

Volume 27 • Number 6 • 2012

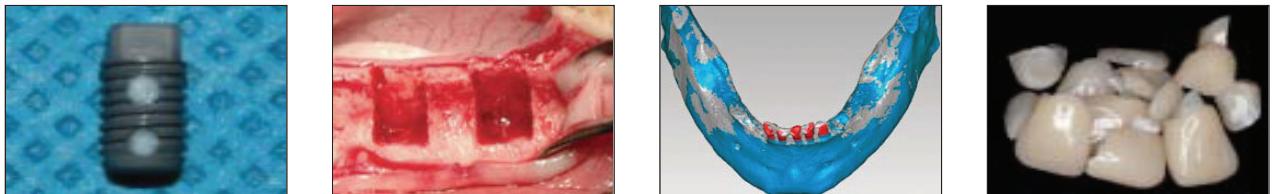
JOMI

The International Journal of
ORAL & MAXILLOFACIAL IMPLANTS

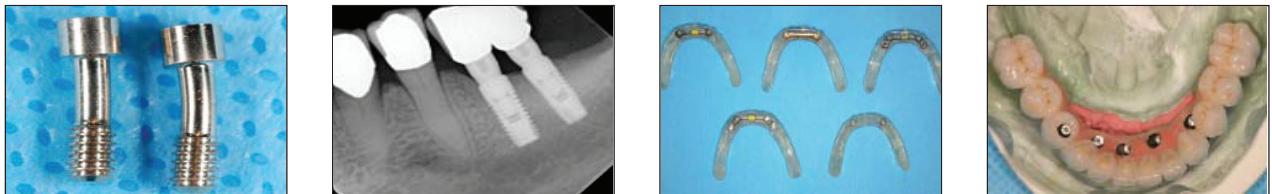
Steven E. Eckert
Editor-in-Chief

OFFICIAL JOURNAL OF THE ACADEMY OF OSSEointegration

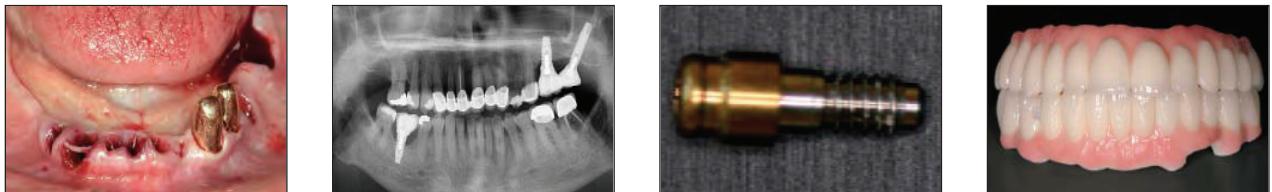
- 1323 Survival of Short Dental Implants for Treatment of Posterior Partial Edentulism: A Systematic Review**
Mohammad A. Atieh/Homayoun Zadeh/Clark M. Stanford/Lyndon F. Cooper
- 1332 Effect of Strontium-Substituted Nanohydroxyapatite Coating of Porous Implant Surfaces on Implant Osseointegration in a Rabbit Model**
Guo-li Yang/Li-na Song/Qiao-hong Jiang/Xiao-xiang Wang/Shi-fang Zhao/Fu-ming He
- 1340 Comparison of Three Inoculation Methods for Bone Tissue Engineering**
Gu Cheng/Xi Chen/Zhi Li/Hui Lu/Ongodia Davide/Zubing Li
- 1351 Evaluation of a Porcine Matrix With and Without Platelet-Derived Growth Factor for Bone Graft Coverage in Pigs**
Alan S. Herford/Mei Lu/Lee Akin/Marco Cicciù
- 1359 Systematic Assessment of Clinical Outcomes in Bone-Level and Tissue-Level Endosseous Dental Implants**
Ioannis D. Vouros/Christos D. R. Kalpidis/Attila Horvath/Aviva Petrie/Nikolaos Donos
- 1375 Effect of Different Alloplast Materials on the Stability of Vertically Augmented New Tissue**
Shing-Zeng Dung/Yu-Kang Tu
- 1382 Increased Intraosseous Temperature Caused by Ultrasonic Devices During Bone Surgery and the Influences of Working Pressure and Cooling Irrigation**
Falk Birkenfeld/Merlind Erika Becker/Sönke Harder/Ralph Lucius/Matthias Kern
- 1389 Bone Regeneration with Rabbit Bone Marrow-Derived Mesenchymal Stem Cells and Bone Graft Materials**
Ji-Eun Lee/Seong-Joo Heo/Jai-Young Koak/Seong-Kyun Kim/Chong-Hyun Han
- 1400 Bone Regeneration in Osteoporotic Conditions: Healing of Subcritical-Size Calvarial Defects in the Ovariectomized Rat**
Sara F. O. Durão/Pedro S. Gomes/José M. Silva-Marques/Hélder R. M. Fonseca/João F. C. Carvalho/José A. R. Duarte/Maria H. R. Fernandes
- 1409 Assessment of Leakage at the Implant-Abutment Connection Using a New Gas Flow Method**
Marie-Alix Fauroux/Bernard Levallois/Jacques Yachouh/Jacques-Henri Torres



- 1413 The Effect of Covering Materials with an Open Wound in Alveolar Ridge Augmentation Using Beta-Tricalcium Phosphate: An Experimental Study in the Dog**
Kenji Inomata/Eriko Marukawa/Yukinobu Takahashi/Ken Omura
- 1422 The Effect of Impression Technique and Implant Angulation on the Impression Accuracy of External- and Internal-Connection Implants**
Pavlos Mpikos/Nikolaos Kafantaris/Dimitrios Tortopidis/Christos Galanis/George Kaisarlis/Petros Koidis
- 1429 Efficacy and Predictability of Short Dental Implants (< 8 mm): A Critical Appraisal of the Recent Literature**
Murali Srinivasan/Lydia Vazquez/Philippe Rieder/Osvaldo Moraguez/Jean-Pierre Bernard/Urs C. Belser
- 1438 Reliability of Voxel Gray Values in Cone Beam Computed Tomography for Preoperative Implant Planning Assessment**
Azin Parsa/Norliza Ibrahim/Bassam Hassan/Alessandro Motroni/Paul van der Stelt/Daniel Wismeijer
- 1443 Effects of Systemic Zoledronic Acid Administration on Osseointegration of Hydroxyapatite-Coated and Resorbable Blast Material Surface Implants in Rabbit Models**
Ferhan Yaman/Serkan Agaçayak/Serhat Atilgan/Emre Benlidayı/Musa Can Ucan/Behçet Erol/Beyza Kaya/Ahmet Gunay/Sedat Guven
- 1448 Fracture Resistance of Crowns Cemented on Titanium and Zirconia Implant Abutments: A Comparison of Monolithic Versus Manually Veneered All-Ceramic Systems**
Francisco Martínez-Rus/Alberto Ferreiroa/Mutlu Özcan/José F. Bartolomé/Guillermo Pradés
- 1456 Comparison of Heat Generation Between Internally Guided (Cannulated) Single Drill and Traditional Sequential Drilling With and Without a Drill Guide for Dental Implants**
Scott E. Bulloch/Russell G. Olsen/Brandon Bulloch
- 1461 Air Powder Abrasive Treatment as an Implant Surface Cleaning Method: A Literature Review**
Ceylin S. Tastepen/Rien van Waas/Yuelian Liu/Daniel Wismeijer



- 1474 Biotribiological Behavior of Two Retrieved Implant Abutment Screws after Long-Term Use In Vivo**
Youssef S. Al Jabbari/Raymond A. Fournelle/Spiros Zinelis/Anthony M. Iacopino
- 1481 Localized Bone Augmentation with Cortical Bone Blocks Tented over Different Particulate Bone Substitutes: A Retrospective Study**
Arash Khojasteh/Hossein Behnia/Yadollah Soleymani Shayesteh/Golnaz Morad/Marzieh Alikhasi
- 1494 Bone Response to Submerged Implants in Organ Transplant Patients: A Prospective Controlled Study**
Lucio Montebugnoli/Mattia Venturi/Fabio Cervellati
- 1501 Use of 8-mm and 9-mm Implants in Atrophic Alveolar Ridges: 10-Year Results**
Christian Mertens/Amelie Meyer-Bäumer/Hannes Kappel/Jürgen Hoffmann/Helmut G. Steveling
- 1509 Retention Characteristics of Different Attachment Systems of Mandibular Overdentures Retained by Two or Three Implants**
Bulent Uludag/Serdar Polat
- 1514 Evaluation of Buccal Alveolar Bone Dimension of Maxillary Anterior and Premolar Teeth: A Cone Beam Computed Tomography Investigation**
Carolina Vera/Ingeborg J. De Kok/Dominik Reinhold/Praephun Limpiphipatanakorn/Alan K. W. Yap/Donald Tyndall/Lyndon F. Cooper
- 1520 Effects of Implant Surgery on Blood Pressure and Heart Rate During Sedation with Propofol and Midazolam**
Daisuke Ueno/Junichi Sato/Jun Nejima/Keisuke Maruyama/Mariko Kobayashi/Toshikazu Iketani/Rei Sekiguchi/Hiroshi Kawahara
- 1527 Restoration of Immediately Loaded Implants in a Minimal Number of Appointments: A Retrospective Study of Clinical Effectiveness**
Carlo Ercoli/Alessandro Geminiani/Heeje Lee/Changyong Feng/Carlo E. Poggio
- 1534 Immediate Loading of Tooth-Implant-Supported Telescopic Mandibular Prostheses**
George E. Romanos/Stephan May/Dittmar May
- 1541 The Influence of Substitute Materials on Bone Density After Maxillary Sinus Augmentation: A Microcomputed Tomography Study**
Sebastian Kühl/Hermann Götz/Christoph Brochhausen/Norbert Jakse/Andreas Filippi/Bernd d'Hoedt/Matthias Kreisler



- 1547 Modified Surgical Protocol for Placing Implants in the Pterygomaxillary Region: Clinical and Radiologic Study of 454 Implants**
Xavier Rodríguez/Victor Méndez/Xavier Vela/Maribel Segalà

- 1554 Two-Year Follow-up of Early- and Conventionally-Placed Two-Stage Implants Supporting Fixed Prostheses**
Burak Bekcioglu/Elcin Sagirkaya/Durdu Karasoy/Murat Cehreli

- 1560 Patient Preference and Satisfaction with Implant-Supported Mandibular Overdentures Retained with Ball or Locator Attachments: A Crossover Clinical Trial**
Gerald Krennmair/Rudolf Seemann/Andres Fazekas/Rolf Ewers/Eva Piehslinger

- 1569 Immediate Restoration of Delayed Placement of Dental Implants in Patients with Treated Periodontal Disease: 1-Year Results**
Jacob Horwitz/Liran Levin/Eran Gabay/Otman Zuabi/Eli E. Machtei

- 1576 Marginal Bone Loss Around Tilted Implants in Comparison to Straight Implants: A Meta-Analysis**
Alberto Monje/Hsun-Liang Chan/Fernando Suarez/Pablo Galindo-Moreno/Hom-Lay Wang

- 1584 All-on-Three Delayed Implant Loading Concept for the Completely Edentulous Maxilla and Mandible: A Retrospective 5-Year Follow-up Study**
Josep Oliva/Xavi Oliva/Josep D. Oliva

Editor-in-Chief

Steven E. Eckert
Professor Emeritus
Mayo Clinic, College of Medicine

Kivanc Akca
Hacettepe University

Tara L. Aghaloo
University of California at Los Angeles

O. Ross Beirne
University of Washington

John B. Brunske
Stanford University

Joke Dyuck
Catholic University of Leuven

Joseph P. Fiorelli
University of Pennsylvania

Robert A. Jaffin
Hackensack, New Jersey

Dean Morton
University of Louisville

Shabrez Ahmed
Tomas Alberktsson

Zvi Artzi

Daniel A. Assad

Oded Bahat

Crawford A. Bain

Edmond Bedrossian
Sérgio R. Bernardes

Paul P. Binon

Hardeep Singh Bidi

Michael S. Block

Donald M. Brunette

Luiz Henrique

Burnett Jr

Daniel Buser

Murat Cavit cehreli

Gavriel Chaushu

Winston chee

David Chvartsaid

Lyndon Cooper

Roberto Crespi

Douglas Deporter

Jocelyne S. Feine

Vania Fontanella

Earl Fu

German Gallucci

Neal Garrett

William V. Giannobile

Julie Glowacki

Stuart L. Graves

Henry Greenwell

Reinhard Gruber

Robert Haas

Siegfried Heckmann

Editor Emeritus

William R. Laney
Professor Emeritus
Mayo Clinic, College of Medicine

Associate Editors

Peter K. Moy
University of California at Los Angeles
Michael R. Norton
London, UK
Clark M. Stanford
University of Iowa
James C. Taylor
Ottawa, Ontario
Minoru Ueda
Nagoya University
Hom-Lay Wang
University of Michigan
Georg Watzek
Medical University of Vienna

Review Board

Kenji W. higuchi
Douglas A. Hock
Rhonda Jacob
Zhimon Jacobson
Ole T. jensen
Asbjorn Jokstad
Susan D karabin
Yavuz Kaya
E. Barrie Kenney
David Kerns
Ameen Khraisat
Seong-Hun Kim
Richard Kinsel
perry Klokkevold
Gerald Krennmaier
Lisa A. Lang
Daniel M. Laskin
Barry P. Levin
Liran Levin
Robert London
David MacDonald
Kenneth A. Mann
Chris Marchack
James T. Mellonig
Craig Misch
Sinan Muftu
Ignace Naert
Ichiro Nishimura
Russeel D. nishimura
Joseph nissan
Joo L. Ong
Stephen M. Patel
Brian Paul
Alan Pollack

Frederick Regennitter
W. Eugene Roberts
George Romanos
Paul Rosen
Edwin S. Rosenberg
Jeggrey E. Rubenstein
steven Sadowsky
Ronald L. Sakaguchi
Thomas J. Salinas
Galen B. Schneider
Tracy Scott
Edward Sevetz
Phillip Sheridan
Roxana Stegaroiu
Robert Taft
Dennis P. Tarnow
Thomas D. Taylor
Khim H. Teoh
Tiziano Testori
Gilbert Triplett
Ned Van Roekel
Keisuke Wads
Stephen Wagner
Mary Walker
Hans P. Weber
Ann Wennerberg
Jonathan Wiens
Harvey A. Wigdor
Thomas G. Wilson
Philip Worthington
Junro Yamashita
Roy Yanase
Yunzhi Yang

Publisher
H. W. Haase

Associate Publisher
Tomoko Tsuchiya

Director, Journal Publications
Lori A. Bateman

Managing Editor
Heather Forkos

Production Manager
Jody Stevens

Director, Advertising Sales
William G. Hartman

For advertising and subscription information contact:

Quintessence Publishing Co, Inc, 4350 Chandler Drive, Hanover Park, Illinois 60133 • Telephone: (630) 736-3600 Toll Free: (800) 621-0387 • Fax: (630) 736-3633 Advertising email: spinski@quintpub.com Subscriptions email: mhartman@quintbook.com Web site: www.quintpub.com.

Subscription rates (includes online version): Regular rate for North America is \$ 185 per year: \$375 institutional (Canadian subscribers add applicable GST). International rate (outside North America) is \$225; \$415 institutional. International subscribers add \$40 to international rate for air mail. Student rate \$85 per year (\$125 international); verification should accompany order. Single issue \$40. Subscription may begin at any time. Claims for missing issues will be serviced only within 6 months of publication date. Otherwise, single-copy price will be charged on missing issues. Subscription orders and changes of address should be sent to the nearest subscription office. Please allow 6 weeks for any change of address notification to be processed.

Copyright © 2012 by Quintessence Publishing Co, Inc. All rights reserved. No part of this journal may be reproduced or transmitted in any form or by any means, electronic or mechanical, including without permission in writing from the publisher. The views expressed herein are those of the individual authors and are not necessarily those of the publisher or the Academy of Osseointegration (AO). Information included herein is not professional advice and is not intended to replace the judgement of a practitioner with respect to particular patients, procedures, or practices. To the extent permissible under applicable laws, the publisher and AO disclaim responsibility for any injury and/or damage to persons or property as a result of any actual or alleged libelous statements, infringement of intellectual property or other proprietary or privacy rights, or from the use or operation of any ideas, instructions, procedures, products, or methods contained in the material therein.

Permission to photocopy items solely for internal or personal use, and for internal or personal use of specific clients, is granted by Quintessence Publishing Co, Inc, for libraries and other users registered with the Copyright Clearance center (CCC) Transaction Reporting Service, provided that the base fee of \$5 per article plus \$.10 per page is paid directly to the CCC, 222 Rosewood Drive, Danvers, MA 01923 (www.copyright.com). Identify this publication by including with your payment the fee code: 0882-2786/12 \$5 + \$10.

Advertising Policy: All advertising appearing in The International Journal of Oral & Maxillofacial Implants must be approved by the editorial staff. The editorial staff retains the right to reject advertising. The publication of an advertisement does not constitute on the part of the journal, publisher, or AO a guaranty or endorsement of the quality or value of the advertised products or services or of any of the representations or the claims made by the advertisers.

Manuscript submission information can be found on the Quintessence Publishing Co website (www.quintpub.com). Submit manuscripts at www.manuscriptmanager.com/jomi. The publisher assumes no responsibility for unsolicited manuscripts.

The International Journal of Oral & Maxillofacial Implants is indexed and/or abstracted in Index Medicus, Science Citation Index, Current Contents/Clinical Medicine, MEDLINE, Index to the Dental Literature, and CINAHL database.

The International Journal of Oral & Maxillofacial Implants (ISSN 0882-2786 [print]; ISSN 1942-4434 [online]) is published bimonthly by Quintessence Publishing Co, Inc, 4350 Chandler Drive, Hanover Park, Illinois 60133, to disseminate current information related to the management of patients utilizing implant modalities and to report the results of basic and clinical research by investigators whose studies embrace the implant concept. Printed in USA.

Postmaster: Send address changes to Quintessence Publishing Co, Inc, 4350 Chandler Drive, Hanover Park, Illinois 60133.

A Truly International Journal

It is always difficult to create a time-sensitive, topical editorial for JOMI. The editorial is created at least a few weeks before the journal is printed and it is often conceived and developed over the months that precede the publication. Consequently, events that promote a series of ideas for an editorial may already be yesterday's news by the time the publication arrives in your mailbox.

This is particularly true as I put the final touches on this editorial. As I sit before the computer, a television is on in the background telling me about the devastation to the Eastern seaboard of the United States caused by Hurricane Sandy. The weather reports are interspersed with reports on the presidential election, which will be conducted on the first Tuesday of November and the results of which will be evident to you before you even pick up this editorial, but obviously remain unknown to me as I write. From the standpoint of an international journal I have to understand that the devastating storm and the implications of a presidential election may be of only minor interest to its readership, and certainly have only minimal impact upon the lives of the international readership.

My schedule for the last few days and for the upcoming week included the Board of Directors meeting for the Academy of Osseointegration, the annual scientific session for the American Academy of Maxillofacial Prosthetics, the scientific session for the American College of Prosthodontists, and the examining session with the American Board of Prosthodontics. So far, I have been able to attend the AO Board of Directors meeting, but the maxillofacial prosthetic meeting was canceled because the oncoming storm created a state of emergency. As I write, I am awaiting a decision from the ACP as to whether or not their meeting will be held, and this will in turn be followed by another decision as to whether or not the Board Certification examination will be held. One meeting is dependent upon another and I remain captive to the events of the day.

When considering the impact that this one storm has had on me, I certainly realize how much more troubling such a state of uncertainty would be to an attendee from the international community. I was able to experience this situation first hand when I was in Switzerland for a meeting during the time that a volcano erupted in Iceland, effectively halting air traffic across Europe. Indeed, the Swiss hosts treated me very well, but the sense of disconnection with home was pervasive.

The point of this editorial is not to wax poetic on the events of the day as they affect my small portion

of the world but is instead to recognize how our international journal impacts the field of osseointegration. As editor-in-chief I have come to appreciate the fact that different parts of the world address situations quite differently.

Consider the concept of standards for comparison. When looking at scientific research it becomes evident that a "gold standard" control exists as a gold standard only for limited communities of interest. Depending upon where you are from, your perspective may change and a gold standard for one investigative team might appear to be completely different than a gold standard for a different team. We see this with materials, techniques, and devices. It can be rather perplexing, as we often think that gold is gold and as such it becomes the standard that we rely upon, but differing perspectives often invalidate this perception.

The situation can be confusing to reviewers, editors, and readers. Approaches that are self-evident to one may be an anathema to another. This is one reason that JOMI often publishes articles that contradict other articles.

Even the method that is used to report information exhibits regional differences. Many authors express concerns with strict editorial policies. The rationale that I use for such policies is that our international readership appreciates a consistent method for presentation of material. Likewise, editorial policies that request simple language and concise descriptions are created with the international reader in mind. It is the editor's impression that complex sentence structure, numerous parenthetical expressions, and use of inconsistent terminology does nothing but complicate the readability of an article for a non-native English speaking reader. Hopefully this perception is correct. Even the creation of acronyms is discouraged unless the acronym is universally accepted within the industry, a condition that rarely exists.

JOMI strives to present an international journal that respects and understands the desires of the international readership. With literally thousands of unique authors from all corners of the world, it appears that the general editorial policy is acceptable to authors. The number of authors who have become electronic friends has certainly gratified me. I think that this indicates that our initial goal in forming this journal, an international collaboration, continues to be met.



Steven E. Eckert, DDS, MS
Editor-in-Chief

Page nos. 1312 and 1313 which include international advertisements of no relevance have been omitted,
to keep the contents limited to academics only.

THEMATIC ABSTRACT REVIEW

Emad W. Estafanous, BDS, MSD

The University of Iowa, Iowa City, Iowa

Section Editor: Clark Stanford, DDS, PhD

The University of Iowa, Iowa City, Iowa

Guy Huynh-Ba, DDS, MS

University of Texas Health Science Center
San Antonio, Texas

Thomas W. Oates, DMD, PhD

University of Texas Health Science Center
San Antonio, Texas

Jan-Eirik Ellingsen, DDS, PhD

University of Oslo
Oslo, Norway

Martin Osswald, BDS, MDent

University of Alberta
Alberta, Canada

Finite Element Modeling and Dental Implant Prosthetics

The predictability of implant treatment success depends mainly on bone support. Dental implants are totally different biomechanically from natural teeth, mainly due to the lack of periodontal ligaments. Understanding the stress and load around dental implants will help preserve the surrounding bone structures and increase the success and longevity of that type of dental restoration.

Pesqueira et al conducted a literature review on the use of stress analysis methods to evaluate the biomechanics of dental implants. Finite element modeling (FEM) was found to be the most commonly used method to serve that goal.

Occlusion was modeled by FEM and predicted to be a major factor affecting stress concentration around dental implants. Klineberg et al explained that load concentration increases with steeper cusp inclination and broader occlusal table.

FEM for the different occlusal patterns in complete dentures supported by dental implants was investigated by Greco et al, where he compared canine guided occlusion (CGO) versus bilateral balanced occlusion (BBO), observing that the BBO occlusal pattern was more favored than CGO in complete dentures supported by implants.

Dos Santos et al evaluated the effect of reline material thickness on the stress distribution in peri-implant bone during function during the implant healing period, concluding that localized application of soft liners in the implant region is more favorable

than relining the entire denture. Likewise, the thicker the soft liner, the less stress occurs in the peri-implant bone.

With the introduction of mini implants to retain complete dentures, the number of implants and the type of attachments are critical parts that need more investigations. Fatalla et al concluded that three mini implants retaining complete dentures with flexible acrylic attachments had more favorable stress distribution when compared to four mini implants with O-ring attachment systems.

Abutment angulation is another factor, especially in fixed prosthetics on dental implants. The results of Sadrimanesh et al revealed that stress values were the highest in 20-degree abutments. Hauchard et al also favored splinting for implant-supported restorations subjected to horizontal or oblique loads.

Ormianer et al concluded that implant diameter and peri-implant bone thickness influence load distribution in bone and the type of implant-abutment connection has no significant effect on the predicted outcomes. Small-diameter implants should be limited to dense bone to minimize stress concentrations.

FEM has several advantages. One of the most important aspects is the ability to address and map the pattern and magnitude of the stresses surrounding dental implants. More *in vivo* studies are needed to validate the role of stress distribution around dental implants in different prosthetic applications.

Emad W. Estafanous, BDS, MSD

Pesqueira A, Goiato M, Gennari-Filho H. The use of stress analysis methods to evaluate the biomechanics of oral rehabilitation with implants.

J Oral Implantol 2012 Mar 1 [epub ahead of print]. Because the biomechanical behavior of dental implants is different from that of natural tooth, clinical problems may occur. The mechanism of stress distribution and load transfer to the implant/bone interface is a critical issue affecting the success rate of implants. Therefore, the aim of this study was to conduct a brief literature review about the available stress analysis methods to study implant-supported prosthesis loading, and to discuss their contributions in the biomechanical evaluation of oral rehabilitation with implants. It was found that several studies have used experimental, analytical and computational models by means of finite element models (FEM), photoelasticity, strain gauges and associations of these methods to evaluate the biomechanical behavior of dental implants. The FEM has been used to evaluate new components, configurations, materials and shape of implants. The greatest advantage of the photoelastic method is the ability to visualize the stresses in complex structures such as oral structures, and to observe the stress patterns in the whole model, allowing to localize and to quantify the stress magnitude. The strain gauges can be used to assess in vivo and in vitro stress in prosthesis, implants and teeth. Some authors use the strain gauge technique associated with either photoelasticity or FEM techniques. These methodologies can be widely applied in Dentistry, mainly in the research field. Therefore, they can guide further researches and clinical studies by predicting some disadvantages and streamlining the clinical time.

Correspondence to: Department of Dental Materials and Prosthodontics, San Paolo State University, UNESP Araraquara Dental School, Araraquara SP Brazil.

Klineberg IJ, Trulsson M, Murray GM. Occlusion on implants - is there a problem? J Oral Rehabil 2012;39:522-537.

Oral rehabilitation restores form and function and impacts on general health. Teeth provide a discriminating sense of touch and directional specificity for occlusal perception, management of food with mastication and swallowing, and awareness of its texture and hardness. Peripheral feedback for control of jaw muscles includes the enamel-dentine-pulp complex and mechanoreceptors in the periodontal tissues. The implications of feedback from periodontal and other intra-oral mechanoreceptors as well as changes in central representation are significant for function and adaptation to oral rehabilitation. With implants, in the absence of the periodontium and periodontal mechanoreceptor feedback, fine motor control of mastication is reduced, but patients are still able to function adequately. Further, there is no significant difference in function with full-arch fixed prostheses on teeth in comparison with implants. Predictable implant outcomes depend on bone support. Optimum restoration design appears to be significant for bone remodelling and bone strains around implants with occlusal loading.

Finite element analysis data confirmed load concentrations at the coronal bone around the upper section of the implant where bone loss is commonly observed clinically. Load concentration increased with steeper cusp inclination and broader occlusal table and decreased with central fossa loading and narrower occlusal table size. It is recommended that occlusal design should follow a narrow occlusal table, with central fossa loading in intercuspal contact and low cusp inclination to minimise lateral loading in function and parafunction. Acknowledging these features should address potential problems associated with the occlusion in implant therapy.

Correspondence to: iven.klineberg@sydney.edu.au

Greco GD, Las Casas EB, Cornacchia TP, Magalhães CS, Moreira AN. Standard of disocclusion in complete dentures supported by implants without free distal ends: Analysis by the finite elements method. J Appl Oral Sci 2012;20:64-69.

The occlusal patterns are key requirements for the clinical success of oral rehabilitation supported by implants. This study compared the stresses generated by the disocclusion in the canine guide occlusion (CGO) and bilateral balanced occlusion (BBO) on the implants and metallic infrastructure of a complete Bränemark protocol-type denture modified with the inclusion of one posterior short implant on each side. A three-dimensional model simulated a mandible with seven titanium implants as pillars, five of them installed between the mental foramen and the two posterior implants, located at the midpoint of the occlusal surface of the first molar. A load of 15 N with an angle of 45 degrees was applied to a tooth or distributed across three teeth to simulate the CGO or BBO, respectively. The commercial program ABAQUS was used for the model development, before and after the processing of the data. The results were based on a linear static analysis and were used to compare the magnitude of the equivalent stress for each of the simulations. The results showed that the disocclusion in CGO generated higher stresses concentrated on the working side in the region of the short implant. In BBO, the stresses were less intense and more evenly distributed on the prosthesis. The maximum stress found in the simulation of the disocclusion in CGO was two times higher than that found in the simulation of the BBO. The point of maximum stress was located in the neck of the short implant on the working side. Under the conditions of this study, it was concluded that the BBO pattern was more suitable than CGO for the lower complete denture supported by implants without free distal ends.

Correspondence to: gustavodgreco@yahoo.com.br

Dos Santos MB, Bacchi A, Consani RL, Mesquita MF. Influence of thickness and area of reline on the stress distribution in peri-implant bone during the healing period: A three-dimensional finite element analysis. Gen Dent 2012;60:e231-236.

This study used finite element analysis to evaluate how the thickness of reline material and the area of its place-

ment in conventional complete dentures affected the stress distribution in peri-implant bone during function in the healing period. For this study, three-dimensional models were created to simulate a severely resorbed mandible with two implants placed recently in the anterior region. Two of these models received a layer of soft liner material that covered the entire length of the denture base (1.5 mm or 3.0 mm); for the other sample models, soft liner material was placed (in thicknesses of 1.5 mm or 3.0 mm) in the implant region only. The models were exported to mechanical simulation software; two simulations were performed by placing a load in the mandibular right canine (35 N) and the mandibular right first molar (50 N). Data were quantitatively and qualitatively evaluated by means of maximum principal stress. In all cases, models that received 3.0 mm of soft liner material showed lower values of stress concentration than those receiving 1.5 mm of soft liner material. Likewise, localized application of soft liner in the implant region showed lower stress concentration compared with models in which the entire denture base was relined. These results indicate that the thickness and area of reline in conventional complete dentures has a direct effect on stress distribution in the peri-implant bone tissue during the healing period.

Correspondence to: mateusbertolini@yahoo.com.br

Fatalla AA, Song K, Du T, Cao Y. A Three-Dimensional Finite Element Analysis for Overdenture Attachments Supported by Teeth and/or Mini Dental Implants. J Prosthodont 2012 Jul 27 [epub ahead of print]

The aim of this study was to establish the optimum design and attachment combination to support an overdenture with minimal stress and flexing produced in the alveolar bone surrounding any natural teeth and/or mini dental implants. Twelve models were included in the study: the six main models (A, B, C, D, E, and F) were categorized according to the support designs of the overdenture prosthesis, and each model was further subdivided according to the attachment combinations into model 1: with Dalbo elliptic and/or O-ring attachments only and model 2: with flexible acrylic attachments. Vertical loads (35 N) and 17.5 N lateral loads under static conditions were applied to the models to simulate the occlusal forces following the concept of lingualized occlusion. All conditions were created using a finite element software program. Maximum von Mises stress at the level of the attachments and at the bone support foundation interfaces were compared in all 12 models. The flexing of the mandible and the attachments were also compared qualitatively. Stress on these models was analyzed after the given loading condition. The results showed that the model with three freestanding mini dental implants and flexible acrylic attachments showed the lowest von Mises stress and flexing, while the models with four freestanding mini dental implants and O-ring attachments showed the highest von Mises stress. Three freestanding mini dental implants with flexible acrylic attachment systems

supporting an overdenture were better choices than four mini dental implants with O-ring attachment systems, which showed the maximum flexing and stress values in this qualitative comparison.

Correspondence to: cyg0729@tjh.tjmu.edu.cn

Sadrimanesh R, Siadat H, Sadr-Eshkevari P, Monzavi A, Maurer P, Rashad A. Alveolar bone stress around implants with different abutment angulation: an FE-analysis of anterior maxilla. Implant Dent 2012 Jun;21:196-201.

To comparatively assess the masticatory stress distribution in bone around implants placed in the anterior maxilla with three different labial inclinations. Three-dimensional finite element models were fabricated for three situations in anterior maxilla: (1) an implant in contact with buccal cortical plate restored by straight abutment, (2) an implant inclined at 15 degrees, and (3) 20 degrees labially restored with corresponding angled abutment. A palatal bite force of 146 N was applied to a point 3 mm below the incisal edge. Stress distribution around the bone-implant interface was determined using ANSYS software. The maximum compressive stress, concentrated in the labial crestal cortical bone, was measured to be 62, 108, and 122 MPa for 0-, 15-, and 20-degree labially inclined implants, respectively. The maximum tensile stress, concentrated in the palatal crestal cortical bone, was measured to be 60, 108, and 120 MPa for 0-, 15-, and 20-degree labially inclined implants, respectively. While all compressive stress values were under the cortical yield strength of 169 MPa, tensile stress values partially surpassed the yield strength (104 MPa) especially when a 20-degree inclination was followed for fixture placement.

Correspondence to: Department of Oral and Maxillofacial Prosthodontics and Implants, Tehran University of Medical Sciences (TUMS), School of Dental Medicine, Tehran, Iran.

Hauchard E, Fournier BP, Jacq R, Bouton A, Pierrisnard L, Naveau A. Splinting effect on posterior implants under various loading modes: A 3D finite element analysis. Eur J Prosthodont Restor Dent 2011;19:117-122.

This three-dimensional finite element study compared stresses, intensities and displacements of three mandibular posterior implants restored with cemented crowns (two molars and a premolar in straight line), splinted versus non-splinted. Hundred newton occlusal loads were vertically or horizontally applied, either on one single crown or on all of them. Maximal stresses and implants displacements were higher under horizontal loading. Splinting major effects appeared under single horizontal load with a decrease in stresses (34-49%) and displacements (16-19%) of the loaded crown. Splinting seems more appropriate for implant-supported restorations submitted to frequent single horizontal or oblique loads than vertical ones.

Correspondence to: Service d'Odontologie, Hôpital Albert Chenevier, 40, rue de Mesly, 94010, Créteil, France.

Ormaner Z, Ben Amar A, Duda M, Marku-Cohen S, Lewinstein I. Stress and strain patterns of 1-piece and 2-piece implant systems in bone: A 3-dimensional finite element analysis. Implant Dent 2012;21:39-45.

The transition from implant to abutment is solid in 1-piece (1P) and broken in 2-piece (2P) implant designs. This difference may affect occlusal load distribution and marginal bone response. The purpose of this study is to determine whether 1P and 2P implants with equivalent geometries exhibited stresses and strains differently under applied loading conditions. Design software simulated 1P and 2P implants restored with metal copings and embedded in 3 cylindrical bone block models that varied in dimensions, density, and percentage of bone-to-implant contact. Three-dimensional, finite element analysis simulated occlusal loading. Experiments evaluated stresses and strains relative to implant design and (1) peri-implant bone thickness, (2) cortical bone thickness, (3) magnitude and direction of occlusal loading, and (4) % bone-to-implant contact. Implants with equivalent dimensions exhibited comparable stresses and strains in all experimental conditions. Implant diameter and peri-implant bone thickness influenced stress levels. Only small-diameter (3.0 mm) 1P implants in low-density bone exhibited stress levels that might adversely affect marginal bone stability. It was concluded that Implant diameter and peri-implant bone thickness influenced load distribution in bone, but the type of implant-abutment transition had no significant effect. Small-diameter 1P implants should be limited to dense bone to minimize stress concentrations.

Correspondence to: drzeev@ormianer.com

FULL TIME FACULTY

Department of Periodontology and Implant Dentistry

NYU COLLEGE OF DENTISTRY

New York University College of Dentistry is one of the most dynamic and robust dental education and research institutions in the world. Today, the College of Dentistry is seeking applications for full-time faculty positions available immediately in the Department of Periodontology & Implant Dentistry. Responsibilities will include research, as well as didactic and clinical teaching in pre-doctoral and post-doctoral programs.

The requirements for this position include a D.D.S./D.M.D. degree and advanced education in periodontics, prosthodontics, or oral surgery from a CODA approved program. Board certification is strongly desired as is a history as well as current research funding, or eligibility for training grants, and a strong publication record. Intramural and extramural practice opportunities are available.

NYU offers an excellent benefits package. Salary and academic rank will be commensurate with qualifications and experience. Applicants should send a letter of intent and curriculum vitae to: **Dr. Steven P. Engebretson, Chair, Department of Periodontology and Implant Dentistry, New York University College of Dentistry, 345 East 24th Street, Suite 3W, New York, NY 10010.**



NEW YORK UNIVERSITY

NYU is an Equal Opportunity/Affirmative Action Employer.

Always One Step Ahead



Always One Step Ahead

AB Dental is a leading developer and manufacturer of dental implants and rehabilitation components, marketing to clients worldwide.

The company's products are based on advanced technologies, and offer comprehensive solutions that are both aesthetic and functional, delivered with the highest level of service, quality and innovation.

AB Dental Devices
+972-8-853-1388
info@ab-dent.com
www.ab-dent.com

Page nos. 1318 and 1322 which include international advertisements of no relevance have been omitted,
to keep the contents limited to academics only.

Survival of Short Dental Implants for Treatment of Posterior Partial Edentulism: A Systematic Review

Mohammad A. Atieh, BDS¹/Homayoun Zadeh, DDS, PhD²/
Clark M. Stanford, DDS, PhD³/Lyndon F. Cooper, DDS, PhD⁴

Purpose: Dental implant therapy for posterior partial edentulism may utilize short implants. The advantages of short implants include the ability to avoid the additional surgical procedures that would be required to place longer implants. The aim of this study was to systematically review studies concerning dental implants of ≤ 8.5 mm placed in the posterior maxilla and/or mandible to support fixed restorations. **Materials and Methods:** English-language articles published between 1992 and May 2011 were identified electronically and by hand search of the PubMed, Embase, and Cochrane libraries. Data were extracted and compared statistically. Forest plots were generated to compare outcomes of short versus long implants. **Results:** An initial screening of 1,354 studies led to direct evaluation of 401 articles. Of these, 33 met the research criteria: 5 randomized clinical studies; 16 prospective, nonrandomized, noncontrolled studies; 12 retrospective, nonrandomized studies; and 1 study with both prospective and retrospective data. These studies indicated that there is no significant difference in the reported survival of short versus long implants. Failure of 59 of 2,573 short implants at 1 year was recorded, with 71% of them failing before loading. Only 101 short implants were followed for 5 years. **Conclusions:** The initial survival rate for short implants for posterior partial edentulism is high and not related to implant surface, design, or width. Short implants may constitute a viable alternative to longer implants, which may often require additional augmentation procedures. INT J ORAL MAXILLOFAC IMPLANTS 2012;27:1323–1331

Key words: posterior partial edentulism, short dental implant, systematic review

Dental implant therapy is currently used for the replacement of missing teeth in diverse clinical situations. The use of osseointegrated dental implants has evolved from its initial application for mandibular edentulism to include all clinical scenarios for tooth replacement. Different scenarios are associated with unique challenges. When considering placement of implants in the posterior maxilla or mandible, the superoinferior dimension of available bone is defined by the extent of alveolar ridge resorption and the location of the maxillary sinus or the inferior alveolar nerve. These factors can limit or preclude dental

implant placement.^{1,2} Additional factors that may add to the risk of osseointegration failure include the lower quality bone that is present in parts of the maxilla.³

Clinical solutions to these problems involve alveolar ridge augmentation procedures.⁴ Additional solutions include the movement of the inferior alveolar nerve (lateral nerve transposition)² and sinus elevation, with or without grafting.⁴ Each of these surgical approaches to increasing the bone volume and vertical dimension of available bone for implant placement has been evaluated in terms of the possible subsequent implant survival rates, and each approach has attendant and specific complications and limitations.

An alternative approach for the treatment of posterior partial edentulism involves the use of short dental implants. The definition of what constitutes a short implant has not reached consensus; however, implants of 10 mm or shorter have generally been considered "short" by existing clinical standards.^{5–8} The use of short dental implants remains controversial, particularly in comparison to alternative approaches to the treatment of posterior partial edentulism. For example, sinus augmentation versus the use of short dental implants was recently considered,⁹ and there is limited evidence that short dental implants provide acceptable and comparable success.

¹Research Assistant, Department of Prosthodontics, University of North Carolina, Chapel Hill, North Carolina, USA.

²Associate Professor, Division of Periodontology, Diagnostic Sciences and Dental Hygiene, University of Southern California School of Dentistry, Los Angeles, California, USA.

³Associate Dean for Research and Centennial Fund Professor, College of Dentistry, University of Iowa, Iowa City, Iowa, USA.

⁴Chair and Stallings Distinguished Professor, Department of Prosthodontics, University of North Carolina, Chapel Hill, North Carolina, USA.

Correspondence to: Dr Lyndon F. Cooper, Department of Prosthodontics, University of North Carolina, Chapel Hill, NC 27518, USA. Fax: +919-966-3821. Email: lyndon_cooper@dentistry.unc.edu

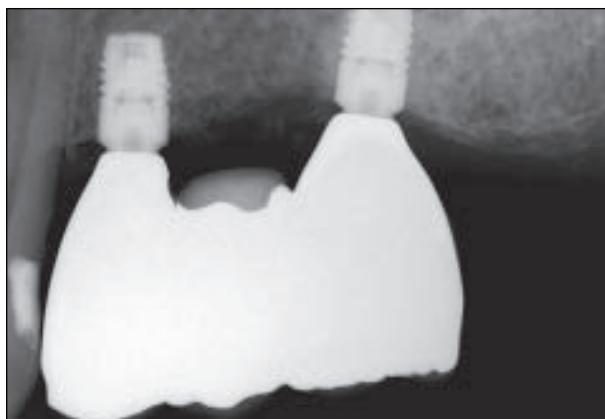


Fig 1 Radiographic and clinical illustrations of the use of short dental implants for the treatment of posterior partial edentulism. Two 6-mm implants in the edentulous posterior maxilla support a three-unit fixed dental prosthesis. The implants do not invade the superior maxillary sinus and are well distributed to eliminate a posterior cantilever. Continued study of short implant survival, including mechanical complications, is required. Additional investigation of possible prosthodontic complications, as well as patient-based outcomes, of this alternative treatment of the atrophic posterior maxilla or mandible is needed (care provided by Dr Chris Barwacz, DDS, University of Iowa).

Irrespective of other approaches available, the use of short implants in the treatment of posterior partial edentulism offers some advantages (Fig 1). Included are the reduced surgical risks of paresthesia, contact with adjacent tooth roots, and overheating of bone; the reduced exposure to bone grafting and reduced time, discomfort, and cost; and improved surgical placement by expanding surgical access and reducing implant inventories.¹⁰ However, these advantages could be irrelevant if the survival of short implants is significantly lower than that of the facilitated use of longer implants.

Therefore, the aim of the present study was to determine whether there is a significant difference in the survival of short implants (≤ 8.5 mm) and longer implants for the treatment of posterior partial edentulism. The treatment of the maxilla and mandible using single implants and fixed partial dentures was evaluated by completing a systematic review of prospective, retrospective, and randomized clinical studies published in English up to May 2011.

MATERIALS AND METHODS

The search for articles included in this systematic review was divided into primary and secondary stages. The primary stage was initiated by searching the National Library of Medicine database (Medline) through its online site (PubMed). This investigation was followed by searches of the Cochrane Library and Embase databases.

Key words and search inquiries that were used during primary stage were as follows:

- Posterior dental implant
- (Posterior dental implant) AND (short OR ultra-short OR ultra-wide OR wide OR length OR width OR diameter OR 5 mm OR 6 mm OR 7 mm OR 8 mm OR 8.5 mm)
- Posterior dental implant AND (retrospective OR prospective OR clinical trial)
- Short implant survival

The choice of key words was intended to be broad to collect as much relevant data as possible without relying on electronic means alone to refine the search results. The titles of the articles retrieved were searched manually. After that, manual and electronic searches of the abstracts and full texts were performed to identify relevant articles. Additionally, the references of each article were thoroughly inspected for more possible candidates.

The resulting articles were then subjected to clear inclusion and exclusion criteria by two reviewers as follows.

The included articles:

- Were human prospective or retrospective follow-up studies and clinical trials, published in English
- Investigated implants ≤ 8.5 mm long
- Examined implants in posterior partially edentulous patients restored with fixed restorations

- Followed short implants for at least 1 year after loading and reported clear data regarding follow-up intervals, dropouts, and failures
- Could not be excluded before careful reading

The following articles were excluded:

- Studies that targeted dental implants in medically compromised patients
- Studies that did not separate the data of edentulous from partially edentulous and anterior from posterior implant cases
- Studies that did not attribute implant loss to specific implant length
- Case reports
- Studies that included unclear data, with authors who could not be contacted for any reason

From the included articles, data were collected and arranged in the following fields: implant system, design, and surface; implant length and diameter; implant location; type of surgical procedure used; healing time; type of restoration; number of short implants, number of failed short implants, and the time to failure; and survival criteria. Other factors that were planned to be included but were not obvious in most of the studies were: type of placement (immediate or late) and type of loading (immediate, early, or late).

Two tables were created initially with the data: one for short dental implants (≤ 8.5 mm) and the other for dental implants that were both short and wide (short-wide) (≤ 8.5 mm in length and ≥ 4.8 mm in diameter). The previous data were also used to construct different life table analyses.

RESULTS

The initial search, after duplicates were removed, resulted in 1,354 articles. After manual search of the article titles, manual and electronic searches of the abstracts and full text were done, resulting in 331 possibly relevant articles. Additionally, the reference section of each article was thoroughly inspected, resulting in 70 new articles. After the inclusion and exclusion criteria were applied to the 401 articles, 33 articles were included.

A total of 3,573 short dental implants was reported in the 33 studies that fulfilled the inclusion criteria. Of those implants, 38% were in the maxilla, 51% were in the mandible, and the location of the remaining implants was unclear. The majority of short dental implants (59%) were 8 mm long, and a majority (56%) of the implants with known diameters were wide (≥ 4.8 mm). The distribution of these implants according to length,

Table 1 Implant Distribution According to Length

Length	No. of implants
5 mm	41
6 mm	380
7 mm	809
8 mm	2,104
8.5 mm	239
Total	3,573

Table 2 Implant Distribution According to Diameter

Diameter	No. of implants
≥ 4.8 mm	887
< 4.8 mm	700
Unknown	1,986

diameter, and location is shown in Tables 1 to 3. Regarding the surfaces of the reported implants, only 4.6% of the reported implants had a machined surface. More than 64% of the reported short implants were represented by titanium plasma spray (TPS) surfaces or the SLA surface (sandblasted, large-grit, acid-etched; Straumann) (Table 4). Information about posterior partially edentulous restorations for Kennedy Class I, II, and III situations was extracted from the reviewed papers. The total number of restorations was distributed nearly equally between single crowns and fixed partial restorations (Table 5).

Implant Survival and Life Table Analyses

Only two studies were excluded from the life table analyses of short dental implants. Data from 16 of 21 studies were used in the life table analyses for the short-wide dental implants. The reported average follow-up period was 3.9 years (range, 1 to 7 years). Of the 3,573 implants studied, 67 failures were reported. The majority (71%) of failures occurred before loading. Based on the information available, it is apparent that many short implants were not followed for the duration of the investigation. To better understand the potential limitations in interpreting these data, life tables were constructed to include censored implants (implants that were not continuously reported, as well as dropouts recorded by the investigators). All of the included papers contained data that were censored; however, 16 studies provided information (including dropouts) concerning all implants for all time points (78% of the reported implants).

Table 3 Implant Distribution According to Location

Location	No. of implants
Maxilla	1,373
Mandible	1,820
Unknown	380

Table 5 Implant Distribution According to Type of Restoration

Prosthesis	No. of implants
Single tooth	1,952
Fixed partial	1,198
Cantilever	63
Unspecified fixed restoration	360

Table 4 Implant Distribution According to Surface

Surface	No. of implants
DAE	60
HA-coated	168
Machined	163
Roughened (HA-blasted)	30
SLA	405
SLActive	40
SPS	317
TiO ₂ blasted	10
TiUnite	511
TPS	14
TPS or SLA	1,851
Unknown	4

DAE = dual acid-etched; HA = hydroxyapatite; SLActive = the SLA surface, conditioned with nitrogen and kept in isotonic solution (Straumann); SPS = sintered porous surface; TiUnite = porous anodized, highly crystalline, and phosphate-enriched titanium dioxide (Nobel Biocare); TPS = titanium plasma spray.

Table 6 Life Table Analysis of Short Dental Implants, Combined from the Reviewed Papers

Interval (y)	Implants at risk	Failed	Censored	ISR	CSR
0–1	3,457	53 (38)	35	98.5%	98.5%
1–2	2,288	7	1,116	99.7%	98.2%
2–3	1,297	3	984	99.8%	97.9%
3–4	786	0	508	100.0%	97.9%
4–5	338	0	448	100.0%	97.9%
5–6	101	0	237	100.0%	97.9%
6–7	27	0	74	100.0%	97.9%
7–8	1	0	26	100.0%	97.9%

Numbers in parentheses indicate implants that failed before loading.

ISR = interval survival rate; CSR = cumulative survival rate.

A 5-year cumulative survival rate of 98% was calculated for all short implants (Table 6). When short (≤ 8.5 mm) and longer (> 8.5 mm) implants were compared from the aggregate data set, comparable 5-year cumulative survival rates were observed (98.3% and 97.7%, respectively) (Table 7). An additional comparison of short implants (< 4.8 mm in diameter) versus short-wide implants (≥ 4.8 mm in diameter) is reported in Table 8 and revealed similar 5-year cumulative survival rates (98.9% and 98.6%, respectively).

Forest Plots

Six of the 33 examined studies included a comparison of short versus long implants as the objective of the study. Among these studies, the definition of short implants varied. Two of them defined ≤ 8.5 -mm implants as "short," another two studies reported ≤ 9 -mm implants

as "short," one compared ≤ 10 -mm implants as "short" versus other longer implants, and the last one compared 7-mm implants to ≥ 10 -mm implants. A meta-analytic representation of these studies in the form of forest plots was performed; risk ratio was used as the effect size measure, and the tested outcome was implant survival risk ratio. The implant survival risk ratios were used instead of implant survival rates because the length of follow-up periods varied between studies and these studies included censored data. However, the total number of placed and failed implants was known (since it was an inclusion criterion for the selected studies). Calculations were adjusted to unify the criteria for "short implant" to ≤ 8.5 mm. The resultant forest plot is shown in Table 9.^{11–16} The result showed that the overall risk ratio was equal to 1, meaning that the survival rate of the surveyed implants was not related to length.

Table 7 Life Table Analysis for Short Versus Long Dental Implants from Papers that Included Both

Interval (y)	Implants at risk	Failed	Censored	ISR	CSR
Short					
0–1	2,662	33 (30)	28	98.8%	98.8%
1–2	1,626	5	1,003	99.7%	98.5%
2–3	1,054	2	567	99.8%	98.3%
3–4	635	0	417	100.0%	98.3%
4–5	290	0	345	100.0%	98.3%
5–6	86	0	204	100.0%	98.3%
6–7	24	0	62	100.0%	98.3%
Long					
0–1	3,058	64 (35)	71	97.9%	97.9%
1–2	1,921	5	1,073	99.7%	97.7%
2–3	1,368	0	548	100.0%	97.7%
3–4	709	0	659	100.0%	97.7%
4–5	400	0	309	100.0%	97.7%
5–6	185	0	215	100.0%	97.7%
6–7	28	0	157	100.0%	97.7%

Numbers in parentheses indicate implants that failed before loading.

ISR = interval survival rate; CSR = cumulative survival rate.

Short was defined as ≤ 8.5 mm; long was defined as > 8.5 mm.

Table 8 Life Table Analysis for Short Versus Short-Wide Dental Implants Using Combined Data from the Reviewed Papers

Interval (y)	Implants at risk	Failed	Censored	ISR	CSR
Short					
0–1	351	4 (4)	11	98.9%	98.9%
1–2	269	0	78	100.0%	98.9%
2–3	187	0	82	100.0%	98.9%
3–4	135	0	52	100.0%	98.9%
4–5	99	0	36	100.0%	98.9%
Short-wide					
0–1	710	7 (7)	11	99.0%	99.0%
1–2	472	2	231	99.6%	98.6%
2–3	236	0	234	100.0%	98.6%
3–4	59	0	177	100.0%	98.6%
4–5	4	0	55	100.0%	98.6%

Numbers in parentheses indicate implants that failed before loading.

ISR = interval survival rate; CSR = cumulative survival rate.

Short-wide was defined as ≤ 8.5 mm in length and ≥ 4.8 mm in width.

Another comparison of short and long implants was attempted using all available data presented in 24 studies that included both long and short implants (Table 10).^{11–32} The overall risk ratio for short versus long implants was 1.00 (pooled confidence interval of 0.98 to 1.01). In this broader analysis that included more diverse studies, the mean survival rates were similar for short and long implants.

DISCUSSION

The main observation in this investigation was the reported survival of short implants, defined as ≤ 8.5 mm in length, for the treatment of posterior partial edentulism. This reiterates the findings of similar reports. Among the greatest confounding factor in evaluating these different reports is the definition of a “short” dental

Table 9 Meta-analytic Representation of Short versus Long Implant Survival Data from Comparative Studies

Study/subgroup	Short implants		Long implants		Weight (%)	Risk ratio M-H, fixed, 95% CI
	Events	Total	Events	Total		
Bischof et al ¹¹	78	81	157	159	10.8	0.98 (0.93, 1.02)
Jung et al ¹²	19	19	276	281	3.7	0.99 (0.93, 1.07)
Fugazzotto ¹³	1,835	1,851	327	330	56.4	1.00 (0.99, 1.01)
Felice et al ¹⁴	59	60	58	61	5.8	1.03 (0.97, 1.10)
Sohn et al ¹⁵	33	33	86	89	4.8	1.03 (0.97, 1.09)
Koo et al ¹⁶	122	122	384	399	18.4	1.04 (1.01, 1.06)
Total (95% CI)		2,166		1,319	100.0	1.01 (1.00, 1.02)
Total events	2,146		1,288			

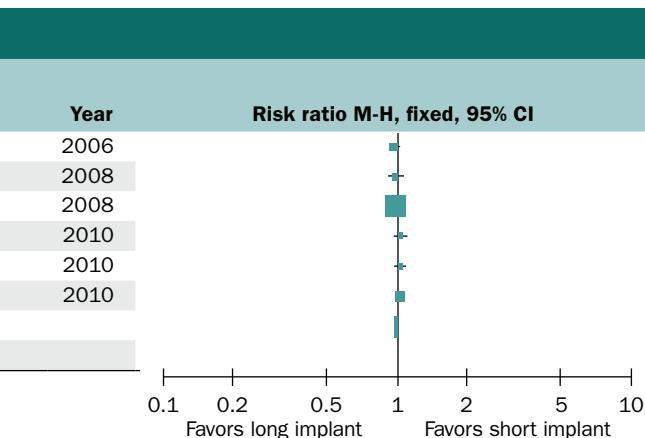
Heterogeneity: $\chi^2 = 10.32$, df = 5 ($P = .07$), $I^2 = 52\%$ Test for overall effect: $Z = 1.33$ ($P = .18$)**Table 10** Meta-analytic Representation of Short versus Long Implant Survival Data from Studies Reporting

Study/subgroup	Short implants		Long implants		Weight (%)	Risk ratio M-H, fixed, 95% CI
	Events	Total	Events	Total		
Bahat and Handelsman ¹⁷	27	27	29	31	1.7	1.07 (0.95, 1.19)
Renouard et al ¹⁸	57	62	29	31	2.3	0.98 (0.87, 1.11)
Wennerberg and Jemt ¹⁹	60	69	337	353	6.7	0.91 (0.83, 1.00)
Van Steenberghe et al ²⁰	16	16	78	79	1.7	0.99 (0.91, 1.08)
Deporter et al ²¹	32	32	16	16	1.3	1.00 (0.91, 1.10)
Polizzi et al ²²	12	13	44	45	1.2	0.94 (0.80, 1.11)
Romeo et al ²³	14	14	146	155	1.6	1.03 (0.93, 1.14)
Roccuzzo and Wilson ²⁴	9	9	26	27	0.8	1.00 (0.85, 1.19)
Rocci et al ²⁵	10	10	94	105	1.1	1.07 (0.93, 1.24)
Salvi et al ²⁶	3	3	64	64	0.5	1.00 (0.69, 1.45)
Bischof et al ¹¹	78	81	157	159	6.4	0.98 (0.93, 1.02)
Misch et al ²⁷	30	30	707	715	3.6	1.00 (0.95, 1.04)
Levine et al ²⁸	246	252	253	255	15.3	0.98 (0.96, 1.01)
Jung et al ¹²	19	19	276	281	2.2	0.99 (0.93, 1.07)
Fugazzotto ¹³	1,835	1,851	327	330	33.7	1.00 (0.99, 1.01)
Nedir et al ²⁹	44	44	10	10	1.0	1.00 (0.88, 1.14)
Felice et al ³⁰	10	10	13	13	0.7	1.00 (0.85, 1.18)
Felice et al ¹⁴	59	60	58	61	3.5	1.03 (0.97, 1.10)
Zembic et al ³¹	2	3	39	41	0.3	0.70 (0.31, 1.56)
Sohn et al ¹⁵	33	33	86	89	2.9	1.03 (0.97, 1.09)
Koo et al ¹⁶	122	122	384	399	11.0	1.04 (1.01, 1.06)
Nedir et al ³²	4	4	21	21	0.5	1.00 (0.74, 1.35)
Total (95% CI)		2,764		3,280	100.0	1.00 (0.98, 1.01)
Total events	2,722		3,194			

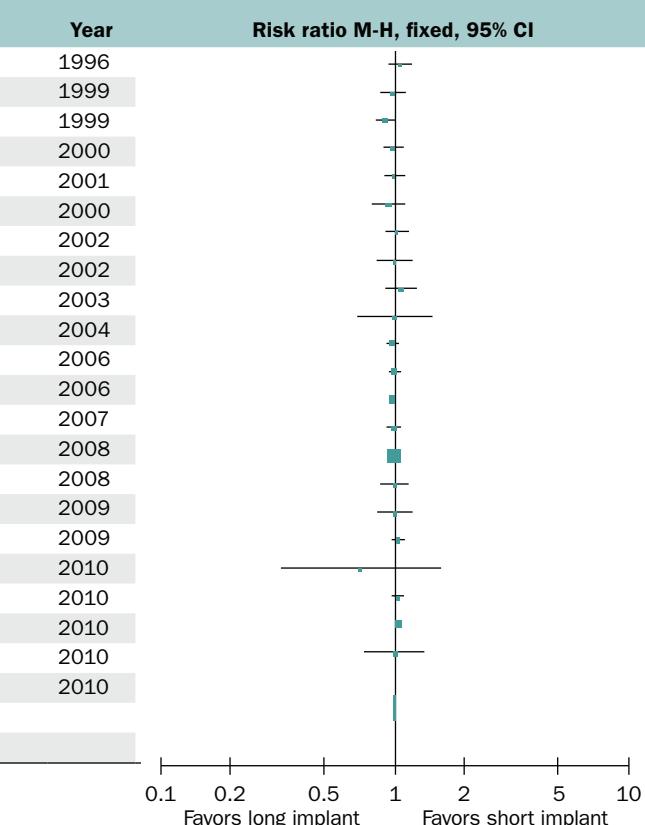
Heterogeneity: $\chi^2 = 23.93$, df = 21 ($P = .30$), $I^2 = 12\%$ Test for overall effect: $Z = 0.72$ ($P = .47$)

implant. Studies have defined short implants to include a wide range, from 5 to 10 mm.^{6–8,33} The present investigation included studies reporting on the outcomes of implants 8.5 mm and shorter, for the pragmatic reason that the implant manufacturers who represent a large share of the international market include an 8.5-mm implant for selection. Many of the reports also included short implants with a range of diameters. While it was

not feasible to segregate the different diameters, it was possible to report here on all short implants and short-wide implants, with “wide” defined as ≥ 4.8 mm. Again, the pragmatic reason for selecting 4.8 mm was that implant manufacturers representing the majority of the international market share include implant diameters ≥ 4.8 mm for selection. The results of this and previous investigations indicate that there is little difference in



on Survival of Short and Long Dental Implants



the survival of short versus long implants, regardless of the definition of a short implant. Ultimately, it will be valuable to define a short implant according to known anatomic restrictions or, alternatively, by assignment of added risk to an implant of known alternative (shorter) dimension. The existing data suggest that, in the short term, implant survival rates are incrementally reduced below 8 mm (Table 11).

This systematic review was not limited to the inclusion of only randomized controlled clinical trials. The reviewed prospective and retrospective, nonrandomized, uncontrolled studies provide evidence of the high survival rate of short implants in posterior partially edentulous patients. The included studies are of relatively short duration. Despite this, the constructed life table analyses revealed a high cumulative survival rate of 98% after up to 7 years of loading. In the included studies, only one was a randomized clinical trial.¹⁴ It compared 7-mm (short) implants with ≥ 10-mm (long) implants, with placement dependent upon interpositional block grafting. Both procedures showed comparable clinical results 1 year after loading, and the authors advocated the use of short implants because of their advantages over long implants, which required additional surgical procedures, cost, and effort.

Some of the variables believed to affect therapy involving short implants may be relevant to these studies. Romeo et al²³ indicated that the length and diameter of the implant, the surface topography of the implant, the crown-to-implant ratio, the prosthesis type, splinting to other implants, and occlusal/parafunctional loads are additional important factors to consider. The placement of implants in host vs grafted bone may also be important,³⁵ and the impact of systemic factors and habits such as smoking are of additional consequence.³⁶ It is also interesting to speculate that the length of bone-to-implant contact measured after prosthetic connection may be more relevant to the survival of the implant than the length of the implant placed into bone.

The forest plot of the studies that compared short and long dental implants (Table 9) showed that short dental implants have no more statistically significant risk of failure than their longer counterparts. This graphic representation of a meta-analysis is typically applied to randomized controlled trials of combinable data sets. Here, a variety of clinical reports were included. It appears from a previous analysis³⁶ that the data were sufficiently homogenous to permit this meta-analytic approach, despite the obvious inclusion of studies using different definitions of "short implants."

Several other investigations have recently analyzed the reported success of short implants. Most recently, Telleman et al³⁶ defined short implants as less than 10 mm and evaluated a similar data set involving 29 studies involving 2,611 implants up to 9.5 mm in length. Three hundred six of the implants were 9 or 9.5 mm in length. Using a main outcome of survival rates after 2 years on a per-implant basis, the authors concluded that there was a significant negative association between implant length and failure rate within the range of 5 to 8.5 mm. In a recent meta-analysis of the survival of short implants, where short implants were

Table 11 Cumulative Survival Rate According to Length

Implant length	0–1 y			1–2 y			2–3 y			3–4 y		
	n	ISR	CSR	n	ISR	CSR	n	ISR	CSR	n	ISR	CSR
5 mm	28	100.0%	100.0%	22	95.5%	95.5%	17	94.1%	89.8%	14	100.0%	89.8%
6 mm	359	97.2%	97.2%	161	99.4%	96.6%	39	100.0%	96.6%	8	100.0%	96.6%
7 mm	713	97.8%	97.8%	250	99.2%	97.0%	73	98.6%	95.6%	67	100.0%	95.6%
8 mm	2,095	99.2%	99.2%	1,654	99.9%	99.2%	1,055	100.0%	99.2%	656	100.0%	99.2%
8.5 mm	225	98.2%	98.2%	71	100%	98.2%	7	100.0%	98.2%	2	100.0%	98.2%

ISR = interval survival rate; CSR = cumulative survival rate.

defined as 10 mm or less, a larger number of implants was included (7,392). The results were largely focused on implant surface-related effects on the cumulative success rate and did not report the effect of stratified implant length upon survival.³⁷ A systematic review concluded that placement of short, rough-surfaced implants (< 8 mm) was not less efficacious than placement of rough-surface implants at least 10 mm long.⁵ A similar conclusion was developed by a recent literature review of 13 studies.³⁴ The report of Telleman et al³⁶ provided insight into factors affecting reported implant survival. The interactions of implant length (5 to 9.5 mm) with implant surface, maxilla versus mandible, smoking, and augmentation procedures were reported, and it was found that the heterogeneity was insufficient to reject the result of failure rates per implant length. They did conclude that, in partially edentulous patients, short dental implants had a better prognosis in the mandible than in the maxilla and that studies that excluded smokers achieved higher survival rates than those studies that included heavy smokers. Augmentation procedures preceding implant placement did not affect the survival of short implants. Surface topography has a controversial role in the survival of short implants. Mecherevo-Cantalejo et al³⁷ argued that the cumulative success rate of machined-surface implants is lower than that of rough-surfaced short implants. Studies that examined implant survival using machined implants for the treatment of posterior partial edentulism reported relatively low cumulative survival rates for short dental implants.^{38,39} In the present analysis, only 4.6% of the included implants possessed a machined surface.

A key observation made among all of these studies is that, in aggregate, 70% of the failed implants failed before loading. This suggests that the impact of loading and notions of biomechanical inferiority of the shorter bone-implant interface may not be the major factors in the failure of short implants. Other mechanical factors merit consideration but have not

been fully disclosed in the majority of studies. One of them is crown-to-implant ratio. A large amount of bone loss leads to restorations with increased crown-to-implant ratios. In this context, a recent retrospective cohort study on 5.7- or 6-mm-long plateau-design implant-supported restorations was conducted on 194 patients. The crown-to-implant ratio ranged between 0.9 and 3.2. However, the study showed that crown-to-implant ratio had no effect on the success of those implants.⁴⁰ This study was also preceded by a literature review, which showed the same result.⁴¹

CONCLUSION

Short dental implants, defined as 8.5 mm or shorter, demonstrated success rates that were comparable to those of longer implants, irrespective of design, surface, and width. The use of implants that are 8.5 mm or shorter for the treatment of posterior partial edentulism may be considered as a possible alternative to the use of longer implants, which require additional surgical procedures or involve safety concerns.

ACKNOWLEDGMENTS

The authors reported no conflicts of interest related to this study.

REFERENCES

- Tasoulis G, Yao SG, Fine JB. The maxillary sinus: Challenges and treatments for implant placement. *Compend Contin Educ Dent* 2011;32:10–14,16,18–19.
- Chrcanovic BR, Custódio AL. Inferior alveolar nerve lateral transposition. *Oral Maxillofac Surg* 2009;13:213–219.
- Fuh LJ, Huang HL, Chen CS, et al. Variations in bone density at dental implant sites in different regions of the jawbone. *J Oral Rehabil* 2010;37:346–351.
- McAllister BS, Haghigiat K. Bone augmentation techniques. *J Periodontol* 2007;78:377–396.

5. Kotsovilis S, Fourmousis I, Karoussis I K BC. A systematic review and meta-analysis on the effect of implant length on the survival of rough-surface dental implants. *J Periodontol* 2009 Nov;80:1700–1718.
6. Renouard F, Nisand D. Impact of implant length and diameter on survival rates. *Clin Oral Implants Res* 2006 Oct;17(suppl 2):35–51.
7. Das Neves FD, Fones D, Bernardes SR, do Prado CJ, Neto AJ. Short implants—An analysis of longitudinal studies. *Int J Oral Maxillofac Implants* 2006;21:86–93.
8. Hagi D, Deporter DA, Pilliar RM, Arenovich T. A targeted review of study outcomes with short (< or = 7 mm) endosseous dental implants placed in partially edentulous patients. *J Periodontol* 2004 Jun;75:798–804.
9. Felice P, Checchi V, Pistilli R, Scarano A, Pellegrino G, Esposito M. Bone augmentation versus 5-mm dental implants in posterior atrophic jaws. Four-month post-loading results from a randomised controlled clinical trial. *Eur J Oral Implantol* 2009;2:267–281.
10. Grant BT, Pancko FX, Kraut R. Outcomes of placing short dental implants in the posterior mandible: A retrospective study of 124 cases. *J Oral Maxillofac Surg* 2009 Apr;67:713–717.
11. Bischof M, Nedir R, Najim SA, Szumukler-Moncler S, Samson J. A five-year life-table analysis on wide neck ITI implants with prosthetic evaluation and radiographic analysis: Results from a private practice. *Clin Oral Implants Res* 2006;17:512–520.
12. Jung UW, Choi JY, Kim CS, et al. Evaluation of mandibular posterior single implants with two different surfaces: A 5-year comparative study. *J Periodontol* 2008;79:1857–1863.
13. Fugazzotto PA. Shorter implants in clinical practice: Rationale and treatment results. *Int J Oral Maxillofac Implants* 2008;23:487–96.
14. Felice P, Pellegrino G, Checchi L, Pistilli R, Esposito M. Vertical augmentation with interpositional blocks of anorganic bovine bone vs. 7-mm-long implants in posterior mandibles: 1-year results of a randomized clinical trial. *Clin Oral Implants Res* 2010;21:1394–1403.
15. Sohn D-S, Kim W-S, Lee W-H, Jung H-S, Shin I-H. A retrospective study of sintered porous-surfaced dental implants in restoring the edentulous posterior mandible: Up to 9 years of functioning. *Implant Dent* 2010;19:409–418.
16. Koo K-T, Wikesjö UME, Park J-Y, et al. Evaluation of single-tooth implants in the second molar region: A 5-year life-table analysis of a retrospective study. *J Periodontol* 2010;81:1242–1249.
17. Bahat O, Handelsman M. Use of wide implants and double implants in the posterior jaw: A clinical report. *Int J Oral Maxillofac Implants* 1996;11:379–386.
18. Renouard F, Arnoux JP, Sarment DP. Five-mm-diameter implants without a smooth surface collar: Report on 98 consecutive placements. *Int J Oral Maxillofac Implants* 1999;14:101–107.
19. Wennerberg A, Jemt T. Complications in partially edentulous implant patients: A 5-year retrospective follow-up study of 133 patients supplied with unilateral maxillary prostheses. *Clin Implant Dent Relat Res* 1999;1:49–56.
20. Van Steenberghe D, Mars GD, Quirynen M, Jacobs R, Naert I. A prospective split-mouth comparative study of two screw-shaped self-tapping pure titanium implant systems. *Clin Oral Implants Res* 2000;11:202–209.
21. Deporter D, Pilliar RM, Todescan R, Watson P, Pharoah M. Managing the posterior mandible of partially edentulous patients with short, porous-surfaced dental implants: Early data from a clinical trial. *Int J Oral Maxillofac Implants* 2001;16:653–658.
22. Polizzi G, Rangert B, Lekholm U, Gualini F, Lindström H. Bränemark System wide platform implants for single molar replacement: Clinical evaluation of prospective and retrospective materials. *Clin Implant Dent Relat Res* 2000;2:61–69.
23. Romeo E, Chiapasco M, Ghisolfi M, Vogel G. Long-term clinical effectiveness of oral implants in the treatment of partial edentulism. Seven-year life table analysis of a prospective study with ITI dental implants system used for single-tooth restorations. *Clin Oral Implants Res* 2002;13:133–143.
24. Rocuzzo M, Wilson T. A prospective study evaluating a protocol for 6 weeks' loading of SLA implants in the posterior maxilla: One year results. *Clin Oral Implants Res* 2002;13:502–507.
25. Rocci A, Martignoni M, Gottlow J. Immediate loading of Bränemark System TiUnite and machined-surface implants in the posterior mandible: A randomized open-ended clinical trial. *Clin Implant Dent Relat Res* 2003;5(suppl 1):57–63.
26. Salvi GE, Gallini G, Lang NP. Early loading (2 or 6 weeks) of sandblasted and acid-etched (SLA) ITI implants in the posterior mandible. A 1-year randomized controlled clinical trial. *Clin Oral Implants Res* 2004;15:142–149.
27. Misch CE, Stegenga J, Barboza E, Misch-Dietsh F, Cianciola LJ, Kazor C. Short dental implants in posterior partial edentulism: A multicenter retrospective 6-year case series study. *J Periodontol* 2006;77:1340–1347.
28. Levine RA, Ganeles J, Jaffin RA, Clem DS, Beagle, J. R. & Keller GW. Multicenter retrospective analysis of wide-neck dental implants for single molar replacement. *Int J Oral Maxillofac Implants*. 2007;22: 736–742.
29. Nedir R, Nurdin N, Szumukler-Moncler S, Bischof M. Placement of tapered implants using an osteotome sinus floor elevation technique without bone grafting: 1-year results. *Int J Oral Maxillofac Implants* 2009;24:727–733.
30. Felice P, Pistilli R, Lizio G, Pellegrino G, Nisii A, Marchetti C. Inlay versus onlay iliac bone grafting in atrophic posterior mandible: A prospective controlled clinical trial for the comparison of two techniques. *Clin Implant Dent Relat Res* 2009;11(suppl 1):e69–82.
31. Zembic A, Gläuser R, Khraisat A, Hämerle CHF. Immediate vs. early loading of dental implants: 3-year results of a randomized controlled clinical trial. *Clin Oral Implants Res* 2010;21:481–489.
32. Nedir R, Nurdin N, Vazquez L, Szumukler-Moncler S, Bischof M, Bernard J-P. Osteotome sinus floor elevation technique without grafting: A 5-year prospective study. *J Clin Periodontol*. 2010;37: 1023–1028.
33. Morand M, Irinakis T. The challenge of implant therapy in the posterior maxilla: Providing a rationale for the use of short implants. *J Oral Implantol* 2007;33:257–266.
34. Griffin TJ, Cheung WS. The use of short, wide implants in posterior areas with reduced bone height: A retrospective investigation. *J Prosthet Dent* 2004;92:139–144.
35. Becktor JP, Isaksson S, Sennerby L. Survival analysis of endosseous implants in grafted and nongrafted edentulous maxillae. *Int J Oral Maxillofac Implants* 2004;19:107–115.
36. Tellemann G, Raghoebar GM, Vissink A, den Hartog L, Huddleston Slater JJ, Meijer HJ. A systematic review of the prognosis of short (<10 mm) dental implants placed in the partially edentulous patient. *J Clin Periodontol* 2011;38:667–676.
37. Menchero-Cantalejo E, Barona-Dorado C, Cantero-Álvarez M, Fernández-Cáliz F, Martínez-González JM. Meta-analysis on the survival of short implants. *Med Oral Patol Oral Cir Bucal* 2011;16: e546–551.
38. Naert I, Koutsikakis G, Quirynen M, et al. Biologic outcome of implant-supported restorations in the treatment of partial edentulism. Part I: A longitudinal clinical evaluation. *Clin Oral Implants Res* 2002;13:381–389.
39. Bahat O. Bränemark System implants in the posterior maxilla: Clinical study of 660 implants followed for 5 to 12 years. *Int J Oral Maxillofac Implants* 2000;15:646–653.
40. Birdi H, Schulte J, Kovacs A, Weed M, Chuang SK. Crown-to-implant ratios of short-length implants. *J Oral Implantol* 2010;36:425–433.
41. Blanes R. To what extent does the crown-implant ratio affect the survival and complications of implant-supported reconstructions? A systematic review. *Clin Oral Implants Res* 2009;20(suppl 4):67–72.

Effect of Strontium-Substituted Nanohydroxyapatite Coating of Porous Implant Surfaces on Implant Osseointegration in a Rabbit Model

Guo-li Yang, PhD, DDS¹/Li-na Song, BA, DDS²/Qiao-hong Jiang, PhD, DDS²/
Xiao-xiang Wang, DE³/Shi-fang Zhao, PhD, DDS⁴/Fu-ming He, MD, DDS⁵

Purpose: This study investigated the effects of a strontium-substituted nanohydroxyapatite (Sr-HA) coating, deposited onto porous implant surfaces using an electrochemical process, on implant osseointegration in a rabbit model. **Materials and Methods:** The surfaces were analyzed by field-emission scanning electron microscopy, x-ray diffractometry (XRD), Fourier transform infrared spectroscopy (FT-IR), a portable surface roughness tester, and inductively coupled plasma atomic emission spectroscopy (ICP-AES). Thirty implants (half HA-coated and half Sr-HA-coated) were inserted into femurs of 15 rabbits. After 2, 4, and 8 weeks, the femurs were retrieved and prepared for histomorphometric evaluation. **Results:** Microscopic examination showed a surface topography of rodlike crystals on both surfaces. XRD and FT-IR showed that the phase of the deposits was HA. No differences were found in surface roughness between the two groups. ICP-AES showed that the Sr/(Ca+Sr) molar ratio of Sr-HA coating was 10.1 mol%. Histologic observation showed that new bone appeared on both surfaces after 2 weeks and became mature after 8 weeks. Histomorphometric analysis showed no differences between the two groups in bone-to-implant contact at 2 weeks or in bone area within all threads at 2 and 4 weeks. The Sr-HA coated group had significantly higher bone-to-implant contact at 4 and 8 weeks. Significant differences were also found in bone area at 8 weeks. **Conclusion:** The present study showed that this Sr-HA coating, deposited using an electrochemical process, has the potential to enhance implant osseointegration. INT J ORAL MAXILLOFAC IMPLANTS 2012;27:1332–1339

Key words: dental implant, electrochemical process, hydroxyapatite coating, osseointegration, strontium

Increasing attention has been paid to strontium (Sr) because of its beneficial effects on bone. Sr is a trace element found in the skeleton that possesses the dual capacities of promoting osteoblast-mediated bone formation¹ and inhibiting osteoclast-mediated bone

resorption.^{2,3} In vitro studies indicate that Sr appears to act by enhancing preosteoblast differentiation, promoting the synthesis of osteogenic proteins, and inhibiting both osteoclast differentiation and mature osteoclast function.⁴ Preclinical studies have employed Sr salts in the treatment of postmenopausal osteoporosis^{5–7} and have demonstrated that Sr improves bone marker profiles,⁸ bone histology, and bone architecture,⁹ resulting in a reduced fracture risk^{10,11} compared with placebo.

The effects of Sr on implant osseointegration have also been investigated. Oral administration of Sr ranelate increased mechanical fixation of implants in normal and osteoporotic rats.¹² However, there are several drawbacks associated with oral administration of Sr.^{13–15} Consequently, the development of implants that release strontium locally is desirable. One study produced a film of strontianite (SrCO_3) by exposing a sodium titanate surface to strontium acetate.¹⁶ In another study, well-ordered strontium titanate (SrTiO_3) nanotube arrays were prepared by hydrothermal treatment of anodized titania nanotubes. These nanotube arrays released Sr over a 4-week period.¹⁷

¹Attending Doctor, Department of Implantology, Stomatology Hospital, Medical School, Zhejiang University, Hangzhou, China.

²Resident Doctor, Department of Implantology, Stomatology Hospital, Medical School, Zhejiang University, Hangzhou, China.

³Professor, Department of Materials Science and Engineering, Zhejiang University, Hangzhou, China.

⁴Professor, Department of Implantology, Stomatology Hospital, Medical School, Zhejiang University, Hangzhou, China.

⁵Associate Chief Physician, Department of Implantology, Stomatology Hospital, Medical School, Zhejiang University, Hangzhou, China.

Correspondence to: Dr Fu-ming He, Department of Implantology, Stomatology Hospital, Medical School, Zhejiang University, Yan'an Road, Hangzhou, 310006 China.
Fax: +571-87217218. Email: hfm@zju.edu.cn

Hydroxyapatite (HA) is the most commonly described implant coating in the literature. Many investigations have demonstrated that the addition of an HA coating to implant surfaces was beneficial for bone integration with implants.^{18,19} Recently, nano-HA coatings have been of interest because of the similarity of nano-HA to HA in the body. In vivo experiments showed that nano-HA coatings improved early bone formation, even if implants were placed in a gap-healing model.²⁰⁻²² Strontium-HA (Sr-HA) coatings on titanium (Ti) or Ti alloy substrates have been synthesized via pulsed-laser deposition,²³ plasma spray,²⁴ or a biomimetic method.²⁵ Previous studies have shown that nano-HA coatings can be deposited onto porous implant surfaces via an electrochemical process.²⁶⁻³⁰ This process has many advantages, including good control of the composition and structure of coatings, relatively low processing temperatures that enable formation of highly crystalline deposits with low residual stresses, and the ability to coat porous or complex surfaces. Coatings produced using this process have rodlike HA crystals with a hexagonal cross section, similar to the structure of HA in bone, and they also show increased bone formation around coated implants, resulting in increased mechanical strength between implant and bone. This electrochemical method is capable of depositing Sr into or onto HA by adding Sr salt into the electrolytes.

The thickness of the described HA coating was 5 to 6 μm , which is unsuitable clinically, as the coating can be lost when the implant is placed into an undersized osteotomy. To resolve this drawback, the authors modified the electrochemical process to deposit a coating with a thickness of approximately 1 to 2 μm that cannot be destroyed during implant placement.³¹

It is hypothesized that a Sr-HA coating can be successfully deposited onto implant surfaces and improve bone integration with implant surfaces. The aims of the present study were to deposit a thin Sr-HA coating onto porous implant surfaces using an electrochemical process and to investigate the effects of this Sr-HA coating on implant osseointegration in a rabbit model.

MATERIALS AND METHODS

Surface Treatment of Ti Implants and Plates

Screw-shaped Ti implants with an external diameter of 4.1 mm and a length of 8 mm ($n = 30$) and plates of 10 \times 10 \times 1 mm ($n = 36$) were roughened as previously described by Yang et al.³⁰ In brief, samples were polished, sandblasted, and washed in acetone, 75% alcohol, and distilled water in an ultrasonic cleaner. Subsequently, samples were treated with a solution containing hydrofluoric acid and nitric acid for 10 minutes and then treated with a solution contain-

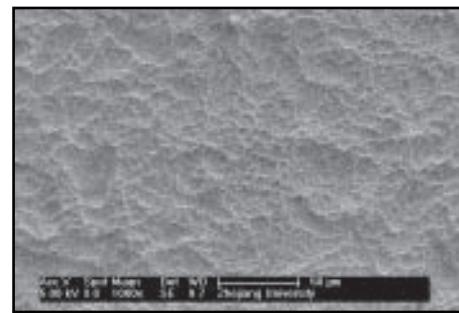


Fig 1 FSEM image of sandblasted and etched samples (original magnification $\times 1,000$).

ing hydrochloric acid and sulfuric acid for 30 minutes. Samples were dried in an oven at 50°C for 24 hours. Field-emission scanning electron microscopy (FSEM) observation showed that irregular porous structures appeared on the implant surfaces (Fig 1).

Preparation of HA and Sr-HA Coatings

The preparation of HA coatings was similar to previous studies.³² In brief, the Ti samples were used as the working electrode (cathode), while a platinum plate functioned as the counterelectrode. The electrolytes were prepared by dissolving analytic-grade calcium nitrate (1.2 mmol/L) and ammonium phosphate (0.72 mmol/L) into distilled water to a calcium/phosphorus ratio of 1.67. Sodium nitrate (0.1 mol/L) was added to improve the conductivity of the electrolytes. The deposition process was conducted with a direct-current power source at 3.0 V at 85°C for 30 minutes. Preparation of Sr-HA coatings used the same process except that strontium chloride (SrCl_2) with an $\text{Sr}/(\text{Ca}+\text{Sr})$ molar ratio of 10% was added to the electrolyte solution.

Surface Analysis

The surface morphology of the treated samples was examined using FSEM (FEI, SIRION100). The surface crystal structure was analyzed using an x-ray diffractometer (XRD) (Philips XD-98, Cu $\text{K}\alpha$ radiation). The goniometer was set a scan rate of 4 degrees/minute over a 20° range of 5 to 55 degrees. Spectroscopic analysis of both coatings was carried out by Fourier transform infrared spectroscopy (FT-IR) (Bruker Tenson 27) using the potassium bromide pellet technique. The coatings on the Ti specimens ($n = 3$ each group) were dissolved in 100 mL

of 0.1 mol/L hydrochloric acid solution. The chemical composition was calculated by analyzing the solution by inductively coupled plasma atomic emission spectroscopy (ICP-AES) (IRIS Intrepid II, Thermo Fisher Scientific), assuming that the coating was stoichiometric HA.

Animals and Surgical Procedure

This experiment was approved by the Institutional Animal Care and Use Committee of Zhejiang University. Fifteen adult white rabbits weighing 2.5 to 3.0 kg each were used. Surgery was performed under sterile conditions in a veterinary operating theater.

The surgical procedure has been reported in detail previously.²⁸ Briefly, 30 implants were inserted into the femurs of 15 rabbits bilaterally. General anesthesia was induced by intramuscular injection of SuMianXin II (0.1 to 0.2 mL/kg, The Military Veterinary Institute, Quartermaster University of PLA). Lidocaine was injected locally at the surgical site before the operation. The distal aspect of the femur was surgically exposed by incisions through the skin, fascia, and periosteum. The flat surface on the lateral aspect of the femur was selected for implant placement. The HA-coated implants were placed in the right femurs, while the Sr-HA coated implants were placed in the left femurs. With intermittent drilling with a low rotary speed and under profuse saline irrigation, each site was prepared and enlarged to 4.1 mm in diameter. The implants were inserted without tapping until the implant shoulders were level with the bone surface. After implantation, the animals received antibiotics (penicillin, 400,000 IU/day) for 3 days. At 2, 4, and 8 weeks after the operation, animals ($n = 5$ at each time point) were euthanized by an intramuscular overdose of SuMianXin (1.0 mL). The tissues were then retrieved and prepared for histomorphometric analysis.

Histomorphometric Analysis

The specimens were stored in 10% neutral buffered formalin for 5 to 7 days. Undecalcified sections containing the central portion of each implant were produced at a final thickness of 30 μm using a cutting and grinding system (Exakt 310 CP series, Exakt Apparatebau). The ground sections were stained with Stevenel blue and van Gieson picro fuchsin. One experienced blinded examiner performed the histometric analysis by means of a computerized image analysis system (Image-Pro Plus, Media Cybernetics). Histomorphometric measurements of bone associated with the implants were made in the region where the implant was juxtaposed to cancellous bone. The percentage of bone-to-implant contact (BIC) along the threads and the percentage of area between threads filled with bone were measured. BIC was measured as the percentage of the length of bone in direct contact with the implant surface. Bone area was mea-

sured as the percentage of the area within the threads located inside the cancellous bone containing bone.

Statistical Analysis

Surface roughness and histomorphometric data were analyzed statistically using SPSS version 16.0 software (IBM). Group means and standard deviations were used to calculate each parameter. Differences between experimental samples were analyzed using the paired Student *t* test. A *P* value $< .05$ was considered significant.

RESULTS

Surface Characteristics

The surface topography of both coatings appeared similar under FSEM (Fig 2). At high magnification, rodlike crystals could be seen covering the irregular surfaces. However, the surface morphology was still clear and demonstrated that the coatings were thin and were mostly located in the porous structures. Sr did not affect the general morphology of the HA crystals.

The XRD patterns confirmed that the phase of the deposits was HA (Fig 3). The XRD patterns showed that the pure HA (Fig 3a) had narrower diffraction peaks than Sr-HA (Fig 3b), suggesting that while the particle size of the two products was not very different, the crystallinity of the Sr-HA was lower than that of pure HA.

The FT-IR spectra of both groups are shown in Fig 4. These were typical spectra of HA showing PO_4^{3-} -derived bands at 566, 605, 963, and 1,030 to 1,090 cm^{-1} . Low intensity OH^- -derived bands were visible at 630 and 3,570 cm^{-1} in both coatings. CO_3^{2-} and CO_2 were present in both coatings because all steps of the electrochemical process had been carried out in air.

ICP-AES analysis of the dissolved coatings was carried out to determine the elemental ratio composition of the two coatings in the present work. The results indicated that Sr was present in the Sr-HA coatings at a $\text{Sr}/(\text{Ca}+\text{Sr})$ molar ratio of 10.1 mol%, which was approximately equal to the molar ratio of Sr in the electrolytes.

Histologic Observation

Evaluation of the bone healing around both implants after 2 weeks showed no clear differences (Fig 5). Woven bone was found between the screw threads of both implant surfaces, with extensive bone contact along the length of the implant. Osteoblasts were seen on the circumference of marrow cavities, indicating active bone formation.

After 4 weeks, bone around both types of implants appeared to be remodeling into a more mature lamellar form, and osteoblastlike cells were less common. Some differences were noted between the two groups; there appeared to be more bone in contact with the Sr-HA-coated implants (Fig 6).

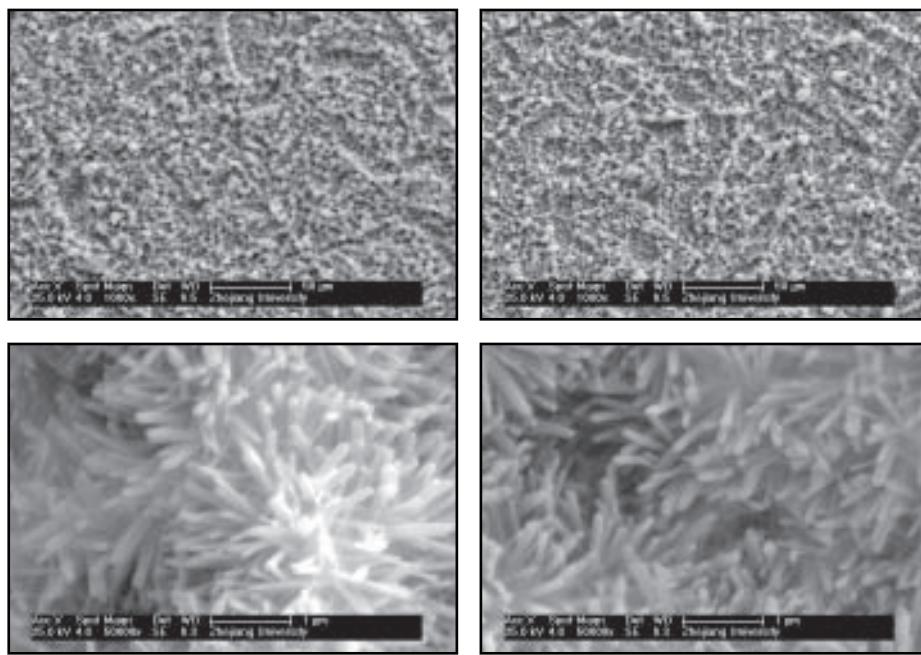


Fig 2 FSEM images of (left) HA-coated and (right) Sr-HA-coated surfaces. Surface topography of both coatings appeared similar, and Sr did not affect the general morphology of the HA crystals. Magnification: top row, $\times 1,000$; bottom row, $\times 50,000$.

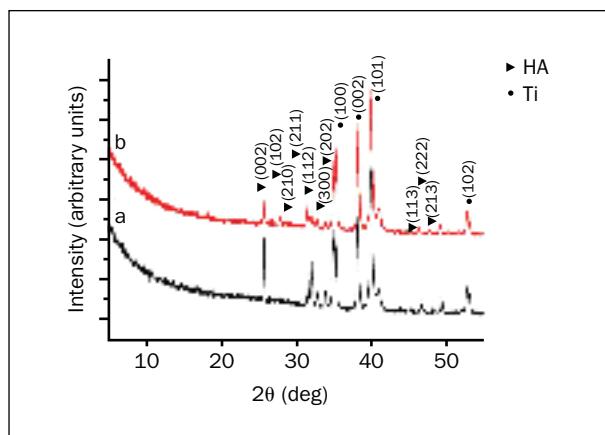


Fig 3 XRD patterns of the coatings. a = HA-coated implant surface; b = Sr-HA-coated implant surface.

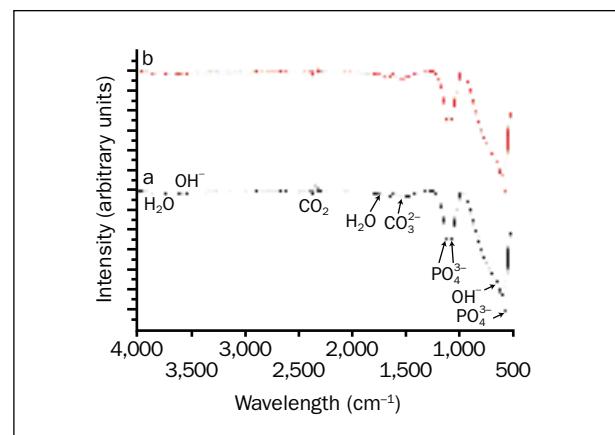


Fig 4 FT-IR spectra of the two coatings. a = HA coating; b = Sr-HA coating.

After 8 weeks, mature bone tissue was seen along both implant surfaces (Fig 7), and it was not possible to distinguish the recently formed bone from the adjacent older bone. Extensive direct contact of bone with implant surfaces was seen in both groups, and it appeared that there was more bone present and in contact with Sr-HA-coated implants than with HA implants.

Histometric Analysis

The percentage BIC values for each time point are shown in Table 1. At 2 weeks, no differences were found between the two groups ($P = .985$). However,

the Sr-HA-coated group had significantly higher BIC at 4 and 8 weeks ($P = .016$ and $.033$, respectively) (Table 1). For the HA-coated group, there were no differences between 2 weeks and 4 weeks ($P = .505$), between 2 weeks and 8 weeks ($P = .532$), or between 4 weeks and 8 weeks ($P = .966$). In the Sr-HA-coated group, no differences were found between 2 weeks and 4 weeks ($P = .915$), between 2 weeks and 8 weeks ($P = .168$), or between 4 weeks and 8 weeks ($P = .200$).

The percentage bone area values within all threads are shown in Table 2. At 2 and 4 weeks, there were no evident differences between two groups ($P = .968$ and

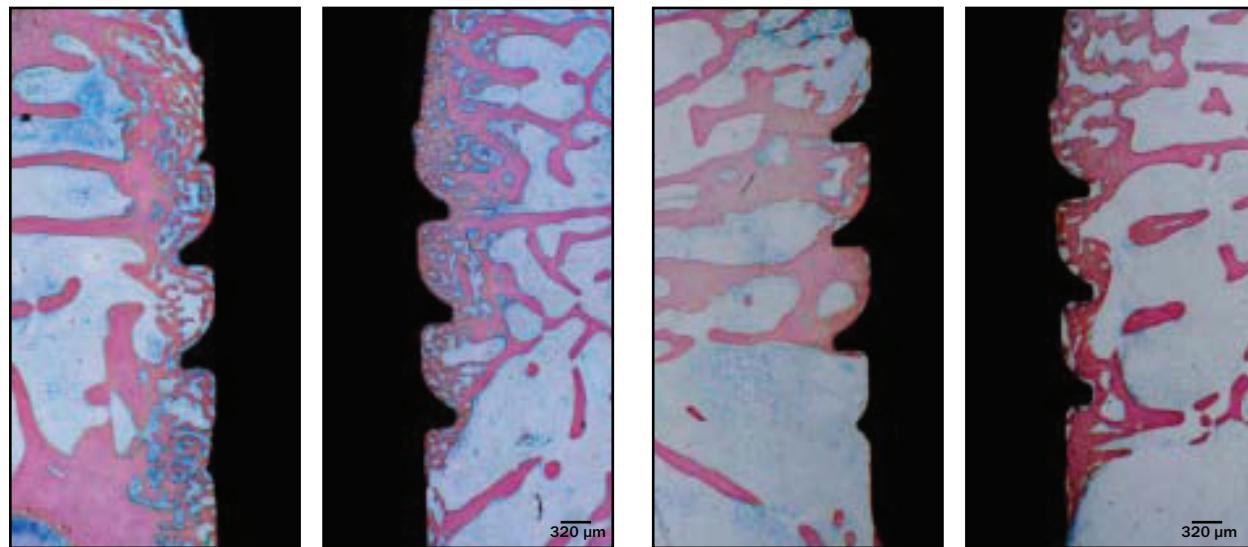


Fig 5 Histologic sections of the two groups after 2 weeks (left: HA-coated implants; right: Sr-HA-coated implants). Woven bone was found between the threads of both implant surfaces, with extensive bone contact along the implants' length. Above: bar = 320 µm; below: bar = 100 µm.

.089, respectively). However, significant differences were found between the two groups after 8 weeks ($P = .003$) (Table 2). Within the HA-coated group, there were no differences in bone area between 2 weeks and 4 weeks ($P = .447$), between 2 weeks and 8 weeks ($P = .550$), or between 4 weeks and 8 weeks ($P = .867$). In the Sr-HA-coated group, no differences were found in bone area between 2 weeks and 4 weeks ($P = .566$), between 2 weeks and 8 weeks ($P = .434$), or between 4 weeks and 8 weeks ($P = .830$).

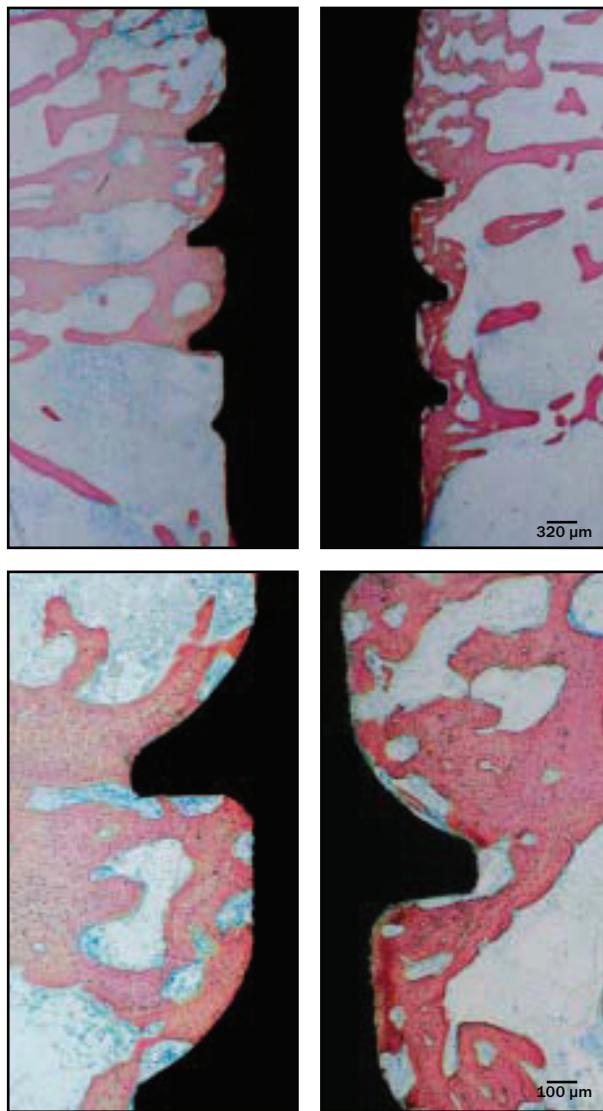


Fig 6 Histologic sections of the two groups after 4 weeks (left: HA-coated implants; right: Sr-HA-coated implants). Bone along both types of implants appeared to be remodeling into a more mature lamellar form, and osteoblastlike cells were less common. Above: bar = 320 µm; below: bar = 100 µm.

DISCUSSION

In this study, an Sr-HA-coated Ti implant surface was created using an electrochemical process, and the effects of the Sr-HA coating on implant osseointegration were investigated. The results showed that the process successfully produced a thin coating on the implant surfaces and the coating significantly increased new bone formation and BIC after 4 and 8 weeks *in situ* in a rabbit model.

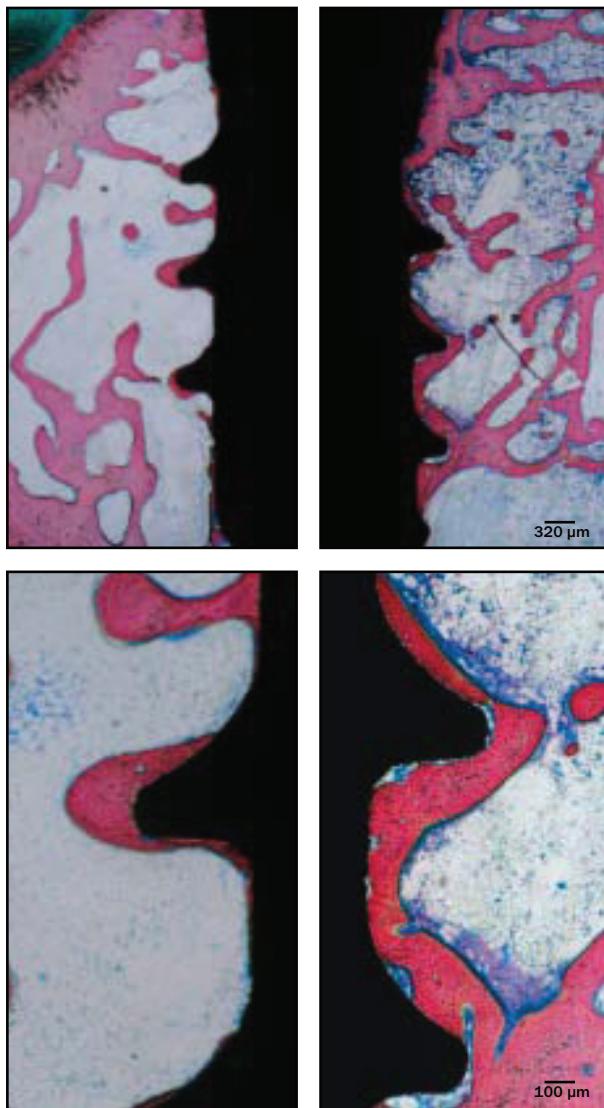


Fig 7 Histologic sections of the two groups after 8 weeks (left: HA-coated implants; right: Sr-HA-coated implants). Mature bone tissue was seen along both implant surfaces, and it was not possible to distinguish the recently formed bone from the adjacent older bone. Extensive direct contact of bone with implant surfaces was seen in both groups. Above: bar = 320 μm ; below: bar = 100 μm .

The demonstration that Sr-HA coatings increased osseointegration compared to HA coatings was in agreement with previous reports. Ten-percent Sr-HA coatings produced by sol-gel methods enhanced implant osseointegration in ovariectomized rats, suggesting that Sr-HA coatings could improve implant fixation in osteoporotic bone.³³ Hydrothermally produced phosphorus and Sr ion-incorporated Ti oxide surfaces improved implant osseointegration in rabbit cortical and cancellous bone by increasing bone

Table 1 Percent BIC at Each Time Point for Both Implants

Time	HA-coated implants	Sr-HA-coated implants	P
2 wk	48.06 \pm 18.02	48.19 \pm 11.48	.985
4 wk	42.08 \pm 8.02	49.00 \pm 7.71	.016
8 wk	42.46 \pm 13.41	59.15 \pm 15.09	.033

Table 2 Percent Bone Area Within All Threads of the Implants

Time	HA-coated implants	Sr-HA-coated implants	P
2 wk	39.42 \pm 20.44	39.05 \pm 14.08	.968
4 wk	29.73 \pm 5.46	46.59 \pm 20.57	.089
8 wk	31.84 \pm 26.17	49.38 \pm 24.55	.003

apposition.³⁴ Therefore, strontium-substituted apatite coatings improve the osseointegration of implant surfaces.

During the process of implant osseointegration, resorption of necrotic bone damaged during implant placement occurs, followed by a phase of bone formation.¹² If bone resorption is overactive, the implant can become loose and fail. Bone resorption is associated with the recruitment and activation of osteoclasts, so suppression or minimization of osteoclast activity is important. Sr may promote this action, as it is known to decrease markers of bone resorption in human studies,⁸ reduce osteoclastic bone resorption,^{1,35-37} and decrease osteoclast formation³⁷ as well as induce osteoclast apoptosis³⁸ *in vitro*. Future studies are needed to investigate the effects of Sr-HA coating on osteoclast function and the relative mechanism.

It is also important to promote osteoblast proliferation and activity, ie, increasing the amount of bone around the implant, to ensure adequate fixation of an implant. Studies have shown that Sr can stimulate the proliferation and differentiation of osteoblastic cells.^{39,40} The authors assume that this is the main reason that Sr-HA-coated implants had higher BIC and bone area compared to the HA coating.

The mechanism of action of Sr is not well understood, with the most likely explanation relating to effects on the calcium-sensing receptor (CaR).^{41,42} Several types of preosteoblastic cells and marrow stromal cells express the CaR, which is also expressed at all stages of osteoblast development, including proliferation, differentiation, and matrix mineralization. As an agonist of the CaR, Sr could increase osteoblast proliferation, differentiation, and matrix mineralization, thereby improving bone formation. Caverzasio suggested that cell replication induced by Sr ranelate

involves a protein kinase C/protein kinase D pathway in MC3T3-E1 cells and represents another potential mechanism for inducing osteoblastic cell replication.⁴³ Studies have also demonstrated that Sr can induce osteoclast apoptosis.⁴⁴ Future studies are needed to investigate which signal path plays a part in improving osteoblast function by Sr.

The bonding of crystalline HA with bone tissue may also play a role in the improved implant osseointegration seen with the Sr-HA coating.⁴⁵ This occurs via a dissolution-precipitation process: (1) the crystalline HA transforms into amorphous HA; (2) the amorphous HA dissolves into the surrounding solution, resulting in oversaturation; and (3) the nanocrystallites are precipitated from the oversaturated solution in the presence of collagen fibers. Therefore, the transition from crystalline to amorphous HA might be the determining step in the bone bonding of crystalline HA. In the Sr-HA coating, a portion of Ca²⁺ was replaced by Sr²⁺, which resulted in an improvement of dissolution of the Sr-HA coating.^{46,47} Therefore, the high dissolution rate of the Sr-HA coating was appropriate for ingrowth of bone into the implant surfaces. These may be a reason for the high BIC and increased bone area seen with the Sr-HA coating.

There were no significant differences in BIC and bone area at 2 weeks. Surface roughness and morphology play roles in the formation of implant osseointegration.⁴⁸ FSEM and roughness profile analysis showed no clear differences between the two coating surfaces, so these surfaces can be assumed to have a similar ability to improve implant osseointegration at the early stage of implantation. With the gradual dissolution of the coatings, Sr was released from the coatings, thereby improving implant osseointegration.

While studies have shown that oral administration of Sr can increase new bone formation around implants, there are some potential adverse reactions with oral Sr salts, including toxic epidermal necrolysis,¹³ drug rash with eosinophilia, and systemic symptoms syndrome.^{14,15} Thus, local application of Sr might be an alternative method to enhance implant osseointegration that avoids these potential adverse reactions. The results of this study showed that it is possible to generate Sr-HA coatings that enhance implant osseointegration via electrochemical deposition. This coating method is suitable for commercial coating of clinical implants, as it can generate thin coatings on complex or porous surfaces. In addition, the electrochemical process did not destroy the prepared implant surface. Moreover, the majority of the Sr-HA coating was located in the concavities of the porous structures, making it a good candidate for clinical application. Therefore, this coating represents an excellent prospect for clinical development of implants.

CONCLUSION

The present study has shown that the creation of a thin strontium-substituted nanohydroxyapatite (Sr-HA) coating on porous implant surfaces using the electrochemical process has the potential to enhance implant osseointegration.

ACKNOWLEDGMENTS

The authors thank Zhejiang Guangci Medical Appliance Company for delivering the experimental implants and disks. This work was supported by grants from the Excellent Youth Science program of Zhejiang Provincial Natural Science Foundation (Grant no: R2110374) and Ministry and Province Foundation (Grant no: WKJ2011-2-009). The authors reported no conflicts of interest related to this study.

REFERENCES

- Brennan TC, Rybchyn MS, Green W, Atwa S, Conigrave AD, Mason RS. Osteoblasts play key roles in the mechanisms of action of strontium ranelate. *Br J Pharmacol* 2009;157:1291–1300.
- Gentleman E, Fredholm YC, Jell G, et al. The effects of strontium-substituted bioactive glasses on osteoblasts and osteoclasts in vitro. *Biomaterials* 2010;31:3949–3956.
- Capuccini C, Torricelli P, Sima F, et al. Strontium-substituted hydroxyapatite coatings synthesized by pulsed-laser deposition: In vitro osteoblast and osteoclast response. *Acta Biomater* 2008;4: 1885–1893.
- Canalis E, Hott M, Deloffre P, Tsouderos Y, Marie PJ. The divalent strontium salt S12911 enhances bone cell replication and bone formation in vitro. *Bone* 1996;18:517–523.
- Cortet B. Use of strontium as a treatment method for osteoporosis. *Curr Osteoporos Rep* 2011;9:25–30.
- Dimai HP, Pietschmann P, Resch H, et al. Austrian guidance for the pharmacologic treatment of osteoporosis in postmenopausal women: Addendum 2010. *Wien Med Wochenschr* 2010;160: 586–589.
- Reginster J Y, Neuprez A. Strontium ranelate: A look back at its use for osteoporosis. *Expert Opin Pharmacother* 2010;11:2915–2927.
- Meunier PJ, Slosman DO, Delmas PD, et al. Strontium ranelate: Dose-dependent effects in established postmenopausal vertebral osteoporosis—A 2-year randomized placebo controlled trial. *J Clin Endocrinol Metab* 2002;87:2060–2066.
- Arlot M E, Jiang Y, Genant HK, et al. Histomorphometric and microCT analysis of bone biopsies from postmenopausal osteoporotic women treated with strontium ranelate. *J Bone Miner Res* 2008;23:215–222.
- Roux C, Fechtenbaum J, Kolta S, Isaia G, Andia JB, Devogelaer JP. Strontium ranelate reduces the risk of vertebral fracture in young postmenopausal women with severe osteoporosis. *Ann Rheum Dis* 2008;67:1736–1738.
- Meunier PJ, Roux C, Seeman E, et al. The effects of strontium ranelate on the risk of vertebral fracture in women with postmenopausal osteoporosis. *N Engl J Med* 2004;350:459–468.
- Maimoun L, Brennan TC, Badoud I, Dubois-Ferriere V, Rizzoli R, Ammann P. Strontium ranelate improves implant osseointegration. *Bone* 2010;46:1436–1441.
- Lee HY, Lie D, Lim KS, Thirumoorthy T, Pang SM. Strontium ranelate-induced toxic epidermal necrolysis in a patient with postmenopausal osteoporosis. *Osteoporos Int* 2009;20:161–162.
- Jonville-Béra AP, Crickx B, Aaron L, Hartingh I, Autret-Leca E. Strontium ranelate-induced DRESS syndrome: First two case reports. *Allergy* 2009;64:658–659.

15. Pernicova I, Middleton ET, Aye M. Rash, strontium ranelate and DRESS syndrome put into perspective. European Medicine Agency on the alert. *Osteoporos Int* 2008;19:1811–1812.
16. Forsgren J, Engqvist H. A novel method for local administration of strontium from implant surfaces. *J Mater Sci Mater Med* 2010;21:1605–1609.
17. Xin Y, Jiang J, Huo K, Hu T, Chu PK. Bioactive SrTiO(3) nanotube arrays: Strontium delivery platform on Ti-based osteoporotic bone implants. *ACS Nano* 2009;3:3228–3234.
18. Kim S, Jung UW, Lee YK, Choi SH. Effects of biphasic calcium phosphate bone substitute on circumferential bone defects around dental implants in dogs. *Int J Oral Maxillofac Implants* 2011;26:265–273.
19. Wennerberg A, Jimbo R, Allard S, Skarnemark G, Andersson M. In vivo stability of hydroxyapatite nanoparticles coated on titanium implant surfaces. *Int J Oral Maxillofac Implants* 2011;26:1161–1166.
20. Araujo MV, Mendes VC, Chattopadhyay P, Davies JE. Low-temperature particulate calcium phosphates for bone regeneration. *Clin Oral Implants Res* 2010;21:632–641.
21. Meirelles L, Albrektsson T, Kjellin P, et al. Bone reaction to nano hydroxyapatite modified titanium implants placed in a gap-healing model. *J Biomed Mater Res A* 2008;87:624–631.
22. Meirelles L, Arvidsson A, Andersson M, Kjellin P, Albrektsson T, Wennerberg A. Nano hydroxyapatite structures influence early bone formation. *J Biomed Mater Res A* 2008;87(2):299–307.
23. Capuccini C, Torricelli P, Boanini E, Gazzano M, Giardino R, Bigi A. Interaction of Sr-doped hydroxyapatite nanocrystals with osteoclast and osteoblast-like cells. *J Biomed Mater Res A* 2009;89:594–600.
24. Xue WC, Hosick HL, Bandyopadhyay A, et al. Preparation and cell-materials interactions of plasma sprayed strontium containing hydroxyapatite coating. *Surf Coat Technol* 2007;201:4685–4693.
25. Oliveira AL, Reis RL, Li P. Strontium-substituted apatite coating grown on Ti6Al4V substrate through biomimetic synthesis. *J Biomed Mater Res B Appl Biomater* 2007;83:258–265.
26. Yang GL, He FM, Song E, Hu JA, Wang XX, Zhao SF. In vivo comparison of bone formation on titanium implant surfaces coated with biomimetically deposited calcium phosphate or electrochemically deposited hydroxyapatite. *Int J Oral Maxillofac Implants* 2010;25:669–680.
27. Yang GL, He FM, Hu JA, Wang XX, Zhao SF. Biomechanical comparison of biomimetically and electrochemically deposited hydroxyapatite-coated porous titanium implants. *J Oral Maxillofac Surg* 2010;68:420–427.
28. He F, Yang G, Wang X, Zhao S. Effect of electrochemically deposited nanohydroxyapatite on bone bonding of sandblasted/dual acid-etched titanium implant. *Int J Oral Maxillofac Implants* 2009;24:790–799.
29. Yang GL, He FM, Hu JA, Wang XX, Zhao SF. Effects of biomimetically and electrochemically deposited nano-hydroxyapatite coatings on osseointegration of porous titanium implants. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2009;107:782–789.
30. Yang GL, He FM, Yang XF, Wang XX, Zhao SF. Bone responses to titanium implants surface-roughened by sandblasted and double-etched treatments in a rabbit model. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2008;106:516–524.
31. Cheng ZP, Guo CH, Dong WJ, He FM, Zhao SF, Yang GL. Effect of thin nano-hydroxyapatite coating on implant osseointegration in ovariectomized rats. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2012;113:e48–53.
32. Mingjie J, Xiaoxiang W. Electrolytic deposition of magnesium-substituted hydroxyapatite crystals on titanium substrate. *Mater Lett* 2009;63:2286–2289.
33. Li Y, Li Q, Zhu S, et al. The effect of strontium-substituted hydroxyapatite coating on implant fixation in ovariectomized rats. *Biomaterials* 2010;31:9006–9014.
34. Park JW. Increased bone apposition on a titanium oxide surface incorporating phosphate and strontium. *Clin Oral Implants Res* 2011;22:230–234.
35. Baron R, Tsouderos Y. In vitro effects of S12911-2 on osteoclast function and bone marrow macrophage differentiation. *Eur J Pharmacol* 2002;450:11–17.
36. Barbara A, Delannoy P, Denis BG, Marie PJ. Normal matrix mineralization induced by strontium ranelate in MC3T3-E1 osteogenic cells. *Metabolism* 2004;53:532–537.
37. Bonnelye E, Chabadel A, Saltel F, Jurdic P. Dual effect of strontium ranelate: Stimulation of osteoblast differentiation and inhibition of osteoclast formation and resorption in vitro. *Bone* 2008;42:129–138.
38. Hurtel-Lemaire AS, Mentaverri R, Caudrillier A, et al. The calcium-sensing receptor is involved in strontium ranelate-induced osteoclast apoptosis. New insights into the associated signaling pathways. *J Biol Chem* 2009;284:575–584.
39. Park JW, Kim YJ, Jang JH. Enhanced osteoblast response to hydrophilic strontium and/or phosphate ions-incorporated titanium oxide surfaces. *Clin Oral Implants Res* 2010;21:398–408.
40. Park JW, Kim HK, Kim YJ, Jang JH, Song H, Hanawa T. Osteoblast response and osseointegration of a Ti-6Al-4V alloy implant incorporating strontium. *Acta Biomater* 2010;6:2843–2851.
41. Brown EM. Is the calcium receptor a molecular target for the actions of strontium on bone? *Osteoporosis Int* 2003;14S:S25–34.
42. Chattopadhyay N, Quinn SJ, Kifor O, Ye C, Brown EM. The calcium-sensing receptor (CaR) is involved in strontium ranelate-induced osteoblast proliferation. *Biochem Pharmacol* 2007;74:438–447.
43. Caverzasio J. Strontium ranelate promotes osteoblastic cell replication through at least two different mechanisms. *Bone* 2008;42:1131–1136.
44. Bergamini P, Marchesi E, Pagnoni A, et al. Synthesis, characterization of strontium-bile acid salts and their bioactivity vs. the anti-osteoporosis drug strontium ranelate. *J Inorg Biochem* 2009;103:891–897.
45. Chen QZ, Wong CT, Lu WW, Cheung KM, Leong JC, Luk KD. Strengthening mechanisms of bone bonding to crystalline hydroxyapatite in vivo. *Biomaterials* 2004;25:4243–4254.
46. Christoffersen J, Christoffersen MR, Kolthoff N, Barenholdt O. Effects of strontium ions on growth and dissolution of hydroxyapatite and on bone mineral detection. *Bone* 1997;20:47–54.
47. Ni GX, Lu WW, Xu B, et al. Interfacial behaviour of strontium-containing hydroxyapatite cement with cancellous and cortical bone. *Biomaterials* 2006;27:5127–5133.
48. Yang GL, He FM, Zhao SS, Wang XX, Zhao SF. Effect of H₂O₂/HCl heat treatment of implants on in vivo peri-implant bone formation. *Int J Oral Maxillofac Implants* 2008;23:1020–1028.

Comparison of Three Inoculation Methods for Bone Tissue Engineering

Gu Cheng, MD¹/Xi Chen, MD²/Zhi Li, DDS, PhD³/Hui Lu, MD¹/Ongodia Davide, MD¹/Zubing Li, DDS, PhD⁴

Purpose: The purpose of this study was to compare the effectiveness of three methods of cell inoculation on cell growth and bone formation: inoculation of seed cells into the scaffolds from two sides (two-side inoculation method), inoculation of seed cells from one side (single-side inoculation method), and inoculation of a compound of seed cells and type 1 collagen gel from one side (type 1 collagen inoculation method).

Materials and Methods: Bone marrow stromal cells were isolated from 1-month-old male New Zealand rabbits and implanted into three-dimensional chitosan/beta-tricalcium phosphate scaffolds using the three different methods. Cultures were analyzed by various methods. **Results:** The type 1 collagen group expressed the best uniformity of cell distribution among all the three methods during a 1-week culture period, and the two-side group expressed the best uniformity during a 2- to 3-week culture period. The number of inoculated cells in the type 1 collagen group outpaced that of the other groups. With respect to the depth of penetration of the inoculated cells, the cells of the type 1 collagen group were concentrated on the surface of the scaffold and formed multiple layers, whereas the two-side group accounted for the deepest cell penetration.

Conclusion: The two-side inoculation method improves the number and distribution of seed cells *in vitro* and enhances the quality and rate of bone formation *in vivo*. This method is the most suitable seed method for bone tissue engineering. *INT J ORAL MAXILLOFAC IMPLANTS* 2012;27:1340–1350

Key words: bone marrow stromal cells, distribution, inoculation, scaffold

The development of tissue engineering has opened new avenues for the reconstruction of bone defects and transplantation. The combination of cells and bone tissue engineering scaffolds is the first and foremost step. The ability to reconstruct defects caused by accidents, trauma, and neoplasms is of utmost importance

to orthopedic and maxillofacial surgeons. Several grafting materials have been reported for the repair of bone defects, including autografts, allografts, and synthetic composite materials. Autologous bone transplantation is regarded as the most promising treatment¹; however, problems at donor sites are common.^{2,3} Allografts are limited by their scarcity and potential for immune reactions.^{4,5} To make up for the drawbacks of autografts and allografts, many synthetic composite scaffolds are being developed and used in patients with jawbone defects.⁶ However, several critical problems with the use of bone tissue engineering scaffolds to restore bone defects, especially large bone defects, hinder their usage. One of them is that cells at the center of the scaffold may not survive because the nutrients and oxygen required for cell survival can diffuse only 50 to 200 μm.^{7–9} Another is the poor distribution and penetration of seed cells, which also result in low cell densities and necrosis at the center of the scaffold. And third, bone tissue engineering products form only a limited tissue layer on the scaffold surface.⁸

Seed cells and biomaterial scaffolds are the basic components of bone tissue engineering; the inoculation of seed cells into scaffolds is the first and critical step. Three main inoculation methods are currently in use in bone tissue engineering: two-side inoculation,¹⁰ single-side inoculation,^{11,12} and gel-compound inocu-

¹Researcher, The State Key Laboratory Breeding Base of Basic Science of Stomatology (Hubei-MOST) and Key Laboratory of Oral Biomedicine, Ministry of Education, Wuhan, China; Department of Oral and Maxillofacial Surgery, School and Hospital of Stomatology, Wuhan University, Wuhan, China.

²Researcher, School of Public Health, Wuhan University, Wuhan, China.

³Assistant Professor, The State Key Laboratory Breeding Base of Basic Science of Stomatology (Hubei-MOST) and Key Laboratory of Oral Biomedicine, Ministry of Education, Wuhan, China; Department of Oral and Maxillofacial Surgery, School and Hospital of Stomatology, Wuhan University, Wuhan, China.

⁴Professor, The State Key Laboratory Breeding Base of Basic Science of Stomatology (Hubei-MOST) and Key Laboratory of Oral Biomedicine, Ministry of Education, Wuhan, China; Department of Oral and Maxillofacial Surgery, School and Hospital of Stomatology, Wuhan University, Wuhan, China.

Correspondence to: Dr Zubing Li, Department of Oral and Maxillofacial Surgery, School of Stomatology, Wuhan University, 237 Luoyu Road, Wuhan, China 430079. Fax: +86-27-8787-3849. Email: lizubing@sina.com

lation methods. The effectiveness of these techniques is yet to be evaluated. Therefore, the present study sought to compare cell viability and cell distribution on scaffolds inoculated with the three aforementioned methods to determine the best and most effective inoculation method.

MATERIALS AND METHODS

Preparation of Type 1 Collagen Gel Populated with Bone Marrow Stromal Cells

Type 1 collagen has the same characteristics as the extracellular matrix of natural bone, so it is a natural candidate for a scaffold or a coating material for scaffolds.¹³ Type 1 collagen gel populated with bone marrow stromal cells (BMSCs) (1 mg/mL) was prepared according to specifications¹⁴. Briefly, 200 µL of sterile type 1 rat-tail collagen (5 mg/mL) (Shanghai Canspec Scientific Instruments Co, Ltd) were mixed with 12 µL of sterile 0.1 mol/L sodium hydroxide, 760 µL of cell suspension, and 28 µL of 10× Dulbecco modified Eagle medium (Sigma) on ice. The resulting concentrations of BMSCs and fetal bovine serum (Invitrogen) were $3.925 \times 10^6/\text{mL}$ and 10%, respectively, at a pH of 7.0.

Fabrication and Characterization of Chitosan/Beta-Tricalcium Phosphate Scaffolds

Porous scaffolds of degradable chitosan/beta-tricalcium phosphate (CS/β-TCP) in a ratio of 4:2.7 were prepared according to previously reported methods.¹⁵ This method results in an interconnected open-pore microstructure and macropore structure. The porosity of the scaffolds was determined by the Archimedes method.¹⁶

Cross-sectional images of all the developed scaffolds were analyzed using a scanning electron microscope (Leica Cambridge S360, Leica) to examine the microstructure of the scaffolds. Cylindrical scaffolds ($n = 5$) with a 2:1 aspect ratio (5 mm length, 10 mm radius) were coated with gold/palladium using a Hummer V sputtering system.

Isolation and Identification of Rabbit BMSCs

Primary BMSCs were isolated from the femurs of 30-day-old New Zealand rabbits that had received an overdose of pentobarbital sodium through the auricular vein. In brief, the femurs were cut at both ends with a sterile bone-ribbing rongeur; then the bone marrow was flushed out with a 5-mL sterile syringe with high-glucose Dulbecco modified Eagle medium containing 10% (by volume) fetal bovine serum, 100 U/mL penicillin, and 100 U/mL streptomycin (Sigma). The marrow solution was centrifuged at 1,000 rpm for 7 minutes, suspended in fresh complete medium, seeded on culture

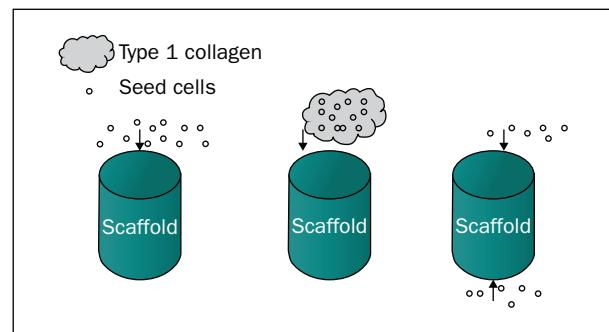


Fig 1 Diagram of the three different inoculation methods. (Left to right) Single-side group, in which cells were inoculated into the scaffolds from the front side; type 1 collagen, in which cell-seeded collagen gel was added to the front side of each scaffold; two-side group, in which seed cells were inoculated into the scaffold from both the front and back sides.

flasks, and incubated at 37°C in 5% carbon dioxide (CO₂). After 48 hours, any nonadherent cells were removed through changes of media. At a confluence of 80% to 100%, the attached BMSCs were further expanded by subculturing, and the second generations were used in this study.

Experimental Groups

After about 80% to 90% confluence was reached, the cells were digested by 0.25% trypsin, and the cell density was adjusted to $3.925 \times 10^6/\text{mL}$. The sterilized scaffolds were shaped into cylinders (5 mm length, 10 mm radius) and transferred into six-well plastic culture plates. Three different experimental groups and a control group were then developed as follows and as shown in Fig 1.

Single-Side Group. BMSCs were inoculated onto the scaffolds from the front side as follows: 100 µL of cell suspension was added to one side of each scaffold in each well in a six-well culture plate. The culture was set at 37°C in a 5% CO₂ humidified atmosphere. After 1.5 hours of incubation, 900 µL of culture medium was supplied and the culture was again set at 37°C in a 5% CO₂ humidified atmosphere.

Two-Side Group. BMSCs were inoculated on two sides of the scaffold. On the front side, 50 µL of cell suspension was added. After 1.5 hours of incubation, 50 µL of cell suspension was seeded onto the back side of the scaffold. After another 1.5 hours of incubation, 900 µL of culture medium was supplied and the culture was set at 37°C in a 5% CO₂ humidified atmosphere.

Type 1 Collagen Group. A total of 100 µL of cell-seeded collagen gel was added to the front side of each scaffold. After 1.5 hours of incubation, 900 µL of culture medium was supplied.

Control Group. One hundred microliters of cell suspension were dropped into a six-well plate. Then 900 µL

of culture medium was supplied and the scaffolds were placed into the culture plate.

Measurement of Initial Cell Seeding Efficacy

The percentage of BMSCs anchored to CS/ β -TCP scaffolds as a function of initial cell seeding efficacy was established. Holy et al¹ demonstrated that tissue formation of polylactic-co-glycolic acid scaffolds seeded with 1×10^6 cells/cm³ was similar to that seen on scaffolds seeded with higher initial cell seeding densities; therefore, the initial cell seeding density chosen for the present study was 1×10^6 /cm³. Because the volume of the cylindric scaffolds was 1.57 cm³, 1.57×10^6 cells were inoculated into the scaffolds in all groups with the different inoculation methods. Initial cell seeding efficacy was determined according to a previous study.¹⁷

Detection of Cell Viability

Cell proliferation was quantitatively analyzed by 2-(2-methoxy-4-nitrophenyl)-3-(4-nitrophenyl)-5-(2, 4-disulfophenyl)-2H-tetrazolium monosodium salt (WST-8) assay (Cell Counting Kit-8, Dojindo).¹⁸ On days 4, 8, and 12, five scaffolds of each group were taken out of the culture, washed twice with phosphate-buffered saline (PBS), and moved into a new six-well plate. Subsequently, 300 μ L of the WST-8 reagent were added to each well at a 1:10 ratio to the cell culture medium and incubated for 1.5 hours at 37°C in a humidified 5% CO₂ atmosphere. Then 200 μ L of solution from each well were transferred into a 96-well plate, and the optical density was determined at 490 nm on a microplate reader (Biotek-mQuant, Bio-Tek Instruments).

Alkaline Phosphatase Activity and Total DNA Content

Alkaline phosphatase (ALP) activity of the BMSCs induced into osteoblasts for 7, 14, 21, and 28 days on each specimen was determined by detecting the formation of p-nitrophenol following the procedure of p-nitrophenyl phosphate substrate solution (Sigma)¹⁹ and normalized by the corresponding DNA content,²⁰ which was assayed by the Quant-iT PicoGreen Kit (Invitrogen). The solutions were read at 490 nm using a microplate reader (Biotek-mQuant, BioTek Instruments). Briefly, after washing three times with PBS and treating with a cell lysis reagent, the cell-scaffold compounds were ground in a grinder with liquid nitrogen. Then, aliquots of lysates were sonicated for 30 seconds, and the suspensions were collected for analysis of ALP activity and total DNA content.

Confocal Laser Scanning Microscopic Analysis

The sections were analyzed with a confocal laser scanning microscope (Leica LCS Sp2 AOBS MP, Leica). The barrier filters had a band-pass of 530/30 nm and long-

pass of 590 nm combined with double dichroic 488/568 activation; the photomultipliers for each band of fluorescence were 534 nm (calcein) and 357 nm (alizarin red).

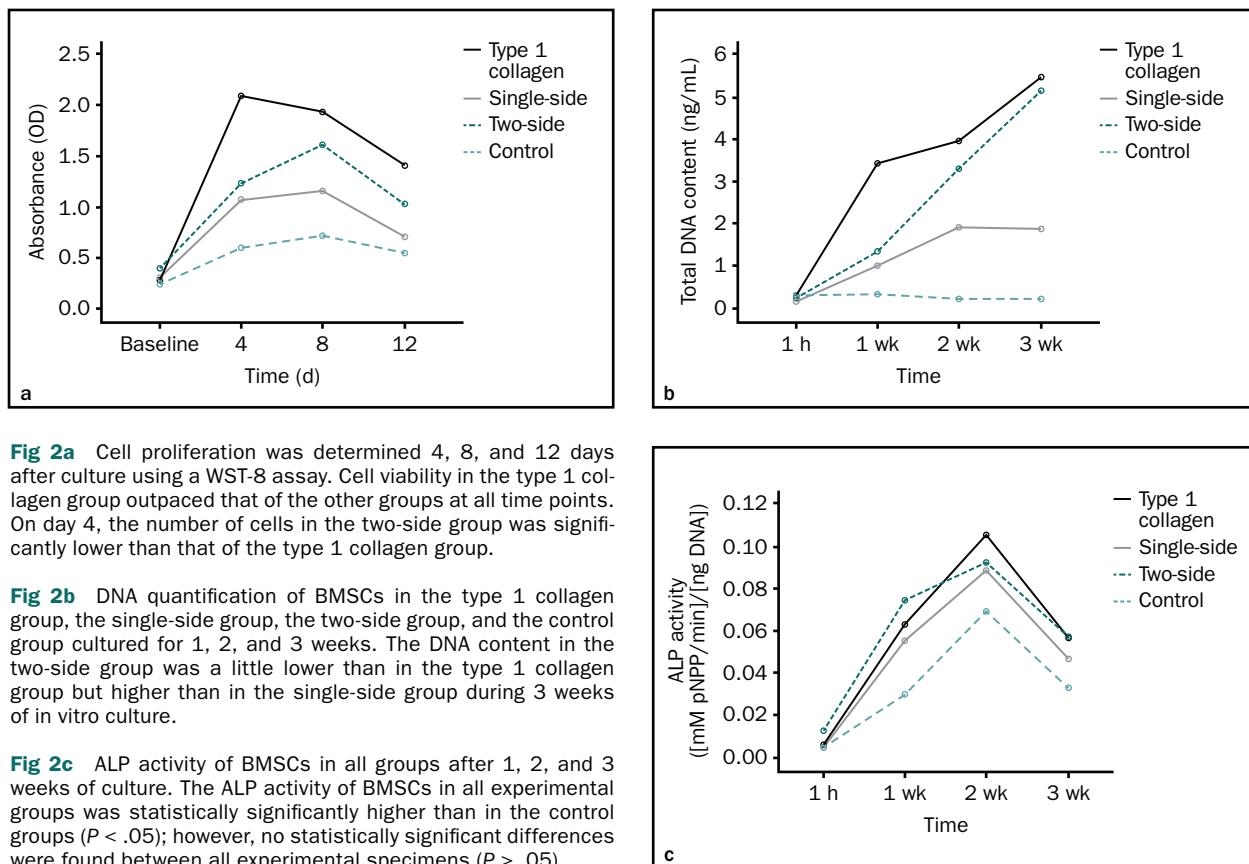
In the context of this study, the back side accounts for the side of the scaffolds close to the underside of the plates, and the front side accounts for the side of the scaffolds far from the underside of the plates.

In Vivo Study

Ninety adult China white rabbits were randomly divided into six groups (type 1 collagen, two-side, single side; and empty, negative, and positive control groups) (randomization done with Statistics Analysis System version 9.1). Five animals in each group were housed for 1 week before surgery. All surgical procedures followed protocols approved by Wuhan University's Animal Care and Use Committee. Surgery was performed under sterile conditions. Briefly, all animals were anesthetized with pentobarbital sodium (Sigma; 40 mg/kg intravenous) via the carotid artery. A small incision was made longitudinally along the skin of the lower margin of the mandible to expose the mandibular bone, and critical-size defects with radii of 10 mm^{21,22} were created using a fissure bur according to the methods of Young et al and Zhang and Zhang.^{15,23} The surrounding bone was cooled using sterile PBS to prevent overheating-related damage. Then, the tissue-engineered scaffolds of all the groups were implanted and anchored in the defects using resorbable suture material. In the empty group, the defects were created but left untreated; autologous bone was used to repair the defects in the positive control group. In the negative control group, CS/ β -TCP scaffolds without BMSCs were used to repair the defects. All animals were given intramuscular injections of penicillin (400,000 IU/mL; 0.1 mL/kg per day) and streptomycin (400,000 IU/mL; 0.1 mL/kg per day) in the first 3 days after operation. In the first, second, and third months after surgery, the mandibles of all rabbits were radiographed with panoramic apparatus (Department of Radiology, Hospital of Stomatatology, Wuhan University) with an exposure time of 0.04 seconds and a working distance of 1 meter. A radiograph analysis system (Soredex, Orion) was used to evaluate the process of healing in the defect region.

Statistical Analysis

Repeated-measures analysis of variance (ANOVA) was used to test the difference between various groups with respect to ALP activity over time and to compare the different groups with respect to the penetration depth of cells. The methods for multiple comparisons were least significant difference and Bonferroni tests, descriptive statistics, and means \pm standard deviations (SD). Statistical analyses were performed with SPSS software (version 13.0, IBM). All probability values were two-tailed ($\alpha = .05$).



RESULTS

Characteristics of Scaffolds

Scaffolds with a 2.7:4 (by weight) ratio of CS/ β -TCP were prepared and their mesh size and mechanical properties characterized. These compound scaffolds had open-cell pores with a high degree of interconnectivity, ensuring access to nutrients and transport of waste products.²⁴ The mean porosity of the CS/ β -TCP scaffold was 87.5% and the relative mesh size was 100.2 μm . Therefore this scaffold met the requirements for bone tissue engineering.^{25,26}

Efficacy of Initial Cell Seeding

The initial cell seeding efficacy (% of attachment) values of all the groups were as follows: type 1 collagen, $93.7\% \pm 8.49\%$; single-side, $67.9\% \pm 5.12\%$; two-side, $80.1\% \pm 4.62\%$; control, $5.27\% \pm 3.16\%$.

Cell Viability

The quantitative cell proliferation data obtained over a short time (12 days) through the WTS-8 assay are shown in Fig 2a. Cell viability over a longer time (21 days), as determined by total DNA content, is shown in Fig 2b. On day 4, the number of cells in the two-side

group was significantly lower than that of the type 1 collagen group (Fig 2a). However, by day 14, the two-side group showed cell numbers comparable to those seen in the type 1 collagen group (Fig 2b). At all time points, the DNA content in the type 1 collagen group outpaced that of the other groups. The two-side group showed slightly lower DNA content than the type 1 collagen group, but it was higher than the single-side group during 3 weeks of in vitro culture.

ALP Activity

Figure 2c shows that the ALP activity of BMSCs in all experimental groups was statistically significantly higher than in the control group. However, no statistical difference was found among all experimental specimens. Over time, the ALP activity of the specimens increased (Fig 2c); there were statistically significant differences ($F = 60.795$, $P < .001$) at all time points. ALP activity peaked at day 14 and decreased slightly at day 21 ($P < .05$).

Microscopic Observations

Repeated-measures ANOVA showed that the quantity of cells on the front side of the scaffolds was sig-

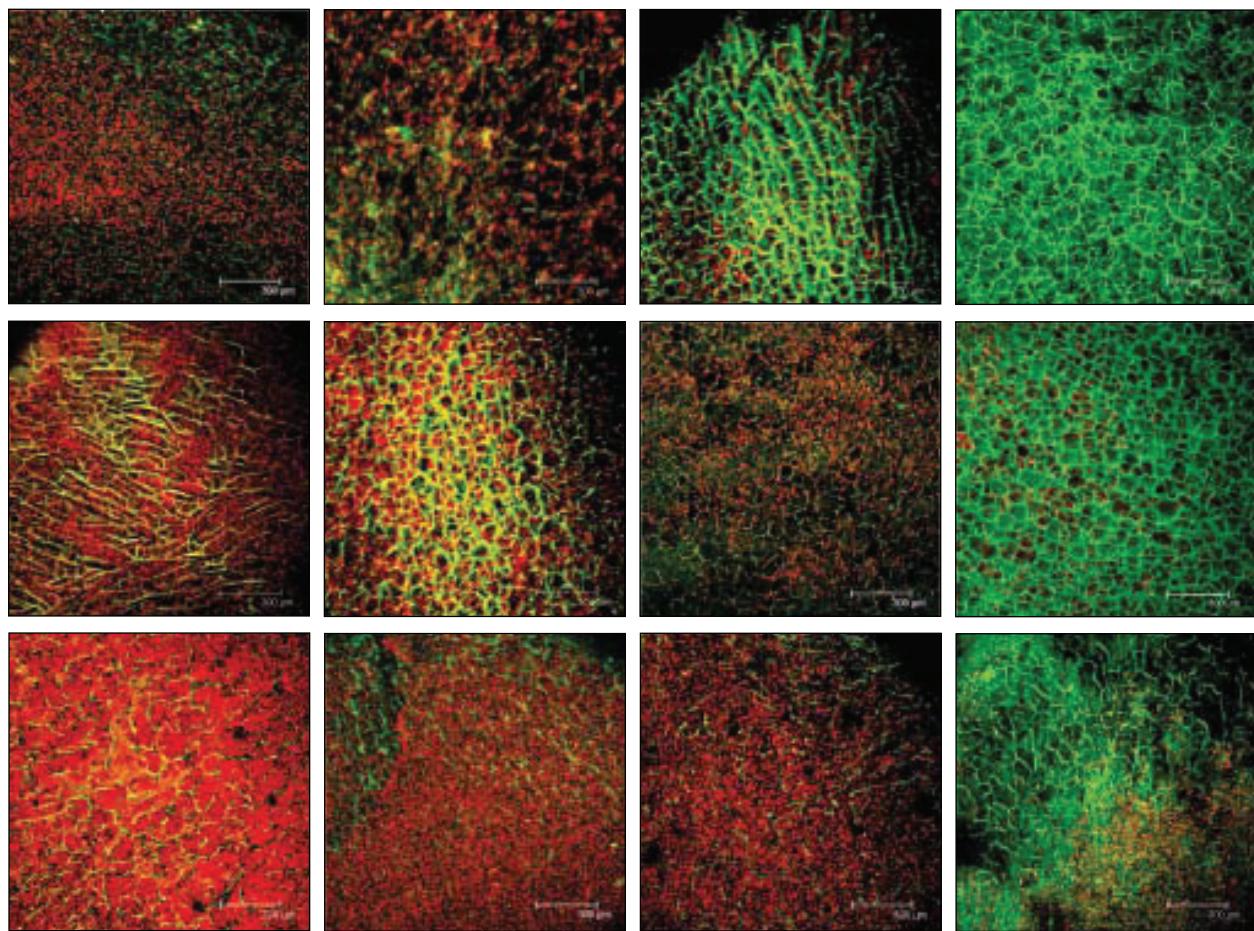


Fig 3 Confocal microscopic appearance of the front side of scaffolds. (Left to right) Inoculated with the type 1 collagen method; inoculated with the single-side method; inoculated with the two-side method; negative control. Inoculation time (top to bottom): 1 week, 2 weeks, 3 weeks. Red denotes the nuclei of BMSCs, stained by propidium iodide revealing BMSCs attached on the scaffolds; CS/β-TCP scaffolds appear green (autofluorescence). The number of BMSCs in the front side of scaffolds in the type 1 collagen group was greater than that of the other groups at all time points. BMSCs were scarcer in the two-side group than in the single-side group during week 1 and week 2, but they were nearly equal in these groups by week 3.

nificantly different among all four groups ($F = 887.096$, $P < .0001$). Furthermore, the quantity of cells on the front side of the scaffolds in the two-side group was lower than that of the single-side group, with significant differences on days 7 ($P < .0001$) and 14 ($P < .0001$) by Bonferroni test; (Figs 3 and 5). By the 21st day, however, the BMSC quantities on the front side showed no significant differences between the two-side and the single-side groups ($P = .714$) (Figs 3 and 5, Table 1).

At all time points, there were almost no cells on the back of the scaffolds of the control group, type 1 collagen group, and single-side group (Figs 4 and 6). However, a great number of cells were found on the back side of the scaffolds of the two-side group (Figs 5 and 6; Table 2). The penetration depth of cells on the front side of all scaffolds is shown in Table 3. The cell penetration depth on the back side of the two-side scaffolds was the highest among all the groups from the very first week of

inoculation; the type 1 collagen group ranked second, and the single-side group lagged behind (Fig 6, Table 4).

With respect to the total depth of cell penetration (cell penetration depth of the front side plus the back side), ANOVA showed a significant difference between the three test groups ($F = 179.88$, $P < .0001$); the least significant difference test showed that any two of the three groups were significantly different in the second week ($P < .0001$). The total depth of cell penetration was greatest in the two-side group, and the single-side group ranked second (Table 5). By the third week, no significant difference was found between the single-side group and the type 1 collagen group in terms of total cell penetration depth ($P = .717$).

In Vivo Observations

In the first month, the mandibular defects in rabbits of the type 1 collagen and the two-side group showed

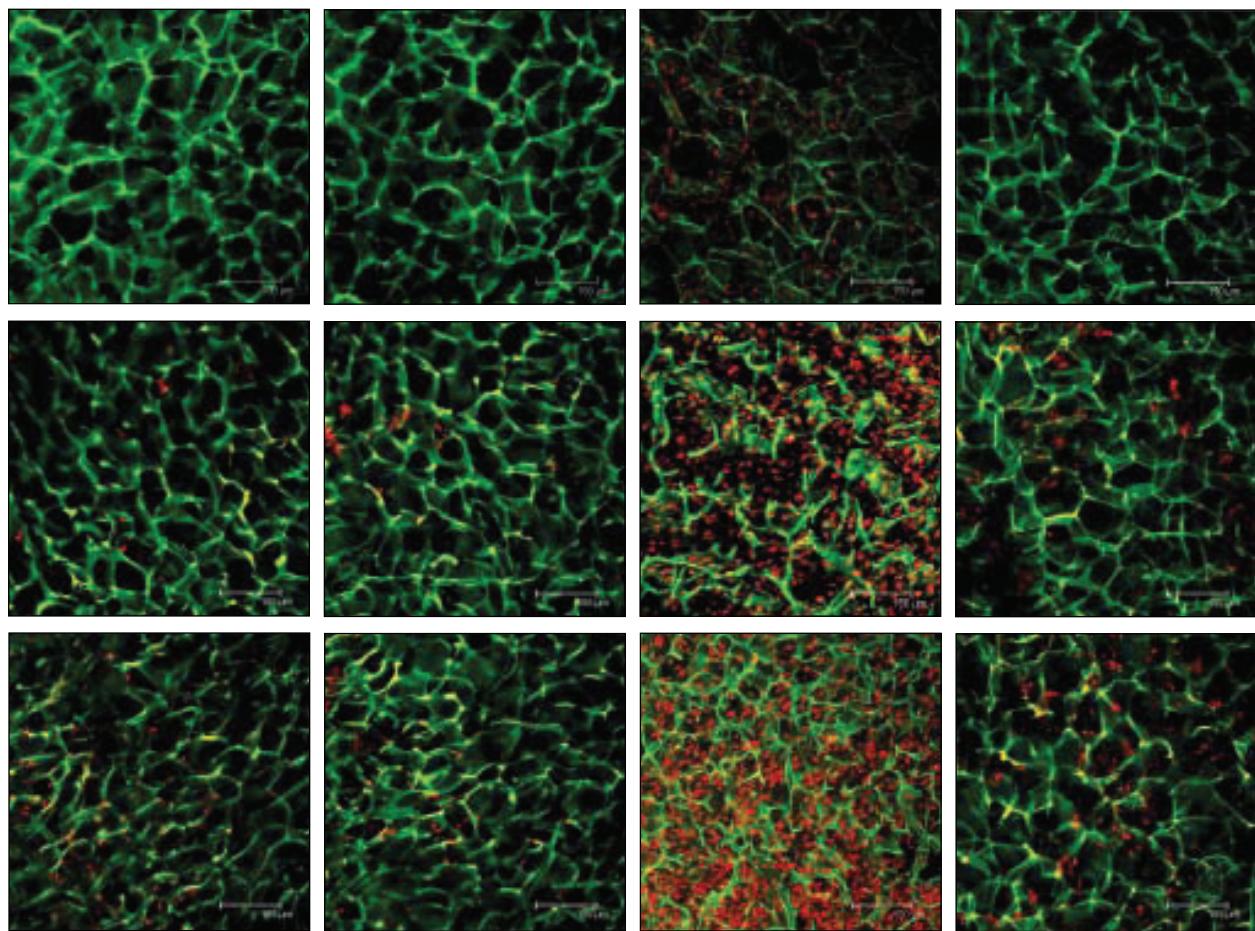


Fig 4 Confocal microscopic appearance of the back side of scaffolds. (Left to right) Inoculated with the type 1 collagen method; inoculated with the single-side method; inoculated with the two-side method; negative control. Inoculation time (top to bottom): 1 week, 2 weeks, 3 weeks. Only the scaffolds of (third column from left) the two-side group show some cells, especially at 3 weeks after inoculation. Almost no BMSCs were observed in the back side of scaffolds in the other groups during the study period.

similar bone density ($P > .05$). The bone density of these two groups was higher than that in the single-side and negative control groups. The defect areas in the experimental groups had a higher density than the defects in the blank group, which were radiolucent. Compared with the positive control group, the defects of all experimental groups were lower in bone density ($P < .0001$).

In the second month, callus tissue of the two-side and type 1 collagen groups occupied almost the whole area of the defect, which was now barely visible on the radiograph. The bone density of the defect area in the two-side group was similar to the host bone, and higher than that of other groups ($P < .001$). The bone density in the type 1 collagen group was lower than that of the two-side group ($P < .05$) but higher than that of the single-side group ($P < .01$). The defect area of the scaffolds in the blank group remained empty, with no bone formation.

There was enhanced bone mineral density after 3 months in all the experimental groups and positive control groups compared with the negative control group ($P < .001$). The bone density of the defect area in the positive control at the third month was the same as that in the first month ($P > .05$) but higher than that in the second month ($P < .001$). The healing rate of the two-side group was the fastest among all the groups; the defect areas were smaller than those of the other groups at the third month (Fig 7). The bone density of the defect area in the two-side group was higher than that of the host bone. The bone density in the type 1 collagen group was similar to that of the host bone and lower than that of the two-side group at the third month postoperatively ($P < .001$) (Fig 7). There was no significant increase in bone mineral density between the positive control and the negative control groups at the third month (Fig 7).

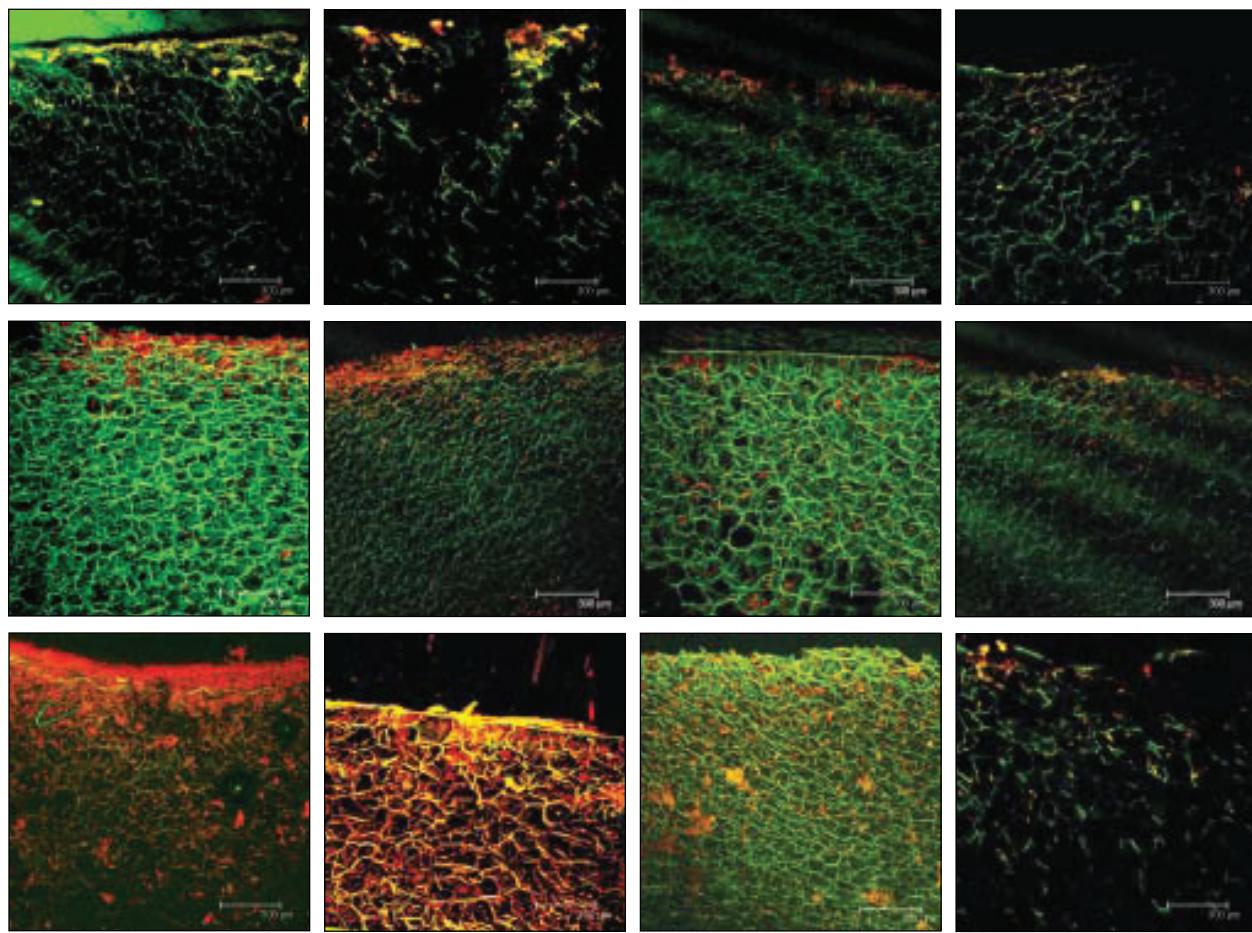


Fig 5 Confocal microscopic appearance of the front side of the scaffolds observed from the sagittal plane. (Left to right) Inoculated with the type 1 collagen method; inoculated with the single-side method; inoculated with the two-side method; negative control. Inoculation time (top to bottom): 1 week, 2 weeks, 3 weeks. In the first week (top row), cells inoculated in the front side of the scaffolds began to creep into the middle area of the scaffolds. Cells in the front side of the scaffolds in the two-side groups were scarcer than in the type 1 collagen and single-side groups in the first and second weeks. By the third week, however, most of the BMSCs in the type 1 collagen group had formed multiple layers on the surface of scaffolds, and the number of cells inside the scaffolds (not including cells on the surface) was nearly equal to those in the two-side and single-side groups.

Table 1 Cell Density in the Front Side of the Scaffolds at Three Time Points

Group	Time point (means \pm SD) (cells/cm ²)		
	Wk 1	Wk 2	Wk 3
Type 1 collagen	487.50 \pm 24.25	1,148.75 \pm 43.26	1,480.41 \pm 43.26
One-sided	381.33 \pm 14.14	940.00 \pm 32.91	1,199.83 \pm 23.31
Two-sided	175.42 \pm 17.76	676.25 \pm 9.15	1,207.08 \pm 29.74
Control	7.08 \pm 2.53	303.75 \pm 21.37	513.75 \pm 17.40

Table 2 Cell Density in the Back Side of Scaffolds at Three Time Points

Group	Time point (means \pm SD) (cells/cm ²)		
	Wk 1	Wk 2	Wk 3
Type 1 collagen	6.67 \pm 2.83	4.58 \pm 1.59	50.83 \pm 5.30
One-sided	5.00 \pm 1.61	2.92 \pm 0.78	39.58 \pm 4.77
Two-sided	105.00 \pm 18.02	404.58 \pm 32.29	594.17 \pm 44.84
Control	7.08 \pm 1.41	12.08 \pm 2.95	145.83 \pm 17.43

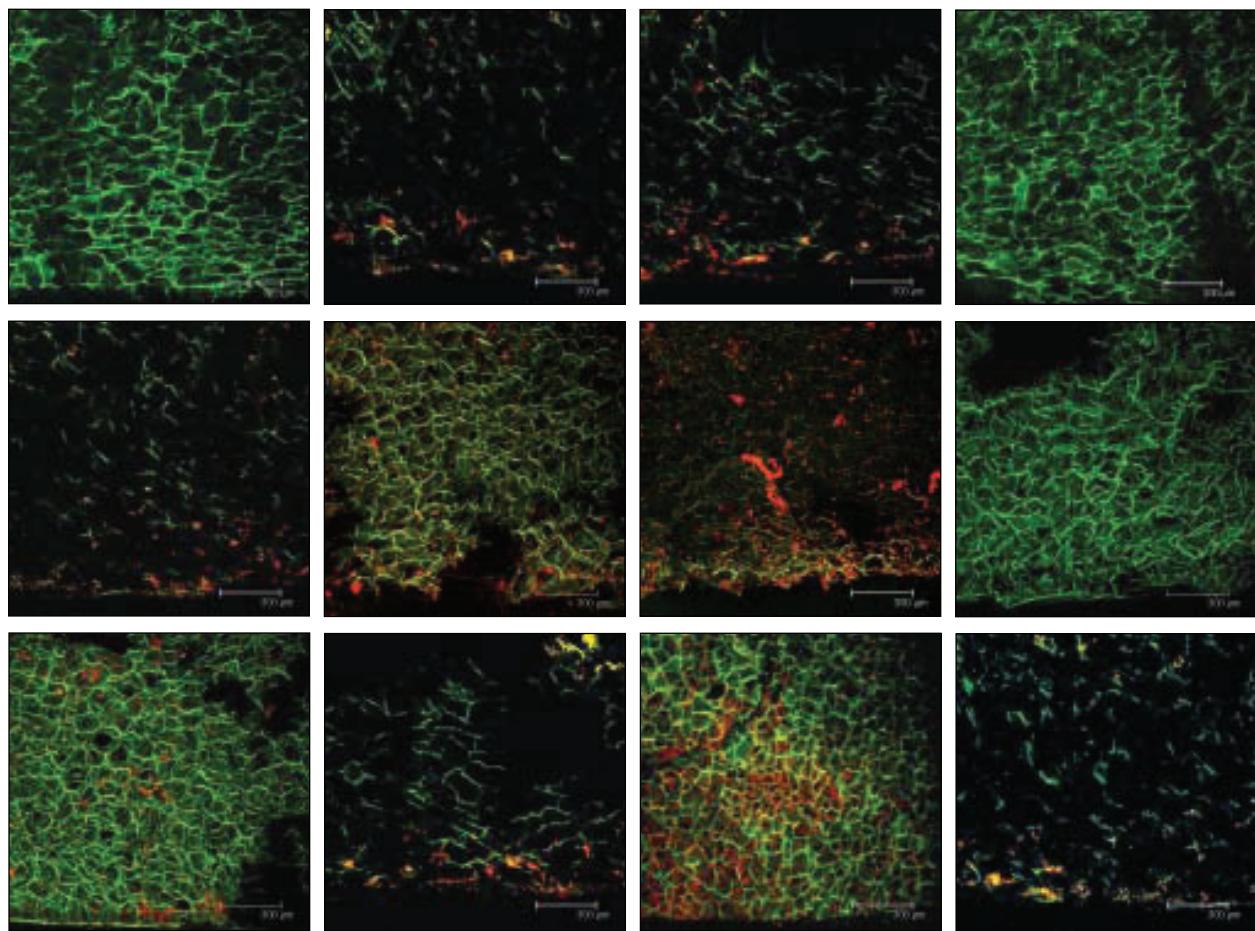


Fig 6 Confocal microscopic appearance of the back side of scaffolds observed from the sagittal plane. (Left to right) Inoculated with the type 1 collagen method; inoculated with the single-side method; inoculated with the two-side method; negative control. Inoculation time (top to bottom): 1 week, 2 weeks, 3 weeks. Only the scaffolds of the two-side group show some cells, whereas there are almost no cells on the back of the scaffolds of the type 1 collagen, single-side, and negative control groups at all time points. In addition, the BMSCs in the two-side groups exhibited the greatest uniformity of cell distribution and penetration.

Table 3 Penetration Depth of BMSCs in the Front Side of Scaffolds, Observed from the Sagittal Plane

Group	Time point (means \pm SD) (μm)		
	Wk 1	Wk 2	Wk 3
Type 1 collagen	252 \pm 13.64	391 \pm 18.15	1,269 \pm 24.60
One-sided	478 \pm 38.14	504 \pm 34.74	1,294 \pm 50.67
Two-sided	366 \pm 13.87	366 \pm 14.90	1,183 \pm 96.47
Control	123 \pm 19.24	133 \pm 30.77	362 \pm 21.95

Table 4 Penetration Depth of BMSCs in the Back Side of Scaffolds, Observed from the Sagittal Plane

Group	Time point (means \pm SD) (μm)		
	Wk 1	Wk 2	Wk 3
Type 1 collagen	—	15.50 \pm 2.12	29.00 \pm 2.13
One-sided	16.13 \pm 2.26	21.00 \pm 2.12	19.63 \pm 2.64
Two-sided	132.00 \pm 18.72	421.00 \pm 22.75	451.00 \pm 25.51
Control	—	—	108.00 \pm 17.93

Table 5 Penetration Depth of BMSCs in the Front and Back Sides of Scaffolds, Observed from the Sagittal Plane

Group	Time point (means \pm SD) (μm)		
	Wk 1	Wk 2	Wk 3
Type 1 collagen	252.00 \pm 13.64	406.50 \pm 18.55	1,298.00 \pm 25.88
One-sided	494.13 \pm 36.33	525.00 \pm 38.50	1,313.63 \pm 52.89
Two-sided	498.00 \pm 31.10	787.00 \pm 36.53	1,634.00 \pm 99.17
Control	123.00 \pm 19.24	133.00 \pm 30.77	407.00 \pm 22.33

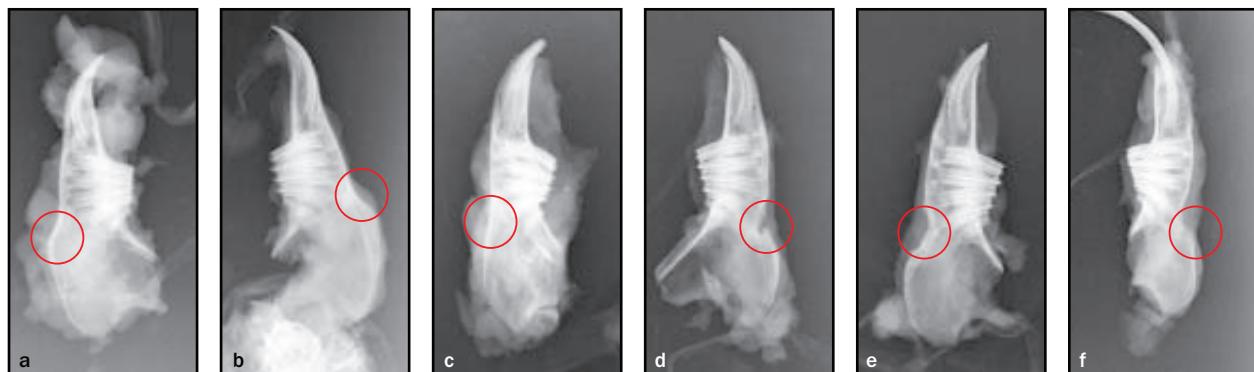


Fig 7 Radiographs of the defect areas of rabbit mandibles inoculated with BMSCs through different methods after 3 months. (a) two-side group, (b) type 1 collagen group, (c) single-side group, (d) positive control group, (e) negative control group, (f) empty control group. Light areas indicate enhanced x-ray absorption and higher bone density, while dark areas indicate less absorption of x-ray and lower bone density. Bone defect of two-side group (a) shows significantly improved healing in comparison with other groups (the defect areas are smaller than in the other groups). Round defect of type 1 collagen group (b) at 3 months shows complete healing. Empty and negative control groups (e, f) show oval defects and a lack of bridging.

DISCUSSION

The selection of a suitable material to produce a scaffold for bone tissue engineering is a critical step. A biologic ceramic such as β -TCP has a composition and structure similar to that of natural bone; therefore, it has been considered an ideal biomaterial because of its osteoconductivity and osteoinductivity.¹⁵ However, its fragility and poor mechanical stability limit its use. On the other hand, biocompatible polymers have the disadvantages of low efficacy of cell seeding, cytotoxicity of the breakdown products, and poor mechanical properties.²⁷ To overcome the drawbacks of bioceramics and biopolymers, it is prudent to fabricate ceramic/polymer composite materials.^{28,29} The use of chitosan as a scaffolding material for tissue engineering has been reported.³⁰ Calcium phosphates can bond to bone and stimulate osteogenesis and bone regeneration.^{31,32} Additionally, their chemical composition is similar to the inorganic component of bone³³; it has been proven that CS-coated β -TCP porous ceramics show enhanced newly formed bone tissue.³⁴ Therefore, a compound scaffold of CS and β -TCP is based on the biomimetic properties of the unique structure of hydroxyapatite/collagen in natural bone.¹⁵

The number of BMSCs in the type 1 collagen group was higher than that in the other groups at all time points; the large number of initial seeding cells in the collagen gel may account for this. However, the total depth of cell penetration (the depth of the front and back sides) in the type 1 collagen group was less than that of the two-side group. This is because most of the BMSCs in the type 1 collagen group formed multiple layers on the surface of scaffolds (Fig 5) but could not penetrate down to the middle areas of the scaffolds. It is also possible that type 1 collagen gel on the surface of CS/ β -TCP scaffolds may have behaved as another kind of scaffold, thereby confining the BMSCs within the gel scaffold. Therefore, in the third week, cells in the inner part of the scaffolds in type 1 collagen group were fewer than those in the two-side group. Ohno et al have already investigated the use of type 1 collagen as a tissue engineering scaffold.³⁵

During the process of in vitro culture, the BMSCs in the two-side group had a faster proliferation rate than in the other groups until the end of the third week. At the third week, the number of BMSCs was similar to that of type 1 collagen according to the total DNA content. Of the four groups, although the BMSCs cultured in type 1 collagen gel showed the highest percentage

of attachment efficacy ($93.7\% \pm 8.49\%$), the cell growth rate was markedly reduced by the nonuniformity of cell distribution. It indicated that the well-distributed BMSCs proliferated faster.

The two-side group expressed the best uniformity during the 1- to 3-week culture period. Furthermore, BMSCs in collagen formed multiple layers on the surface of the scaffold, but type 1 collagen hindered the growth of BMSCs when the proliferation of BMSCs in the collagen reached a certain degree, as they could not easily penetrate into the scaffold over a period of time. Cells in the front side of scaffolds in the two-side group were less numerous than in the single-side group in the first and second weeks. However, the front side of the scaffolds in the two-side group showed similar cell numbers as the single-side group by the third week. The results suggested that the scaffolds, which were inoculated with BMSCs at densities of $1 \times 10^6/\text{cm}^3$ and $0.5 \times 10^6/\text{cm}^3$, respectively, showed the same numbers of BMSCs after 3 weeks culture in vitro. At all time points, there were almost no cells on the back side of the scaffolds in the negative control group, the type 1 collagen group, and the single-side group. However, a large number of cells was found on the back side of the scaffolds in the two-side group. This indicated that cells on the front side cannot penetrate into the other side of a scaffold (the back side) with an average pore size of $100.2 \mu\text{m}$. To ensure more uniform distribution of BMSCs in scaffolds, one must inoculate seed cells from both the front and back sides of scaffolds.

At early time points (days 7 and 14), type 1 collagen and the two-side groups exhibited higher levels of ALP expression compared to the single-side group. The number of cells plays an important role in ALP activity.¹ However, there was no statistically significant difference in ALP activity ($F = 3.874$, $P = .056$) among all the groups. The small sample size may have accounted for this; a larger sample size may have shown different results. It is also quite possible that the influence of different inoculation methods on ALP activity was not obvious. As time passed, the ALP activity of all specimens increased, and there were statistically significant differences ($F = 60.795$, $P < .0001$) within each group at all time points.

The in vivo study showed that the two-side inoculation method enhanced bone formation significantly when compared with the control and other experimental groups. The method of inoculating a compound of BMSCs and type 1 collagen gel from one side (type 1 collagen group) also resulted in a more ideal osteogenesis effect than that of inoculating cells from one side without type 1 collagen gel (single-side group).

It has already been shown that increased bone formation is induced by increasing osteoblastic differ-

entiation or by increasing the number of osteoblastic cells.³⁶ In this study, all the experimental scaffolds succeeded in repairing the mandibular defect. However, the scaffolds treated with the two-side inoculation method provided more new bone of a higher quality than the scaffolds of the other groups. New bone formation of the scaffolds alone in the negative control group or autografts alone in the positive control group was dependent only on the ingrowth of host bone, which is known as "creeping substitution."³⁷ Hardly any osteogenesis effects were achieved in the center of these scaffolds because of the dependence on creeping substitution from the host bone. Scaffolds that were preseeded with BMSCs (all experimental groups) achieved new bone formation not only from the host bone but also from the preseeded cells. Therefore, the scaffolds with a uniform cell distribution (ie, the two-side scaffolds) attained a higher quality and quantity of new bone formation than the other groups. This study has further proven that two-side and type 1 collagen inoculation methods, and not the single-side method, can supply enough seed cells for bone formation. Furthermore, not only cell number but also cell distribution in scaffolds contributed to effective bone formation in this study.

The technology of bone tissue engineering, which is used to repair bony defects, is likely to significantly impact the field of craniofacial surgery. To date, most studies on bone tissue engineering have focused on scaffolds and growth factors; the interconnection between cells and scaffolds has rarely been mentioned. This study will serve as a starting point for future studies in bone tissue engineering by channeling the attention of researchers into the field of inoculation methods. It is also the first study to compare the effectiveness of osteogenesis with different inoculation methods.

CONCLUSION

The two-side method of inoculation of bone marrow stromal cells resulted in an improved number and distribution of seed cells in vitro and enhanced quality and rate of bone formation in vivo. This method would appear to be the most suitable seed method for bone tissue engineering.

ACKNOWLEDGMENT

This work was supported by the National Natural Science Foundation of China (grants 30872892 and 30672341). The authors reported no conflicts of interest related to this study.

REFERENCES

1. Holy CE, Shoichet MS, Davies JE. Engineering three-dimensional bone tissue in vitro using biodegradable scaffolds: Investigating initial cell-seeding density and culture period. *J Biomed Mater Res* 2000;51(3):376–382.
2. De Long WG Jr, Einhorn TA, Koval K, et al. Bone grafts and bone graft substitutes in orthopaedic trauma surgery. A critical analysis. *J Bone Joint Surg Am* 2007;89(3):649–658.
3. Huffer WE, Benedict JJ, Turner AS, et al. Repair of sheep long bone cortical defects filled with COLLOSS, COLLOSS E, OSSAPLAST, and fresh iliac crest autograft. *J Biomed Mater Res B Appl Biomater* 2007;82(2):460–470.
4. Meyer U, Joos U, Wiesmann HP. Biological and biophysical principles in extracorporeal bone tissue engineering. Part I. *Int J Oral Maxillofac Surg* 2004;33(4):325–332.
5. Tomford WW, Doppelt SH, Mankin HJ, Friedlaender GE. 1983 bone bank procedures. *Clin Orthop Relat Res* 1983;174:15–21.
6. Zhang X, Jia W, Gu Y, et al. Teicoplanin-loaded borate bioactive glass implants for treating chronic bone infection in a rabbit tibia osteomyelitis model. *Biomaterials* 2010;31(22):5865–5874.
7. Laschke MW, Harder Y, Amon M, et al. Angiogenesis in tissue engineering: breathing life into constructed tissue substitutes. *Tissue Eng* 2006;12(8):2093–2104.
8. Fan W, Crawford R, Xiao Y. Enhancing in vivo vascularized bone formation by cobalt chloride-treated bone marrow stromal cells in a tissue engineered periosteum model. *Biomaterials* 2010;31(13):3580–3589.
9. Wu F, Wei J, Guo H, Chen F, Hong H, Liu C. Self-setting bioactive calcium-magnesium phosphate cement with high strength and degradability for bone regeneration. *Acta Biomater* 2008;4(6):1873–1884.
10. Arpornmaeklong P, Pripatnanont P, Suwatwirote N. Properties of chitosan-collagen sponges and osteogenic differentiation of rat-bone-marrow stromal cells. *Int J Oral Maxillofac Surg* 2008;37(4):357–366.
11. Costa-Pinto AR, Salgado AJ, Correlo VM, , et al. Neves NM: Adhesion, proliferation, and osteogenic differentiation of a mouse mesenchymal stem cell line (BMC9) seeded on novel melt-based chitosan/polyester 3D porous scaffolds. *Tissue Eng Part A* 2008;14(6):1049–1057.
12. Nukavarapu SP, Kumbar SG, Brown JL, et al. Polyphosphazene/nano-hydroxyapatite composite microsphere scaffolds for bone tissue engineering. *Biomacromolecules* 2008;9(7):1818–1825.
13. Douglas T, Heinemann S, Bierbaum S, Scharnweber D, Worch H. Fibrillogenesis of collagen types I, II, and III with small leucine-rich proteoglycans decorin and biglycan. *Biomacromolecules* 2006;7(8):2388–2393.
14. Richards J, Pasco D, Yang, J, Guzman R, Nandi S. Comparison of the growth of normal and neoplastic mouse mammary cells on plastic, on collagen gels and in collagen gels. *Exp Cell Res* 1983;146:1–14.
15. Zhang Y, Zhang M. Synthesis and characterization of macroporous chitosan/calcium phosphate composite scaffolds for tissue engineering. *J Biomed Mater Res* 2001;55(3):304–312.
16. Wang JW, Hon MH. Sugar-mediated chitosan/poly(ethylene glycol)-beta-dicalcium pyrophosphate composite: Mechanical and microstructural properties. *J Biomed Mater Res A* 2003;64(2):262–272.
17. Shimizu K, Ito A, Honda H. Mag-seeding of rat bone marrow stromal cells into porous hydroxyapatite scaffolds for bone tissue engineering. *J Biosci Bioeng* 2007;104(3):171–177.
18. Irie T, Takahata M, Majima T, et al. Effect of selective estrogen receptor modulator/raloxifene analogue on proliferation and collagen metabolism of tendon fibroblast. *Connect Tissue Res* 2010;51(3):179–187.
19. Li J, Song Y, Zhang S, et al. In vitro responses of human bone marrow stromal cells to a fluoridated hydroxyapatite coated biodegradable Mg-Zn alloy. *Biomaterials* 2010;31(22):5782–5788.
20. Zhao L, Weir MD, Xu HH. Human umbilical cord stem cell encapsulation in calcium phosphate scaffolds for bone engineering. *Biomaterials* 2010;31(14):3848–3857.
21. Rabie AB, Deng YM, Samman N, Hagg U. The effect of demineralized bone matrix on the healing of intramembranous bone grafts in rabbit skull defects. *J Dent Res* 1996;75(4):1045–1051.
22. Dean D, Wolfe MS, Ahmad Y, et al. Effect of transforming growth factor beta 2 on marrow-infused foam poly(propylene fumarate) tissue-engineered constructs for the repair of critical-size cranial defects in rabbits. *Tissue Eng* 2005;11(5–6):923–939.
23. Young S, Bashoura AG, Borden T, et al. Development and characterization of a rabbit alveolar bone nonhealing defect model. *J Biomed Mater Res A* 2008;86(1):182–194.
24. Silva GA, Coutinho OP, Ducheyne P, Reis RL. Materials in particulate form for tissue engineering. 2. Applications in bone. *J Tissue Eng Regen Med* 2007;1(2):97–109.
25. Bucholz RW. Nonallograft osteoconductive bone graft substitutes. *Clin Orthop Relat Res* 2002;(395):44–52.
26. Freed LE, Vunjak-Novakovic G, Biron RJ, et al. Biodegradable polymer scaffolds for tissue engineering. *Biotechnology (N Y)* 1994;12(7):689–693.
27. Jansen EJ, Sladek RE, Bahar H, et al. Hydrophobicity as a design criterion for polymer scaffolds in bone tissue engineering. *Biomaterials* 2005;26(21):4423–4431.
28. Sun L, Xu HH, Takagi S, Chow LC. Fast setting calcium phosphate cement-chitosan composite: Mechanical properties and dissolution rates. *J Biomater Appl* 2007;21(3):299–315.
29. Lian Q, Li DC, He JK, Wang Z. Mechanical properties and in-vivo performance of calcium phosphate cement–chitosan fibre composite. *Proc Inst Mech Eng H* 2008;222(3):347–353.
30. Muzzarelli R, Baldassarre V, Conti F, et al. Biological activity of chitosan: Ultrastructural study. *Biomaterials* 1988;9(3):247–252.
31. Yuan H, de Bruijn JD, Zhang X, van Blitterswijk CA, de Groot K. Bone induction by porous glass ceramic made from Bioglass (45S5). *J Biomed Mater Res* 2001;58(3):270–276.
32. Yao J, Radin S, Reilly G, Leboy PS, Ducheyne P. Solution-mediated effect of bioactive glass in poly(lactic-co-glycolic acid)-bioactive glass composites on osteogenesis of marrow stromal cells. *J Biomed Mater Res A* 2005;75(4):794–801.
33. Gazdag AR, Lane JM, Glaser D, Forster RA. Alternatives to autogenous bone graft: Efficacy and indications. *J Am Acad Orthop Surg* 1995;3(1):1–8.
34. Abarategui A, Moreno-Vicente C, Ramos V, Aranaz I, Sanz Casado JV, Lopez-Lacomba JL. Improvement of porous beta-TCP scaffolds with rhBMP-2 chitosan carrier film for bone tissue application. *Tissue Eng Part A* 2008;14(8):1305–1319.
35. Ohno T, Tanisaka K, Hiraoka Y, Ushida T, Tamaki T, Tateishi T. Effect of type I and type II collagen sponges as 3D scaffolds for hyaline cartilage-like tissue regeneration on phenotypic control of seeded chondrocytes in vitro. *Materials Science and Engineering: C*. 2004;24:407–411.
36. Zakhary K, Motakis D, Hamdy RH, Campisi P, Amar Y, Lessard ML. Effect of recombinant human bone morphogenetic protein 7 on bone density during distraction osteogenesis of the rabbit mandible. *J Otolaryngol* 2005;34(6):407–414.
37. Li Z, Li ZB. Repair of mandible defect with tissue engineering bone in rabbits. *ANZ J Surg* 2005;75(11):1017–1021.

Evaluation of a Porcine Matrix With and Without Platelet-Derived Growth Factor for Bone Graft Coverage in Pigs

Alan S. Herford, DDS, MD¹/Mei Lu, DDS, PhD²/Lee Akin, DDS³/Marco Cicciù, DDS, PhD⁴

Purpose: The aim of this investigation was to compare three different techniques for soft tissue closure over intraoral particulated bone grafts in a pig model: primary closure and nonprimary closure utilizing a porcine collagen matrix (Mucograft), with or without the addition of platelet-derived growth factor (PDGF). An additional aim was to determine whether the addition of PDGF to the collagen matrix would prevent the need for primary closure or later soft tissue grafting. **Materials and Methods:** Twenty-four bilateral mandibular alveolar defects were created in 12 minipigs. These defects were reconstructed with a mixture of autogenous bone and bovine bone and secured with a titanium mesh. The animals were randomly assigned to group A (Mucograft + PDGF), group B (Mucograft alone), or group C (primary closure and no Mucograft). In groups A and B the collagen matrix was placed directly over the mesh, and the soft tissue was closed passively. Exposure of the titanium mesh, height of new bone, and the percentage of keratinized mucosa covering the bone graft were analyzed. **Results:** Average new bone formation in group A was 7.0 mm, whereas groups B and C had less regenerated bone (4.7 mm and 2.5 mm, respectively). Group A had the thickest keratinized mucosa (1.6 mm), versus 0.9 mm for group B and 0.4 mm for group C. Group A had an average of 95% regenerated keratinized tissue, whereas group B had 41% and group C had 22%. **Conclusion:** The addition of PDGF to the collagen matrix appeared to accelerate soft tissue healing and promote bone formation. Mucograft provided an adequate alternative to autogenous soft tissue grafts or primary closure to cover bone grafts intraorally while eliminating adverse effects, namely disruption of the adjacent soft tissue architecture, loss of vestibular height, and the need for further surgery. *INT J ORAL MAXILLOFAC IMPLANTS* 2012;27:1351–1358

Key words: collagen matrix, platelet-derived growth factor, soft tissue

Intraoral bone grafting is often compromised by exposure of the graft during the postoperative period. Techniques such as tension-free closure and placement of various membranes have been performed in attempts to reduce the incidence of exposure.^{1–23} Bone grafting of alveolar defects is often associated with deficient soft tissue at the recipient site. Extensive soft tissue undermining is often necessary to provide primary

tension-free closure over the bone graft to facilitate bone graft healing and minimize the likelihood of exposure of the graft during healing. However, this significant undermining destroys the normal architecture and often results in a later need for additional soft tissue procedures or vestibuloplasty. Even with tension-free closure, a significant amount of exposures of the underlying graft will occur, which may lead to graft failure. The earlier the exposure occurs, the greater the risk of graft resorption or complete graft failure.

The purpose of this investigation was to compare primary closure to the use of a porcine collagen matrix (Mucograft, Geistlich Pharma) with and without platelet-derived growth factor (PDGF) for soft tissue healing over intraoral bone grafts in a pig model. The potent stimulatory effects of PDGF as a chemoattractant and mitogen, in addition to its ability to promote angiogenesis, position it as a key mediator in tissue repair that may improve soft tissue healing over a bone graft. Mucograft is a bilayered porcine collagen matrix membrane that is recommended as a substitute for autogenous soft tissue grafts for intraoral mucogingival defects. Previous studies have found that Mucograft

¹Chairman and Program Director, Department of Oral and Maxillofacial Surgery, Loma Linda University, Loma Linda, California, USA.

²Assistant Professor, Department of Oral and Maxillofacial Surgery, Loma Linda University, Loma Linda, California, USA.

³Resident, Advanced Education Program in Oral and Maxillofacial Surgery, School of Dentistry, Loma Linda University, Loma Linda, California, USA.

⁴Assistant Professor, Human Pathology Department, University of Messina, ME, Italy.

Correspondence to: Dr Alan Herford, Department of Oral and Maxillofacial Surgery, Loma Linda University School of Dentistry, Room 3306, 11092 Anderson St, Loma Linda CA 92350, USA. Fax: +909-558-0285. Email: aherford@llu.edu

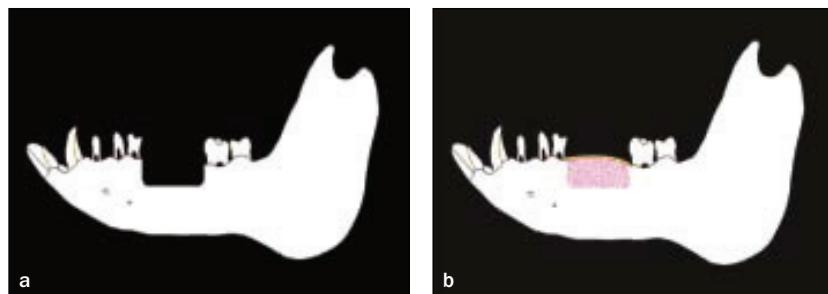


Fig 1a Defect model created in the mandibular body.

Fig 1b Reconstruction of the defect with bone graft and titanium mesh.

can be an effective means of increasing vestibular depth as well as regenerating keratinized tissue to a degree comparable to that of free connective tissue grafts.^{24–27} Therefore, the present investigation evaluated whether Mucograft would allow tension-free partial closure over bone grafts, thus limiting disruption of soft tissue architecture and minimizing the incidence of postoperative bone graft exposure. This study also sought to determine whether the addition of PDGF to the Mucograft would improve soft tissue healing over particulated bone grafts, thus avoiding the need for autogenous soft tissue grafting and primary closure.

MATERIALS AND METHODS

Twelve 24-week-old micropigs underwent a surgical procedure to create bilateral mandibular defects (24 defects total). The micropigs were chosen because of the easy management afforded by the fact that they do not exceed 30 lbs. The nontransgenic animals were randomly assigned to receive one of three procedures: group A, Mucograft + PDGF-BB (eight sites); group B, Mucograft alone (eight sites); or group C, Primary closure (no matrix) (eight sites).

The animals were allowed to heal for 3 months after the creation of defects prior to the reconstructive surgery. For all of the defects, the lost alveolar bone was restored with autogenous bone harvested from the defect, combined with bovine bone (Bio-Oss, Geistlich), and secured in place with titanium mesh. A collagen matrix was used to cover the bone graft and mesh, or the tissue was closed primarily, depending on the treatment group.

Surgical Procedures

The first procedure involved extraction of the right and left posterior mandibular teeth, plus the removal of alveolar bone, to create the defects (Fig 1). After 4 weeks of healing, a second surgical procedure was performed to restore the bony defect with autogenous bone and bovine bone (Bio-Oss). A horizontal supracrestal incision was performed in the mandibular mucosa, extending to the periosteum overlying the defect. The

width of the keratinized tissue along the alveolar ridge was measured, and care was taken to evenly divide the band of keratinized tissue. This undermining incision was continued along the alveolar ridge in the area of the defect. Careful elevation of the mucosa was performed to expose the bony defect with minimal elevation and disruption of the adjacent soft tissue. Following visualization of the defect, a surgical stent was used to remove bone and create a standardized 10 × 20-mm defect. Approximately 5 mL of bone was removed, morselized, and then combined with 5 mL of Bio-Oss. A titanium mesh crib was used to secure the graft and prevent mobility of the graft during healing. The surgical site was then closed (Fig 2).

For groups A and B sites, the Mucograft was placed over the titanium mesh. The mucosa was sutured without undermining the tissue, and incomplete closure, with exposure of some of the collagen matrix, was performed (Fig 3). The Mucograft in group A was saturated with 2.5 mL of 0.3 mg/mL PDGF-BB (GEM 21S, Osteohealth) (0.75 mg).

The PDGF-BB provides the biologic stimulus for tissue repair by increasing angiogenesis and the proliferation of osteoblasts, the cells responsible for the formation of bone. It stimulates chemotaxis and new gene expression in monocytes (macrophages) and fibroblasts. It has been suggested that it enhances the tissue repair process, improves healing of soft tissue and bony wounds, and, when delivered exogenously, stimulates collagen production, improves wound strength, and initiates callous formation.^{11,25,27} Moreover, PDGF-BB can easily be incorporated into the Mucograft membrane.

After 3 months of healing, the pigs were sacrificed and radiographs were taken of the surgical sites (Fig 4). Histologic sections of bone and soft tissue were prepared and analyzed. The specimens were fixed in neutral buffered 10% formalin, dehydrated and infiltrated in resin, and embedded and polymerized in resin blocks. The blocks were cut and ground using the Exakt cutting-grinding system (Exakt Apparatebau) to a thickness of 50 µm and stained with Mayer hematoxylin and eosin or Masson trichrome. Histologic evaluation included identification of any residual matrix as well as any evidence of inflammation.



Fig 2a Mixture of autogenous and bovine bone.



Fig 2b Titanium mesh holds the particulate graft in place.



Fig 2c Placement of PDGF onto the collagen matrix in a group A defect.

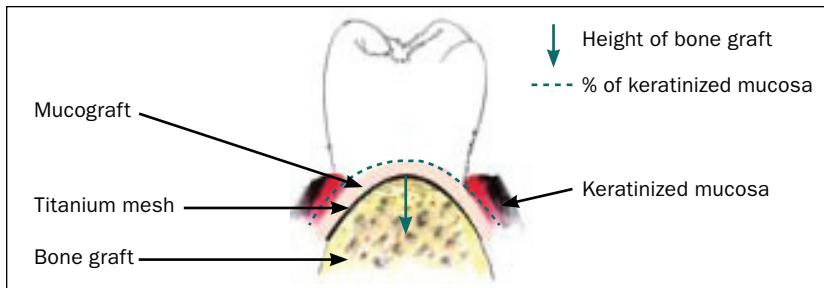


Fig 2d Diagram of the placement of Mucograft over the titanium mesh and bone graft in groups A and B.



Fig 2e Radiograph of a grafted defect.

Fig 3a Passive closure over graft. Note exposure of collagen matrix.



Fig 3b Primary closure over a group C graft. Note undermining, with loss of vestibule.



Fig 4a Measurement of regenerated tissue.



Fig 4b Regenerated tissue over a grafted area.



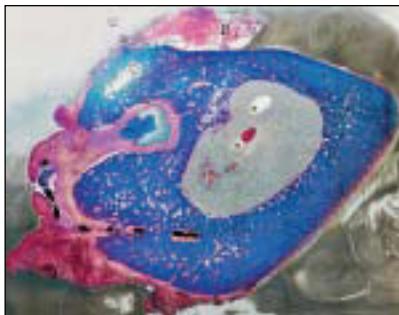
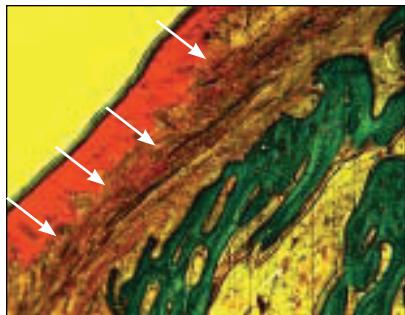
Fig 4c Jaw displaying an exposed graft in the left mandible (group C) and a covered regenerated area on the right side (group A).

The thickness of the keratinized mucosa was measured under 10 \times magnification. Ten areas of regenerated tissue were randomly selected per section. The percentage of keratinized mucosa that covered the bone graft area was calculated in three coronal sections of the specimen. The total amount of regenerated keratinized tissue over the grafted ridge was determined by measuring the entire amount of tissue

covering the ridge and dividing that number by the total length of tissue covering the regenerated area. The quantity of grafted bone was also evaluated. The height of new bone was measured in three separate sections. The height was reported as an average by measuring the distance from the crest of the regenerated ridge to the junction of regenerated bone to residual nongrafted bone.

Table 1 Coverage and Thickness of Keratinized Tissue, Amount of Bone Formation, and Incidence of Graft Exposure

Group/specimen	Bone graft healing	Mesh exposure	Percentage of keratinized mucosa	Thickness of mucosa
Group A				
17R	8 mm	No	100	174.6
18R	5 mm	Yes	60	167.51
21R	7.5 mm	Yes	90	164.09
22R	5 mm	Yes	100	180.1
23L	7 mm	Yes	100	158.21
140R	7 mm	No	100	179.06
141L	8 mm	Yes	90	141.52
143R	6 mm	No	100	117.7
Group B				
16R	6 mm	Yes	60	84.61
17L	5 mm	Yes	20	72.61
18L	4 mm	Yes	50	100.16
20R	4 mm	Yes	40	121.91
22L	4 mm	Yes	40	99.87
140L	4 mm	Yes	20	52.48
142L	5 mm	Yes	25	62.9
143L	5 mm	Yes	95	130.21
Group C				
16L	2 mm	Yes	20	20.23
19L	1.5 mm	Yes	20	12.51
19R	2 mm	Yes	20	12.18
20L	3 mm	Yes	20	15.05
21L	2 mm	Yes	20	11.22
23R	3 mm	Yes	15	5.98
141R	2 mm	Yes	25	10.01
142R	2.5 mm	Yes	30	4.01

**Fig 5a** (Left) Measurement of the thickness of the mucosa (magnification $\times 10$).**Fig 5b** (Right) A whole specimen captured by a scanning microscope showing the cross section of titanium mesh, regenerated bone, and keratinized soft tissue (magnification $\times 2$).

Statistical Analysis

The data were analyzed using one-way analysis of variance (SPSS statistical software, IBM), and the results were plotted and compared with those reported in the literature. Qualitative and quantitative histologic evaluations of soft tissue ingrowth and bone regeneration were performed on nondecalcified ground sections. For statistical analysis, the Mann-Whitney-Wilcoxon test, the Kruskal-Wallis test, and the paired *t* test were applied. *P* values were adjusted using the Dunnett-Hsu adjustment.

RESULTS

Coverage and thickness of keratinized tissue, amount of bone formation, and incidence of graft exposure in all animals are reported in Table 1. Ten areas of regenerated tissue were randomly selected per section (Figs 5 and 6). Group A had the thickest amount of keratinized mucosa (mean, 1.6 mm), whereas group B had 0.9 mm and group C had 0.4 mm (Fig 7). Group A had an average of 95% regenerated keratinized tissue, group B had 41%, and group B had 22% (Fig 8). The

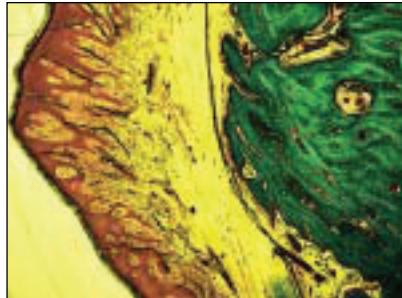


Fig 6a Group A specimen. Extensive and thick keratinized tissue has developed over the graft.

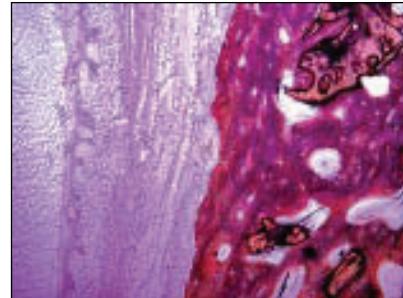


Fig 6b Group B specimen. A thin layer of mucosa is over the graft. Note the residual particles of bovine bone in the regenerated bone area.

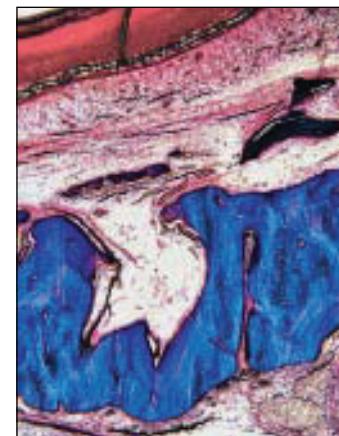


Fig 6c Group C specimen. Thin or no mucosa is present over the bone graft.

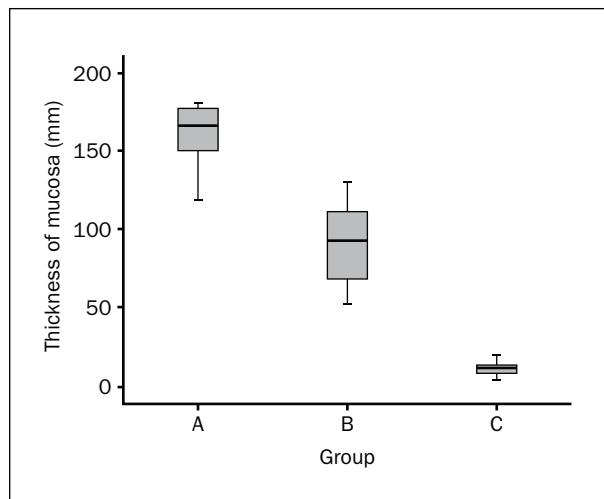


Fig 7 Thickness of mucosa over the grafted area.

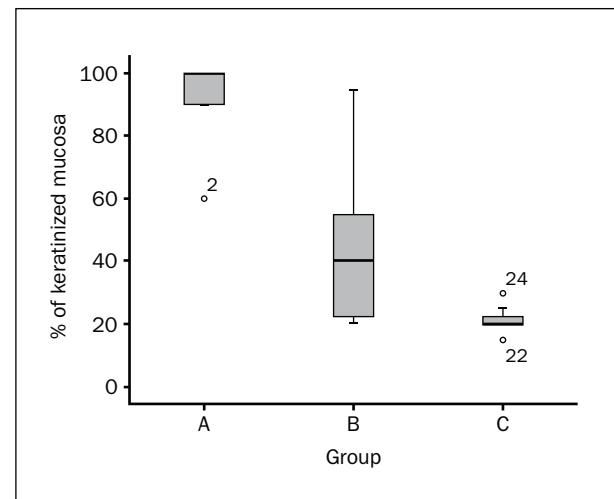
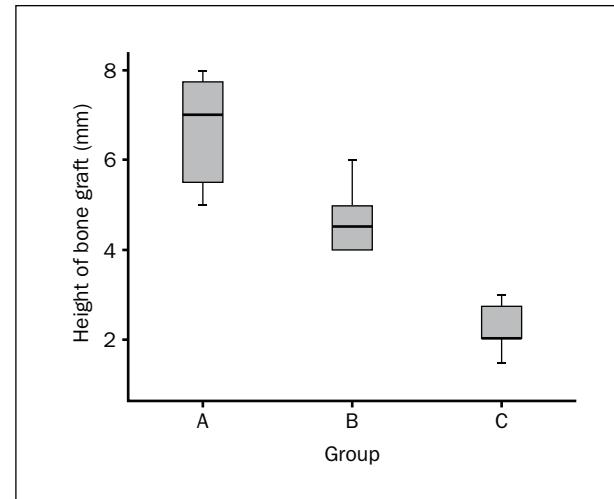


Fig 8 Percentage of regenerated keratinized mucosa.

Fig 9 (Right) Height of regenerated bone.



group A treatment thus resulted in significantly more keratinized tissue formation than in groups B and C.

With respect to new bone formation, group A sites showed an average of 7.0 mm of new bone, whereas groups B and C had less regenerated bone (4.7 mm and 2.5 mm, respectively) (Fig 9). Group A sites (Mucograft + PDGF) showed significantly more bone formation than groups B and C.

Exposure of the titanium mesh occurred postoperatively in the majority of animals. In this model, the exposure rates were 62.5% in group A and 100% in groups B and C. Group C sites, which had been subjected to significant undermining and primary closure, exhibited earlier mesh exposure and less bone formation.

DISCUSSION

Alveolar defects often require bone grafting prior to placement of dental implants, especially non-space-making bone defects rated classes V or VI according to the Cawood and Howell system.²⁸ There is often insufficient soft tissue to completely cover the bone graft without aggressive undermining of the adjacent tissue. However, the normal soft tissue architecture is disrupted by this treatment, resulting in a decrease or elimination of the vestibule. Consequently, after the bone graft heals, soft tissue grafting is often required to reposition the tissue and re-establish the correct vestibular architecture.^{28,29} The harvesting of graft tissue may also necessitate an additional surgical site. Exposure of the bone graft frequently occurs. The earlier this occurs during the postoperative period, the more detrimental it is to the survival of the graft. Collagen membranes may improve the thickness of the tissue over the graft, resulting in a lower incidence of graft exposure.^{29,30}

Various biomaterials have been used to cover wounds and function as a biologic "bandage" to allow the growth of host epithelial cells beneath the graft. However, most of these merely protect wounds and reduce pain, and their antigenicity, biocompatibility, and handling remain problematic. Kim et al reported on a double-layer collagen membrane technique for overlaying bone grafts.³¹ They found that the collagen was more helpful in enhancing the efficacy of the on-lay block bone graft technique in terms of both bone resorption and augmentation compared with a single-layer collagen membrane. A study of Thoma et al evaluated whether a synthetic, biodegradable membrane made of polyethylene glycol would prevent soft tissue ingrowth into alveolar defects used in a minipig animal model. The biodegradable membrane successfully prevented collapse of the covering soft tissues.³²

The collagen material used in the present study (Mucograft) is a bioresorbable, bilayer matrix. This product is made from porcine types I and III collagen and consists of two functional layers: a smooth collagen layer in a compact arrangement, and a porous layer. This material biodegrades over a period of 3 to 10 weeks, depending on the surgical site and the manner in which the matrix is utilized.²⁴⁻²⁶ Biodegradation of the product occurs with very little, if any,

inflammatory cellular response. The use of the collagen matrix almost completely eliminates the negative sequelae associated with a second surgical site, including pain, swelling, and bleeding. Other advantages include decreased length of surgery, unlimited size of autogenous graft because of donor site anatomy, and "off-the-shelf" availability. Recent clinical studies have demonstrated that Mucograft can be used as an effective grafting material to increase both keratinized and nonkeratinized mucosa and features a rapid degradation and healing process.^{25,33}

It was the authors' hypothesis that the addition of PDGF to the Mucograft would improve the efficacy and rate of soft tissue healing. Platelets are known to contain a variety of growth factors, including transforming growth factor beta, vascular endothelial growth factor, and PDGF. These growth factors are released from the platelets when they are activated. PDGF is a naturally occurring factor that has been shown to be a potent activator for cells of mesenchymal origin.³⁴⁻⁴¹ PDGF binds to cell-surface receptors on most cells of mesenchymal origin and stimulates the reparative process in multiple types of tissue. PDGF stimulates chemotaxis, proliferation, and new gene expression in monocytes (macrophages) and fibroblasts. It has been suggested that PDGF enhances the tissue repair process by improving the healing of soft tissue and bony wounds. Platelets release PDGF-BB into the developing blood clot. The PDGF acts early in the wound cascade by attracting neutrophils and macrophages and aiding in angiogenesis, chemotaxis, and mitogenesis. PDGF also up-regulates vascular endothelial growth factor, further enhancing angiogenesis. When delivered exogenously, PDGF stimulates collagen production, improves wound strength, and initiates callus formation.

Bone morphogenic proteins (BMPs) also play a role in chemotaxis and cell proliferation. Attraction of osteoprogenitor cells (chemotaxis) and increases in their number (mitogenesis) provide a pool of cells that are responsive to BMPs.⁴² BMPs and PDGF are primary and powerful coregulatory controls for healing and regeneration of bone. Mucograft combined with PDGF resulted in an increased volume of grafted bone in the present study. This may be secondary to improved soft tissue healing and resultant superior coverage of the bone graft, with a decreased incidence of resorption. Alternatively, it may be related to some osteoinductivity of the growth factor. Controversy remains regarding the osteoinductive properties of PDGF.

The pig model offers certain challenges with respect to postoperative compliance. Although the animals were maintained on a soft diet, they continued to masticate throughout the day, chewing on the cages and food bowls. Exposure of mesh was significantly more common in this animal model than clinically, which is

likely a result of this factor. However, the group with significant undermining and primary closure (group C) exhibited earlier mesh exposure and less bone formation.

CONCLUSIONS

Mucograft (collagen matrix), both alone and in combination with platelet-derived growth factor (PDGF), resulted in significantly thicker soft tissue covering bone grafts in a pig model. The clinical implications include a decreased need for additional soft tissue grafting to augment thin tissue over grafted sites. Mucograft allowed tension-free partial closure over the bone grafts, thereby limiting the disruption of soft tissue architecture. The addition of PDGF to Mucograft appeared to accelerate soft tissue healing and promote bone graft healing. Mucograft combined with PGDF may therefore provide an adequate alternative to autogenous soft tissue grafts or primary closure to cover bone grafts intraorally while eliminating adverse effects, namely disruption of the adjacent architecture, loss of vestibular height, and the need for further surgery.

ACKNOWLEDGMENTS

The authors reported no conflicts of interest related to this study.

REFERENCES

- Von Arx T, Cochran DL, Schenk RK, Buser D. Evaluation of a prototype trilayer membrane (PTLM) for lateral ridge augmentation: An experimental study in the canine mandible. *Int J Oral Maxillofac Surg* 1992;31:190–199.
- Chiapasco M, Abati S, Romeo E, Vogel G. Clinical outcome of autogenous bone blocks or guided bone regeneration with e-PTFE membranes for the reconstruction of narrow edentulous ridges. *Clin Oral Implants Res* 1999;10:278–288.
- Nowzari H, Slots J. Microbiologic and clinical study of polytetrafluoroethylene membranes for guided bone regeneration around implants. *Int J Oral Maxillofac Implants* 1995;10:67–73.
- Hürzeler MB, Kohal RJ, Naghshbandi J, et al. Evaluation of a new bioresorbable barrier to facilitate guided bone regeneration around exposed implant threads. An experimental study in the monkey. *Int J Oral Maxillofac Surg* 1998;27:315–320.
- Bessho K, Murakami K, Iizuka T. The use of a new bilayer artificial dermis for vestibular extension. *Br J Oral Maxillofac Surg* 1998;36:457–459.
- Hall HD, Steen AN. Free grafts of palatal mucosa in mandibular vestibuloplasty. *J Oral Surg* 1970;28:565–574.
- Kaspar DW, Laskin DM. The effect of porcine skin and autogenous epithelial grafts on the contraction of experimental wounds. *J Oral Maxillofac Surg* 1983;41:143–152.
- Dougherty WR, Chalabian JR. Skin substitutes. *West J Med* 1995;162:540–541.
- Murashita T, Nakayama Y, Hirano T, Ohashi S. Acceleration of granulation tissue ingrowth by hyaluronic acid in artificial skin. *Br J Plast Surg* 1996;49:58–63.
- Sheridan RL, Tompkins RG. Skin substitutes in burns. *Burns* 1999;25:97–103.
- Muhart M, McFalls S, Kirsner RS. Behavior of tissue-engineered skin: A comparison of a living skin equivalent, autograft, and occlusive dressing in human donor sites. *Arch Dermatol* 1999;135:913–918.
- Machens HG, Berger AC, Mailaender P. Bioartificial skin. *Cells Tissues Organs* 2000;167:88–94.
- Kirsner RS. The use of Apligraf in acute wounds. *J Dermatol* 1998;25:805–811.
- Trent JF, Kirsner RS. Tissue engineered skin: Apligraf, a bi-layered living skin equivalent. *Int J Clin Pract* 1998;52:408–413.
- Camargo PM, Melnick PR, Kenney EB. The use of gingival grafts for aesthetic purposes. *Periodontol* 2000 2001;27:72–96.
- Elliot RA Jr, Hoehm JG. Use of commercial porcine skin for wound dressing. *Plast Reconstr Surg* 1973;52:401–405.
- Silverstein LH, Kraft JD, Wand R. Bone regeneration and tissue acceptance of human fascia lata grafts adjacent to dental implants: A preliminary case report. *J Oral Implantol* 1992;18:394–398.
- Gregory EW, Triplett RG, Connole PW. Comparisons of fresh autogenous and freeze-dried allogenic skin for mandibular vestibuloplasty. *J Oral Maxillofac Surg* 1983;41:75–79.
- Dordick B, Coslet JG, Seibert JS. Clinical evaluation of free autogenous gingival grafts placed on alveolar bone. Part I. Clinical predictability. *J Periodontol* 1976;47:559–567.
- Maurer S, Hayes C, Leone C. Width of keratinized tissue after gingivoplasty of healed subepithelial connective tissue grafts. *J Periodontol* 2000;71:1729–1736.
- Laskin D, Kaspar D. The effect of porcine skin and autogenous epithelial grafts on the contraction of experimental oral wounds. *J Oral Maxillofac Surg* 1983;41:143–152.
- Shulman J. Clinical evaluation of an acellular dermal allograft for increasing the zone of attached gingiva. *Pract Periodontics Aesthet Dent* 1996;8:201–208.
- Yannas IV, Burke JF. Design of an artificial skin. I. Basic design principles. *J Biomed Mater Res* 1980;14:65–81.
- Herford AS, Cooper TC, Maiorana C, Cicciù M. Vascularized connective tissue flap for bone graft coverage. [epub ahead of print June 16 2010]. *J Oral Implantol*. 2011;37:279–85.
- Herford AS, Akin L, Cicciù M, et al. Use of a porcine collagen matrix as an alternative to autogenous tissue for grafting oral soft tissue defects. *J Oral Maxillofac Surg* 2010;68:1463–1470.
- Sanz M, Lorenzo R, Aranda JJ, Martin C, Orsini M. Clinical evaluation of a new collagen matrix (Mucograft prototype) to enhance the width of keratinized tissue in patients with fixed prosthetic restorations: A randomized prospective clinical trial. *J Clin Periodontol* 2009;36:868–876.
- Rutkowski JL, Thomas JM, Bering CL, et al. Analysis of a rapid, simple, and inexpensive technique used to obtain platelet-rich plasma for use in clinical practice. *J Oral Implantol* 2008;34:25–33.
- Cawood JL, Howell RA. A classification of the edentulous jaws. *Int J Oral Maxillofac Surg* 1988 Aug;17:232–236.
- Louis PJ, Gutta R, Said-Al-Naief N, et al. Reconstruction of the maxilla and mandible with particulate bone graft and titanium mesh for implant placement. *J Oral Maxillofac Surg* 2008;66:235–245.
- Chaushu G, Mardinger O, Peleg M, et al. Analysis of complications following augmentation with cancellous block allografts. *J Periodontol* 2010;81:1759–1764.
- Kim SH, Kim DY, Kim KH, et al. The efficacy of a double-layer collagen membrane technique for overlaying block grafts in a rabbit calvarium model. *Clin Oral Implants Res* 2009;20:1124–1132.
- Thoma DS, Halg GA, Dard MM, et al. Evaluation of a new biodegradable membrane to prevent gingival ingrowth into mandibular bone defects in minipigs. *Clin Oral Implants Res* 2009;20:7–16.
- McGuire MK, Scheyer ET. Xenogeneic collagen matrix with coronally advanced flap compared to connective tissue with coronally advanced flap for the treatment of dehiscence-type recession defects. *J Periodontol* 2010;81:1108–1117.
- Kakudo N, Minakata T, Mitsui T, Kushida S, Notodihardjo FZ, Kusumoto K. Proliferation-promoting effect of platelet-rich plasma on human adipose-derived stem cells and human dermal fibroblasts. *Plast Reconstr Surg* 2008 Nov;122:1352–1360.
- Hollinger JO, Hart CE, Hirsch SN, Lynch S, Friedlaender GE. Recombinant human platelet-derived growth factor: Biology and clinical applications [review]. *J Bone Joint Surg Am* 2008 Feb;90(suppl 1):48–54.

36. Pierce GF, Mustoe TA, Altrock BW. Role of platelet-derived growth factor in wound healing. *J Cell Biochem* 1991;45:319–26.
37. Marx RE, Carlson ER, Eichstaedt RM, Schimmele SR, Strauss JE, Georgeff KR. Platelet rich plasma-growth factor enhancement for bone grafts. *Oral Surg* 1998;85:638–646.
38. Marx RE. Platelet-rich plasma: Evidence to support its use. *J Oral Maxillofac Surg* 2004;62:489–96.
39. Kaigler D, Avila G, Wisner-Lynch L, et al. Platelet-derived growth factor applications in periodontal and peri-implant bone regeneration. *Expert Opin Biol Ther* 2011;11:375–385.
40. Schwarz F, Sager M, Ferrari D, et al. Influence of recombinant human platelet-derived growth factor on lateral ridge augmentation using biphasic calcium phosphate and guided bone regeneration: A histomorphometric study in dogs. *J Periodontol* 2009;80:1315–1323.
41. Nevins ML, Reynolds MA. Tissue engineering with recombinant human platelet-derived growth factor BB for implant site development. *Compend Contin Educ Dent* 2011;32:18,20–27.
42. Lynch SE, Wisner-Lynch L, Nevins M, et al. A new era in periodontal and periimplant regeneration: Use of growth-factor enhanced matrices incorporating rhPDGF. *Compend Contin Educ Dent* 2006; 27:672–678.

Systematic Assessment of Clinical Outcomes in Bone-Level and Tissue-Level Endosseous Dental Implants

Ioannis D. Vouros, DDS, Dr Med Dent¹/Christos D. R. Kalpidis, DDS, DSc²/Attila Horvath, DDS³/Aviva Petrie, BSc, MSc, CStat, CSci⁴/Nikolaos Donos, DDS, MS, PhD⁵

Purpose: The aim of the present systematic review was to address the following question: in patients treated with dental implants placed in pristine bone, what are the clinical and radiographic outcomes of bone-level (BL) implants in comparison to tissue-level (TL) implants after restoration with dental prostheses? **Materials and Methods:** Scanning of online literature databases from 1966 to January 2012, supplemented by hand searching, was conducted to identify relevant prospective randomized controlled trials, controlled clinical trials, and cohort studies. Sequential screenings at the title, abstract, and full-text levels were performed independently and in duplicate. A meta-analysis was conducted to compile data from the primary studies included in this systematic review.

Results: The search strategy revealed a total of 5,998. Screening at the title level resulted in 752 papers, while screening at the abstract level yielded 92 publications. Full-text reading identified nine articles that fulfilled the inclusion criteria of this review. The pooled estimated difference between BL and TL implants in mean marginal bone loss was 0.05 mm (95% confidence interval [CI], -0.03 to 0.13 mm), with no statistically significant difference between the groups at 1 year after placement of the definitive prostheses. The relative risk of implant loss was estimated at 1.00 (95% CI, 0.99 to 1.02) at 1 year and at 1.01 (95% CI, 0.99 to 1.03) at 3 years after restoration, indicating no evidence of an increased risk of implant loss in BL compared to TL implants. **Conclusions:** No statistically significant differences in bone loss and survival rates were detected between BL and TL dental implants over a short-term observation period (1 to 3 years). Thus, both implant systems fulfill the requirements for the replacement of missing teeth in implant dentistry. *INT J ORAL MAXILLOFAC IMPLANTS* 2012;27:1359–1374

Key words: bone-level implants, bone loss, dental implants, implant outcomes, implant survival, systematic review, tissue-level implants

¹Associate Professor, Department of Preventive Dentistry, Periodontology and Implant Biology, School of Dentistry, Aristotle University, Thessaloniki, Greece.

²Lecturer, Department of Preventive Dentistry, Periodontology and Implant Biology, School of Dentistry, Aristotle University, Thessaloniki, Greece.

³Clinical Research Fellow, Periodontology Unit, Department of Clinical Research, University College London Eastman Dental Institute, London, United Kingdom; Clinical Lecturer, Department of Periodontology, Semmelweis University, Budapest, Hungary.

⁴Head of Biostatistics Unit and Senior Lecturer, University College London Eastman Dental Institute, London, United Kingdom.

⁵Professor and Head of Periodontology, Chair, Division of Clinical Research, Periodontology Unit, Department of Clinical Research, University College London Eastman Dental Institute, London, United Kingdom.

This material was presented at the 88th General Session and Exhibition of the International Association for Dental Research, held July 14–17, 2010, in Barcelona, Spain.

Correspondence to: Dr Ioannis Vouros, Department of Preventive Dentistry, Periodontology and Implant Biology, School of Dentistry, Aristotle University of Thessaloniki, 54124 Thessaloniki, Greece. Fax: +30-2310999613. Email: jvou@med.auth.gr

The use of osseointegrated dental implants to replace missing teeth has been proven to be successful in recent decades. Dental implants are available in different body designs, lengths/diameters, surface characteristics, and platforms. Conventionally, bone-level (BL), two-part implants were placed at the bone crest during the first-stage surgical procedure and allowed to heal submerged during the osseointegration period to minimize implant failures.¹ A second surgery was then performed to uncover the implants for the prosthetic reconstruction. Subsequently, BL implants were placed in a single-stage approach, with survival rates similar to those observed for the two-stage placement approach, to minimize morbidity and shorten treatment time.² Tissue-level (TL), one-part implants are typically placed transmucosally in a single-stage procedure, and the soft tissue attachment is established on the supracrestal part of the implant.³

Crestal bone resorption is typically observed around the neck of BL implants 1 year after surgical uncovering.^{1,4} The characteristic "saucerization" seen around BL implants has vertical and horizontal components.⁵ The

observed bone remodeling is thought to be related to the establishment of the biologic width around the implants.^{6,7} In addition, it has been suggested that the microgap and the micromovement between the implant and the abutment in BL dental implant systems play a dominant role in the development of marginal bone loss and subsequent soft tissue recession.^{4,8} The concept of platform switching (also called platform shifting or horizontal offset) was proposed to prevent bone resorption around BL implants. Clinicians have observed that when BL implants are restored with narrower prosthetic abutments, peri-implant marginal bone loss is minimized.⁹ The centripetal displacement of the microgap and the associated microbial shift away from bone might protect against crestal bone destruction.

The transmucosal location of the microgap in TL implants seems to be advantageous because it is positioned at a distance from the bone crest.³ However, long-term radiographic studies of TL dental implants also demonstrated peri-implant bone loss ranging from 0.6 to 1.0 mm during the first year of function and < 0.2 mm per year thereafter.^{10,11}

The soft tissue collar around dental implants, consisting of the epithelial and connective tissue attachment, is of great importance with regard to protection of the underlying osseointegration.^{12,13} The behavior of peri-implant soft tissue is influenced by marginal bone loss because of the underlying osseous support.⁵

Although both BL and TL implants have been used successfully for decades to replace missing natural teeth, the treatment outcomes of these two major implant types have not been evaluated with an evidence-based approach. A number of clinical trials have reported over the years on the short- and long-term clinical outcomes of both implant types. However, no firm conclusions, based on a systematic appraisal of the available literature, on the clinical performance of BL and TL implants have yet been drawn. Therefore, the present systematic review was carried out to investigate possible differences in clinical outcomes between TL and BL implants after at least 1 year of function. The answer to the following question was sought: In patients treated with dental implants placed in pristine bone, what are the clinical and radiographic outcomes of BL implants in comparison to TL implants after restoration with dental prostheses?

MATERIALS AND METHODS

Design of the Study

Before commencing the present systematic review, a comprehensive protocol was developed and successively approved by all authors. This detailed protocol

incorporated several sections and research methods, including the search strategy, definition of eligibility, inclusion criteria, screening techniques, data extraction, quality assessment, and data synthesis/analysis.

Inclusion Criteria

1. All prospective controlled longitudinal studies reporting on clinical survival/success and radiographic outcomes of TL and BL osseointegrated dental implants were included (randomized controlled trials [RCTs], controlled clinical trials [CCTs], cohort studies, and case-control studies).
2. All included studies had to report on implants followed for at least 12 months after loading to observe long-term tissue behavior, rather than early tissue remodeling after loading.
3. Patients were partially or completely edentulous with fixed implant-supported prostheses supported by BL or TL implants. The arbitrary "cutoff" number of patients was set at 15 individuals per group (control/test, ie, a minimum of 30 patients in total for each study).
4. Studies with smokers and patients with a history of periodontitis were included.
5. Studies utilizing titanium endosseous implants with various surface modifications were included.

Exclusion Criteria

1. Case reports, case series, reviews, editorials, and retrospective studies were excluded.
2. Studies in patients with medical conditions possibly affecting implant therapy, such as cancer, uncontrolled diabetes mellitus, and intake of certain medications, were excluded.
3. Studies with transmandibular or zygomatic implants or with implants utilized for anchorage in orthodontics, for maxillofacial prostheses, or any other nondental use were also excluded.
4. Studies that reported on any form of soft tissue augmentation procedure done in conjunction with implant placement were excluded.
5. Studies that reported on simultaneous or staged implant placement in sites augmented laterally or vertically with bone augmentation techniques were excluded.
6. Studies of immediate loading or immediate implantation in extraction sites were excluded.
7. Studies that reported on implant-supported removable overdentures or partial dentures were excluded.
8. Studies that described the treatment of peri-implantitis were also excluded.

Types of Interventions. The following implant placement types were considered: (1) submerged two-stage placement of BL implants and (2) nonsubmerged single-stage placement of TL and BL implants.

Outcome Measures. Radiographically assessed marginal bone loss was considered as the primary outcome measure of the present systematic review. In addition, cumulative survival rates indicating that a certain percentage of implants were still present in the mouth at the end of the observation period were also regarded as an important outcome measure. Pocket probing depth (PPD), bleeding on probing (BoP), plaque scores, peri-implant soft tissue levels, and recession were considered secondary clinical outcomes.

Search Strategy

The search strategy incorporated examinations of electronic databases, supplemented by hand searches. A search on MEDLINE and EMBASE using the Ovid interface was conducted from 1966 up to and including the 30th of January 2012. The search strategy used a combination of MeSH terms and text words. The initial electronic search strategies formulated for MEDLINE were adapted from Esposito and coworkers¹⁴ and later modified as appropriate for EMBASE. The following key words/search terms and their combinations were used: transmucosal, submucosal, tissue level, bone level, submerged, nonsubmerged, one stage, 1 stage, single stage, two stage, 2 stage, one piece, 1 piece, two piece, 2 piece, single piece, one part, 1 part, single part, two part, microgap, micro gap, microleakage, micro leakage, micromovement, micro movement, marginal bone, implant abutment interface, platform switch\$, platform shift\$, horizontal offset, non matching implant abutment, butt joint connection, Morse taper connection, external hexagonal connection, internal connection, alveolar bone loss, bone resorption, bone remodeling, gingival recession, healing, implant, placement, dental implant, dental implantation. Filters for RCT and CCT were applied.

These terms were then combined as: population/exposure AND intervention AND types of studies. The Cochrane Oral Health Group's Trial Register and the Cochrane Central Register of Controlled Trials were also screened for related studies following adapted search strategies.

In addition, the following journals were considered potentially important and were hand-searched for the present review: *British Journal of Oral and Maxillofacial Surgery*, *Clinical Implant Dentistry and Related Research*, *Clinical Oral Implants Research*, *European Journal of Oral Implantology*, *Implant Dentistry*, *International Journal of Oral & Maxillofacial Implants*, *International Journal of Oral and Maxillofacial Surgery*, *International Journal of Periodontics & Restorative Dentistry*, *International Journal*

of Prosthodontics, *Journal of Clinical Periodontology*, *Journal of Dental Research*, *Journal of Oral Implantology*, *Journal of Oral and Maxillofacial Surgery*, *Journal of Periodontology*, and *Journal of Prosthetic Dentistry*.

Assessment of Study Eligibility and Data Extraction

Sequential Search Strategy. The comprehensive nature of the search methodology would result in a large volume of published studies on the topic. As such, a sequential screening process was performed independently and in duplicate (by JV and CK) to increase the relevance of the extracted data. Following the initial literature search, all article titles were screened (JV and CK) to eliminate irrelevant publications, review articles, case reports, and animal studies. Next, studies were excluded based on data from screening of the abstracts (JV and CK). The final stage of screening involved full-text reading and was performed by two reviewers (JV and CK) using a predetermined data extraction form to confirm the study's eligibility based on the inclusion and exclusion criteria.

The level of agreement regarding inclusion of potential studies was calculated by kappa statistics for all steps of the screening process. During each stage, all disagreements were resolved by discussion, and, if necessary, a third reviewer was consulted (AH). If consensus on the exclusion of an article was not achieved, the article was included in the next stage of screening.

Assessment of Methodologic Quality. Quality assessment of all the included studies was performed independently and in duplicate by two reviewers (JV and CK) during the data extraction process. The technique of assessment of the methodologic quality of the included studies has been used in other systematic reviews.^{15,16} Briefly, the quality appraisal evaluated the methodologic elements that might influence the outcomes of each study, including sample size and power calculation, baseline homogeneity, explicitness of both inclusion and exclusion criteria, randomization methods, standardization of outcome assessment, reproducibility of measurements, examiner calibration and masking, follow-up details, and similarity of dropouts between groups. The reviewers assigned an overall score to each study to indicate a low, medium, or high risk of bias. A trial with low risk of bias fulfilled all the proposed quality assessment criteria. A study with a high risk of bias satisfied only some or none of the evaluated methodology factors.

Confounding Factors. Confounding factors, including medical history, smoking, and periodontal status, were also screened to determine whether they had been included and the appropriate adjustments made for them in the primary statistical analysis.

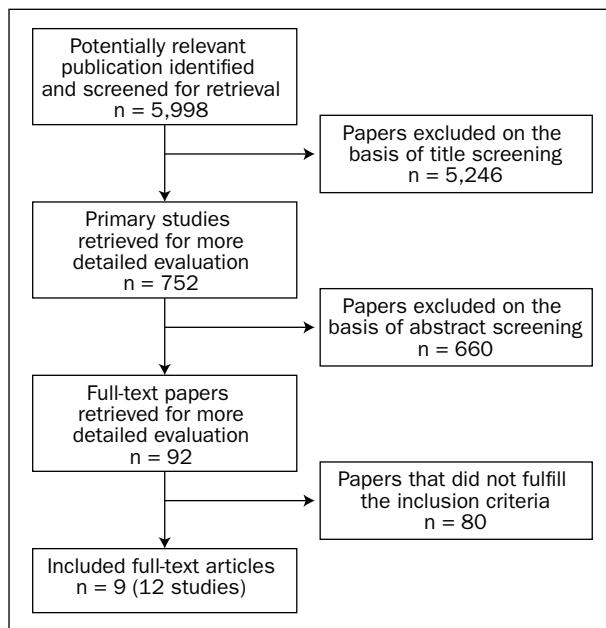


Fig 1 Flow chart of literature search and the selection of relevant clinical trials.

Data Extraction and Synthesis. Evidence tables were structured containing original data from the included studies. Descriptive analysis was undertaken to evaluate variations of the study characteristics, including populations, design, interventions, outcomes, and quality.

Statistical Analysis

A meta-analysis was performed to identify potential differences between BL and TL implants in relation to clinical and radiographic outcomes. To summarize and compare the studies included in this systematic review, primary data for continuous variable outcomes were pooled and analyzed using weighted mean differences and 95% confidence intervals (95% CI). The estimates of the effect were expressed as risk ratios and 95% CI for dichotomous variable outcomes. If a significant heterogeneity was not evident, the fixed effect model was adopted, whereas in cases of statistical heterogeneity, a random-effects meta-analysis was performed.

For each study, the outcome of interest was the mean difference between BL and TL implants. Means and standard deviations of both implant groups and for each outcome measure were required from all included studies to perform the meta-analysis. Forest plots were constructed to graphically present study-specific mean differences and summary estimates of the meta-analysis. All the meta-analyses were performed with STATA (StataCorp LP) statistical software, and the significance level was set at $P < .05$.

RESULTS

Study Characteristics

The electronic and manual searches of the literature provided 5,998 studies in total. Following screening of the article titles, 752 potentially relevant articles were identified. Independent screening of abstracts resulted in the selection of 92 publications for possible inclusion. Following full-text screening, 9 of the 92 studies met the predefined criteria and were included in the systematic review (Fig 1).

The nine studies consisted of four RCTs,¹⁷⁻²⁰ three CCTs,²¹⁻²³ and two prospective cohort studies.^{24,25} Three of the publications were multicenter trials,^{19,21,23} three were conducted in a private practice setting,^{21,22,25} and six presented data from patients treated at respective university dental clinics.^{17-20,23,24} Three additional publications fulfilled the inclusion criteria but were not eventually included because they covered the same patient populations of included studies at different time periods.²⁶⁻²⁸

The calculated interreviewer kappa values were 0.85 at the title level, 0.82 at the abstract level, and 0.92 for the final screening, indicating good agreement between the reviewers for all steps of the literature search strategy.²⁹

Patient Characteristics

Table 1 describes the characteristics of the patients and interventions. In the four RCTs, 294 BL implants were placed in 153 patients and 273 TL implants were positioned in 161 patients. In the remaining prospective cohort studies, 244 patients received 501 TL implants and 239 individuals were treated with 631 BL implants. A few publications provided information on the smoking habits of patients. In the study of Åstrand and co-workers,¹⁹ 7 of 28 patients (25%) were smokers (< 20 cigarettes daily), and two TL implants failed in smoking patients. In the study of Baelum and Ellegaard,²² most of the participants (65%) were smokers, and TL and BL implants were equally distributed in smoking patients. In the study of Ozkan and coworkers,²⁴ 15 of 63 patients (23.8%) were light smokers (< 10 cigarettes/day), but the distribution of TL and BL implants among smokers was not provided. Bilhan et al excluded heavy smokers (> 20 cigarettes/day) from their study.²⁵

The periodontal condition of patients was not discussed in six publications, while one study excluded patients with periodontitis.¹⁹ In the Baelum and Ellegaard trial,²² 57 BL and 201 TL implants were placed in periodontally compromised patients. All participants received periodontal therapy, including surgery, to eliminate pathologically deep pockets and were considered able to maintain high standards of oral hygiene at the time of implant insertion.²²

The observation period ranged from 1 to 3 years in five studies with 671 BL and 454 TL implants in total.^{18,19,21,22,24} Two studies with 119 BL and 90 TL implants reported 1-year results,^{17,20} while one publication projected results over 5 and 10 years utilizing Kaplan-Meier estimates.²² In the latter study, the 57 BL implants were observed for an average of 5.6 years (range, 0 to 10.6 years), while the 201 TL implants were followed for an average of 6.1 years (range, 0 to 14 years).²² In another study, 78 BL implants (two different systems) and 29 TL implants were followed for 2 years.²⁵

Intervention Characteristics

Eight different implant systems were utilized in the nine publications that fulfilled the inclusion criteria of this systematic review (Table 1).

BL Implant Systems. The most commonly used BL system was the Bränemark System (Nobel Biocare). In all, 276 Bränemark implants were placed in 195 patients.^{18,19,21,23,25} The standard Bränemark machined surface was used in three studies, one trial used implants with the rough TiUnite surface,²⁵ and in one publication, the implant surface characteristics were not reported.¹⁸

Astra BL implants (Astra Tech Dental Implant Systems, Astra Tech) were utilized in three studies.^{17,22,25} The Astra implant system is provided with a platform-switched abutment connection, with the manufacturer claiming that less bone loss will occur compared with conventional butt-joint connections.³⁰ In total, 145 Astra implants were positioned in 95 patients. A titanium oxide-blasted surface was used in two trials,^{22,25} but no information was provided on surface characteristics in another study.¹⁷

Four additional BL systems were used in the remaining studies: the Frialit System (Friatec)²⁴; the Ankylos System (Ankylos, Friadent), which is characterized by a rough-surfaced body with a progressive thread design and a machined neck²⁰; the Camlog System (Camlog Biotechnologies)²⁴; and the Oneplant System (Oneplant, Warantec), which has a sandblasted, acid-etched surface and a microthreaded neck.²⁰ In total, 45 Frialit, 35 Ankylos, 53 Camlog, and 38 Oneplant implants were placed in 63, 68, 63, and 68 patients, respectively.^{20,24}

BL implants were customarily placed with a two-stage surgical protocol. However, BL implants were inserted in a single-stage surgical procedure in three of the included publications: 80 BL implants were placed in 29 patients by Becker et al,²¹ 120 BL implants were placed in one group of 30 patients by Engquist et al,²³ and two groups of 38 and 35 BL implants were positioned in 68 patients by Shin et al.²⁰

TL Implant Systems. The most frequently used TL implant system was the Straumann Dental Implant System (Straumann), which was utilized in seven studies.^{17–19,21,22,24,25} In all, 652 Straumann implants were

positioned in 315 patients. In two of the publications, 155 original titanium plasma-sprayed implants were placed in 53 patients.^{19,21} Bilhan et al²⁵ placed 29 implants with a sandblasted, large grit, acid-etched surface (SLA, Straumann) in 26 patients. In another trial, Ozkan et al placed 105 Straumann implants but did not provide information on the surface characteristics or implant design.²⁴

Two additional TL systems were used in the remaining studies. In one publication, 34 Lifecore TL implants (Lifecore Biomedical), characterized by a surface blasted with calcium phosphate ceramics, were placed in 68 patients.²⁰ Finally, the Bränemark conical TL implant (Nobel Biocare) was used in one publication, without further information regarding surface characteristics.²³ All TL implants were placed in all patients of the included trials in a nonsubmerged, single-stage protocol.

Outcome Variables

Outcome variables of the included studies are detailed in Table 2.

Primary Outcome Characteristics. Radiographic changes expressing marginal bone levels (MBLs) were provided in all studies incorporated in this systematic review. In most trials, MBL changes were evaluated from placement of the prosthesis to the time of various follow-up examinations (usually 1, 2, or 3 years). Two trials reported additional MBL measurements at implant insertion.^{19,23} One study evaluated the proportion of implants with bone loss over longer observation periods utilizing Kaplan-Meier statistics.²² The authors concluded that 95% of the BL implants and 94.4% of the TL implants did not show radiographic bone loss ≥ 3.5 mm at 5 years after insertion. The corresponding values at the 10-year examination remained stable for BL implants and dropped to 86.4% for the TL group.²²

A random-effects meta-analysis was performed on bone loss from baseline to 1 year after placement of the definitive prosthesis because there was evidence of statistical heterogeneity ($\chi^2 = 977.9$, degrees of freedom [df] = 9, $P < .001$, $I^2 = 99.1\%$). The weighted mean difference and 95% CI of MBL changes between BL and TL implants of the studies are presented in Fig 2. For trials that used two different BL implant systems^{20,24,25} or placed a BL implant system in both single- and two-stage protocols,²³ individual differences were calculated in relation to the same TL implant group in each respective study (Fig 2). The pooled estimated difference between BL and TL implants in mean bone loss was 0.05 mm (95% CI: -0.03 to 0.13 mm), with no significant difference ($P = .2$) between the two implant groups (Fig 2). A meta-analysis on mean differences in MBL at 3 years after functional loading was not performed because of insufficient data from the included publications.

Table 1 Trial, Population, and Intervention Characteristics of the Included Studies

Study	Study design	Country	Recruitment	Implant manufacturer, type, surface	No. of surgeries
Kemppainen et al (1997) ¹⁷	RCT parallel	Finland	University dental clinic	AST, BL, TiOB ITI, TL, TPS	Two One
Becker et al (2000) ²¹	Not randomized MC (3 C)	USA	Private offices	BRS, BL, MAC BRS, BL, MAC ITI, TL, TPS	Two One One
Moberg et al (2001) ¹⁸	RCT parallel	Sweden	University dental clinic	BRS, BL, MAC ITI, TL, TPS	Two One
Åstrand et al (2004) ¹⁹ (Åstrand et al [2002] ²⁷)	RCT, MC (5 C) Split-mouth	Sweden	University dental clinic	BRS, BL, MAC ITI, TL, TPS	Two One
Baelum and Ellegaard (2004) ²² (Ellegaard et al [1997] ²⁶)	Not randomized case-control	Denmark	Private office	AST, BL, TiOB ITI, TL, TPS	Two One
Engquist et al (2005) ²³ (Engquist et al [2002] ²⁸)	CCT, MC (2 C) parallel	Sweden	University hospital dental clinics	BRS, BL, MAC BRS, BL, MAC BRS, TL, MAC	One Two One
Shin et al (2006) ²⁰	RCT	South Korea	University hospital dental clinics	1PL, BL, Microthreads ANK, BL, MAC neck LIF, TL, Rough neck	One One One
Ozkan et al (2007) ²⁴	Not randomized	Turkey	University dental clinic	FRI, BL, Unclear CAM, BL, Unclear ITI, TL, Unclear	Two Two One
Bilhan et al (2010) ²⁵	Not randomized	Turkey	Private office	AST, BL, TiOB BRS, BL, TU ITI, TL, SLA	Two Two One

ANK = Ankylos (Dentsply Friadent); AST = Astra (Astra Tech); BRS = Bränemark (Nobel Biocare); C = center; CAM = Camlog; CCT = controlled clinical trial; FPD = fixed partial denture; FRI = Frialit (Dentsply Friadent); IMP = implant; ITI = ITI (Straumann); LIF = Lifecore; MAC = machined; MC = multicenter; RCT = randomized controlled trial; SC = single crown; SLA = sandblasted/acid-etched (Straumann); TiOB = TiOblast (Astra Tech); TPS = titanium plasma-sprayed; TU = TiUnite (Nobel Biocare); 1PL = Oneplant (Warantec).

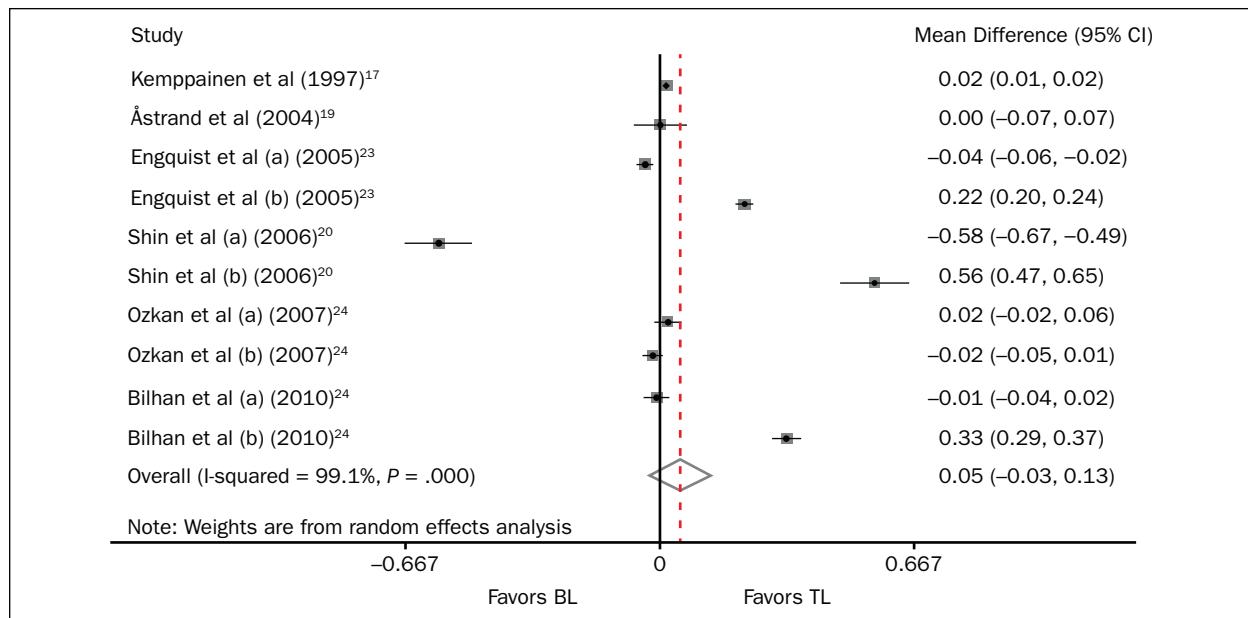


Fig 2 Meta-analysis of mean marginal bone loss at 1 year after restoration. Mean differences and 95% CI (in mm) for BL minus TL implants are presented for each study. For trials that employed two different BL implant systems^{20,24,25} or placed a BL implant system in both single- and two-stage protocols,²³ individual weighted mean differences (a, b) were calculated.

Survival rate was defined as the percentage of implants present over the observation period in each study. A fixed-effects meta-analysis was conducted on

implant survival at both 1 and 3 years after functional loading, because no evidence of statistical heterogeneity was detected ($\chi^2 = 3.48$, $df = 8$, $P = .90$,

No. of pts	Gender	Age (y) (range)	No. of IMP	Implantation site	Type of prosthesis	Prosthesis placed (mo)
37	16 M, 21 W	22 (18–37)	46	Most in the anterior maxilla	SC	7
45	17 M, 28 W	23 (19–51)	56			
29	9 M, 20 W	(23.0–74.0)	78	Unclear	Unclear	Maxilla: 6 Mandible: 3–4
29	11 M, 18 W	(24.0–82.0)	80			
25	15 M, 10 W	(40.0–83.0)	78			
20	10 M, 10 W	62.6 ± 7.0 (44.2–75.2)	102	Edentulous mandible	Full-arch fixed prosthesis	≈ 7.5
20	11 M, 9 W	64.0 ± 6.8 (44.0.2–77.2)	106			
28	13 M, 15 W	61.7 (36–76)	73	Partially edentulous maxilla (anterior teeth present)	FPD	≈ 7.0
32	8 M, 24 W	58.1 (34–87)	57	Mostly maxillary molars and premolars	SC, FPD	3
108	37 M, 71 W	59.5 (44–78)	201			–
30	17 M, 13 W	51 to > 70	120	Edentulous mandible	Full-arch fixed prosthesis	–
30	16 M, 14 W	41 to > 70	120			2
22	9 M, 13 W	41 to > 70	88			–
68	39 M, 29 W	48	38	Unclear	Unclear	Maxilla: 3 Mandible: 2
			35			
			34			
63	25 M, 38 W	46 ± 9 (18–63)	45	Posterior maxilla (91 imp), posterior mandible (112 imp)	81 FPD (153 imp), 50 SC	Maxilla: 6 Mandible: 3
			53			
			105			
26	9 M, 17 W	M: 52.6 W: 49.1	42	Unclear	Unclear	≈ 4
			36			
			29			

$I^2=0.0\%$ for implant survival at 1 year; chi-squared = 2.72, df = 7, $P = .91$, $I^2 = 0.0\%$ for implant survival at 3 years). For each study, the risk ratio and 95% CI of implant loss between BL and TL groups are presented in Figs 3 and 4 for 1 and 3 years, respectively. For trials that placed a BL implant system with both single- and two-stage protocols^{21,23} or two different BL implant systems,²⁴ individual relative risks were calculated with respect to the same TL implant group in each respective study (Figs 3 and 4). The studies by Shin and coworkers²⁰ and Bilhan and coworkers²⁵ were excluded from the meta-analysis of implant survival at 1 year (Fig 3) because no implants failed in either trial. The relative risks of implant survival were 1.003 (95% CI: 0.99 to 1.02, $P = .78$) at 1 year and 1.005 (95% CI: 0.99 to 1.03, $P = .63$) at 3 years, with no statistically significant evidence of an increased risk of implant failure in BL compared to TL implants.

The statistical unit of analysis for the survival rate was the implant in four publications,^{17,18,22,23} the patient in two studies,^{19,24} and unclear in the remaining publications.^{20,21,25} Censored implants and dropouts were not considered for the estimation of survival rates. One study reported a remarkably large number of censored implants during the 2- to 3-year evaluation period.²¹ More specifically, 40 of 78 TL, 71 of 80 nonsubmerged BL, and 53 of 78 submerged BL im-

plants in the respective clinical groups were withdrawn in the last year of the observation period for reasons not clearly discussed by the authors.

Secondary Outcome Characteristics. Most papers provided data on clinical periodontal parameters, including PPD, Plaque Index, BoP, and soft tissue recession. In general, no statistically significant differences in plaque accumulation, bleeding, or sulcus depth were reported between TL and BL implants in the primary investigations included in the present systematic review (Table 2). A meta-analysis of the secondary outcome measures was not performed because of insufficient data for compilation.

Ozkan and coauthors reported mean implant sulcus depths of 2.16 mm and 1.87 mm for their two BL groups and 1.80 mm for their TL group 1 year after implant placement.²⁴ In the study of Kemppainen et al,¹⁷ 73% of the BL and 69% of the TL implants presented PPDs of 2 to 3 mm at the 1-year examination. PPD of 3 to 4 mm were present in 2% of the BL and 1% of the TL group, while there were no peri-implant sulcus recordings deeper than 4 mm in any of the investigated groups.¹⁷ Moberg et al reported that the frequency distribution of sites exhibiting sulcus depth ≤ 3.5 mm was 96% for the BL implants and 97.5% for the TL implants 3 years after implant insertion.¹⁸

Table 2 Outcome Characteristics of the Included Studies

Study	Implant data	No. of surgeries	No. of failed implants			Implant survival (%)		No. of implants with PIM
			NOS	PIM	CEN	1 y	3 y	
Kempainen et al (1997) ¹⁷	AST, BL	Two	1	—	—	97.8% (45/46)	—	Unclear
	ITI, TL	One	—	—	—	100% (56/56)	—	
Becker et al (2000) ²¹	BRS, BL	One	1	1	71	97.5% (78/80)	97.5% (78/80)	Unclear
	BRS, BL	Two	1	2	40	96.2% (75/78)	96.2% (75/78)	
	ITI, TL	One	1	1	53	97.4% (76/78)	97.4% (76/78)	
Moberg et al (2001) ¹⁸	BRS, BL	Two	1	1	5	—	(95/97) 97.9%	0
	ITI, TL	One	—	1	12	—	(93/94) 98.9%	2
Åstrand et al (2004) ¹⁹ (Åstrand et al [2002] ²⁷)	BRS, BL	Two	2	—	—	97.26% (71/73)	97.26% (71/73)	0
	ITI, TL	One	—	2	—	98.7% (76/77)	97.4% (75/77)	7 (9.1%)*
Baelum and Ellegaard (2004) ²² (Ellegaard et al [1997] ²⁶)	AST, BL	Two	—	18	—	100%	100%	39
	ITI, TL	One	—	—	—	99.5% (96.4%–99.9%)	95.0% (89.0%–99.3%)	
Engquist et al (2005) ²³ (Engquist et al [2002] ²⁸)	BRS, BL	One	5	3	4	93.3% (112/120)	93.3% (112/120)	Unclear
	BRS, BL	Two	3	8	—	97.5% (117/120)	97.5% (117/120)	
	BRS, TL	One	5	1	4	93.2% (82/88)	93.2% (82/88)	
Shin et al (2006) ²⁰	1PL, BL	One	—	—	—	100%	—	Unclear
	ANK, BL	One	—	—	—	100%	—	
	LIF, TL	One	—	—	—	100%	—	
Ozkan et al (2007) ²⁴	FRI, BL	Two	—	—	—	100% (45/45)	100% (45/45)	0
	CAM, BL	Two	—	—	—	100% (53/53)	100% (53/53)	0
	ITI, TL	One	1	—	—	99.0% (104/105)	99.0% (104/105)	0
Bilhan et al (2010) ²⁵	AST, BL	Two	—	—	—	100% (42/42)	—	0
	BRS, BL	Two	—	—	—	100% (36/36)	—	0
	ITI, TL	One	—	—	—	100% (29/29)	—	0

ANK = Ankylos (Dentsply Friudent); AST = Astra (Astra Tech); BoP = bleeding on probing; BRS = Brånemark (Nobel Biocare); CAM = Camlog; CEN = censored (dropout, loss to follow-up, deceased patient); FRI = Frialit (Dentsply Friudent); ITI = ITI (Straumann); LIF = Lifecore; NOS = nonosseointegrated; PI = Plaque Index; PIM = peri-implantitis; PPD = probing pocket depth; 1PL = Oneplant (Warantec).

*Statistically significant difference.

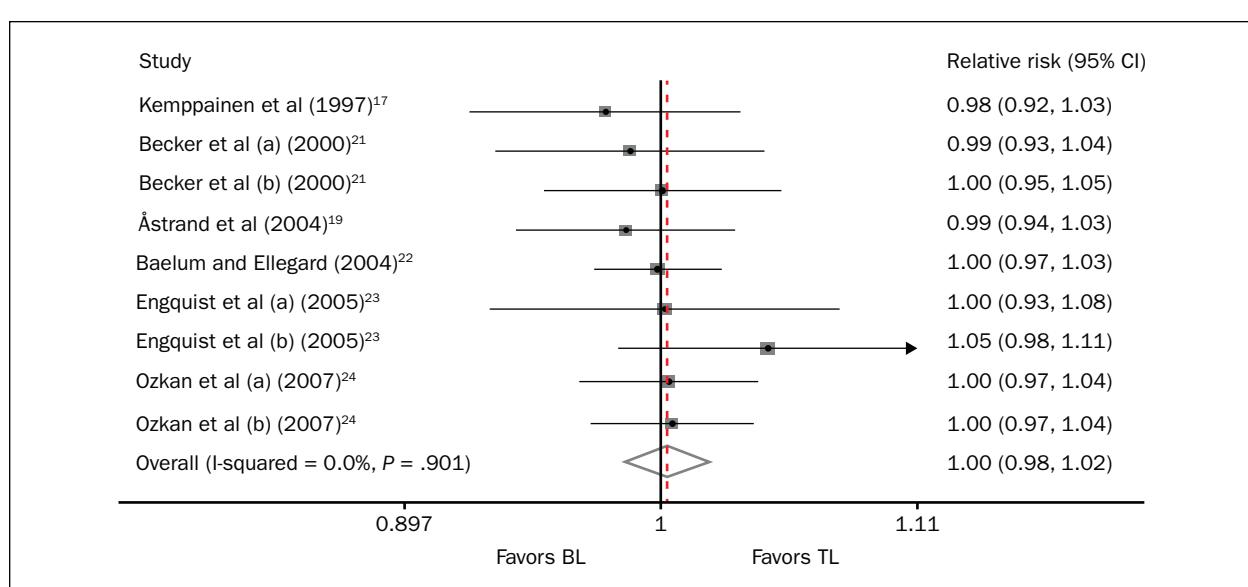


Fig 3 Meta-analysis of relative risk for implant loss at 1 year from functional loading. Relative risk and 95% CI for BL compared to TL implants are presented for each study. In studies that placed a BL implant system in both single- and two-stage protocols^{21,23} or used two different BL implant systems,²⁴ separate relative risks (a, b) were calculated.

MBL change (mm) from prosthesis to reevaluation (\pm SD)					
1 y	3 y	Reevaluation	PI (3 y)	BoP (3 y)	PPD
Maxilla: 0.14 ± 0.10	–	1 y	25%	26%	2-3 mm 1 y: 73%
Mandible: 0.10 ± 0.09	–		34%	29%	2-3 mm 1 y: 69%
Maxilla: 0.12 ± 0.09	–				
Mandible: 0.09 ± 0.03	–				
Maxilla: -0.16	–	1-2 y	Unclear	Unclear	Unclear
Mandible: -0.43^*	–	0-1 y			
Maxilla: -0.11	–				
Mandible: 0.07	–				
Maxilla: 1.31^*	–	2-3 y			
Mandible: 0.98^*	–				
	$1.2 \text{ mm: } 8.9\% (8/90)$ $\geq 1.2 \text{ mm: } 5.4\% (5/93)$	1 y 3 y	37% 36%	14% 20%	$> 3 \text{ mm: } 4.0\%^*$ $> 3 \text{ mm: } 2.5\%^*$
$0.2 \pm 0.09 (n = 28)$	$0.1 \pm 0.09 (n = 26)$	1 y	11.9%	7.9%	–
$0.2 \pm 0.16 (n = 28)$	$0.2 \pm 0.25 (n = 26)$	3 y	7.5%	9.1%	–
$< 3.5 \text{ mm: } 100\%$	$< 3.5 \text{ mm: } 100\%$	1 y 5 y 10 y	Unclear	5 y: 51.0% 10 y: 90.5%	$(\geq 4.0 \text{ mm}) 5 \text{ y: } 45.5\%$ $10 \text{ y: } 75.4\%$
$< 3.5 \text{ mm: } 100\%$	$< 3.5 \text{ mm: } 95.7\%$ (83.8%-98.9%)			5 y: 45.5% 10 y: 69.5%	$(\geq 4.0 \text{ mm}) 5 \text{ y: } 59.6\%$ $10 \text{ y: } 76.5\%$
$0.09 \pm 0.05 (n = 106)$	$0.18 (n = 106)$	1 y	Unclear	Unclear	Unclear
$0.35 \pm 0.06 (n = 107)$	$0.27 (n = 96)$	2 y			
$0.13 \pm 0.08 (n = 76)$	$0.26 (n = 71)$	3 y			
0.18 ± 0.16	–	1 y	Unclear	Unclear	Unclear
1.32 ± 0.27	–				
0.76 ± 0.21	–				
0.19 ± 0.11	0.28 ± 0.16	1 y	61.5%	BoP 0: 46.2%	2.16 ± 0.36
0.16 ± 0.08	0.25 ± 0.11	2 y	40.0%	BoP 0: 60.0%	1.87 ± 0.36
0.17 ± 0.08	0.26 ± 0.13	3 y	42.9%	BoP 0: 54.3%	1.80 ± 0.23
0.46 ± 0.07	–	1 y	–	–	–
0.80 ± 0.08	–	2 y	–	–	–
0.47 ± 0.07	–		–	–	–

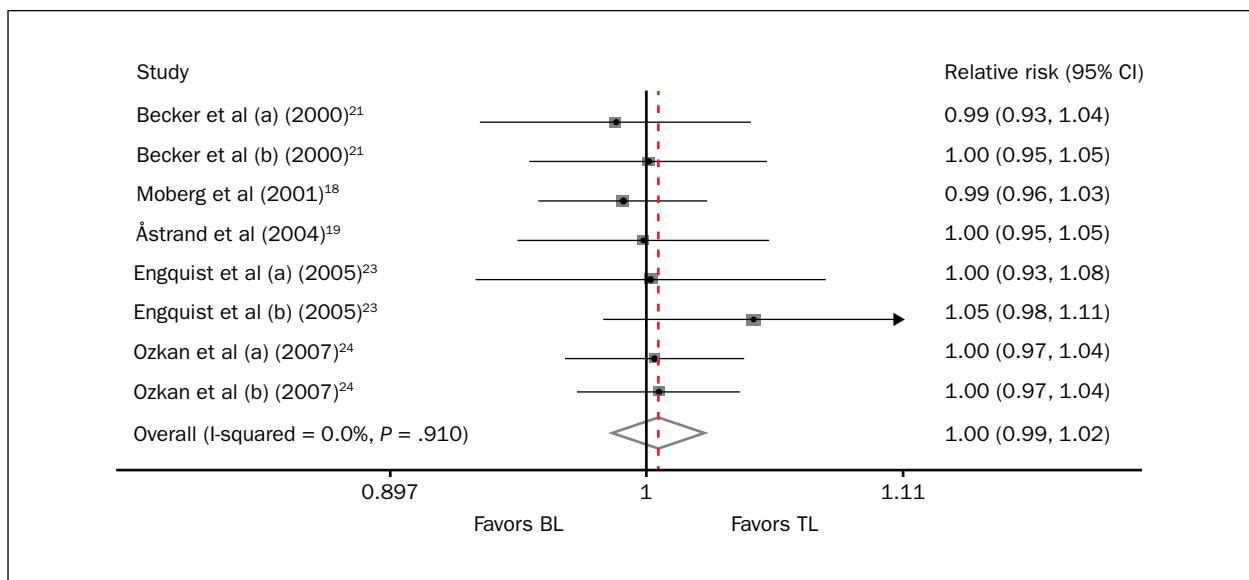


Fig 4 Meta-analysis of relative risk for implant loss at 3 years after placement of the definitive prostheses. Relative risk and 95% CI for BL compared to TL implants are presented for each study. In studies that placed a BL implant system in both single- and two-stage protocols^{21,23} or placed two different BL implant systems,²⁴ individual relative risks (a, b) were calculated.

Table 3a Results of the Quality Assessment of the Included Studies

Study	Sample size/power calculation	Ethical approval	Informed consent	Inclusion criteria explicit
Kemppainen et al (1997) ¹⁷	Unclear	Unclear	Unclear	Yes
Becker et al (2000) ²¹	Unclear	Unclear	Yes	No
Moberg et al (2001) ¹⁸	Unclear	Unclear	Yes	No
Åstrand et al (2004) ¹⁹ (Åstrand et al [2002] ²⁷)	28 pts per group to detect a 0.3-mm change in BL (90% power, $P = .05$)	Yes	Yes	Yes
Baelum and Ellegaard (2004) ²² (Ellegaard et al [1997] ²⁶)	Unclear	Unclear	Unclear	Unclear
Engquist et al (2005) ²³ (Engquist et al [2002] ²⁸)	Unclear	Unclear	Yes	Yes
Shin et al (2006) ²⁰	Unclear	Unclear	Unclear	Yes
Ozkan et al (2007) ²⁴	Unclear	Yes	Yes	Yes
Bilhan et al (2010) ²⁵	Unclear	Unclear	Yes	Yes

BL = bone level; IMP = implant; Pt = patient.

Table 3b Results of the Quality Assessment of the Included Studies

Study	Standardized radiographic assessment	Reproducibility of measurements
Kemppainen et al (1997) ¹⁷	Custom film holders and bite blocks for standardized intraoral x-rays Radiographic measurements independently performed by two EXM (mean values calculated)	Surgeries performed by the same surgeon Radiographic measurements of the two observers coincided < 0.4 mm in 80% of the sites
Becker et al (2000) ²¹	BL changes mesially and distally measured with electronic software on digitized x-rays	X-rays evaluated by one EXM
Moberg et al (2001) ¹⁸	Radiographic measurements on panoramic and intraoral x-rays using the thread distance	Each of the two surgeons and the two prosthodontists treated half cases in each IMP group
Åstrand et al (2004) ¹⁹ (Åstrand et al [2002] ²⁷)	Modified Eggen holder Radiographic measurements independently performed by two EXM Mean values used if difference was ≤ 0.5 mm, a consensus was obtained by the two EXMs if difference was ≥ 0.5 mm	Unclear
Baelum and Ellegaard (2004) ²² (Ellegaard et al [1997] ²⁶)	BL changes mesially and distally (using the thread distance) rounded to the nearest 0.5 mm	Unclear
Engquist et al (2005) ²³ (Engquist et al [2002] ²⁸)	Modified Eggen holder Radiographic measurements independently performed by two EXM Mean values used if difference was ≤ 0.5 mm, a consensus was obtained by the two EXM if difference was ≥ 0.5 mm	Unclear
Shin et al (2006) ²⁰	Parallel technique BL changes mesially and distally measured to the nearest 0.01 mm with electronic software on digitized x-rays	All surgical prosthetic procedures performed by the same clinician
Ozkan et al (2007) ²⁴	Occlusal index attached to standard film holder for standardized intraoral x-rays Radiographic measurements independently performed by two EXM (mean values calculated) BL changes evaluated with electronic software on digitized x-rays using known thread distances	All surgeries performed by the same clinician
Bilhan et al (2010) ²⁵	BL changes evaluated under 7 \times magnification on digitized x-rays using known thread distances	Unclear

Examiner calibration was unclear for all studies.

BL = bone level; EXM = examiner; IMP = implant; Pt = patient; x-ray = radiograph.

Exclusion criteria explicit	Baseline homogeneity	Randomization method	Allocation concealment
Yes	Gender, age, IMP location, prosthetic needs	Not specified	Unclear
Yes	Gender, age	No randomization	Unclear
Yes	Gender, age, IMP location, prosthetic needs	Not specified	Unclear
Yes	Gender, age, IMP location, prosthetic needs	Split mouth Block size of 4	Unclear
Unclear	Two nonmatched groups (32 and 108 pts)	Unclear	Unclear
Yes	Gender, age, IMP location, prosthetic needs	No randomization	No
Yes	Gender, IMP location	Pts were randomized in blocks	No
Yes	Prosthetic needs	No randomization	No
Yes	Unclear	No randomization	No

Similarity of dropouts and reasons for dropouts	Statistical unit	Risk of bias	Other potential sources of heterogeneity and methodological issues
No dropouts	IMP	High	Randomization inadequately defined Unfavorable IMP positioning in nine cases
Radiographic evaluation not performed for many IMPs Significant number of drop-outs, inadequate info provided	Unclear	High	Each center was assigned one group Cumulative survival rates were based on minimal no. of IMP at the 3-y eval Significant number of dropouts
TL group: two pts died (12 IMP) BL group: one pt died (5 IMP), one pt did not attend the x-ray exam (5 IMP)	IMP	High	Randomization inadequately defined Unclear radiographic exam
Two pts died	Patient	Medium	Potential reproducibility problems between five centers The number of pts was reduced from 50 to 28 pts per group, thus decreasing the power to detect a change in bone level from 0.3 to 0.2 mm (90% power, $P = 0.05$)
Several dropouts, but no numbers provided	IMP	High	IMP placement in periodontally compromised pts Unclear radiographic standarization Extremely wide range of observation periods Possible effect of unreported dropouts in the outcomes of the study
10 of 108 pts were lost to follow-up: 5 dies, 1 severely ill, 3 uncooperative, 1 lost all IMP (unclear distribution among groups)	Relative frequency of IMP loss in each pt	High	No randomization or allocation concealment
No dropouts	Unclear	High	Randomization inadequately defined
No dropouts	Pt	High	No randomization
Unclear	Unclear	High	No randomization Unclear radiographic standarization

Tables 4 Confounding Factors and Postsurgical Patient Management in the Included Studies

Study	Smoking	Periodontitis	Systematic disease	Medication
Kempainen et al (1997) ¹⁷	Unclear	Unclear	Unclear	Unclear
Becker et al (2000) ²¹	Unclear	Unclear	Unclear	Unclear
Moberg et al (2001) ¹⁸	Unclear	Unclear	Unclear	Unclear
Åstrand et al (2004) ¹⁹ (Åstrand et al [2002] ²⁷)	7 of 28 pts were smokers (< 20 cigarettes/day)	No	Two pts diabetes One pt osteoporosis	Unclear
Baelum and Ellegaard (2004) ²² (Ellegaard et al [1997] ²⁶)	65% of 140 pts were smokers	Pts received periodontal treatment including Sx	During follow-up 10 pts developed systematic diseases (cardiovascular, diabetes, asthma, bronchitis)	Unclear
Engquist et al (2005) ²³ (Engquist et al [2002] ²⁸)	Pts smoking ≥ 20 cigarettes/day excluded	Unclear	Unclear	Unclear
Shin et al (2006) ²⁰	Unclear	Unclear	Unclear	Unclear
Ozkan et al (2007) ²⁴	15 of 63 pts smoked < 10 cigarettes/day	Unclear	No	Unclear
Bilhan et al (2010) ²⁵	Heavy smokers (> 20 cigarettes/day excluded)	No history of periodontal Sx	Unclear	Unclear

CHX = chlorhexidine; D = denture; Pt = patient; S-removal = suture removal; Sx = surgical procedure.

Data on soft tissue recession after implant placement was provided by two publications.^{18,19} In one study, the authors registered, at baseline, a visible crown margin in 18.3% of BL and 29.9% of TL implants.¹⁹ At the 1-year examination, the buccal mucosa margin remained stable for BL implants, while in the TL group the recession progressed, leading to visible margins in 37.7% of the cases. In contrast, in the second trial, a more pronounced increase of mucosal margin recession was reported in BL implants, and at the 3-year examination the recession amounted to 2.4 mm for BL and 0.8 mm for TL implants.¹⁸

Complications

Only a few articles provided information on biologic and technical complications during the follow-up period. All peri-implantitis cases were considered biologic complications. In one study, two TL implants with peri-implantitis responded favorably to antimicrobial treatment but one BL implant was removed at 1 year.¹⁸ In another study, peri-implantitis with purulent discharge and bone loss was reported for 7 of 77 TL implants (9.1%), while none of the BL implants exhibited

any biologic complications.¹⁹ In one of the trials that reported on periodontally compromised patients, 39 implants were treated surgically for peri-implantitis in 20 participants, but the number of affected implants in the BL or TL groups was not clarified.²²

Methodologic Quality of the Studies

Data concerning quality assessment criteria of the included studies are presented in Table 3. The reviewers agreed that the included studies were at high risk of bias because they did not fulfill most of the quality assessment criteria presented in Table 3. Only one study was classified as being at medium risk because it satisfied several quality assessment criteria, including a prospective statistical power and sample size calculation (Table 3).¹⁹

Confounding Factors

Adjustment for the effect of confounding factors on implant survival rate was carried out in only one study (Table 4).²² A multivariable full model was utilized, and the significance of eight covariates was evaluated using the partial likelihood ratio test.

Antibiotics	Healing management	Adverse events	Maintenance intervals
Pts received 2×10^6 IU phenoxyethyl penicillin 1 h before Sx (orally) and 3×10^6 IU daily for 10 d	CHX gluconate (0.12%) rinses S-removal after 14 d	No	Unclear
	Unclear	S-removal after 7 d	Unclear
	Unclear	No D for 7–10 d post-Sx	One pt with paresthesia until 1y exam, one pt with paresthesia at final eval, three cases with tissue hyperplasia
Pts received penicillin V (2 g twice daily) or clindamycin (300 mg twice daily) for 10 d	S-removal after 7–10 d CHX 0.1% 4×/d, then gel No D for 14 d	No	Unclear
	Unclear	CHX 0.2% for 2 wk post-Sx	Unclear 3-mo recall by dental hygienist. Treatment provided as needed.
	Unclear	Unclear	Unclear
Pts received antibiotics for 7–10 d post-Sx	S-removal after 7–10 d CHX 0.1% 2×/d for 2 wk Soft diet post-Sx No D for 10 d post-Sx	Unclear	Unclear
Unclear	Unclear	Small tissue inflammation in one pt at 3-mo recall	Unclear
Unclear	Unclear	No	Unclear
Pts received antibiotics for 3 d post-Sx	CHX gluconate (0.2%) rinses S-removal after 7 d	Unclear	Unclear

The remaining studies either did not report on patient smoking habits^{17,18,20,21} or failed to carry out an appropriate statistical analysis to adjust for smoking as a confounding factor.^{19,23,24} The periodontal status of patients was provided in only one trial,²² whereas two studies discussed the systemic diseases of their patient populations.^{19,22} Therefore, based on the limited available information, it is not possible to evaluate the effect of possible confounding factors such as smoking, periodontal condition, and systemic diseases on implant clinical outcomes.

DISCUSSION

In recent decades, BL and TL dental implants have been successfully employed to replace missing natural teeth. However, in spite of the broad use of both implant types worldwide, there is no systematic comparison of the outcomes in the literature. This systematic review investigated possible differences in clinical and radiographic outcomes between TL and BL implants placed

in pristine bone. MBLs were considered as the primary outcome of the present systematic review because peri-implant crestal bone loss has been proposed by several investigators as a benchmark of implant success.^{3,11,16,31} All the primary studies included in this systematic review provided relevant radiographic data. Assessment of MBL changes was based on radiographic findings 1 and 3 years after restoration. However, several methodologic differences were observed between the clinical studies with respect to the evaluation of radiographic MBL changes, and only four trials provided adequate information on the standardization of the radiographic assessment.^{17,19,23,24}

The meta-analytic processing of available data revealed no significant differences in peri-implant bone level changes between BL and TL implants at 1 year after restoration. Based on radiographic observations from six primary studies included in the present systematic review,^{17,19,20,23–25} the pooled estimated difference between BL and TL implants in mean bone loss was 0.05 mm (95% CI: –0.03 to 0.13 mm), with no significant difference ($P = .2$) between the two implant groups (Fig 2).

A mean bone loss of ≤ 1.5 mm is generally accepted as a result of osseous remodeling during the first year of implant function; thereafter, an annual bone loss not exceeding 0.2 mm is consistent with successful implant treatment.³¹ The reported MBL changes in the included publications 1 year after restoration ranged from -0.43 to 1.32 mm for BL and 0.11 to 1.31 mm for TL implants (Table 2), which are within the accepted limits of bone loss.³¹ The 3-year MBL changes ranged between 0.10 and 0.28 mm for BL and 0.20 to 0.26 mm for TL implants (Table 2). These values correspond to a mean annual bone loss of approximately 0.09 mm, which is below the suggested threshold value of 0.2 mm.³¹ Unfortunately, insufficient data from the included publications prohibited analysis of mean MBL differences at 3 years after functional loading.

Implant survival rates were also regarded as an important outcome measure of the present systematic review. The reported 3-year postloading survival rate ranged from 93.3% to 100% for BL implants and was identical for TL implants (93.2% to 99%) (Table 2).^{18,19,21-24} Meta-analysis of data from six primary studies included in this systematic review^{17,19,21-24} revealed no evidence of an increased risk of implant failure in BL compared to TL implants at 1 year after placement of the definitive prostheses (Fig 3). Similarly, based on observations from five primary studies,^{18,19,21,23,24} the meta-analysis failed to detect an increased risk of implant failure in BL compared to TL implants at 3 years after functional loading (Fig 4).

Meta-analysis of the secondary outcome measures was not feasible because the included publications did not provide adequate data for statistical processing. However, most papers reported clinical periodontal parameters, including PPD, Plaque Index, BoP, and soft tissue recession. With the exception of one study of periodontally compromised patients,²² PPD values ranged between 2 and 4 mm in the remaining trials during the observation period of 1 to 3 years (Table 2). Half of the included studies provided data on the peri-implant indices regarding plaque and inflammation (Table 2).^{17,18,22,24,25} Although high plaque levels may influence the amount of bone resorption in relation to the vertical position of the implant-abutment connection, no correlation was reported between plaque scores and MBL in the statistical analysis of the primary studies. Finally, no statistically significant differences in clinical parameters were reported between BL and TL implants in the original statistical analyses of the studies included in this systematic review.

The concept of platform switching or horizontal offset has been proposed to reduce peri-implant marginal bone loss in BL implants. Utilization of a reduced-diameter prosthetic abutment shifts the microgap and the microbial presence horizontally, away from

the surrounding tissues, acting as a protective mechanism against the resorption of peri-implant marginal bone.⁹ Among the BL implants used in the included studies, only the Astra and Ankylos systems incorporated a platform-switched abutment connection. The Astra System was utilized in three studies included in the present systematic review,^{17,22,25} and the radiographic evaluation of MBL changes demonstrated no statistically significant differences in comparison to TL implants (Fig 2).^{17,25} However, the Astra system showed favorable effects on bone loss in comparison with conventional BL abutment connections (Fig 2),²⁵ a behavior that might be attributable to the platform-switching effect. These observations are in agreement with the meta-analytic results of a recent publication reporting 0.24 mm of MBL change for Astra BL, 0.75 mm for Bränemark BL, and 0.48 mm for Straumann TL implants at 5 years after functional loading, with statistically significant differences between these systems.³²

The Ankylos System was employed in a study comparing three systems: one TL implant with a roughened neck, one BL implant with a machined neck (Ankylos), and one BL implant with a microroughened neck.²⁰ Unexpectedly, the Ankylos System featuring the protective platform switch presented the most significant bone loss at the 1-year examination, in comparison to the other two implant systems (Fig 2). The authors attributed the differences in MBL between groups to the microstructure of the implant neck rather than to the pattern of abutment connection.²⁰ Additionally, in contrast to the subcrestal insertion recommended by the manufacturer, the Ankylos implants were placed crestally in this specific study.

Essentially, the majority of the available primary clinical studies present mostly indirect evidence to address the association between the basic two implant types and outcome variables. Other differences between BL and TL dental implants, including surface morphology (threading or roughness), type of abutment connection (flat or Morse taper), and platform switching/horizontal offset (inherent or prosthetically established), may influence implant success and other outcome variables. Only one study presented direct evidence regarding this association.²³ The authors stated that survival rates and MBL changes were not statistically significantly different between TL and BL implants manufactured by the same implant company. Therefore, clinical outcomes in this trial are clearly associated with the TL or BL feature, because the remaining technical characteristics of the implants were identical.

The surgical placement of BL implants following single- or two-stage surgical procedures may also affect MBL of this implant type. However, in two studies that used both submerged and nonsubmerged healing

conditions with BL implants, no differences in survival rates and MBL changes were detected (Figs 2 to 4).^{21,23} This conclusion is consistent with findings from other studies that support that healing of BL implants is independent of the surgical protocol utilized.^{33,34}

The trials included in the present systematic review were characterized by marked heterogeneity in the study designs, which rendered an assessment of methodologic quality difficult. Most of the studies did not provide detailed data on randomization methods and allocation concealment. However, masking of the assessors would be nearly impossible because abutment and implant characteristics are obvious during both clinical and radiographic assessments. Other issues that impaired the strength of evidence of the incorporated studies include a lack of proper radiographic standardization, insufficient reproducibility of the measurements, and inadequacies in statistical analysis and power calculation. In four publications, detailed information on standardized radiographic measurements and reproducibility methods were provided.^{17–19,23} In only one study, a sample size calculation was performed to allow detection of 0.3-mm differences in MBL changes with 90% power and a 5% level of significance.¹⁹ Three of the included publications analyzed implant survival and success rate data on a patient level.^{19,23,24} Three other studies used the implant as a statistical unit,^{17,18,22} increasing the risk to exhibit favorable implant survival percentages because the prevalence calculated on implant-based results is diluted by the large number of implants placed in the sample population.³⁵ In two studies, it was not clear whether the statistical analysis was implant- or patient-based.^{20,21} The studies included in the present systematic review were judged to be at high risk of bias because they failed to fulfill basic quality assessment criteria, with the exception of one publication that was classified as being at medium risk.¹⁹

CONCLUSIONS

1. The meta-analysis performed in the present systematic review did not identify a statistically significant difference in mean marginal bone loss between bone-level and tissue-level implants at 1 year after placement of the definitive prostheses.
2. Similarly, there was no evidence of a statistically significant increased risk of implant loss in bone-level compared to tissue-level implants at both 1 and 3 years after functional loading.
3. The meta-analytic results of bone loss and implant survival rates, in addition to the descriptive analysis of secondary clinical outcomes evaluated in this systematic review, indicate that both implant

types meet the requirements for tooth replacement in implant dentistry.

4. The strength of evidence of this systematic review is moderate to low because of risks of bias and significant variations observed in the included primary investigations.

ACKNOWLEDGMENTS

The authors declare that there are no financial or other conflicts of interest related to this publication. The study was supported by a partial grant from the Periodontology Unit, University College London Eastman Dental Institute, Research Discretionary account. This work was partially undertaken at University College London Hospitals/University College London with a proportion of funding from the Department of Health's National Institute for Health Research Biomedical Research Centers funding scheme.

REFERENCES

1. Adell R, Lekholm U, Rockler B, Bränemark P-I. A 15-year study of osseointegrated implants in the treatment of the edentulous jaw. *Int J Oral Surg* 1981;10:387–416.
2. Esposito M, Grusovin MG, Chew YS, Coulthard P, Worthington HV. Interventions for replacing missing teeth: 1- versus 2-stage implant placement. *Cochrane Database Syst Rev* 2009;CD006698.
3. Buser D, Mericske-Stern R, Bernard JP, et al. Long-term evaluation of non-submerged ITI implants. Part 1: 8-year life table analysis of a prospective multi-center study with 2359 implants. *Clin Oral Implants Res* 1997;8:161–172.
4. Hermann JS, Cochran DL, Nummikoski PV, Buser D. Crestal bone changes around titanium implants. A radiographic evaluation of unloaded nonsubmerged and submerged implants in the canine mandible. *J Periodontol* 1997;68:1117–1130.
5. Tarnow DP, Cho SC, Wallace SS. The effect of inter-implant distance on the height of inter-implant bone crest. *J Periodontol* 2000;71: 546–549.
6. Berglundh T, Lindhe J. Dimension of the periimplant mucosa. Biological width revisited. *J Clin Periodontol* 1996;23:971–973.
7. Hermann JS, Buser D, Schenk RK, Higginbottom FL, Cochran DL. Biologic width around titanium implants. A physiologically formed and stable dimension over time. *Clin Oral Implants Res* 2000;11:1–11.
8. Ericsson I, Persson LG, Berglundh T, Marinello CP, Lindhe J, Klinge B. Different types of inflammatory reactions in peri-implant soft tissues. *J Clin Periodontol* 1995;22:255–261.
9. Lazzara RJ, Porter SS. Platform switching: A new concept in implant dentistry for controlling postrestorative crestal bone levels. *Int J Periodontics Restorative Dent* 2006;26:9–17.
10. Brägger U, Häfeli U, Huber B, Hämmeler CH, Lang NP. Evaluation of postsurgical crestal bone levels adjacent to non-submerged dental implants. *Clin Oral Implants Res* 1998;9:218–224.
11. Karoussis IK, Brägger U, Salvi GE, Bürgin W, Lang NP. Effect of implant design on survival and success rates of titanium oral implants: A 10-year prospective cohort study of the ITI Dental Implant System. *Clin Oral Implants Res* 2004;15:8–17.
12. Berglundh T, Lindhe J, Ericsson I, Marinello CP, Liljenberg B, Thomsen P. The soft tissue barrier at implants and teeth. *Clin Oral Implants Res* 1991;2:81–90.
13. Listgarten MA, Lang NP, Schroeder HE, Schroeder A. Periodontal tissues and their counterparts around endosseous implants. *Clin Oral Implants Res* 1991;2:1–19.
14. Esposito M, Coulthard P, Thomsen P, Worthington HV. Interventions for replacing missing teeth: Different types of dental implants. *Cochrane Database Syst Rev* 2005;CD003815.

15. Ong CT, Ivanovski S, Needleman IG, et al. Systematic review of implant outcomes in treated periodontitis subjects. *J Clin Periodontol* 2008;35:438–462.
16. Donos N, Mardas N, Chadha V. Clinical outcomes of implants following lateral bone augmentation: Systematic assessment of available options (barrier membranes, bone grafts, split osteotomy). *J Clin Periodontol* 2008;35(8 suppl):173–202.
17. Kempainen P, Eskola S, Ylipaavalniemi P. A comparative prospective clinical study of two single-tooth implants: A preliminary report of 102 implants. *J Prosthet Dent* 1997;77:382–387.
18. Moberg LE, Kondell PA, Sagulin GB, Bolin A, Heimdahl A, Gynther GW. Bränemark System and ITI Dental Implant System for treatment of mandibular edentulism. A comparative randomized study: 3-year follow-up. *Clin Oral Implants Res* 2001;12:450–461.
19. Åstrand P, Engquist B, Anzén B, et al. A three-year follow-up report of a comparative study of ITI Dental Implants and Bränemark System implants in the treatment of the partially edentulous maxilla. *Clin Implant Dent Relat Res* 2004;6:130–141.
20. Shin YK, Han CH, Heo SJ, Kim S, Chun HJ. Radiographic evaluation of marginal bone level around implants with different neck designs after 1 year. *Int J Oral Maxillofac Implants* 2006;21:789–794.
21. Becker W, Becker BE, Ricci A, et al. A prospective multicenter clinical trial comparing one- and two-stage titanium screw-shaped fixtures with one-stage plasma-sprayed solid-screw fixtures. *Clin Implant Dent Relat Res* 2000;2:159–165.
22. Baelum V, Ellegaard B. Implant survival in periodontally compromised patients. *J Periodontol* 2004;75:1404–1412.
23. Engquist B, Åstrand P, Anzén B, et al. Simplified methods of implant treatment in the edentulous lower jaw: A 3-year follow-up report of a controlled prospective study of one-stage versus two-stage surgery and early loading. *Clin Implant Dent Relat Res* 2005;7:95–104.
24. Ozkan Y, Ozcan M, Akoglu B, Ucankale M, Kulak-Ozkan Y. Three-year treatment outcomes with three brands of implants placed in the posterior maxilla and mandible of partially edentulous patients. *J Prosthet Dent* 2007;97:78–84.
25. Bilhan H, Kutay O, Arat S, Cekici A, Cehreli MC. Astra Tech, Bränemark, and ITI implants in the rehabilitation of partial edentulism: Two-year results. *Implant Dent* 2010;19:437–446.
26. Ellegaard B, Baelum V, Karring T. Implant therapy in periodontally compromised patients. *Clin Oral Implants Res* 1997;8:180–188.
27. Åstrand P, Engquist B, Anzén B, Bergendal T, Hallman M, Karlsson U, Kvist S, Lysell L, Rundcrantz T. Nonsubmerged and submerged implants in the treatment of the partially edentulous maxilla. *Clin Implant Dent Relat Res* 2002;14:115–127.
28. Engquist B, Åstrand P, Anzén B, et al. Simplified methods of implant treatment in the edentulous lower jaw. A controlled prospective study. Part I: One-stage versus two-stage surgery. *Clin Implant Dent Relat Res* 2002;4:93–103.
29. Landis JR, Koch GG. The measurement of observer agreement for categorical data. *Biometrics* 1977;33:159–174.
30. Arvidson K. A subsequent two-stage dental implant system and its clinical application. *Periodontology* 2000 1998;17:96–105.
31. Albrektsson T, Zarb G, Worthington P, Eriksson AR. The long-term efficacy of currently used dental implants: A review and proposed criteria of success. *Int J Oral Maxillofac Implants* 1986;1:11–25.
32. Laurell L, Lundgren D. Marginal bone level changes at dental implants after 5 years in function: A meta-analysis. *Clin Implant Dent Relat Res* 2011;13:19–28.
33. Ericsson I, Randow K, Nilner K, Petersson A. Some clinical and radiographical features of submerged and non-submerged titanium implants. A 5-year follow-up study. *Clin Oral Implants Res* 1997;8:422–426.
34. Cecchinato D, Olsson C, Lindhe J. Submerged or non-submerged healing of endosseous implants to be used in the rehabilitation of partially dentate patients. *J Clin Periodontol* 2004;31:299–308.
35. Fransson C, Lekholm U, Jemt T, Berglundh T. Prevalence of subjects with progressive bone loss at implants. *Clin Oral Implants Res* 2005;16:440–446.

Effect of Different Alloplast Materials on the Stability of Vertically Augmented New Tissue

Shing-Zeng Dung, BDS, PhD¹/Yu-Kang Tu, DDS, Msc, PhD²

Purpose: Vertical ridge augmentation is a technique to enhance alveolar bone growth or to correct bone defects.

However, its long-term predictability and stability are still unknown. The aim of this study was to evaluate the impact of three alloplastic grafting materials on the retention of vertically augmented bone tissue. **Materials**

and Methods: Four titanium caps (3 mm in radius), filled with different alloplastic materials (resorbable hydroxyapatite [HA], porous or nonporous nonresorbable HA) or peripheral blood (control) were placed on the calvaria of seven male New Zealand rabbits. Three months after implant placement, mucoperiosteal flaps were raised to expose the defect sites. The titanium caps were carefully removed and the tissue was covered by repositioned flaps. Two months later, the animals were sacrificed and the augmented new bone was retrieved and prepared for histomorphometric examination. The highest point of each augmented area was measured directly with a Boley gauge. Bone healing was evaluated by a semiquantitative bone score according to the relative proportion of newly formed bone in the cap (0%, 25%, 50%, and 75% of new bone).

Results: All substitutes promoted supracranial bone augmentation. Some specimens from nonresorbable HA-augmented tissues fractured at the time of cap removal, indicating that these newly augmented tissues were fragile and less flexible. Height of the augmented tissue for nonresorbable HA, resorbable HA, and controls was 2.3, 1.5, and 1.4 mm, respectively. Most augmented tissue contained less than 25% new bone.

Conclusions: Data from this experiment indicated that, while all materials conducted new bone formation predictably, new tissue augmented by resorbable hydroxyapatite and control sites were less stable. Further investigations are encouraged to search for new materials and techniques, which enhance the long-term stability of vertically augmented tissue. *Int J Oral Maxillofac Implants* 2012;27:1375–1381

Key words: bone formation, vertical ridge augmentation, alloplasts, long-term stability

In many clinical situations, the residual alveolar ridge may not be of adequate volume for the placement of dental implants. Ridge augmentation prior to dental implant therapy has therefore become an important field. The technique of guided tissue regeneration, developed to reconstruct periodontal defects, has been used successfully to reconstruct oral and maxillofacial defects, deficient alveolar ridges, and peri-implant bone defects both horizontally^{1–5} and vertically.^{6,7}

The idea of vertical bone augmentation was first introduced by Linde et al, who used an osteopromotive membrane technique in an experimental rat model.⁸

Later, Kostopoulos and Karring and Lundgren et al performed studies in rats and rabbits and also demonstrated that it was possible to form jawbone or calvarial tuberosities using hemispheric expanded polytetrafluoroethylene (e-PTFE) capsules or titanium domes as barriers.^{9,10} In addition, vertical bone augmentation around implants was successfully achieved in rat mandibles with mini-implants to support an e-PTFE barrier membrane.^{11,12} Other researchers also achieved increased peri-implant bone height and showed that the new bone was closely integrated with implants in two different canine models.^{7,13} Finally, three human case studies demonstrated the possibility of supracrestal bone regeneration up to 4 to 7 mm with titanium-reinforced membranes as barriers and exposed implants as space providers.^{6,14,15} Whether bone grafting materials should be used in conjunction with barrier materials for vertical bone augmentation is still controversial.

Alloplasts are synthetic grafting materials and include resorbable hydroxyapatite (HA) and tricalcium phosphate (eg, OsteoGen, Impladent); nonresorbable, nonporous HA (eg, Osteograft, Dentsply Friadent); porous HA (eg, Interpore 200, Interpore Orthopaedics); and bioactive glass (eg, BioGran, Biomet 3i, and

¹Associate Professor, Dental Department, Buddist Tzu-Chi General Hospital, Taipei Branch, Taiwan; School of Medicine, Tzu Chi University, Hualian, Taiwan; School of Dentistry, Yang-Ming University, Taipei, Taiwan; School of Dentistry, Taipei Medical University, Taipei, Taiwan.

²Associate Professor, Graduate Institute of Epidemiology & Preventive Medicine, College of Public Health, National Taiwan University, Taipei, Taiwan.

Correspondence to: Dr Shing-Zeng Dung, Dental Department, Buddist Tzu-Chi General Hospital, No. 289, Jianguo Rd., Xindian District, New Taipei City 231, Taiwan. Fax: +886-2-26241730. Email: tony.angela@msa.hinet.net

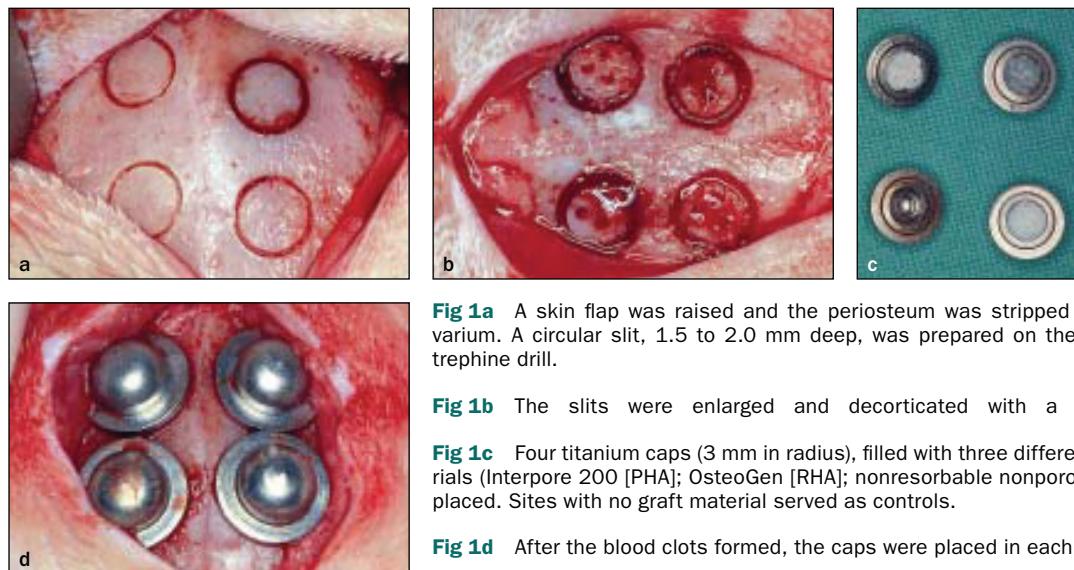
Fig 1 Surgical procedure.

Fig 1a A skin flap was raised and the periosteum was stripped to expose the calvarium. A circular slit, 1.5 to 2.0 mm deep, was prepared on the calvarium using a trephine drill.

Fig 1b The slits were enlarged and decorticated with a small round bur.

Fig 1c Four titanium caps (3 mm in radius), filled with three different alloplastic materials (Interpore 200 [PHA]; OsteoGen [RHA]; nonresorbable nonporous HA [NHA]), were placed. Sites with no graft material served as controls.

Fig 1d After the blood clots formed, the caps were placed in each slit by press fit.

PerioGlas, NovaBone). While alloplasts usually are rather safe and well-tolerated and have sufficient supply, they possess minimal osteoinductive activity and minimal capacity to promote new connective tissue attachment.¹⁶ The efficacy of OsteoGen in sinus augmentation has been evaluated in several studies.^{17–20} However, the relative efficacy of OsteoGen and other grafting materials has not been studied extensively in periodontal or supra-alveolar bone defects. Interpore is a synthetic coralline HA derived from coral by a hydrothermal exchange reaction with phosphate. The materials are available as granules or blocks. Interpore 200, with a pore size of 190 to 230 µm and granule size of 425 to 1,000 µm, is indicated for reconstruction of periodontal or alveolar ridge defects.^{21–24} The predictability and long-term stability of vertical ridge augmentation is still unknown. Moreover, whether bone grafting materials promote the long-term stability of newly augmented tissues remains to be answered. Therefore, the aim of this study was to evaluate the effect of three alloplastic grafting materials on the retention of vertically augmented bone tissue.

MATERIALS AND METHODS

Animals and Anesthesia

The study was approved by the Animal Research Ethics Committee at Yang-Ming University, Taipei, Taiwan. Adult male New Zealand white rabbits weighing 3 to 4 kg were used. Anesthesia was induced by intramuscular injection of ketamine (1 mL/kg) and an equal amount of xylazine (Rompun, Bayer). In addition, 0.5 mL of xylo-

caine (20 mg/mL with 12.5 µg/mL adrenalin) was deposited under the skin of the calvarium as a local anesthetic.

Surgical Procedures

All surgery was performed under aseptic conditions. Following the onset of anesthesia, the dorsum of the head of each animal was shaved with electric clippers and cleaned with a povidone-iodine solution (China Chemicals & Pharmaceutical). In each animal, a midsagittal incision was made through the skin and periosteum.

The surgical procedures are illustrated in Fig 1. A skin flap was raised and the periosteum was stripped to expose the calvarium. A circular slit, 1.5 to 2.0 mm deep, was prepared on the calvarium using a trephine drill (Biomet 3i) with a diameter of 3 mm under generous irrigation with saline. This slit was prepared with a round bur to ensure proper sealing of the titanium caps. Two circular slits were prepared on each side of the sagittal cranial suture, posterior to the transversal frontal suture. A small round bur was then used to penetrate the cortical plate to induce bleeding from marrow spaces. Peripheral blood was aspirated in a syringe from the ear and injected into the titanium caps of all study groups.

After blood clots had formed, the caps were placed into each slit by press fit. Four titanium caps (3 mm in radius), filled with three different alloplastic materials (Interpore 200, a nonresorbable porous HA [PHA]; OsteoGen, a resorbable HA [RHA]; and nonresorbable nonporous HA [NHA]) were placed on the calvaria of seven male New Zealand rabbits. Sites with no grafting material served as controls. Flaps were replaced to cover the domes and secured with 3-0 polyglycolic acid sutures (Unik). Postoperatively, the animals received an intra-

Fig 2 Three months after implant placement, mucoperiosteal flaps were raised to expose the surgical sites. The titanium caps were carefully removed. All groups promoted supracrural bone augmentation.

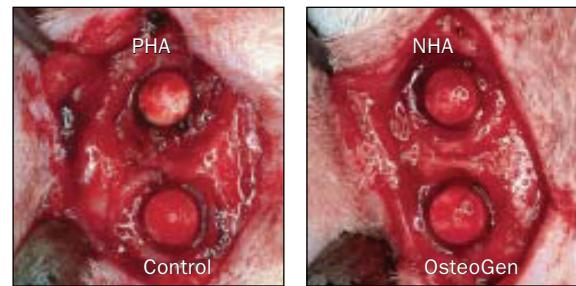


Table 1 Effect of Various Alloplast Materials on the Stability of Vertically Augmented Tissue

Animal	Nonresorbable HA*		Resorbable HA		Controls	
	Height (mm)	Score	Height (mm)	Score	Height (mm)	Score
1	2.1	1	2.3	3	2.1	1
2	2.7	1	1.8	1	1.3	1
3	2.4	1	1.0	1	1.2	1
4	2.4	2	1.3	1	1.1	1
5	2.3	1	1.4	1	1.5	1
6	2.1	2	0.9	1	1.1	1
7	2.1	2	2.1	1	x	x
Mean	2.3	1.4	1.5	1.3	1.4	1.0

*Porous + nonporous HA.

muscular injection of antibiotic at a dose of 30 mg/kg (amoxicillin, Servipharm) to control infection.

Specimen Preparation

Three months after implant placement, mucoperiosteal flaps were raised to expose the surgical sites. The titanium caps were carefully removed and the sites were covered by repositioned flaps. Two months later, the animals were sacrificed, and the augmented new bone was retrieved en bloc, fixed in 10% formalin for 10 to 14 days, then decalcified in 5% formic acid. It normally took a few weeks for the specimens to be decalcified. Ammonium oxalate was used to verify complete decalcification. Following decalcification in 5% formic acid, the specimens were processed for routine paraffin embedding. Coronal sections were cut at a thickness of 7 µm. The cuts were made through the center of the augmented tissue. Alternate slides were stained with hematoxylin-eosin and trichrome.

Histologic Evaluation

Three sections from specimens with the greatest defect diameter were selected randomly from each site for further measurements. To study the effect of the various bone grafts on the stability of vertically augmented tissue, the highest point of the augmented tissue was measured directly with a Boley gauge. Bone healing was evaluated by a semiquantitative bone score according to the relative proportion of newly formed bone in the dome. Scores of 0, 1, 2, and 3 represented 0%, < 25%, 25% to 50%, and > 75% new bone, respectively.

Statistical Analysis

Two dependent variables—the height of newly formed bone and the relative proportion of new bone—were analyzed. Individual specimens were assayed in triplicate. Differences among means for all experiments were analyzed using the Student *t* test for matched-pair parametric data and the Wilcoxon matched-pairs, signed-ranks test for nonparametric data (bone scores).

RESULTS

Healing was uneventful in all animals. Three months after graft placement, the capsules were removed. Dome-shaped bonelike tissue had formed on the cranium in all specimens (Fig 2). The new tissue felt rather hard by palpation and looked similar among all groups. Some specimens augmented with the nonresorbable HA fractured at the time of cap removal, which indicated that these newly formed tissues were rigid and less flexible. These specimens were excluded from the calculations. Data from the nonresorbable porous and nonporous HA groups were pooled together for further analysis.

Two months following cap removal, the mean height of augmented tissue for the nonresorbable HA, resorbable HA, and controls was 2.3, 1.5, and 1.4 mm, respectively (Table 1). The dome-shaped bone tissue appeared resorbed and flattened in both resorbable HA and control sites. In groups grafted with resorbable or nonresorbable HA materials, the HA particles



Fig 3 Following removal of the titanium caps, newly augmented tissue was covered by repositioned flaps. Two months later, the animals were sacrificed and augmented new bone was retrieved en bloc. The sites grafted with (above) porous (PHA) and nonporous nonresorbable HA (NHA) remained stable. However, the two sites (below) grafted with resorbable nonporous HA (RHA) and no graft (control) showed different degrees of tissue resorption.

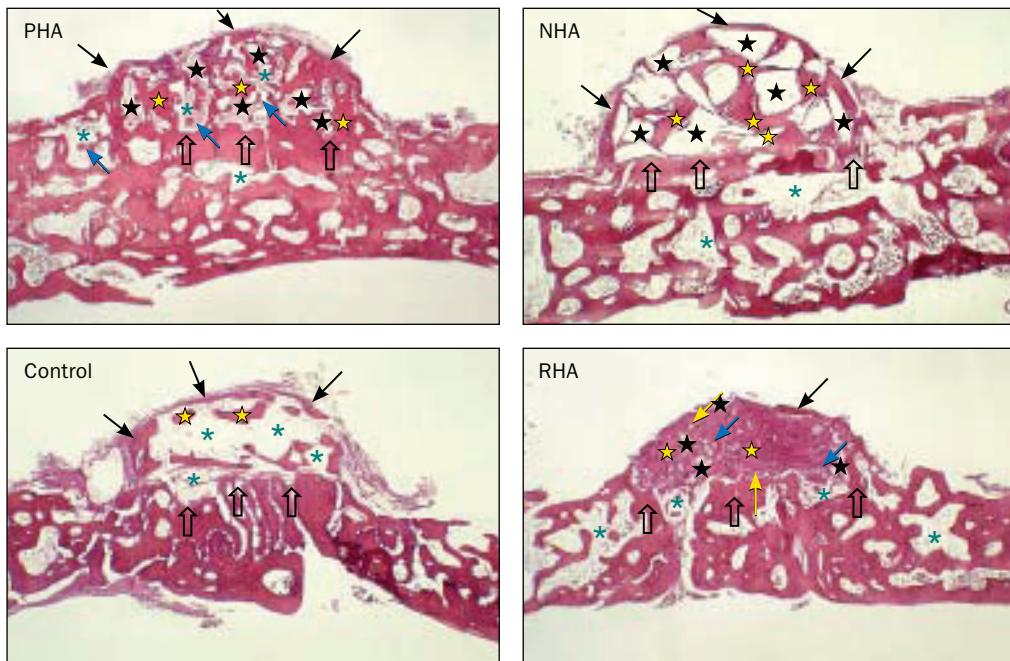


Fig 4 Effects of the different graft materials on the stability of newly augmented tissue. Two months after following cap removal, different amounts of tissue resorption were observed at sites grafted with different alloplast materials. Most augmented tissue contained less than 25% new bone. In the specimens of all groups, bone formation could be seen in the upper periphery of the dome-shaped tissue (arrows). In the nonresorbable HA-grafted animals (PHA, NHA), the newly formed bone (yellow star) had grown in continuity with the host bone (hollow arrow). New bone with marrow and vascular elements had grown into the inner space (yellow arrow) of the porous PHA particles (black star). In the specimens of the nonporous HA-implanted animals (NHA, RHA), the newly formed bone, with minimum bone marrow space, was in continuity with HA particles. With resorbable HA (RHA), the new bone appeared to be more of a replacement of the graft materials. The newly formed tissue had undergone an enormous amount of remodeling. Graft particles (black star) could be observed that were either surrounded by osteoclasts (blue arrow) or incorporated into a provisional matrix that harbored large amounts of osteoblastlike cells (yellow arrow). In the center of the biomaterials, foci of mineralized tissue could be identified. In the control specimens, new bone had grown in continuity with the host bone. The new bone consisted of mature lamellar bone with a trabecular pattern and large marrow spaces filled with fat cells and vascular elements (asterisk) (hematoxylin and eosin).

on newly formed bonelike tissue were distinguishable (Fig 3). Most augmented tissue contained less than 25% new bone (Fig 4). No statistically significant differences in bone scores were noted among the experimental groups. The height of augmented new tissue in sites treated with nonresorbable HA was significantly greater than in the other groups ($P < .01$, Fig 5).

There were no signs of progressive resorption of the particles or foreign-body reactions around any par-

ticles. The bone tended to form through apposition on nonresorbable HA particles. In the animals grafted with nonresorbable HA, the newly formed bone had grown in direct contact with the grafted particles, which in many cases were totally incorporated into the bone. In most specimens, bone formation could be found in the upper periphery of the dome-shaped tissue, with minimal marrow space. In the specimens implanted with RHA and NHA, the newly formed bone

in the space originally created by the capsules was in continuity with the host bone. The newly formed tissue had undergone an enormous amount of remodeling. With resorbable HA, the new bone appeared to be more of a replacement of the graft materials. Graft particles could be observed that were either surrounded by osteoclasts or incorporated into a provisional matrix that harbored large amounts of osteoblastlike cells. In the center of the biomaterials, foci of mineralized tissue could be identified. In the control specimens, new bone had grown in continuity with the host bone. The new bone consisted of lamellar mature bone with a trabecular pattern and large marrow spaces filled with fat cells and vascular elements.

DISCUSSION

Data from this experiment suggested that, while new bone developed in all groups, the new tissue in sites grafted with resorbable HA and controls was less stable. Factors affecting the stability of augmented tissue may include different bone type (intramembranous or long bone), the use of various barrier and graft materials, type and size of osseous defects, healing time, and animal model.

The barriers utilized in this study were titanium caps, and all groups promoted supracrural bone augmentation. Rigid, nonresorbable materials with space-making ability appeared to result in a greater amount of vertical bone augmentation than resorbable materials. However, these newly formed tissues were rigid and less flexible. The possible impact of this correlation on the osseointegration process and long-term success of dental implants is unclear.

In a rat mandibular ramus model, Mardas et al evaluated the effect of demineralized bone matrix on vertical bone augmentation through the use of either cell-permeable (height 2.5 mm) or nonpermeable (0.3 mm needle holes) e-PTFE capsules. After 1, 2, and 4 months of healing, new bone volume was measured histometrically.²⁵ Similar to the present study, the authors showed that after 4 months of healing, new bone had formed in both groups, and no significant difference in the percentage of newly formed bone was found.

Yamada et al used a different animal model, a different defect size (height 4 mm), and titanium caps with different-sized holes (1.5 mm) to evaluate the effects of the occlusive nature of the titanium cap on bone regeneration beyond the skeletal envelope in a rabbit skull model. The titanium caps were filled with peripheral blood only and fitted onto the calvaria.²⁶ Rabbits were sacrificed after 1 or 3 months of healing, and mineralized new bone was measured histologically. After 3 months of healing, more new tissue had formed under nonper-

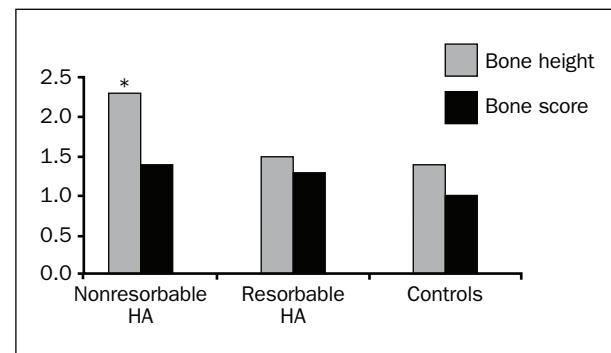


Fig 5 Effect of different alloplast materials on the stability of newly augmented tissue. The height of augmented new tissue in the sites treated with nonresorbable HA were significantly greater than that seen in the other groups (* $P < .01$).

forated caps (90%) than under perforated caps (56%). More mineralized new bone was generated under nonperforated caps (34%) than under perforated ones (24%). In addition to different animal model and defect size, one may speculate that the difference between these two studies could be explained by whether the defects were filled with grafting materials or not. While bone grafting materials may have the osteoconductive ability to enhance the volume of bone augmentation, they unfortunately may retard new bone formation.²⁷

Barboza et al studied the effect of recombinant human bone morphogenetic protein 2 in an absorbable collagen sponge (rhBMP-2/ACS) or rhBMP-2/ACS combined with HA on the reconstruction of class III alveolar defects in dogs.²⁷ Twelve weeks after augmentation, limited bone formation was observed following implantation of rhBMP-2/ACS (0.7 ± 0.6 mm). In contrast, sites that received rhBMP-2/ACS with HA exhibited clinically relevant ridge augmentation (5.5 ± 1.6 mm). Defects implanted with rhBMP-2/ACS exhibited no evidence of expansion into the defect area. Defects that received rhBMP-2/ACS with HA exhibited sparse bone trabeculae amidst HA particles, fibrovascular tissue, and marrow. The results suggested that ACS did not have sufficient structural strength to withstand soft tissue compression at specific anatomic sites and, alone, had a limited effect in this augmentation model of class III alveolar ridge defects. Inclusion of HA in the rhBMP-2 construct resulted in significantly greater bone augmentation; however, the quality of bone was compromised. In addition, the stability of the augmented new tissues is of greater clinical concern.

Similar to the present findings, resorption of the newly augmented tissue by guided tissue regeneration has been demonstrated in studies of peri-implant tissue augmentation, lateral ridge augmentation, sinus augmentation, and vertical ridge augmentation.

Rasmusson et al placed Bränemark-type implants in the tibial metaphyses of 12 rabbits with five threads exposed and treated the exposed areas with e-PTFE and titanium devices without bone grafting materials.²⁸ The membranes were removed after 2 months and the sites were observed for 16 more weeks. Impressions and study models were obtained to evaluate dimensional changes. Histologic specimens were examined to determine bone maturation. It was found that bone volume decreased by 45% during the 16-week follow-up period after barrier removal. Healing of long bone may be different from that of intramembranous bone such as calvaria; therefore, extrapolation of data from long bone to intramembranous bone must be done with caution. Araujo et al studied lateral ridge augmentation in dogs. Defects were grafted with autogenous bone blocks (8 mm in diameter, 3 mm thick) or xenogeneic onlay graft, then covered with collagen membrane.²⁹ Results showed that only 43% of autografts were retained at 6 months, while xenogeneic onlay grafts maintained their volume during healing but only 23% new bone formed within the grafted area. Although autografts provided significantly more new bone, the mineral bone block appeared to provide more volume and better stability of the augmented tissue. Bragger et al investigated the radiographic tissue remodeling around the augmented sinus using an osteotome technique. Results indicated that the mean distance between the implant apex and the initial sinus floor was 4.0 mm.³⁰ The mean height of the new bone reaching apically to the implant was 1.5 mm at surgery but had decreased significantly to 1.2 mm at 3 months and to 0.3 mm after 12 months as the graft area apical to the implants underwent shrinkage and remodeling. In a rabbit calvarial model, van Steenberghe et al studied vertical bone formation beyond a skull envelope treated with a titanium dome (height 6 mm).³¹ No grafting materials were used. The titanium domes were removed 3 months after surgery, and the animals were sacrificed 3 or 9 months later. Data indicated that 75% and 59% of the newly created tissue volume was maintained after 3 and 9 months, respectively.

In contrast to the present findings, the augmented tissue of empty control sites from the studies of Lioubavina et al and Stavropoulos et al showed minimal resorption 6 months after reentry. Possible reasons for the different results may be the different defect types and sizes or the inclusion of sufficient healing time (6 to 12 months) for bone stabilization and remodeling.^{32,33} In addition, rodents may have greater bone healing potential than rabbits. Lioubavina et al placed nonporous oval-shaped e-PTFE capsules (4 mm in height) in thirty 6-month-old albino rats using a mandibular ramus model. The caps were removed after 6 months of healing and the rats continued to heal for 3, 6, 9, and

12 months. The periosteum was preserved at test sites and denuded at control sites. Histology and subtraction radiography were used to evaluate new bone formation. Less than 4% to 8% of the augmented tissue had resorbed 12 months after removal of the capsules, regardless of the presence or absence of the periosteum. In a similar model, Stavropoulos et al evaluated the fate of vertically augmented and new bone in rigid hemispheric e-PTFE (3-mm-high) capsules with or without grafting with Bio-Oss or Biogran. After 1 year, the capsules were removed. Bone volume was measured immediately after capsule removal and at 3 or 6 months after reentry. The mean volume percentages of newly formed bone were 23%, 13%, and 94% of the original capsule spaces grafted with Bio-Oss, Biogran, and no grafting material, respectively. Six months after capsule removal, the corresponding values were 22%, 13%, and 92%, respectively.

Data from the present experiment indicated that while all the tested materials predictably formed new bone, the new tissue at the control sites and that augmented by resorbable HA were less stable. Ideal graft materials should exhibit osteoinductive ability, immediate osteogenesis, good physical stability, safety, unlimited supply, predictable clinical success, and long-term stability. While nonresorbable HA materials are not osteoinductive and thus cannot be replaced by new bone, they are safe, stable, and do not require a second surgical site (as with autografts). An increasing variety of synthetic and natural bone grafting materials is being marketed.³⁴ However, most manufacturers proclaim the usefulness of their products without satisfactory scientific evidence. Methods for evaluating the effects of these materials should be developed and standardized.³⁵ In addition, little information is available concerning the relative biologic activity and comparative efficacy of different grafting materials, both *in vitro* and *in vivo*.^{13,36,37} Furthermore, most available grafting materials have a limited ability to induce or accelerate new bone maturation and mineralization. Recent advanced tissue engineering approaches have incorporated recombinant growth factors, adhesive proteins, or gene therapy into grafting procedures to accelerate bone maturation and mineralization.³⁸

CONCLUSIONS

Data from this experiment indicated that, while all tested materials conducted new bone formation predictably, the new tissue augmented by resorbable hydroxyapatite, as well as that produced in unfilled control sites, was less stable. Further investigations are encouraged to discover new materials and techniques that enhance the long-term stability of vertically augmented tissue.

ACKNOWLEDGMENTS

The authors reported no conflicts of interest related to this study.

REFERENCES

1. Dahlin C, Senneryby L, Lekholm U, Linde A, Nyman S. Generation of new bone around titanium implants using a membrane technique: An experimental study in rabbits. *Int J Oral Maxillofac Implants* 1989;4:19–25.
2. Nyman S, Lang NP, Buser D, Bragger U. Bone regeneration adjacent to titanium dental implants using guided tissue regeneration: A report of two cases. *Int J Oral Maxillofac Implants* 1990;5:9–14.
3. Dahlin C, Andersson L, Lindhe A. Bone augmentation at fenestrated implants by an osteopromotive membrane technique. *Clin Oral Implants Res* 1991;2:159–165.
4. Jovanovic SA, Spiekermann H, Richter EJ. Bone regeneration around titanium dental implants in dehisced defect sites: A clinical study. *Int J Oral Maxillofac Implants* 1992;7:233–245.
5. Mellonig JT, Nevins M. Guided bone regeneration of bone defects associated with implants. *Int J Periodontics Restorative Dent* 1995; 15:168–185.
6. Simion M, Trisi P, Piattelli A. Vertical ridge augmentation using a membrane technique associated with osseointegrated implants. *Int J Periodontics Restorative Dent* 1994;14:497–511.
7. Jovanovic SA, Schenk RK, Orsini M, Kenney EB. Supracrestal bone formation around dental implants: An experimental dog study. *Int J Oral Maxillofac Implants* 1995;10:23–31.
8. Linde A, Thoren C, Dahlin C, Sandberg E. Creation of new bone by an osteopromotive membrane technique. An experimental study in dogs. *J Oral Maxillofac Surg* 1993;51:892–897.
9. Kostopoulos L, Karring T. Augmentation of the rat mandible using guided tissue regeneration. *Clin Oral Implants Res* 1994;5:75–82.
10. Lundgren D, Lundgren AK, Senneryby L, Nyman S. Augmentation of intramembranous bone beyond the skeletal envelope using an occlusive titanium barrier. *Clin Oral Implants Res* 1995;6:67–72.
11. Kostopoulos L, Karring T, Uraguchi R. Augmentation of the rat mandible using guided tissue regeneration. *Clin Oral Implants Res* 1994;5:245–253.
12. Kostopoulos L, Karring T. Role of periosteum in the formation of jaw bone. *J Clin Periodontol* 1995;22:247–254.
13. Jensen SS, Aaboe M, Pinholt EM, Hjortsgård-Hansen E, Melsen F, Ruyter IE. Tissue reaction and material characteristics of four bone substitutes. *Int J Oral Maxillofac Implants* 1996;11:55–66.
14. Tinti C, Parma-Benfenati S, Polizzi G. Vertical ridge augmentation: What is the limit? *Int J Periodontics Restorative Dent* 1996;16: 221–229.
15. Tinti C, Parma-Benfenati S. Vertical ridge augmentation: Surgical protocol and retrospective evaluation of 48 consecutively inserted implants. *Int J Periodontics Restorative Dent* 1998;18:435–443.
16. Yukna RA, Mayer ET, Brite DV. Longitudinal evaluation of Duraparaffin ceramic as an alloplastic implant in periodontal osseous defects after 3 years. *J Periodontol* 1984;55:633–637.
17. Begley CT, Doherty MJ, Mollan RAB, Wilson DJ. Comparative study of the osteoconductive properties of bioceramic, coral, and processed bone graft substitutes. *Biomaterials* 1995;16:1181–1185.
18. Wetzel AC, Stich H, Caffesse RG. Bone apposition onto oral implants in the sinus area filled with different grafting materials. A histologic study in beagle dogs. *Clin Oral Implants Res* 1995;6:155–163.
19. Hurzeler MB, Kirsch A, Ackermann K-L, Quinones CR. Reconstruction of the severely resorbed maxilla with dental implants in the augmented maxillary sinus: A 5-year clinical investigation. *Int J Oral Maxillofac Implants* 1997;11:466–475.
20. Hurzeler MB, Quinones CR, Kirsch A, Schupbach P, Krause A, Strub JR, Caffesse RG. Maxillary sinus augmentation using different grafting materials and dental implants in monkeys. Part III. Evaluation of autogenous bone combined with porous hydroxyapatite. *Clin Oral Implants Res* 1997;8:401–411.
21. Holmes R, Mooney V, Bucholz R, Tencer A. A coralline hydroxyapatite bone graft substitute. Preliminary reports. *Clin Orthop Relat Res* 1984;188:252–262.
22. Kenney EB, Lekovic V, Han T, Carranza FA Jr, Dimitrijevic B. The use of a porous hydroxyapatite implant in periodontal defects. I. Clinical results after 6 months. *J Periodontol* 1985;56:82–88.
23. Martin RB, Chapman MW, Holms RE, Sartoris DJ, Shors EC, Gordon JE, et al. Effects of bone ingrowth on the strength and non-invasive assessment of a coralline hydroxyapatite material. *Biomaterials* 1989;10:481–488.
24. Martin RB, Chapman MW, Sharkey NA, Zissimos SL, Bay B, Shors EC. Bone ingrowth and mechanical properties of coralline hydroxyapatite 1 year after implantation. *Biomaterials* 1993;14:342–348.
25. Mardas N, Kostopoulos L, Stavropoulos L, Karring T. Evaluation of a cell-permeable barrier for guided tissue regeneration combined with demineralized bone matrix. *Clin Oral Implants Res* 2003;14: 812–818.
26. Yamada Y, Nanba K, Ito K. Effects of occlusiveness of a titanium cap on bone generation beyond the skeletal envelope in the rabbit calvarium. *Clin Oral Implants Res* 2003;14:455–463.
27. Barboza EP, Duarte ME, Geolás L, Sorensen RG, Riedel GE, Wiksöö UM. Ridge augmentation following implantation of recombinant human bone morphogenetic protein-2 in the dog. *J Periodontol* 2000;71:488–496.
28. Rasmusson L, Senneryby L, Lundgren D, Nyman S. Morphological and dimensional changes after barrier removal in bone formed beyond the skeletal borders at titanium implants. A kinetic study in the rabbit tibia. *Clin Oral Implants Res* 1997;8:103–116.
29. Araujo MG, Sonohara M, Hayacibara R, Cardaropoli G, Lindhe J. Lateral ridge augmentation by the use of grafts comprised of autologous bone or a biomaterial. An experiment in the dog. *J Clin Periodontol* 2002;29:1122–1131.
30. Bragger U, Gerber C, Joss A, Haenni S, Meier A, Hashorva E, et al. Patterns of tissue remodeling after placement of ITI dental implants using an osteotome technique: A longitudinal radiographic case cohort study. *Clin Oral Implants Res* 2004;15:158–166.
31. Van Steenberghe D, Johansson C, Quirynen M, Molly L, Albrektson T, Naert I. Bone augmentation by means of a stiff occlusive titanium barrier. A study in rabbits and humans. *Clin Oral Implants Res* 2003; 14:63–71.
32. Lioubavina N, Kostopoulos L, Wenzel A, Karring T. Long-term stability of the study of experimental “guided tissue regeneration.” *Clin Oral Implants Res* 1999;10:477–486.
33. Stavropoulos A, Kostopoulos L, Nyengaard JR, Karring T. Fate of bone formed by guided tissue regeneration with or without grafting of Bio-Oss or Biogran. *J Clin Periodontol* 2004;31:30–39.
34. Reddi AH. Symbiosis of biotechnology and biomaterials: Applications in tissue engineering of bone and cartilage. *J Cellular Biochem* 1994;56:192–195.
35. Schwartz Z, Mellonig JT, Carnes DL Jr, de la Fontaine J, Cochran DL, Dean DD, et al. Ability of commercial demineralized freeze-dried bone allograft to induce new bone formation. *J Periodontol* 1996;67:918–926.
36. Zamboni G, Grano M. Biomaterials in orthopaedic surgery: Effects of different hydroxyapatites and demineralized bone matrix on proliferation rate and bone matrix synthesis by human osteoblasts. *Biomaterials* 1995;16:397–402.
37. Schwartz Z, Somers A, Mellonig JT, Carnes DL Jr, Dean DD, Cochran DL, et al. Ability of commercial demineralized freeze-dried bone allograft to induce new bone formation is dependent on donor age but not gender. *J Periodontol* 1998;69:470–478.
38. Mao JJ, Giannobile WV, Helms JA, Hollister SJ, Krebsbach PH, Longaker MT, et al. Craniofacial tissue engineering by stem cells. *J Dent Res* 2006;85(11):966–979.

Increased Intraosseous Temperature Caused by Ultrasonic Devices During Bone Surgery and the Influences of Working Pressure and Cooling Irrigation

Falk Birkenfeld, DMD¹/Merlind Erika Becker, DMD²/Sönke Harder, DMD²/
Ralph Lucius, MD, PhD³/Matthias Kern, DMD, PhD⁴

Purpose: The purpose of this study was to investigate the increases in intraosseous temperature generated by a modern ultrasonic device for bone surgery (UDBS) and the influences of working pressure and cooling irrigation on this temperature. **Materials and Methods:** Twenty human mandibular bone specimens ($20 \times 15 \times 5$ to 7 mm) were used; three vertical cuts were performed for a duration of 12 seconds per cut. Each bone specimen was machined with a different combination of working pressure (1.5, 2.0, 3.0, 4.0, or 6.0 N) and cooling irrigation (0, 30, 60, or 90 mL/min), and intraosseous temperatures were measured. Harmful temperature development was defined as an increase of more than 10°C for the 75th percentile and/or a maximum increase of more than 15°C . Cutting performance was also measured. **Results:** Harmless intraosseous temperature development was identified for working pressures of 1.5 N and 2.0 N with cooling irrigations of 30, 60, and 90 mL/min and for 3.0 N at 90 mL/min. The maximum temperature observed was 72°C (6.0 N with 60 mL/min). The mean cutting performance values were 0.21 ± 0.02 mm/s for 6.0 N, 0.21 ± 0.06 mm/s for 3.0 N, 0.20 ± 0.01 mm/s for 4.0 N, 0.11 ± 0.05 mm/s for 1.5 N, and 0.08 ± 0.03 mm/s for 2.0 N. **Conclusions:** To prevent tissue damage in dental bone surgery, a minimum coolant amount of 30 mL/min is recommended. The working pressure should be chosen with great care because of its significant influence on intraosseous temperature. Doubling of the working pressure from 1.5 to 3.0 N requires a tripling of the coolant (30 to 90 mL/min) to prevent tissue damage. A working pressure above 3.0 N did not result in improved cutting performance. *INT J ORAL MAXILLOFAC IMPLANTS* 2012;27:1382–1388

Key words: cutting performance, intraosseous temperature development, ultrasonic bone surgery

To ensure the success of dental implant therapy, it is necessary to reconstruct atrophic areas with a lack of bone volume.¹ In sinus elevation operations, a bony window osteotomy of the maxilla is performed.² Most autologous bone grafts are prepared in the mandible using the mental region or retromolar area as donor sites. In these areas, the alveolar nerve is threatened by the instruments used for bone harvesting.^{3–5} In the maxilla, the sinus membrane must remain intact after

the access hole is prepared to achieve adequate sinus elevation.^{6,7} Conventional surgical instruments, such as drilling or rotary instruments, may affect the soft tissues. Therefore, adequate results usually depend on the experience of the surgeon. Ultrasonic devices for bone surgery (UDBS) are alternatives to rotary drilling devices and have been used in oral surgery for the past decade.⁸ The low amplitude (300 μm) and frequency (30 kHz) of the microvibrations produced by UDBS allow for selective cutting of hard tissue and minimize potential harm to soft tissues (eg, the alveolar nerve or the maxillary sinus membrane). The use of UDBS may therefore reduce intraoperative problems associated with soft tissue damage.^{7,9–15} Furthermore, UDBS permits the survival of osteocytes and other cells during bone harvesting.^{16,17}

Another problem with bone drilling is that it increases the bone temperature. Several studies have emphasized the importance of cooling irrigation when using rotary and drilling devices.^{18–20} Intraosseous bone temperatures between 40°C and 49°C may result in acute hyperemia, and at a temperature of 50°C , blood flow is reduced. Irreversible resorption

¹Assistant Professor, Institute of Anatomy, Christian-Albrechts University of Kiel, Germany.

²Assistant Professor, Dental School, Department of Prosthodontics, Propaedeutics and Dental Materials, Christian-Albrechts University of Kiel, Germany.

³Professor, Institute of Anatomy, Christian-Albrechts University of Kiel, Germany.

⁴Professor, Dental School, Department of Prosthodontics, Propaedeutics and Dental Materials, Christian-Albrechts University of Kiel, Germany.

Correspondence to: Dr Falk Birkenfeld, Otto-Hahn-Platz 8, 24118 Kiel, Germany. Fax: +49-431-8801557.
Email: f.birkenfeld@anat.uni-kiel.de

of approximately 20% to 30% of the bone is observed as a long-term effect after application of intraosseous bone temperatures of 50°C for 60 seconds and 47°C for 5 minutes.²¹ Harder et al²² investigated the increases in intraosseous temperature during the use of three different UDBS in a bovine femur (temperature increase: approximately 2°C) with the devices used at a working pressure of 3.0 N with 50 mL/min of cooling irrigation.

Because limited data are available on the increase in intraosseous temperature associated with UDBS at different working pressures and cooling irrigations in human mandibular bone, the purpose of this *in vitro* study was to evaluate the influence of the applied pressure and the amount of cooling liquid on the increase in intraosseous temperature and cutting performance.

MATERIALS AND METHODS

For this study, seven human mandibles were used (six women, one man; mean age at time of death: 84.4 ± 8.8 years). All of the bone specimens were taken from body donors at the Institute of Anatomy of the Christian-Albrechts-University at Kiel. The cadavers were used according to the institutionally and nationally available ethical legislative frameworks.²³

The unfixed mandibles had been stored frozen (mean storage period: 11.4 ± 6.5 months; mean time of death prior to freezing: 24 ± 6 hours). Twenty bone specimens (20 × 15 × 5 to 7 mm) were removed from the mental region of the seven mandibles. The cortical bone between the tooth socket and the mandibular border was used. The specimens were prepared using a hand saw (Emil Lux, no. 521501; stainless steel saw blade, 0.4 mm in width, 2.3 mm between saw teeth) with ample saline cooling. Sawing was performed slowly to prevent heating of the cutting edges.

The bone specimens were randomly divided into five groups of different working pressures (1.5, 2.0, 3.0, 4.0, and 6.0 N) and were randomly subdivided into groups with different rates of cooling irrigation with sterile saline solution (0, 30, 60, and 90 mL/min) that had been stored at room temperature (21°C).

In this study, the Piezotome II with a BS 1 working tip (ACTEON-Satelec) was used for vertical cuts for 12 seconds per cut. The operating frequency of the UDBS was between 28 and 36 kHz, and the power rating was 55 W. For each of the five different working pressures, a BS 1 working tip was used, and all cuts were performed with the different cooling irrigations.

Four hours before the test procedure was begun, the bone specimens were thawed and embedded in plaster (Fujirock EP, GC Germany) in a plastic box.

Figure 1 shows the experimental setup, which consisted of a specially designed lifting device (Isel-

Hubvorrichtung, Isel-Automation). The lifting device included a vertically movable carriage in which the handpiece of the UDBS could be mounted. Both the specimen and the handpiece were fixed with screw clamps. The working pressure was applied by placing a corresponding weight near the center of the vertical carriage. To compensate for the weight of the mounted UDBS handpiece, the vertical carriage was balanced by a counterweight.

Test Procedures

Test procedures were performed at room temperature (21°C) as described by Harder et al.²⁴ The bone specimens were placed on the horizontal carriage beneath the working tip of the UDBS. The thermocouple was placed precisely beneath the cutting tip inside the bone specimen. To achieve optimal heat conduction between the bone and the sensor, the thermocouple was embedded in thermal conducting paste (WLP 004 thermal compound, Fischer-Elektronik) with a thermal conductivity of 0.61 W/mK. The working tip was positioned parallel to the cortical bone surface (Fig 2). The tip was brought into contact with the bone specimen by adjusting the vertical carriage of the lifting device such that a 15-μm-thick piece of shim stock foil between the tip and the bone could be removed against slight resistance. The power settings for the UDBS were set to the maximum, as recommended by the manufacturer for very dense and thick cortical bone.

Three cuts (vertical cuts for 12 seconds per cut) were performed for each working pressure/cooling irrigation combination, with intervals of 3 mm between each cut. The thermocouple was placed at a distance of about 0.5 mm from the working tip. After each cut, the thermocouple was replaced exactly beneath the cutting tip of the UDBS. Vertical movements were recorded by displacement transducers and transferred together with the temperature data to an analog-to-digital card connected to a desktop computer. Data were collected with the computer program DIAdem 10.0 (National Instruments).

Scanning Electron Microscopy

After the tests were completed, the morphology of the cutting tips was evaluated using scanning electron microscopy (SEM). The SEM images were taken with a Philips XL 20 (19-fold magnification, 15 KV; Philips).

Statistical Analysis

Statistical analysis was performed with an H test for the nonparametrically distributed (Kolmogorov-Smirnov test) intraosseous temperature data and with a t test for the normally distributed cutting performance data using the WinStat Excel Add-In (version 2007.1, R. Fitch Software) (significance level: $P \leq .05$).



Fig 1a Test setup showing the handpiece of the UDBS fixed with screw clamps. The bone specimens were mounted in the frame of the blue bowl. The working pressures were applied by placing a corresponding weight near the center of the vertical carriage. To compensate for the weight of the mounted UDBS handpiece, the vertical carriage was balanced by a counterweight.

Fig 1b The Piezotome II ultrasonic device (Acteon).

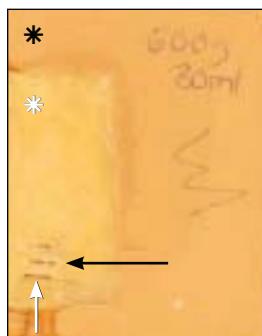


Fig 2 A bone specimen used for the test procedure (6.0 N and 30 mL/min). The black star indicates the plaster, and the white star indicates the bone specimen. The black arrow points toward the middle cut of the three performed cuts. The white arrow shows the direction and position of the thermocouple.

RESULTS

Temperature

The median values (and 25th and 75th percentiles) and maximum intraosseous temperatures measured while the bone specimens were machined with different combinations of working pressure and cooling irrigation are shown in Figs 3 and 4.

Cutting Performance

The mean values and standard deviations of the cutting performance generated by different working pressures independent of cooling irrigation are shown in Fig 5. The values for cutting performance were 0.21 ± 0.02 mm/s for 6.0 N, 0.21 ± 0.06 mm/s for 3.0 N, 0.20 ± 0.01 mm/s for 4.0 N, 0.11 ± 0.05 mm/s for 1.5 N,

and 0.08 ± 0.03 mm/s for 2.0 N. There were no significant differences in cutting performance between 1.5 N and 2.0 N. Moreover, there were also no significant differences in cutting performance among 3.0 N, 4.0 N, and 6.0 N. However, there were significant differences in cutting performance between 1.5 N and 3.0 N, and between 2.0 N and 3.0 N ($P \leq .05$).

Morphology of the Cutting Tips

Prior to being used, the morphology of each cutting tip was evaluated with SEM. The SEM picture of the BS 1 working tip showed homogenous, sharp geometry with a rough surface. The length of the cutting edge was 3.8 mm. After the test procedures, the surfaces and spikes of the tips, with the exception of a few small cavities in the spikes, appeared to be uniform (Fig 6).

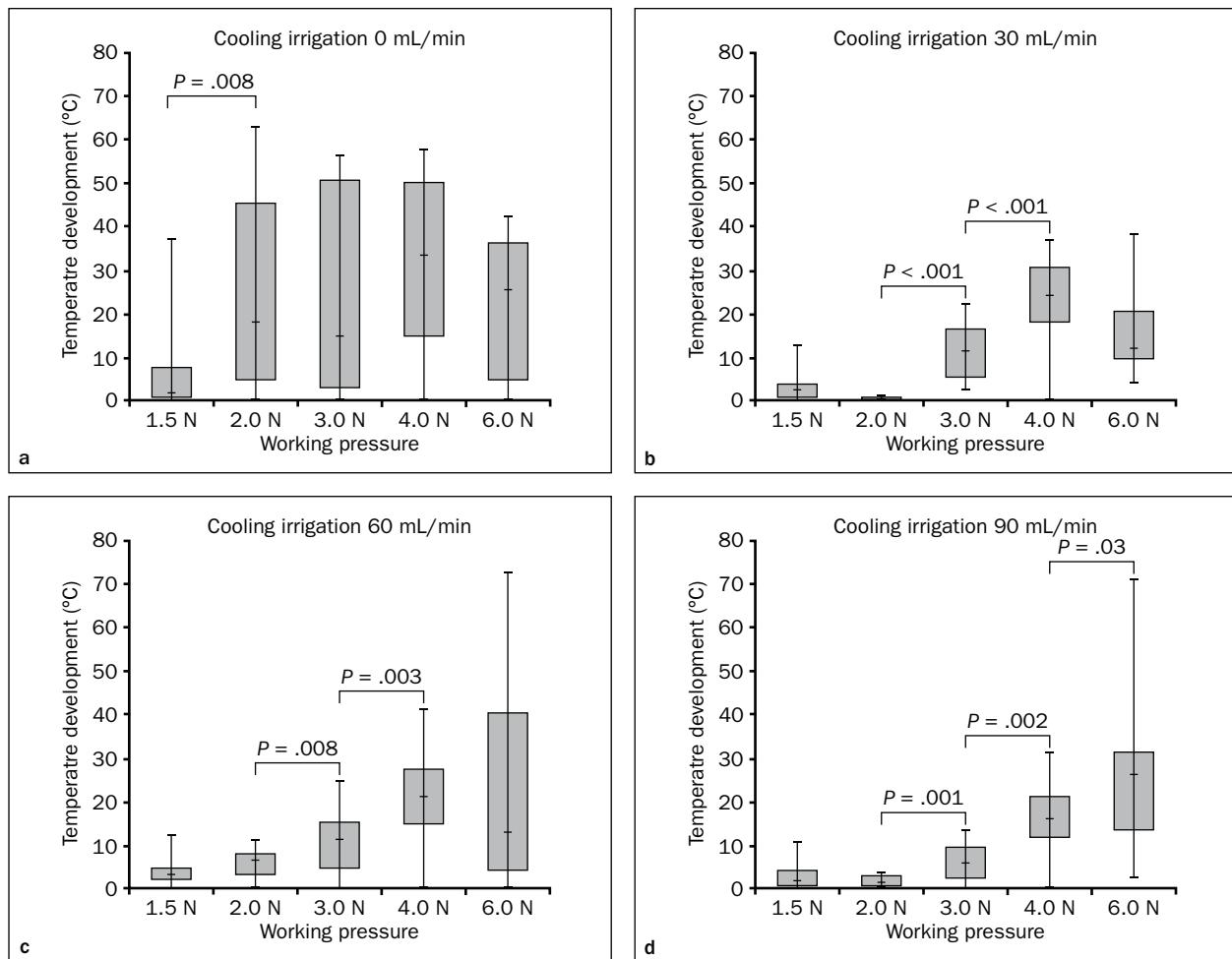


Fig 3 Box plots of the intraosseous temperature with cooling irrigation at (a) 0 mL/min, (b) 30 mL/min, (c) 60 mL/min, and (d) 90 mL/min. Significant differences are indicated by horizontal lines and P values (H test). The maximum intraosseous temperature was observed at a working pressure of 6.0 N, despite the use of the maximum level of cooling irrigation. Working pressures of 1.5 N and 2.0 N yielded the lowest intraosseous temperatures using any amount of coolant.

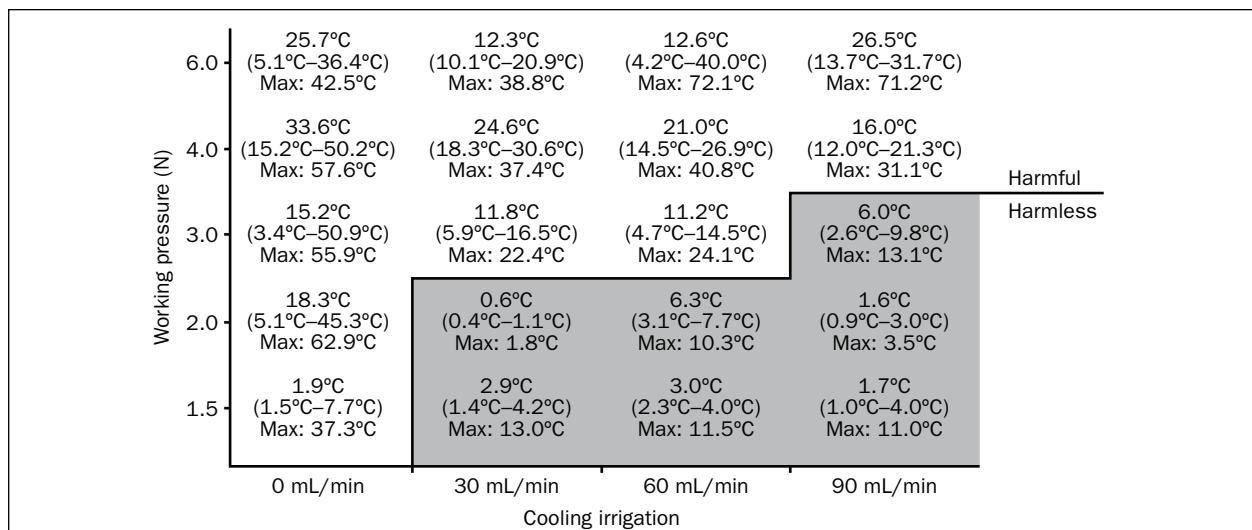


Fig 4 Overview of the measured intraosseous temperatures. Shown are the medians, the 25th and 75th percentiles, and the maximum temperatures. The ordinate shows the working pressures, and the abscissa shows the associated cooling irrigation. The black line separates the working pressure/cooling irrigation combinations that met (below the line) or exceeded (above the line) the requirements for harmless use.

Fig 5 Vertical cutting performance (means \pm standard deviations) for each UDBS setting. Significant differences are indicated by horizontal lines and P values (t test). Increasing the working pressure above 3.0 N did not increase the cutting performance.

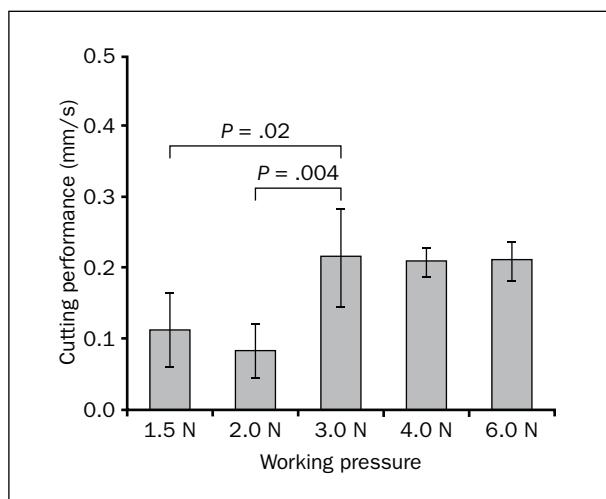
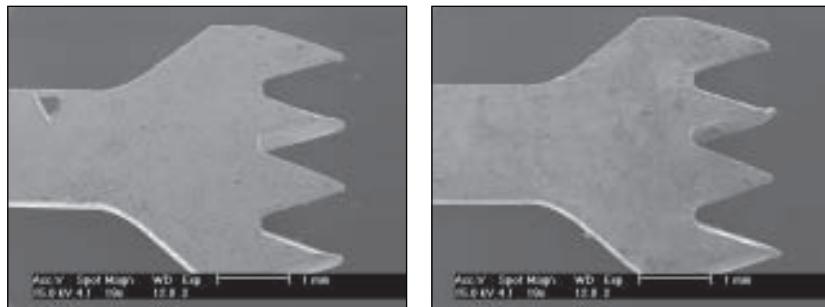


Fig 6 SEM images of (left) the unused BS 1 working tip (Acteon) and (right) the working tip after use at a working pressure of 6.0 N.



DISCUSSION

This study represents the first description of the increases in intraosseous temperature and the cutting performance of a UDBS in unfixed human mandibular bone. Based on the appropriate values for intraosseous temperature in the literature, the authors were able to develop a working protocol for the safer use of UDBS. The clinically critical temperature was described by Grunder and Strub²⁵ in a review of the international literature. It has been reported that intraosseous hyperemia occurs between 40°C and 49°C. An intraosseous temperature of 47°C that is maintained for 5 minutes results in the necrosis of lipocytes and initiates resorption processes.³ Eriksson et al²⁰ observed irreversible bone resorption after exposure to temperatures of 50°C for 1 minute at a distance of 0.5 mm from the cutting site. No resorption was found with a temperature of 44°C that was maintained for 1 minute at the same distance from the cutting site. This indicates that an increase of 10°C or less for 9 seconds (the 75th percentile) and a maximum increase of 15°C in vivo (to 47°C)

should not be harmful. Harmful intraosseous temperature was defined as an increase of over 10°C (the 75th percentile) and/or a maximum increase of more than 15°C. In this study, only seven combinations of working pressure and cooling irrigation met the minimum requirements for harmless use (Fig 4).

Since 2000, UDBS have been used in clinical practice to harvest bone for cortical augmentation in oral rehabilitations.^{7,8} There are some advantages of UDBS; for example, injury to the sinus membrane or the alveolar nerve may be prevented during surgery because of the small amplitude and the selective removal of only hard tissue. However, UDBS have operating frequencies of about 30 kHz. These frequencies may be harmful to soft tissues if the cooling irrigation is insufficient and if the working tip lingers on a single part of the bone.²⁶ The hypothesis that microvibrations generated by UDBS might influence the vitality of collected bone chips was disproven by an in vitro investigation. There was no difference in the cell proliferation time or in cell differentiation into osteoblasts compared to harvested bone chips using rotary drills.²⁶

The present data on the increases in intraosseous temperature suggest that there is a small range in which harmless surgery is possible. Working pressures of 1.5 N and 2.0 N with a minimum of 30 mL/min cooling irrigation fulfilled the requirements for harmless intraosseous temperature. However, a working pressure of 3.0 N, which clinicians are often tempted to use,²⁴ fulfilled the harmless application criteria only in combination with a cooling irrigation of 90 mL/min.

Vertical cutting was performed for 12 seconds without any horizontal movement. Translating this to the 3.8-mm width of the working tip, the cutting time corresponded to the time required to perform a piezoelectric bony osteotomy.⁷ However, during an osteotomy, the working tip is in motion, thus causing intermittent heating. Therefore, these data represent the maximal increase in intraosseous temperature produced directly at the cutting tip. The inconsistent increase in intraosseous temperature and temperature maximums may be attributed to the heterogeneous thickness of the bone specimens; however, heterogeneous thickness represents the most common application of this osteotomy technology.

Bone tissue has a low heat conductivity (0.54 to 0.58 W/mK)²⁷; therefore, the intraosseous heat generated by cutting tips of UDBS dissipates rather slowly. This, in combination with the low value of thermal diffusivity ($\alpha = 4.4$ to 5.6×10^{-7} m²/s),²⁸ could result in a high temperature gradient in the bone area between the cutting edge and the thermocouple. Bone is anisotropic in its structural and mechanical properties, but little is known about the influence of anisotropy on its thermophysical properties. Zelenov observed higher conductivity and diffusivity in the longitudinal direction than in the transverse direction. A higher diffusivity in the longitudinal direction would lead to higher temperatures at the thermocouple.²⁹

A different degree of bone mineralization of the bone tissue and different humidity ratio may also influence the intraosseous temperature development. A higher degree of mineralization or a lower amount of hydration results in about a fourfold lower thermal diffusivity, which leads to a high temperature gradient.²⁵ The blood supply with different sizes of blood vessels may also bias the intraosseous temperature. Larger vessels are constantly cooled off by the passage of well-tempered blood of the mandible; therefore, the present results represent maximal values without cooling by the blood supply only.²¹

Harder et al²⁴ investigated the increase in intraosseous temperature and the cutting performance of three UDBS (Piezosurgery II, Mectron; Piezotome, Acteon; and SurgySonic, American Dental Systems). The Piezotome UDBS by Acteon, also evaluated in the current laboratory study, exhibited the lowest temperature

increase. Therefore, the authors decided to use this UDBS for the study.

The results of these cutting performance experiments suggested an optimal working pressure of 3.0 N. Increases in the working pressure to 4.0 N and 6.0 N did not result in increased performance; however, the temperature increased dramatically, and the harmless working range was exceeded at working pressures of over 4.0 N. This knowledge is important for the use of UDBS, because clinicians commonly use UDBS at a working pressure of 3.0 N in critical areas.

The evaluation of the working tip morphology showed no major alterations from any of the four cutting cycles, with only some small cavities in the spikes. The surfaces of the tips were completely intact, and the cone ends showed no deformations. The small cavities observed in the tips may not affect the intraosseous temperature; however, a noticeable deterioration of the tips was observed after 12 cuts. To maintain a low intraosseous temperature, it is important for the area of contact to be as small as possible. Rapid deterioration of the working tips may increase the risk of thermal damage. The influence of deformed oscillating bone-cutting tips on intraosseous temperature development was investigated by Fuchsberger,³⁰ who showed that these deformed tips led to a greater temperature increase and reduced cutting performance.

CONCLUSION

To prevent tissue damage in dental bone surgery when using an ultrasonic device, a minimum coolant amount of 30 mL/min is recommended. The working pressure should be chosen with great care because of the significant influence of this parameter on increased intraosseous temperature. A working pressure above 3.0 N may not enhance the cutting performance.

ACKNOWLEDGMENTS

The authors would like to thank Christopher Egert and Dr Martin Steiner for their technical assistance and Acteon for supporting this study. The authors reported no conflicts of interest related to this study.

REFERENCES

1. Schultze-Mosgau S, Keweloh M, Wilfang J, Kessler P, Neukam FW. Histomorphometric and densitometric changes in bone volume and structure after avascular bone grafting in the extremely atrophic maxilla. *Br J Oral Maxillofac Surg* 2001;39:439–447.
2. Fugazzotto PA, Vlassis J. Long-term success of sinus augmentation using various surgical approaches and grafting materials. *Int J Oral Maxillofac Implants* 1998;13:52–58.

3. Hirsch JM, Ericsson I. Maxillary sinus augmentation using mandibular bone grafts and simultaneous installation of implants. A surgical technique. *Clin Oral Implants Res* 1991;2:91–96.
4. Jensen J, Sindet-Pedersen S. Autogenous mandibular bone grafts and osseointegrated implants for reconstruction of the severely atrophied maxilla: A preliminary report. *J Oral Maxillofac Surg* 1991; 49:1277–1287.
5. Khouri F. Augmentation of the sinus floor with mandibular bone block and simultaneous implantation: A 6-year clinical investigation. *Int J Oral Maxillofac Implants* 1999;14:557–564.
6. Becker ST, Terheyden H, Steinriede A, Behrens E, Springer I, Wiltfang J. Prospective observation of 41 perforations of the Schneiderian membrane during sinus floor elevation. *Clin Oral Implants Res* 2008;19:1285–1289.
7. Vercellotti T, De Paoli S, Nevins M. The piezoelectric bony window osteotomy and sinus membrane elevation: Introduction of a new technique for simplification of the sinus augmentation procedure. *Int J Periodontics Restorative Dent* 2001;21:561–567.
8. Vercellotti T. Piezoelectric surgery in implantology: A case report—A new piezoelectric ridge expansion technique. *Int J Periodontics Restorative Dent* 2000;20:358–365.
9. Blus C, Szmkler-Moncler S. Split-crest and immediate implant placement with ultra-sonic bone surgery: A 3-year life-table analysis with 230 treated sites. *Clin Oral Implants Res* 2006;17:700–707.
10. Cady WG. Equations of piezoelectricity. *Nature* 1948;162:933.
11. Lambrecht JT. Intraoral piezo-surgery [in French, German]. *Schweiz Monatsschr Zahnmed* 2004;114:28–36.
12. Stubinger S, Kuttnerberger J, Filippi A, Sader R, Zeilhofer HF. Intra-oral piezosurgery: Preliminary results of a new technique. *J Oral Maxillofac Surg* 2005;63:1283–1287.
13. Berengo M, Bacci C, Sartori M, Perini A, Della Barbera M, Valente M. Histomorphometric evaluation of bone grafts harvested by different methods. *Minerva Stomatol* 2006;55:189–198.
14. Vercellotti T. Technological characteristics and clinical indications of piezoelectric bone surgery. *Minerva Stomatol* 2004;53:207–214.
15. Vercellotti T, Pollack AS. A new bone surgery device: Sinus grafting and periodontal surgery. *Compend Contin Educ Dent* 2006;27:319–325.
16. Guillaume B, Gaudin C, Georgeault S, Mallet R, Basle MF, Chappard D. Viability of osteocytes in bone autografts harvested for dental implantology. *Biomed Mater* 2009;4:015012.
17. Labanca M, Azzola F, Vinci R, Rodella LF. Piezoelectric surgery: Twenty years of use. *Br J Oral Maxillofac Surg* 2008;46:265–269.
18. Krause W. Bone cutting: Mechanical and thermal effects [proceedings]. *Bull Hosp Joint Dis* 1977;38:5–7.
19. Huh JB, Eckert SE, Ko SM, Choi YG. Heat transfer to the implant-bone interface during preparation of a zirconia/alumina abutment. *Int J Oral Maxillofac Implants* 2009;24:679–683.
20. Eriksson AR, Albrektsson T, Albrektsson B. Heat caused by drilling cortical bone. Temperature measured *in vivo* in patients and animals. *Acta Orthop Scand* 1984;55:629–631.
21. Eriksson AR, Albrektsson T. Temperature threshold levels for heat-induced bone tissue injury: A vital-microscopic study in the rabbit. *J Prosthet Dent* 1983;50:101–107.
22. Harder S, Wolfart S, Mehl C, Kern M. Performance of ultrasonic devices for bone surgery and associated intraosseous temperature development. *Int J Oral Maxillofac Implants* 2009;24:484–490.
23. McHanwell S, Brenner E, Chirculescu ARM, et al. The legal and ethical framework governing Body Donation in Europe: A review of current practice and recommendations for good practice. *Eur J Anat* 2008;12:1–24.
24. Harder S, Wolfart S, Mehl C, Kern M. Performance of ultrasonic devices for bone surgery and associated intraosseous temperature development. *Int J Oral Maxillofac Implants* 2009;24:484–490.
25. Grunder U, Strub JR. Problems of temperature elevation during the treatment of bone with rotating instruments—A review of the literature [in German]. *Schweiz Monatsschr Zahnmed* 1986;96: 956–969.
26. Chiriac G, Herten M, Schwarz F, Rothamel D, Becker J. Autogenous bone chips: Influence of a new piezoelectric device (Piezosurgery) on chip morphology, cell viability and differentiation. *J Clin Periodontol* 2005;32:994–999.
27. Davidson SR, James DF. Measurement of thermal conductivity of bovine cortical bone. *Med Eng Phys* 2000;22:741–747.
28. Rodriguez G, Arenas A, Sinencio F. Measurement of thermal diffusivity of bone, hydroxyapatite and metals for biomedical application. *Anal Sci* 2001;17:357–360.
29. Zelenov ES. Thermophysical properties of compact bone. *Mech Composite Mater* 1985;21:1092–1095.
30. Fuchsberger A. Effect of temperature on compact bone in saw cutting in relation to the conditions of use [in German]. *Zentralbl Chir* 1987;112:793–804.

Bone Regeneration with Rabbit Bone Marrow-Derived Mesenchymal Stem Cells and Bone Graft Materials

Ji-Eun Lee, DDS, MSD, PhD¹/Seong-Joo Heo, DDS, MSD, PhD²/Jai-Young Koak, DDS, MSD, PhD²/Seong-Kyun Kim, DDS, MSD, PhD³/Chong-Hyun Han, DDS, MSD, PhD⁴

Purpose: This study compared the bone regeneration response of different bone graft materials inside canals within anodized titanium implants in cortical and cancellous bone. **Materials and Methods:** Upper and lower transverse canals were created in anodic oxidized-surface titanium implants to serve as sites for cortical and cancellous bone regeneration, respectively. The canals were filled with bone graft materials—rabbit bone marrow-derived mesenchymal stem cells and platelet-rich plasma, xenograft, or alloplast (micro-macroporous biphasic calcium phosphate)—or left empty (as a control). Eighty implants were surgically placed into the tibiae of 20 New Zealand white rabbits. After 4 and 12 weeks of healing, histomorphometric analysis was performed to measure the newly formed bone areas (NBs) inside the canals. **Results:** Inside the upper canals, the bone graft groups provided significantly higher NBs than the control (no graft). However, there was no significant difference in NBs between the bone graft groups. Inside the lower canals, no significant difference in NBs was shown among the all groups. The NBs inside the upper canals were significantly greater than those inside the lower canals in all groups after 4 and 12 weeks, respectively. **Conclusions:** In the cortical bone, there was significant difference in bone regeneration between the control and the bone graft groups. However, there was no significant difference among the bone graft groups in cortical and cancellous bone regeneration. There was significant difference in bone regeneration between the cortical and cancellous bone regions in the all groups using the titanium canal model. INT J ORAL MAXILLOFAC IMPLANTS 2012;27:1389–1399

Key words: bone graft material, bone regeneration, mesenchymal stem cell, tissue engineering, implant canal model

Bone replacement graft materials have played an important role in regenerative dentistry for many years. Among the various techniques to reconstruct deficient alveolar bone, autogenous bone grafting (autograft) has become a predictable, well-documented surgical approach and the gold standard of care.¹ However, the use of autografts is associated with sub-

stantial morbidity, including infection, malformation, pain, and loss of function.² In addition, autografts are limited in supply, are occasionally not suitable for the proposed reconstruction because of poor tissue quality, and can be extremely difficult to shape.^{3,4} These disadvantages have led to a continuous search for suitable bone substitutes.

An ideal bone substitute should be biologically compatible, nonsupportive of local pathogens or cross-infection, and osteogenic. In addition, it should match the physical composition of natural bone trabeculae and provide scaffolding for new bone ingrowth.⁵ That is, materials that are osteogenic (the cells within a donor graft synthesize new bone at the implantation site), osteoinductive (new bone is formed through the active recruitment of host mesenchymal stem cells [MSCs] from the surrounding tissue, which differentiate into bone-forming osteoblasts), osteoconductive (vascularization and new bone formation in the transplant), and highly biocompatible are necessary.⁶

Various bone graft materials, such as allografts, xenografts, and alloplasts (substitutes), are being extensively studied as alternatives to the harvesting of autogenous bone.⁷ Allografts are tissues taken from

¹Clinical Lecturer, Department of Prosthodontics and Dental Research Institute, School of Dentistry, Seoul National University, Seoul, South Korea.

²Professor, Department of Prosthodontics and Dental Research Institute, School of Dentistry, Seoul National University, Seoul, South Korea.

³Associate Professor, Department of Prosthodontics and Dental Research Institute, School of Dentistry, Seoul National University, Seoul, South Korea.

⁴Professor, Department of Prosthodontics, Kangnam Severance Dental Hospital, College of Dentistry, Yonsei University, Seoul, South Korea.

Correspondence to: Dr Jai-Young Koak, Department of Prosthodontics and Dental Research Institute, School of Dentistry, Seoul National University, 28 Yeongun-dong, Chongno-Gu, Seoul, 110-749, South Korea. Fax: +82-2-2072-3860. Email: young21c@snu.ac.kr

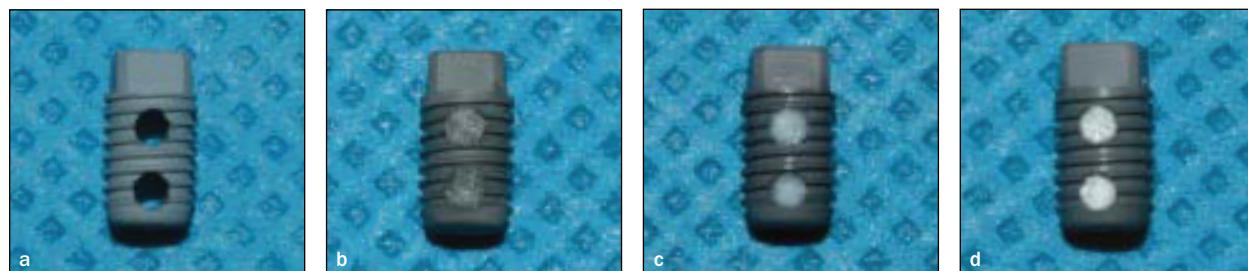


Fig 1 An image of a threaded commercial pure titanium implant with two transverse canals. The implants had a 5-mm threaded body (pitch height, 0.6 mm), a 2-mm unthreaded square top, and a 3.75-mm outer diameter. The implants had two transverse canals, each 1.5 mm in diameter, that were separated by 1.0 mm. The upper and lower transverse canals were filled with various materials (*left to right*): nothing (control), MSCs/PRP, Bio-Oss, and MBCP.

individuals of the same species as the host and are used as a source of type 1 collagen. However, such grafts have the disadvantages of limited supply and potential infectivity (eg, AIDS, hepatitis).⁸ In comparison, xenografts are derived from other species. Bovine hydroxyapatite (HA) is a type of xenograft material obtained from calf bones from which all organic components have been removed. The remaining inorganic structure is an excellent source of calcium and phosphate. It also provides a natural architectural matrix. The bone-conductive properties of bovine HA have been demonstrated in previous studies.^{9,10} Alloplastic materials, such as synthetically manufactured porous HA and tricalcium phosphate, are available in unlimited supply but have the disadvantage of possessing osteoconductivity without osteoinductive properties.^{11,12}

A promising alternative approach to bone regeneration was established by the identification of certain multipotential cells among the stromal cells of bone marrow.¹³ Many studies of tissue engineering have been conducted, and many successful studies using MSCs have been reported.^{14–16} An MSC is an undifferentiated cell that can self-replicate and differentiate into various tissues such as bone, cartilage, nerve, and tendon. It also has many abilities and functions, including immune depression. Studies have confirmed that an undifferentiated MSC can proliferate and differentiate into a desired tissue in a specific environment.^{17,18} Studies on the regeneration of bone defects using MSCs have also been reported.^{19,20}

Bone regeneration by means of tissue engineering can solve problems and disadvantages encountered in autogenous bone grafts, such as limited bone quantity and the need for additional operations. The main factors of bone regeneration using tissue engineering are MSCs, growth factors, and the presence of a three-dimensional scaffold.^{21,22} Yamada et al^{3,23} used MSCs as isolated cells and platelet-rich plasma (PRP) as the growth factor and scaffold (“tissue-engineered injectable bone”).

In the present study, bone regeneration inside canals that had been created within anodized implants

were filled with different grafting materials (MSCs/PRP, xenograft, alloplast) and evaluated. The purposes of this study were: (1) to compare the values of newly formed bone areas (NBs) among the different bone graft materials, and (2) to compare the NBs between the cortical and cancellous bone areas in all groups.

MATERIALS AND METHODS

Implant Preparation (Anodic Oxidation) and Animals

Eighty screw-shaped implants of commercially pure titanium (grade 4) were prepared. The implants had a total length of 7 mm (5 mm threaded and 2 mm unthreaded at the coronal portion), an outer diameter of 3.75 mm, and a thread pitch height of 0.6 mm. The head of the implant was square. Two transverse canals, each 1.5 mm in diameter and 1.0 mm apart, passed through the threaded part of the implant. The implants were treated with anodic oxidation at 300 V in an aqueous electrolytic solution of 0.02 mol/L calcium glycerophosphate and 0.15 mol/L calcium acetate. The implant was attached to the anode, and stainless steel was used as the cathode. All procedures were executed at room temperature, with a total time for anodic oxidation of 3 minutes per implant. The implants were then rinsed ultrasonically with distilled water and absolute alcohol for 5 minutes and dried. The anodized surface morphology was determined using field emission scanning electron microscopy (S-4700, Hitachi) at a 15-kV accelerating voltage. The anodized implants were sterilized in ethylene oxide gas before use. Four different groups were prepared according to the following procedures:

- Group 1: The two transverse canals were left empty as a control (Fig 1a).
- Group 2: The two transverse canals were filled with rabbit bone marrow-derived MSCs that had been mixed with PRP (tissue-engineered injectable bone) (Fig 1b).

- Group 3: The two transverse canals were filled with xenografts (inorganic bovine bone matrix, Bio-Oss, Geistlich Biomaterials) (Fig 1c).
- Group 4: The two transverse canals were filled with alloplasts (micro-macroporous biphasic calcium phosphate [MBCP]) (Fig 1d).

Twenty New Zealand white rabbits aged 6 to 9 months and weighing 3 to 3.5 kg each were used in this study. All of the animals were treated and handled in accordance with the "Recommendations for Handling of Laboratory Animals for Biomedical Research" compiled by the Committee on the Safety and Ethical Handling Regulations for Laboratory Animal Experiments in the College of Dentistry at Seoul National University (approval number: SNU-060615-1).

Bone Replacement Graft Materials

Tissue-Engineered Injectable Bone. Figure 2 provides a diagram of the MSCs/PRP creation process. The rabbits were housed in separate cages and fed a standard diet. Four weeks prior to implant placement surgery, bone marrow was harvested via iliac crest aspiration. During surgery, general anesthesia was induced via an intramuscular injection of 10 mg/kg Zoletil (Vibac Laboratories) and 0.15 mg/kg Rompun (Bayer Korea). The skin and cortical bone of the iliac crest were punctured with a bone marrow aspirator (Klima-Rosegger modified Luer Lock, Unimed) under local anesthesia with lidocaine (Yuhan) containing 1:100,000 epinephrine. After it was confirmed that the bone marrow aspirator was fixed, 8 to 10 mL of bone marrow was aspirated with a 10-mL syringe that contained 1 mL of heparin (Choongwae Pharm) according to a previously reported method.²⁴

The mixture of aspirated bone marrow and 15 mL of basic culture medium (low-glucose Dulbecco modified Eagle medium, 10% fetal bovine serum, and a penicillin-streptomycin mixture) were collected in a T175 flask (Nalge Nunc). The medium was changed after 24 hours to remove nonadherent cells. Subsequently, the medium was changed three times a week. Rabbit bone marrow-derived MSCs were cultured with a technique used in previous studies.³ Primary culture was performed in a humidified atmosphere of 95% air with 5% carbon dioxide at 37°C for 10 to 12 days. After primary culture, the rabbit bone marrow-derived MSCs were released from their culture substratum using 0.05% trypsin-ethylenediaminetetraacetic acid (Sigma-Aldrich). The cells were concentrated via centrifugation at 1,500 rpm for 5 minutes at room temperature and counted. The cells were divided into T175 flasks and subcultured. A quantity of 1×10^7 cells was then placed into each T175 flask, and the cells were cultured in osteogenic induction medium²⁵ (0.1 μmol/L of dexamethasone,

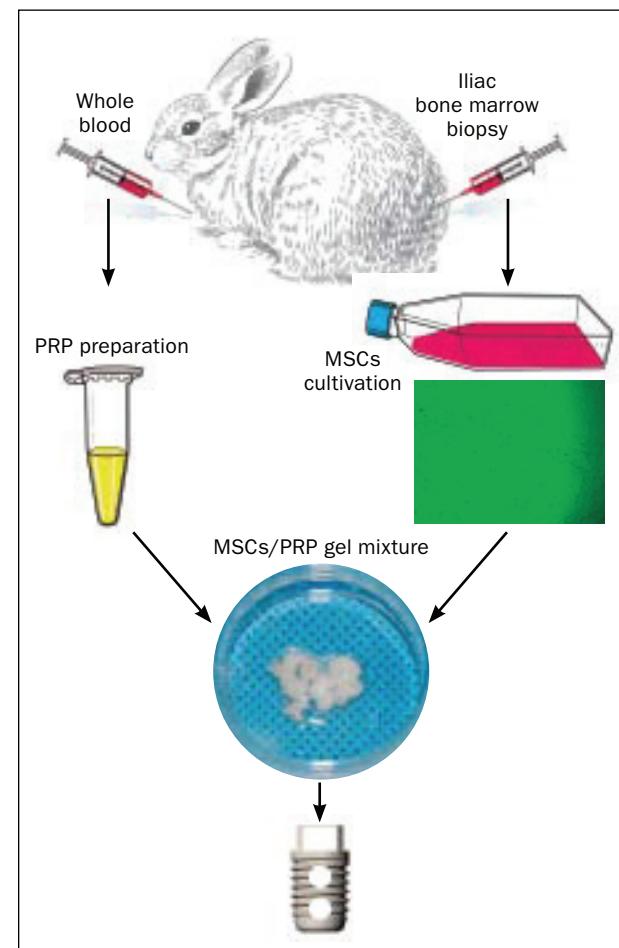


Fig 2 Schematic diagram of the MSCs/PRP group.

0.05 mmol/L of L-ascorbic acid 2-phosphate, and 10 mmol/L of β-glycerophosphate; Sigma-Aldrich) for 2 weeks. Following this, the differentiated MSCs were confirmed through the detection of alkaline phosphatase (ALP) activity using *p*-nitrophenyl phosphatase as a substrate. ALP activity was assayed as the release of *p*-nitrophenol from *p*-nitrophenyl phosphate at a pH of 10.4. The reaction was stopped after 30 minutes using 2 N sodium hydroxide, and the absorbance measurement was performed at 405 nm using an enzyme-linked immunosorbent assay reader (PowerWave X 340, BioTek Instruments). The cells were trypsinized, and 1×10^7 cells/mL were prepared for bone regeneration.

The PRP and gel were prepared according to the method developed by Yamada et al,³ in which 30 mL of whole blood were aspirated with a 50-mL syringe that contained 3 mL of 3.2% sodium citrate under general anesthesia. The sample was then centrifuged at 1,100 rpm for 10 minutes (UNION32R, Hanil Science Industrial). The supernatant that contained the buffy

coat was centrifuged again at 2,500 rpm for 5 minutes to produce a 3-mL pellet of PRP. The PRP was then stored in a conventional shaker (Unimax 1010 DT, Heidolph Instruments) until use.

After powdered thrombin (bovine thrombin, 10,000 U, Sigma-Aldrich) was dissolved into 10 mL of 10% calcium chloride solution, 100 µL of the thrombin/calcium chloride mixture was transferred to a 1-mL syringe. Separately, 600 µL of PRP and rabbit bone marrow-derived MSCs (1×10^7 cells/mL) were collected with a 1-mL syringe. The two syringes were connected with a three-way stopcock (Hyupsung Medical), and the contents were mixed. Within 30 to 60 seconds, the contents assumed a gel-like consistency, because the thrombin affected the polymerization of fibrin to produce an insoluble gel. The MSCs/PRP admixture was injected into the transverse canals of the implants using a syringe.

Other Bone Graft Materials (Xenograft and Alloplast). Anorganic bovine hydroxyapatite (Bio-Oss) is the inorganic component of bovine bone (ie, the minerals) and has a 75% to 80% porosity. All of the organic material from these bones is removed using a stepwise annealing process (up to 300°C), followed by a chemical treatment (sodium hydroxide). The remaining material is porous hydroxyapatite bone chips, the average particle size of which is 0.25 to 2 mm. This material is similar to human cancellous bone and has a crystal size of approximately 10 µm in the form of cortical granules.²⁶

Synthetic biphasic calcium phosphate (MBCP, Biomatlante) is a ceramic composed of two phases of calcium phosphate: 60% HA ($\text{Ca}_{10}[\text{PO}_4]_6[\text{O}]_2$) and 40% β-tricalcium phosphate (β-TCP; $\text{Ca}_3[\text{PO}_4]_2$). The particle sizes of the granules range between 0.5 and 1.00 mm. There are two types of porosity in MBCP: microporosity (30% to 33%, with pores ranging from 1 to 10 µm) and macroporosity (50%, with pore diameters from 300 to 600 µm). The total porosity ratio is about 70%, with micropore sizes similar to those observed in trabecular bone.²⁷

Surgical Implant Placement

Prior to surgery, the operating sites were shaved and carefully washed with iodine solution. Local anesthesia (1.0 mL of 2% lidocaine including 1:100,000 epinephrine, Yu-han) was injected into the tibiae aseptic conditions.

Using sterile surgical techniques, an incision was made in the skin to expose the proximal aspect of each tibia, and the muscles were dissected to allow elevation of the periosteum. The flat surface on the lateral aspect of the proximal tibia was selected for implant placement. The holes were drilled with a low-speed rotary instrument under constant irrigation with sterile saline.

A total of four implants, one from each group, were randomly placed in the right and left tibiae of each rabbit and penetrated only the first cortical layer. The upper canals of the implants were located in the cortical bone region, and the lower canals were located in the marrow. These canals served as sites for the evaluation of bone ingrowth.²⁸ The surgical site was closed in layers: the muscle and fascia were sutured with resorbable suture material (chromic catgut, Ethicon) and the skin was sutured with black silk (Mersilk, Ethicon).

After surgery, all of the rabbits received 50 mg/kg Kanamycin (Dong-A) via intramuscular injection. The rabbits were sacrificed via intravenous injection of potassium chloride (Daihan Pharm) at the scheduled time.

Specimen Preparation and Histomorphometric Analysis

Ten rabbits each were sacrificed after 4 and 12 weeks for histomorphometric analysis. All 80 implants and the surrounding bone were removed en bloc; fixed in neutral buffered formalin; dehydrated in 70%, 90%, 95%, and 100% alcohol; and embedded in light-curing resin (Technovit 7200 VLC, Kulzer). The embedded implants were divided longitudinally with a saw (Exakt, Exakt Apparatebau). The sections were ground to a thickness of approximately 30 µm, as described by Donath and Breuner,²⁹ and were stained with 1% toluidine blue to highlight the collagen content.

The histomorphometric analysis was performed with the aid of an Olympus BX51 microscope (Olympus) connected to a computer onto which the program Kappa Imagebase (Kappa Opto-Electronics) was loaded. All of the measurements were calculated under 100× magnification. The percentages of newly formed bone area (NB), graft materials area (GM), and marrow spaces (MS, ie, the soft marrow spaces containing fatty marrow tissue, connective tissue spaces, and empty spaces). The variables were calculated as follows (Fig 3):

$$\text{NB inside the canals (\%)} = (\text{newly formed bone area in the canal}) / (\text{total area of the canal}) \times 100$$

$$\text{GM inside the canals (\%)} = (\text{graft particles area in the canal}) / (\text{total area of the canal}) \times 100$$

$$\text{MS inside the canals (\%)} = 100 - (\text{NB inside the canals} + \text{GM inside the canals})$$

Statistics

Statistical analyses were carried out using SPSS 12.0 (IBM). Tests of normality and equality of variances were applied, and no violations of those basic assumptions were observed. A mixed-model analysis of variance was used to compare the amounts of newly formed bone inside the canals of the four groups and to

control for the random effects of the individual rabbits. Post hoc analysis was done with the Tukey test. All values were considered significant when $P < .05$.

RESULTS

Histologic Findings

After 4 Weeks. Survey images of the implants confirmed monocortical insertion into the central part of the tibia. The upper canals of the implants were positioned in the first cortical region of the bone in all sections, and the lower canals were positioned in the marrow regions. Both the upper and lower canals demonstrated bone ingrowth, with more bone in the upper canals in all groups (Fig 4).

Figure 5 shows detailed images of the 4-week specimens. The upper canals in group 1 demonstrated newly formed islands of bone and ingrowth into the canal from the outside. In general, the newly formed bone was located on the lateral side of the canal, often in broad close contact with the implant surface of the upper canal (Figs 5a and 5i). Fatty marrow spaces were observed mostly in the lower canals. Only a small amount of newly formed bone could be detected in group 1 (Figs 5e and 5m).

In the upper canals in group 2, the trabeculae of newly formed bone were scattered in the canals. The newly formed bone appeared to be woven or of irregular architecture. The remnants of the scaffold and fibrous connective tissues were dispersed in the canals (Figs 5b and 5j). In the lower canals, sparse and thin trabeculae of bone were rarely observed. An isolated island of newly formed bone was observed in the central part of the canal. The fibrous patchlike scaffold was transversely spread out in the canals (Figs 5f and 5n).

In the upper canals in group 3, Bio-Oss particles could be seen embedded in the newly formed bone. The Bio-Oss particles served as a conductor for the newly formed bone, which interconnected the individual particles. The sizes and shapes of the Bio-Oss particles were used to indicate the differences from the newly formed bone. While the newly formed bone appeared long and thin, the particles of bovine HA were short, thick, and polygonal in shape (Figs 5c and 5k). In the lower canals, a smaller amount of newly formed bone was observed, mostly with a pattern similar to that seen in the upper canals (Figs 5g and 5o).

In the upper canals in group 4, the MBCP particles were surrounded by newly formed bone. No gaps were present at the bone-particle interface, and the bone was in contact with the particles. The MBCP particles presented marked staining differences versus the newly formed bone. The MBCP granules were sharp-edged and relatively dark in color, whereas the newly

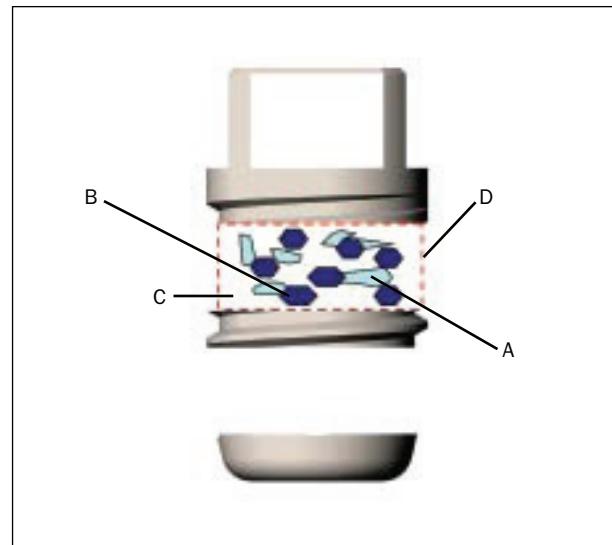


Fig 3 Schematic diagram of the histomorphometric analysis. A = Newly formed bone areas in the canal; B = graft material areas in the canal; C = marrow spaces; D = total area of the canal. Percentage of NB inside the canals (%) = A/D × 100 (%); percentage of GM inside the canals (%) = B/D × 100 (%); percentage of MS inside the canals (%) = C/D × 100 (%) = 100 – [(NB) + (GM)].

formed bone particles were long, with relatively obscure boundaries (Figs 5d and 5l). In the lower canals, a small amount of newly formed bone was observed on the particle surface (Figs 5h and 5p).

After 12 Weeks. The histological views at low magnification (Fig 6) showed that the upper canals were situated in the first cortical region of the bone and the lower canals in the marrow region in all groups. Figures 7 and 8 show the detailed specimens after 12 weeks of healing.

In the upper canals in group 1, newly formed islands of bone showed a configuration extending toward the central part of the canal from the lateral side. Portions of the trabeculae of newly formed bone were in close contact with the superior and inferior anodized surfaces of the upper canal (Figs 7a, 7i, and 8a). Most of the fatty marrow spaces were observed in the lower canals. A thin layer of newly formed bone was observed along the implant surface of the canal (Figs 7e and 7m).

In the upper canals in group 2, islands of newly formed bone were located in the canals. The newly formed bone formed trabeculae, which were dispersed in the scaffold. The remnants of scaffold and fibrous connective tissues were also dispersed in the canal (Figs 7b, 7j, and 8b). In the lower canals, strands of fibrous scaffold were observed running parallel to the canal. Islands of thin trabeculae of newly formed bone were sparsely observed within the fibrous patchlike scaffold (Figs 7f and 7n).

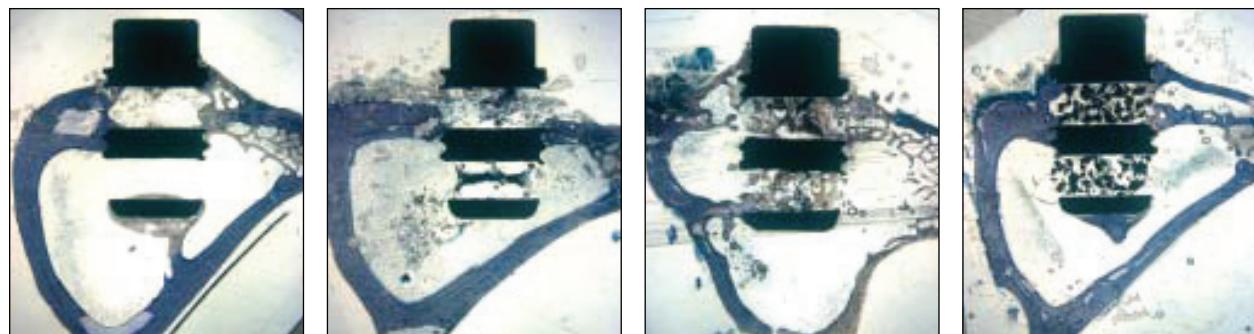


Fig 4 Histologic views of the threaded titanium implants with two transverse canals after implantation in the rabbit tibia for 4 weeks (toluidine blue; magnification $\times 12.5$). (Left to right) Control, MSCs/PRP, Bio-Oss, MBCP.

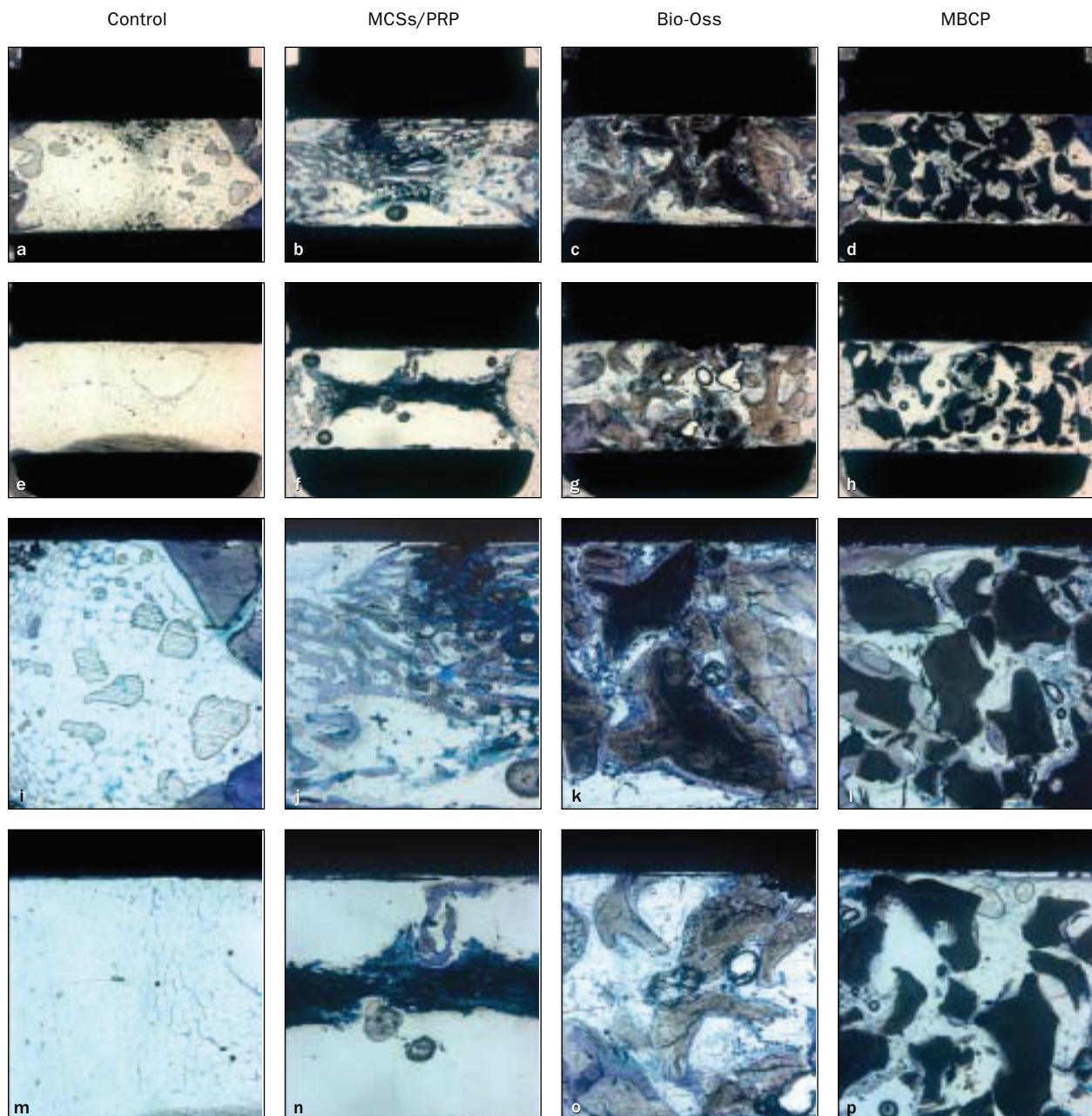


Fig 5 Histologic views after 4 weeks. Columns, left to right: Control, MSCs/PRP, Bio-Oss, MBCP; rows, top to bottom: upper canals, $\times 40$; lower canals, $\times 40$; upper canals, $\times 100$; lower canals, $\times 100$ (toluidine blue).

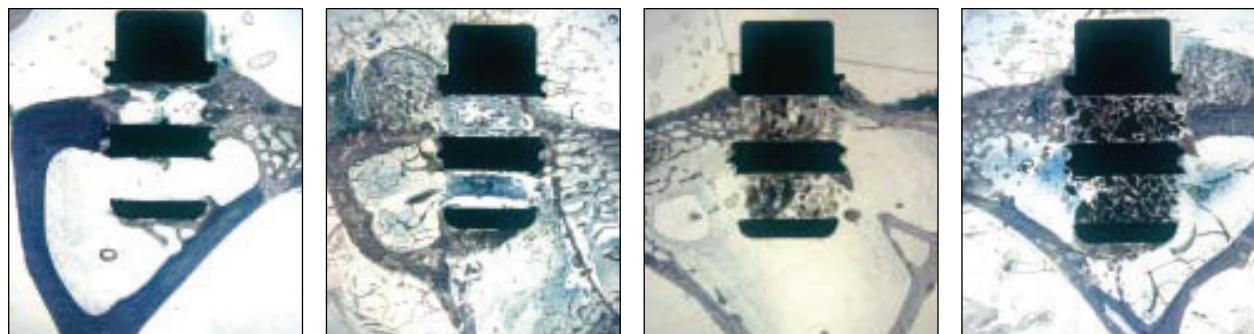


Fig 6 Histologic views of the threaded titanium implants with two transverse canals after implantation in the rabbit tibia for 12 weeks (toluidine blue; magnification $\times 12.5$). (Left to right) Control, MSCs/PRP, Bio-Oss, and MBCP.

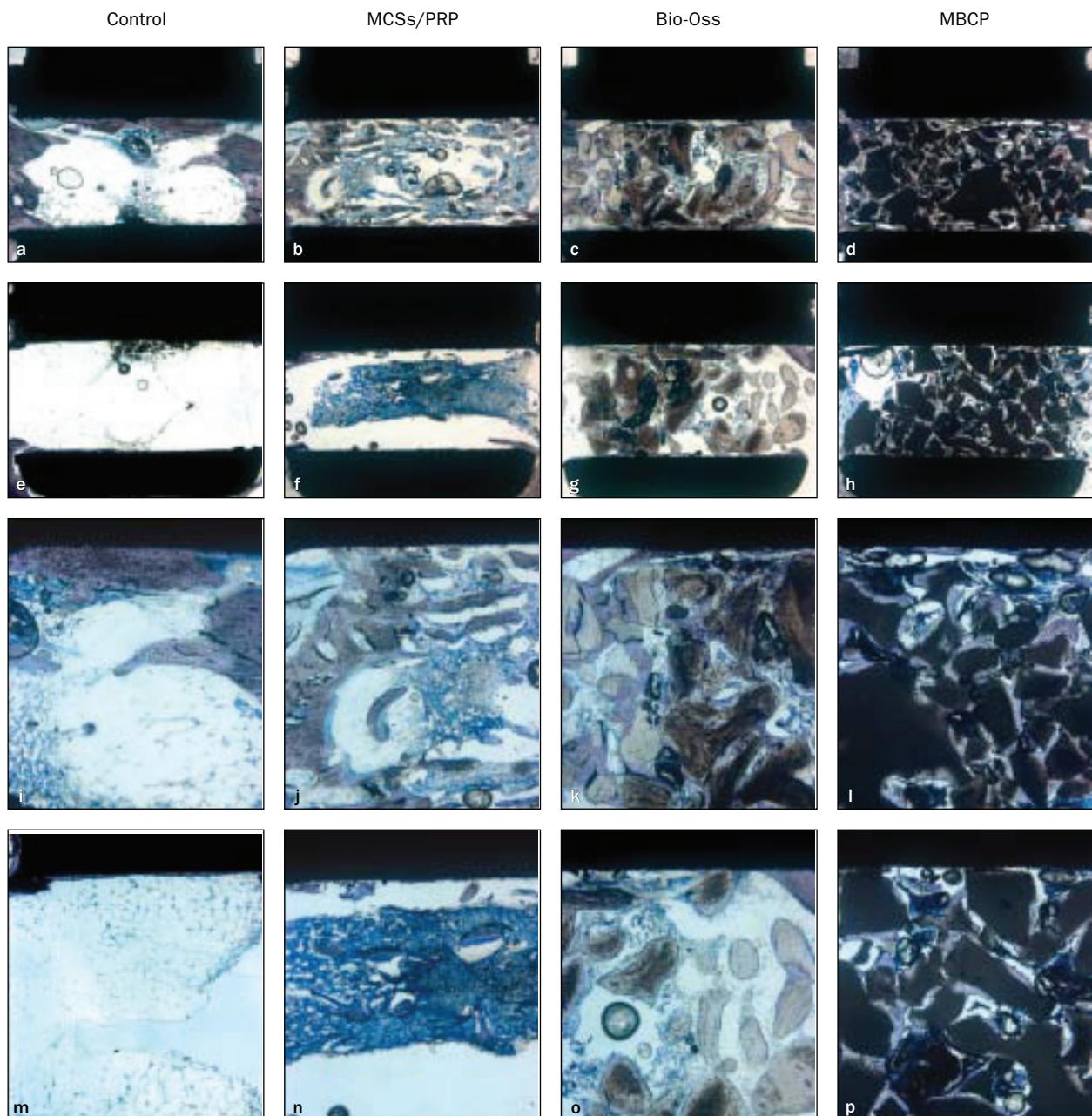


Fig 7 Histologic views after 12 weeks. Columns, left to right: Control, MSCs/PRP, Bio-Oss, MBCP; rows, top to bottom: upper canals, $\times 40$; lower canals, $\times 40$; upper canals, $\times 100$; lower canals, $\times 100$ (toluidine blue).

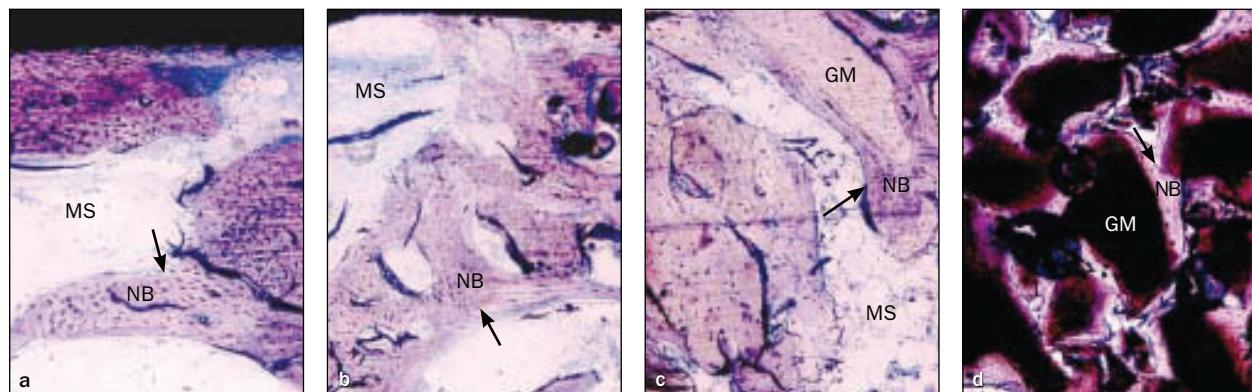


Fig 8 High-power histologic views inside the upper canal after 12 weeks in the (a) control, (b) MSCs/PRP, (c) Bio-Oss, and (d) MBCP specimens (toluidine blue; magnification $\times 200$). Newly formed bone (NB and arrows), graft material (GM), and marrow space (MS) were observed. The trabeculae of NB can be seen in the control and MSCs/PRP sites. The particles of GM were surrounded by NB in the Bio-Oss and MBCP specimens.

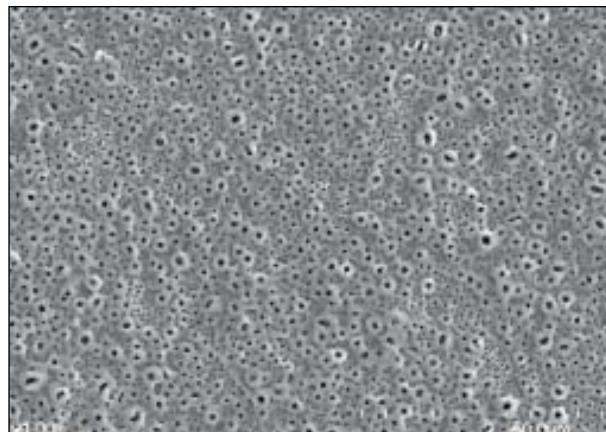


Fig 9 Scanning electron micrograph of anodized implant surface. The surface had a layer of interconnecting pores composed of small craters with holes at the centers (magnification $\times 1,000$).

In the upper canals in group 3, Bio-Oss particles were incorporated in various proportions within newly formed bone. The surfaces of the particles were in contact with newly formed bone, which interconnected the trabeculae (Figs 7c, 7k, and 8c). In the lower canals, a small amount of newly formed bone was observed around the Bio-Oss particles (Figs 7g and 7o).

In the upper canals in group 4, MBCP particles were surrounded by bands of newly formed bone. No gaps were present at the bone-particle interface, and the bone was in contact with the particles (Figs 7d, 7l, and 8d). In the lower canals, the graft materials were in contact with thin bands of newly formed bone. This apposition of newly formed bone in the lower canals exhibited a similar pattern to that observed in the upper canals but was present in smaller quantities (Figs 7h and 7p).

Generally, for the upper canals in groups 3 and 4, bone grew inward from the preexisting cortical bone into the grafted area within the canal.

Table 1 Histomorphometric Values Inside the Canals at 4 Weeks

Location/group	NB (%)	GM (%)	MS (%)
Upper canal			
Control	10.28 \pm 2.08	—	89.72 \pm 2.08
MSCs/PRP	14.96 \pm 2.38	—	85.04 \pm 2.38
Bio-Oss	17.83 \pm 4.62	60.53 \pm 5.29	21.64 \pm 7.37
MBCP	17.11 \pm 5.29	59.32 \pm 4.52	23.58 \pm 7.06
Lower canal			
Control	3.45 \pm 1.61	—	96.55 \pm 1.61
MSCs/PRP	3.92 \pm 1.83	—	96.08 \pm 1.83
Bio-Oss	4.78 \pm 1.49	59.19 \pm 5.43	36.03 \pm 6.43
MBCP	5.03 \pm 1.76	58.01 \pm 5.06	36.96 \pm 5.01

Values are given as means \pm standard deviations.

Table 2 Histomorphometric Values Inside the Canals at 12 Weeks

Location/group	NB (%)	GM (%)	MS (%)
Upper canal			
Control	13.63 \pm 3.90	—	86.37 \pm 3.90
MSCs/PRP	18.94 \pm 3.22	—	81.06 \pm 3.22
Bio-Oss	22.11 \pm 4.18	56.02 \pm 5.63	21.87 \pm 5.65
MBCP	23.03 \pm 5.11	57.84 \pm 4.68	19.13 \pm 7.61
Lower canal			
Control	5.07 \pm 1.31	—	94.93 \pm 1.31
MSCs/PRP	5.76 \pm 1.44	—	94.24 \pm 1.44
Bio-Oss	6.33 \pm 1.50	57.60 \pm 4.70	36.07 \pm 3.75
MBCP	6.95 \pm 1.46	58.10 \pm 4.50	34.95 \pm 4.90

Values are given as means \pm standard deviations.

Implant Surface Morphology and Histomorphometric Results

The surfaces of anodized titanium implants had the typical appearance of uniformly porous surfaces composed of small craters with holes at the centers (Fig 9). The NB, GM, and MS inside the upper and the lower canals of the implants are summarized in Tables 1 and 2.

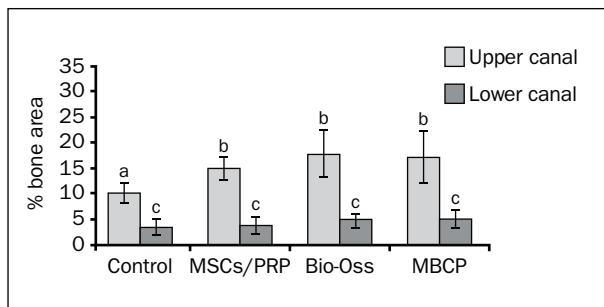


Fig 10 Areas of NB inside the upper and lower canals implanted into the rabbit tibiae for 4 weeks. Values are means \pm standard deviations ($n = 10$).

After 4 weeks, groups 2, 3, and 4 showed significantly higher NB percentages than group 1 in the upper canals (group 2 > group 1, $P = .047$; group 3 > group 1, $P = .001$; group 4 > group 1, $P = .002$). However, there was no significant difference between groups 2, 3, and 4. There were no significant differences between all groups inside the lower canals ($P = .112$) (Fig 10).

After 12 weeks of healing, in the upper canals, groups 2, 3, and 4 showed significantly higher NB percentages than group 1 (group 2 > group 1, $P = .034$; group 3 > group 1, $P < .0001$; group 4 > group 1, $P < .0001$). There was no significant difference between groups 2, 3, and 4. There was no significant difference between the all groups inside the lower canals ($P = .064$) (Fig 11). In addition, the mean values for NB inside the upper canals were significantly higher than those of the lower canals in all groups after 4 and 12 weeks of healing ($P < .0001$).

DISCUSSION

In this study, the authors examined the bone regeneration with various bone replacement materials inside canals created within anodized implants. One of the graft materials used was tissue-engineered injectable bone (ie, MSCs/PRP). The MSCs/PRP group in this study had rabbit bone marrow-derived MSCs and a fibrin network scaffold of PRP gel as the injectable bonelike material. The PRP gel offers numerous advantages: (1) plasticity, (2) flexibility, (3) three-dimensional scaffolding, (4) reduced invasiveness because of the delivery through a syringe, (5) absence of toxicity, and (6) lack of an immune reaction.³ In the osseous defect model, a mixture of MSCs and PRP produced well-formed mature bone and good neovascularization compared to the control (unfilled) defects.³ According to Ito et al,⁵ the MSCs/PRP possess osteogenic characteristics and may repair bone defects. In this study, the MSCs/PRP group also exhibited better bone regeneration inside the upper canals than did the control after 4 and 12 weeks ac-

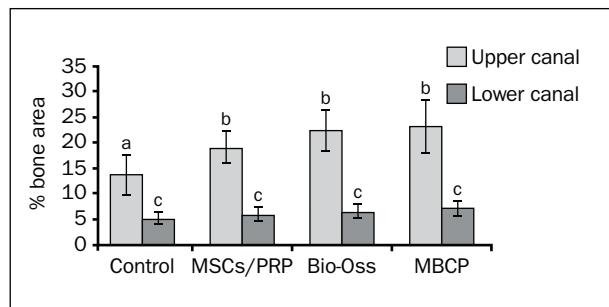


Fig 11 Areas of NB inside the upper and lower canals implanted into the rabbit tibiae for 12 weeks. Values are means \pm standard deviations ($n = 10$).

cording to histomorphometry when transverse canals were used to carry the bone graft materials.

Despite the osteogenic capacity of MSCs, they cannot be used as spatial fillers for bone defects.³⁰ MSCs are usually applied to a scaffold, such as PRP gel. Although the reason for active bone regeneration in the MSCs/PRP group remains unknown, it may be a consequence of the growth factors containing PRP. Therefore, it seems that bone regeneration inside the canals could be promoted by MSCs/PRP because of the presence of osteogenic cells and osteoinductive factors in the MSCs/PRP mixture.

Other bone replacement materials, such as Bio-Oss and MBCP, have been used increasingly often to simplify surgical procedures. Xenogeneic bone matrices and synthetic HA/ β -TCP share several advantages: (1) no donor site is required, (2) unlimited supplies of the materials are available, and (3) the materials are easy to handle.³¹ A majority of the currently available matrix materials for bone grafting are osteoconductive materials that support bone formation by acting as scaffolds for angiogenesis, cell recruitment, and ultimately osteogenesis by host cells. Variables that affect the osteoconductive nature of a bone graft include porosity, surface topography, and chemical composition.³² Bio-Oss possesses important properties, such as biocompatibility and osteoconductivity, that make it a good scaffold for the ingrowth of host cells.^{9,10} In the present study, transverse canals filled with Bio-Oss also displayed osteoconductive bone regeneration. Histologic observation revealed that Bio-Oss particles were incorporated and interconnected by trabeculae of newly formed bone, thereby demonstrating high osteoconductivity. This arises from an interconnecting pore system and from physical and chemical properties similar to those of human cancellous bone.²⁶

A combination of the two primary forms of calcium phosphate has been studied to take advantage of the rapid resorption of β -TCP and the inert scaffold of dense HA. In a histologic study, biphasic calcium phosphate supported active bone replacement from surrounding bone, possibly as the result of a macrophage trigger.³³

In the MBCP group in this study, the particles showed intimate contact with newly formed bone and provided a substrate for bone-forming cells. This material also showed osteoconductive properties. Other experimental studies have detected newly formed bone in the peripheral macropores of the MBCP particles.^{11,12}

Ideally, bone substitutes should maintain their mechanical stability and volume during healing and then be completely resorbed and replaced by newly formed bone.³⁴ Strictly speaking, the MSCs/PRP admixture was the graft material. However, histologic observation showed that the PRP scaffold was biodegradable and was sparsely dispersed in a shrunken pattern, similar to fibrous connective tissue. Except for the newly formed bone, this fibrous scaffold was included in the marrow space area. Therefore, the GM inside the canals could not be measured in the MSCs/PRP group. On the other hand, in the Bio-Oss and MBCP groups, the particles were barely absorbed after 12 weeks of healing and remained as the substratum for the regeneration of bone inward to the canal from the preexisting cortical bone. It seems that the role of a space filler or space maintainer inside the canal was weak in the MSCs/PRP group because of the gel-like consistency, fibrous dispersion, and shrinkage pattern of the material.

Because the healing of severed bone tissue is a complicated process and apparently involves different steps in the cortical and spongy parts of a surgical site,³⁵ in the present study, the implants were surgically placed so that the transverse canals were parallel to the different regions of bone (cortical/cancellous bone). Generally, bone comprises outer cortical bone and inner cancellous bone, and the transverse canals could therefore serve as sites for evaluation of bone ingrowth.²⁸ In this study, the upper canals were positioned within the cortical region of the bone and the lower canals were located in the marrow region, so that the bone ingrowth of the upper canals represented cortical bone regeneration, while the bone ingrowth of the lower canals represented cancellous bone regeneration. In this study, the upper canals showed significantly higher NBs than the lower canals in all groups. However, there were no differences in NBs inside the lower canals located in the cancellous bone of the rabbit tibiae among all groups. These differences may be explained by the nature of the bone in the areas of the canals. Lu et al³⁶ reported that bone growth in rabbits was more pronounced in cortical bone than in the marrow sites. Generally, in rabbit tibiae undergoing implantation experiments, a larger amount of bone is observed in the threads in the old cortical region than in the threads in the marrow cavity.³⁷

In addition to the ratio of cortical/cancellous bone of the rabbit tibia, the bone density and mechanical stability of the canals seem to be affected by the difference between the bone regions. The stiff and compact

outer holding of the cortical bone provides a firm mechanical interlocking of the upper canal, which is important for bone regeneration. The relatively smaller existing bone fragments and weakness of the cancellous bone seem to affect the different bone responses.

In this study, the MSCs/PRP mixture, Bio-Oss, and MBCP inside the upper canals led to more newly formed bone compared to the control group sites. In spite of the fact that the osteogenic and osteoinductive properties of the MSCs/PRP are beneficial to bone regeneration,^{3,5} there was no difference between the three bone graft materials in both upper and lower canals in this study. This may be a consequence of the canal model.

This implant canal model seems to be a useful tool for quantifying bone regeneration. The canals represent a well-defined space that is easy to prepare. The canal dimension is uniform, which allows quantitative measurement of the newly formed bone area inside the canal. These canals also can be filled with various bone grafting materials. The canals served as a space for bone ingrowth evaluation as well as a repository for the materials and carrier. When the canals are placed within the bone, bone regeneration is not affected by the environment of the overlying tissue and mechanical stimuli.^{38,39}

However, the canals have potentially different biologic environments. Inside the canals, the oxygen tension, vascularity, cell activity, etc, are different versus a lesion in bone or beside the threads of an implant. According to Boyan and coworkers,⁴⁰ environmental factors such as oxygen tension help determine whether mesenchymal cells will differentiate into fibroblasts, chondrocytes, or osteoblasts. The environment inside the canals may be unfavorable to bone regeneration adjacent to the implant surface from a bone healing perspective. The canal or chamber itself is an osteoconductive structure,⁴¹ so it also affected the bone ingrowth of all the tested sites. Thus, within the limitations of this canal model study, the results indicate that there was no difference between the bone graft materials. Further studies are required to clarify the osteogenic and osteoinductive capacities as well as the osteoconductive effects of the bone graft materials in the bone defects around implants in clinical bone regeneration.

CONCLUSIONS

In this study, anodized implants were designed with upper and lower transverse canals that were filled with different bone graft materials. The regeneration of cortical and cancellous bone with these bone substitutes inside anodized implant canals was evaluated using histomorphometric analysis of rabbit tibiae after 4 and 12 weeks. From this canal model study, the following conclusions can be drawn:

1. The newly formed bone percentages in the cortical bone were significantly greater in the grafted groups than in control sites, but there was no significant difference among the graft groups.
2. In cancellous bone, there was no significant difference in new bone percentage among all groups.
3. The new bone percentages in cortical bone were significantly higher than those in cancellous bone in all groups.

ACKNOWLEDGMENTS

This study was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (MEST) (No.2011-0028067 & 2011-0004163). The authors reported no conflicts of interest related to this study.

REFERENCES

1. Buser D, Dula K, Hess D, Hirt HP, Belser UC. Localized ridge augmentation with autografts and barrier membranes. *J Periodontol* 1999;19:151–163.
2. Laurie SWS, Kaban LB, Mulliken JB, Murray JE. Donor site morbidity after harvesting rib and iliac bone. *Plast Reconstr Surg* 1984;73: 933–938.
3. Yamada Y, Ueda M, Naiki T, Takahashi M, Hata Ki, Nagasaka T. Autogenous injectable bone for regeneration with mesenchymal stem cells and platelet-rich plasma: Tissue-engineered bone regeneration. *Tissue Eng* 2004;10:955–964.
4. Wang M. Developing bioactive composite materials for tissue replacement. *Biomaterials* 2003;24:2133–2151.
5. Ito K, Yamada Y, Nagasaka T, Bada S, Ueda M. Osteogenic potential of injectable tissue-engineered bone: A comparison among autogenous bone, bone substitute (Bio-Oss), platelet-rich plasma, and tissue-engineered bone with respect to their mechanical properties an histological findings. *J Biomed Mater Res A* 2005;73:63–72.
6. Tadic D, Epple M. A thorough physicochemical characterization of 14 calcium phosphate-based bone substitution materials in comparison to natural bone. *Biomaterials* 2004;25:987–994.
7. Gross JS. Bone grafting materials for dental applications: A practical guide. *Compendium* 1997;18:1013–1036.
8. Hoexter DL. Bone regeneration graft materials *J Oral Implantol* 2002;28:3–7.
9. Hammerle CH, Chiantella G, Karring T, Lang NP. The effect of a deproteinized bovine bone mineral on bone regeneration around titanium dental implants. *Clin Oral Implants Res* 1998;9:151–162.
10. Berglundh T, Lindhe J. Healing around implants placed in bone defects treated with Bio-Oss. An experimental study in the dog. *Clin Oral Implants Res* 1997;8:117–124.
11. Jensen SS, Aaboe M, Pinholt EM, Hjorting-Hansen E, Melsen F, Ruyter LE. Tissue reaction and material characteristics of four bone substitutes. *Int J Maxillofac Implants* 1996;11:55–66.
12. LeGuehenec L, Goyenvalle, Aguado E, et al. Small-animal models for testing macroporous ceramic bone substitutes. *J Biomed Mater Res Appl Biomater* 2005;72:69–78.
13. Ohgushi H, Okumura M, Tamai S, Shors EC, Caplan AI. Marrow cell induced osteogenesis in porous hydroxyapatite and tricalcium phosphate: A comparative histomorphometric study of ectopic bone formation. *J Biomed Mater Res* 1990;24:1563–1570.
14. Ohgushi H, Goldberg VM, Caplan AI. Repair of bone defects with marrow cells and porous ceramic. Experiments in rats. *Acta Orthop Scand* 1989;60:334–339.
15. Young RG, Butler DL, Weber W, Caplan AL, Gordon LI, Fink DJ. Use of mesenchymal stem cells in a collagen matrix for Achilles tendon repair. *J Orthop Res* 1998;16:406–413.
16. Pittenger MF, Mackay AM, Beck SC. Multilineage potential of adult human mesenchymal stem cells. *Science* 1999;284:143–147.
17. Jiang Y, Jahagirdar BN, Reinhardt RL. Pluripotency of mesenchymal stem cells derived from adult marrow. *Nature* 2002;418:41–49.
18. Barry FP, Murphy JM. Mesenchymal stem cells: Clinical applications and biological characterization. *Int J Biochem Cell Biol* 2004;36:568–584.
19. Hasegawa N, Kawaguchi H, Hirachi A, et al. Behavior of transplanted bone marrow-derived mesenchymal stem cells in periodontal defects. *J Periodontol* 2006;77:1003–1007.
20. De Kok IJ, Drapeau SJ, Young R, Cooper LF. Evaluation of mesenchymal stem cells following implantation in alveolar sockets: A canine safety study. *Int J Oral Maxillofac Implants* 2005;20:511–518.
21. Muschler GF, Nitto H, Bohem CA, Easley KA. Age-and gender-related changes in the cellularity of human bone marrow and the prevalence of osteoblastic progenitors. *J Orthop Res* 2001;19:117–125.
22. Langer R, Vacanti JP. Tissue engineering. *Science* 1993;260:920–926.
23. Yamada Y, Ueda M, Naiki T, Nagasaka T. Tissue-engineered injectable bone regeneration for osseointegrated dental implants. *Clin Oral Implants Res* 2004;15:589–597.
24. Kadiyara S, Jaiswal N, Bruder SP. Cultured-expanded bone marrow-derived mesenchymal stem cells can regenerate a critical size segmental bone defect. *Tissue Eng* 1997;3:173–185.
25. Jaiswal N, Haynesworth SE, Calpan AT, Bruder SP. Osteogenic differentiation of purified, culture-expanded human mesenchymal stem cells in vitro. *J Cell Biochem* 1997;64:295–312.
26. Yildrim M, Spiekermann H, Biesterfeld S, Edelhoff D. Maxillary sinus augmentation using xenogenic bone substitute material Bio-Oss in combination with venous blood. A histologic and histomorphometric study in humans. *Clin Oral Implants Res* 2000;11:217–229.
27. Teixeira CC, Nemelivsky Y, Karkia C, Legeros RZ. Biphasic calcium phosphates: A scaffold for growth plate chondrocyte maturation. *Tissue Eng* 2006;12:2283–2289.
28. Stenport VF, Johansson C, Heo SJ, Aspenberg P, Albrektsson T. Titanium implants and BMP-7 in bone: An experimental model in the rabbit. *J Mater Sci Mater Med* 2003;14:247–254.
29. Donath K, Breuner G. A method for the study of undecalcified bones and teeth with attached soft tissues. *J Oral Pathol* 1982;11:318–326.
30. Warren SM, Nacamuli RK, Song HJ, Longaker MT. Tissue-engineered bone using mesenchymal stem cells and a biodegradable scaffold. *J Craniomaxillofac Surg* 2004;15:34–37.
31. Dalkyz M, Özcan A, Yapar M, Gökay N, Yüncü M. Evaluation of the effects of different biomaterials on bone defects. *Implant Dent* 2000;9:226–235.
32. Cornell CN, Lane JM. Current understanding of osteoconduction in bone regeneration. *Clin Orthop* 1998;(355 suppl):S267–S273.
33. Hashimoto-Uoshima M, Ishikawa I, Kinoshita A, Weng TH, Odo S. Clinical and histologic observation of replacement of biphasic calcium phosphate by bone tissue in monkeys. *Int J Periodontics Restorative Dent* 1995;15:204–213.
34. Isaksson S. Aspects of bone healing and bone substitute incorporation: An experimental study in rabbit skull bone defects. *Swed Dent J Suppl* 1992;84:1–46.
35. Albrektsson T, Berglundh T, Lindhe J. Osseointegration: Historic background and current concepts. In: Lindhe J, Karring T, Lang NP (eds). *Clinical Periodontology and Implant Dentistry*, ed 4. Oxford: Blackwell, 2003:809–820.
36. Lu JX, Gallur A, Flautre B, et al. Comparative study of tissue reactions to calcium phosphate ceramics among cancellous, cortical and medullary bone sites in rabbits. *J Biomed Mater Res* 1998;42:357–367.
37. Chun HJ, Cheong SY, Han JH, Heo SJ, Chung JP, Rhyu IC. Evaluation of design parameters of osseointegrated dental implants using finite element analysis. *J Oral Rehabil* 2002;29:565–574.
38. Trisi P, Rao W. The bone growing chamber: A new model to investigate spontaneous and guided bone regeneration of artificial defects in the human jawbone. *Int J Periodontics Restorative Dent* 1998;18:151–159.
39. Hannink G, Aspenberg P, Schreurs BW, Buma P. Development of large titanium bone chamber to study in vivo bone ingrowth. *Biomaterials* 2006;27:1810–1816.
40. Boyan BD, Hummert TW, Dean DD, Schwartz Z. Role of material surfaces in regulating bone and cartilage cell response. *Biomaterials* 1996;17:137–146.
41. Albrektsson T, Johansson C. Osteoinduction, osteoconduction and osseointegration. *Eur Spine J* 2001;10(suppl 2):S96–S101.

Bone Regeneration in Osteoporotic Conditions: Healing of Subcritical-Size Calvarial Defects in the Ovariectomized Rat

Sara F. O. Durão, DDS¹/Pedro S. Gomes, DDS, MSc, PhD²/José M. Silva-Marques, DDS, PhD³/
Hélder R. M. Fonseca, MSc⁴/João F. C. Carvalho, DDS, PhD⁵/
José A. R. Duarte, MD, PhD⁶/Maria H. R. Fernandes, PhD⁷

Purpose: Osteoporosis is a pathologic condition characterized by low bone mass and changes in the microarchitecture of the bone tissue. Although compromised bone strength and increased susceptibility to fracture have been established, little is known regarding the process of bone regeneration in osteoporotic conditions. Accordingly, this study sought to evaluate the intramembranous bone regeneration process in an ovariectomized rat model following the establishment of calvarial subcritical-size defects (sCSDs).

Materials and Methods: Calvarial sCSDs were established in rats that had been ovariectomized (Ovx) or sham-operated 2 months previously and left to heal, unfilled, for 6 months. Bone regeneration was assessed by radiographic, densitometric, histologic, and histometric analyses. **Results:** Radiologic and histologic analyses showed reduced new bone formation in calvarial sCSDs in Ovx animals in comparison to sham animals. Densitometric analysis of radiologic images and histometric analysis showed significant quantitative differences between groups that converged to substantiate reduced bone regeneration in Ovx animals. **Conclusions:** The intramembranous ossification process is impaired in the Ovx rat model. This may suggest an impairment of the bone regeneration process in clinical conditions of postmenopausal osteoporosis and highlight the requirement for selective bone regenerative strategies in affected patients. *INT J ORAL MAXILLOFAC IMPLANTS* 2012;27:1400–1408

Key words: animal models, bone regeneration, osteoporosis

Osteoporosis is a prevalent disease and a major health problem, with high rates of mortality and morbidity worldwide.¹ This pathologic condition is

characterized by low bone mass and changes in the microarchitecture of the bone tissue, which work together to compromise bone strength and increase the susceptibility to fracture.¹

Global epidemiologic data report that 1 in every 3 women and 1 in every 50 men over the age of 50 years have osteoporosis.² Moreover, an estimated 40% of women and 13% of men aged 50 years and older will sustain an osteoporotic fracture in their lifetime. Taking into account future mortality trends, these figures rise to 47% for women and 22% for men.^{2,3} As a health care problem, osteoporosis comprises a large percentage of health spending and is expected to escalate in this century, with projected costs of hip fractures alone reaching US\$131 billion worldwide by 2050.^{4,5}

Even though much attention has been given to preventive approaches and new pharmacologic and physical therapies, which aim to maintain a high level of bone mass, less attention has been directed to the study of the process of bone regeneration in osteoporotic conditions. The available data, despite being sparse, focus mainly on the process of fracture healing; delayed healing and impaired biomechanical strength have been observed in experimental and clinical studies.^{6–8} Moreover, some experimental studies report

¹Lecturer, Faculdade de Medicina Dentária, Universidade do Porto, Porto, Portugal.

²Assistant Professor, Faculdade de Medicina Dentária, Universidade do Porto, Porto, Portugal; Laboratório de Farmacologia e Biocompatibilidade Celular – Faculdade de Medicina Dentária, Universidade do Porto, Porto, Portugal.

³Assistant Professor, Cooperativa de Ensino Superior Egas Moniz. Campus Universitário, Caparica, Portugal.

⁴Researcher, Faculdade de Desporto, Universidade do Porto, Porto, Portugal.

⁵Professor, Faculdade de Medicina Dentária, Universidade do Porto, Porto, Portugal.

⁶Professor, Faculdade de Desporto, Universidade do Porto, Porto, Portugal.

⁷Professor, Faculdade de Medicina Dentária, Universidade do Porto, Porto, Portugal; Laboratório de Farmacologia e Biocompatibilidade Celular – Faculdade de Medicina Dentária, Universidade do Porto, Porto, Portugal.

Correspondence to: Dr Maria Helena Fernandes, Laboratório de Farmacologia e Biocompatibilidade Celular, Faculdade de Medicina Dentária, Universidade do Porto, Rua Dr. Manuel Pereira da Silva, 4200-393 Porto, Portugal. Fax: +351-220-901-101. Email: mhfernandes@fmd.up.pt

a data trend substantiating an impaired biomaterial-mediated bone regeneration process in osteoporotic conditions^{9–11}; nonetheless, some authors found no differences.^{12–14} Regardless, the fundamentals of the de novo bone formation process in osteoporotic conditions have not been adequately detailed.

Animal models play a crucial role in bone-related research, especially within the assessment of the biologic and biomechanical characteristics of bone metabolism, orthopedic implant placement, and bone graft substitutes, in both physiologic and pathologic conditions.^{15–18} Moreover, experimental animals have also been used extensively to model human pathologic states, such as the osteoporotic condition.^{19,20} The ovariectomized (Ovx) rat is the most commonly used model for the study of osteoporosis pathophysiology, diagnosis, and therapy and has been validated as a clinically relevant model of human postmenopausal bone loss.^{21–23} Rodents have also been widely employed in the assessment of the bone regeneration process, in the presence or absence of implanted materials, in the standardized calvarial bone defect.^{17,24,25} The use of the calvarial model implies the selection of a specific defect size, in which the choice between the use of critical-size defects (CSDs) or subcritical-size defects (sCSDs), is crucial.^{24,26} The CSD is broadly described as the smallest wound established intraosseously that does not heal spontaneously during the lifetime of the animal, as a specific condition of failed osteogenesis for overcoming the threshold of the physiologic process of tissue repair.²⁶ It has been used routinely to address the biocompatibility and osteogenic capacity of many candidate materials and tissue engineering approaches for bone regeneration.¹⁷ However, CSDs do not provide data regarding the process of “natural” bone healing, which can be adequately examined only in the appraisal of the regeneration process of unfilled sCSDs.²⁵ Accordingly, sCSDs have been used in the evaluation of bone formation, especially within the assessment of the impact that a wide range of biologic processes, added substances, or pathologic conditions have on the intramembranous ossification process.^{25,27,28}

Therefore, to address the bone regeneration process in an animal model representative of the human condition of osteoporosis, the present study sought to evaluate intramembranous bone regeneration in an Ovx rat model following the establishment of calvarial sCSDs.

MATERIALS AND METHODS

Animals

This experimental study was performed under the authorization of Direcção Geral de Veterinária and upheld the technical standards for the protection of experi-

mental animals, according to Portuguese (decree no. 1005/92) and European (directive 2010/63) legislation.

Fourteen nulliparous female Wistar rats, aged 6 weeks, were purchased from a certified vendor (Charles River Laboratories) and housed in plastic cages in a monitored environment throughout the study period. Animals were given a standard diet (4RF24 GLP, Mucedola) and water ad libitum. After a quarantine period, rats were randomly ovariectomized (Ovx; n = 7) or sham-operated (sham; n = 7). Bilateral ovariectomy was performed as described in the following section.

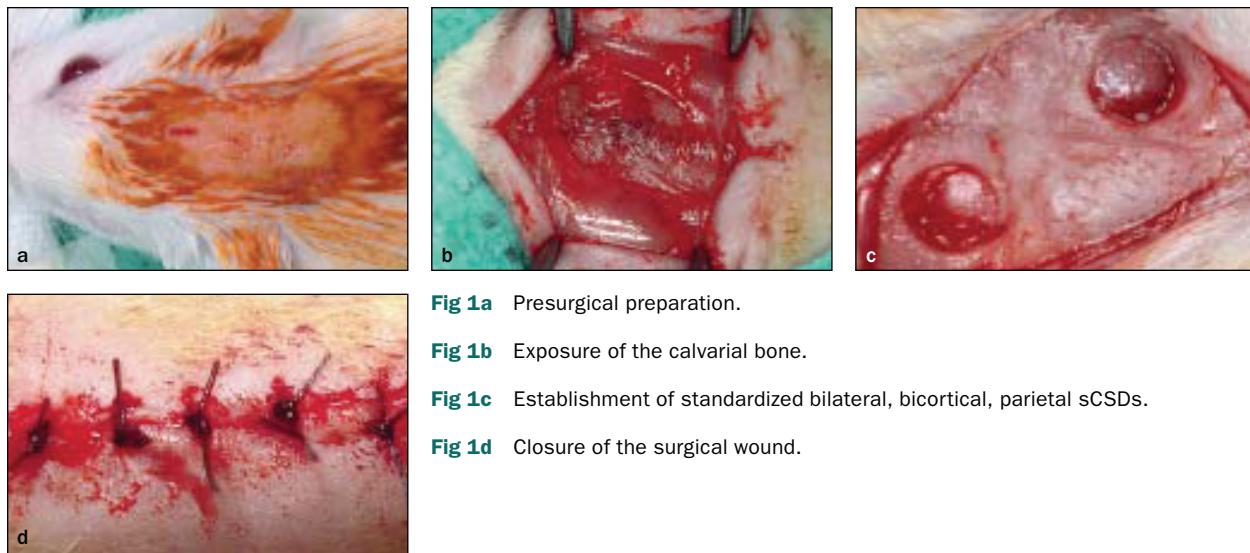
Ovariectomy and Sham Surgical Procedure

At 2 months of age, animals assigned to the Ovx group were anesthetized by an intraperitoneal injection of xylazine (10 mg/kg Rompun 2%, Bayer) and ketamine (90 mg/kg Imalgene 1000, Merial). The abdominal cavity was accessed by a 2-cm midline dorsal skin incision, which allowed for blunt dissection of the connective tissue between the skin and the muscular layer of abdominal wall. Following this, the muscular layers were opened halfway down the sides of the animal. The ovaries were identified surrounded by a considerable amount of fat and pulled out through the incision. Two ligatures were placed with absorbable 4–0 sutures (polyglactin 910, Vicryl Rapide, B Braun): one in the caudal end, between the ovary and the uterine horn, and the other one in the cranial end of the ovary. Following this, the ovaries were safely cut off and the uterine horns were pushed back into the abdominal cavity. Following inspection for abdominal hemorrhage, the abdominal muscle tissue was closed with absorbable 4–0 sutures. Finally, the skin was sutured. The animals were administered tramadol (10 mg/kg Tramal, Grünenthal) intraperitoneally for postoperative analgesia.

Sham surgery, which sought to assess the effect of the intervention under study by neutralizing the placebo effect and reducing bias, consisted of the same surgical protocol with the exception of the placement of ligatures and the removal of ovaries and was performed in all animals of the sham group. In agreement with the experimental protocol, the animals were weighed monthly.

Establishment of Calvarial Subcritical-size Defects

At 4 months of age (2 months following Ovx or sham operation), surgical craniotomies were performed; the surgery sought to establish 3-mm-diameter sCSDs. Both the Ovx and sham animals were submitted to the craniotomy procedure. Animals were anesthetized using sevoflurane (Baxter) inhalation anesthesia (4% to 5% induction; 2% to 3% maintenance) (Fig 1a). A midline incision through the skin allowed access to the calvarial bone. The skin was then reflected bilaterally, and a midline periosteal incision allowed for the division

Fig 1 Surgical craniotomy.

of the subcutaneous fascia and the bilateral reflection of the periosteal flaps, following blunt dissection, to expose the calvarial bone surface (Fig 1b). With a trephine bur with an external diameter of 3 mm, standardized bilateral, bicortical, midparietal defects were created (Fig 1c). The surgical wound was then closed in layers with 4–0 resorbable sutures (Fig 1d). Intraperitoneal administration of tramadol (10 mg/kg) was used for postoperative analgesia.

Animal Euthanasia and Tissue Harvesting

Six months after craniotomy, rats were anesthetized with intraperitoneal administration of xylazine (10 mg/kg) and ketamine (90 mg/kg) and euthanized by exsanguination. Blood was collected from the inferior vena cava into heparinized tubes and further processed for plasma separation, which was later used for biochemical analysis. To address the bone regeneration process, the calvarial bone was harvested for densitometric and histologic analyses; the uterus and the left tibia were also removed for weighing and densitometric evaluation, respectively.

Characterization of the Osteoporosis Animal Model

Biochemical Data. Alkaline phosphatase (ALP) activity and plasma levels of calcium (Ca) and phosphorous (P) were determined in an autoanalyzer. Plasma estrogen levels were determined by an enzyme-linked immunosorbent assay kit (Mouse/Rat Estradiol (E2) ELISA Kit, Calbiotech), according to the manufacturer's specifications.

Radiographic Evaluation and Densitometric Analysis of Tibias. The left tibiae were fixed in 10% buffered formalin. Radiographic imaging was conducted with a RVG intraoral sensor (Kodak RVG 5100)

and the images were processed with software (Kodak Dental Imaging Software 6.8.6.0). With respect to the x-ray beam, a conventional x-ray tube (Trophy, type 708, long cone) was used at 8 mA and 70 kV. The relative position of the sensor and the exposure time were kept constant (film-focus distance of 20 cm and exposure time of 0.2 seconds). Densitometric analysis was conducted with ImageJ (version 1.41o) in a specified region of interest (ROI) in the proximal metaphysis (see Fig 3a). The intensity of the signal was evaluated in unprocessed TIFF files and adequately normalized.

Evaluation of New Bone Formation

Radiographic and Densitometric Evaluations. The calvarial bone was fixed in 10% buffered formalin. Radiographic imaging and computer image analysis were conducted as previously described. Densitometric and regenerated area analyses were conducted with ImageJ (version 1.41o). A circular ROI, 3 mm in diameter (representing the original defect), was defined for the assessment of newly formed bone.

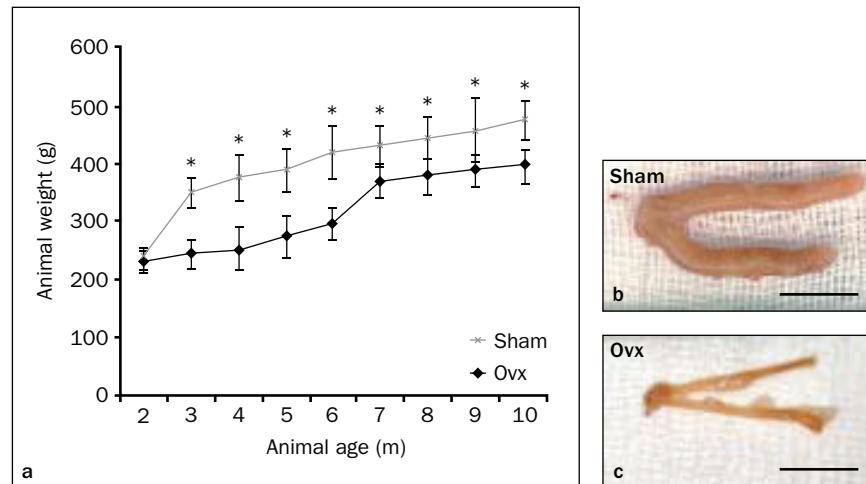
Histologic Processing and Analysis

Following radiographic evaluation, the calvaria samples were processed for undecalcified histologic preparation. They were dehydrated and embedded in methylmethacrylate resin before sectioning and grinding to the appropriate thickness. Sections were then stained with toluidine blue.

Because of the small diameter of the defects and the requirements of the undecalcified technique, rather than using surgically created marks that aimed to identify the center line of the original defect during laboratory processing, as reported by some authors,^{29,30} the authors identified the most central portion of each

Fig 2a Weight of the animals throughout the study period. *Significantly different versus sham group.

Figs 2b and 2c Macroscopic images of representative uteri from sham (b) and Ovx animals (c) at 10 months of age, 6 months after surgery (bar = 1 cm).



osteotomy defect and selected the section displaying the widest extent. This was the area subjected to histologic and histometric analyses, according to the methodology followed by Pryor et al.²⁷

The sections were viewed and evaluated for new bone formation by two calibrated examiners using a binocular microscope (Nikon SMX800) at low magnifications and a light microscope (Olympus CX31 with a DP-25 digital camera) at high magnifications. Histometric analyses, according to the methodology employed by Pryor et al,²⁷ were performed with Image-Pro Plus software (version 6.0.0.260, Media Cybernetics). The following parameters were evaluated: *defect width* (the distance between the margins of the original defect), *bone fill* (the length of newly formed bone tissue along an axis bridging the gap between the defect margins), and *percentage of bone fill* (calculated as the percentage of the ratio between bone fill and defect width parameters).

Statistical Analysis

Hypotheses on the distribution of continuous variables between groups were tested using the Student *t* test or a nonparametric test (Mann-Whitney), as appropriate. Normality distribution of variables was tested by the Shapiro-Wilk test. A significance level of 5% was considered ($P < .05$).

RESULTS

Effects of Ovariectomy

Animals in the sham-operated group reported a slow but steady increase in body weight during the observation period. Following ovariectomy, Ovx rats

Table 1 Plasma Levels of ALP, Ca, P, and Estradiol in Sham and Ovx Animals at 10 Months of Age

	Sham		Ovx	
	Mean	SD	Mean	SD
ALP levels (U/L)	97.81	6.96	101.97	7.14
Ca levels (mg/dL)	9.89	0.34	10.13	0.27
P levels (mg/dL)	6.13	0.26	6.25	0.24
Estradiol levels (pg/mL)	18.15	0.836	ND	—

SD = standard deviation; ND = not detectable.

weighed significantly more than sham rats at the assayed time points (Fig 2a). The uteri removed from Ovx animals at 10 months of age displayed severe atrophy (Figs 2b and 2c) and weighed significantly less (0.084 ± 0.063 g; $P < .05$) than those from the sham animals (0.574 ± 0.121 g).

At 10 months of age, plasma levels of ALP activity, Ca, P, and estradiol were assessed in both groups of animals (Table 1). Estradiol levels were too low to be detected in Ovx animals and were around 18 pg/mL in sham animals. No significant differences were found between the groups regarding ALP, Ca, and P levels.

Radiographic evaluation revealed structural differences between groups in the trabecular architecture of the tibiae (Fig 3a). The Ovx animals displayed decreased trabecular content, which was especially noticeable at the proximal metaphysis and was confirmed by the densitometric analysis performed within the delimited ROI (Fig 3b).

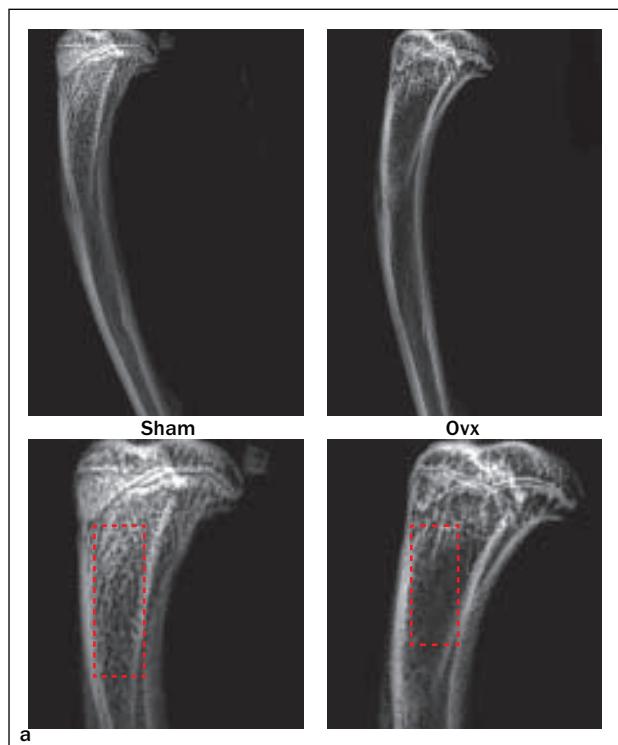
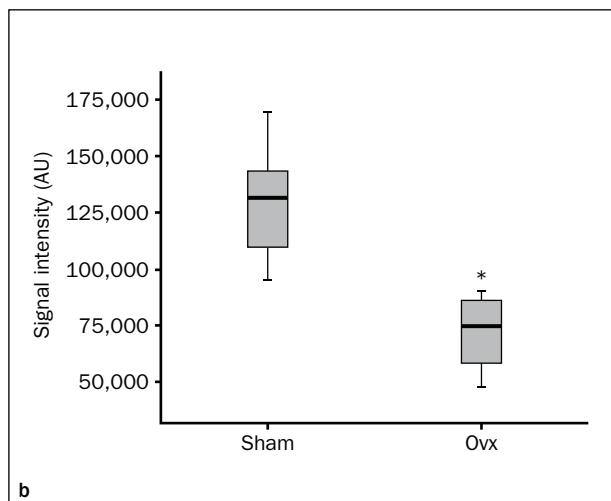


Fig 3a Representative radiographic images of left tibiae of Sham and Ovx animals at 10 months of age.

Fig 3b Densitometric analysis of the signal intensity within the ROI delimited in the proximal metaphysis in Fig 3a. AU = arbitrary units. *Significantly different versus the sham group.



Bone Regeneration

Radiographic images of the surgically created defect, at baseline and after 6 months of healing, are shown in Fig 4a. Image analysis allowed the observation of a centripetal formation of new bone tissue starting from the original margin of the defect in both sham and Ovx animals. In the sham group, the new bone formation process seemed to be in a more advanced stage and closer to filling the original defect compared to the Ovx group. Densitometric analysis of the reported radiographic images revealed significant differences between the two groups, with an increased intensity of signal in sham animals (Fig 4b). Moreover, assessment of the regenerated area within the defect revealed an increased value for sham animals (Fig 4c).

Histologic analysis showed the presence of osteogenic activity along the margins of the defect, with new bone forming by an intramembranous process in both sham and Ovx animals (Fig 5). The typical formation of a cone with the vertex oriented toward the center of the defect could be seen, in which centripetal tissue growth was evident. In the sham animals, the regenerative process seemed to be in a more advanced stage, with more newly formed mineralized bone tissue and less fibrous tissue bridging the two margins of the defect. In the Ovx group, nonetheless, new bone formation was verified, but a larger area between the margins of the defect was occupied by fibrous tissue.

Histometric analysis showed a higher percentage of bone fill in sham animals ($67.69\% \pm 8.247\%$) compared to Ovx animals ($50.24\% \pm 9.766\%$). High-magnification images revealed the formation of well-organized regenerating trabeculae of woven and lamellar bone within the area of newly formed bone (Fig 6).

DISCUSSION

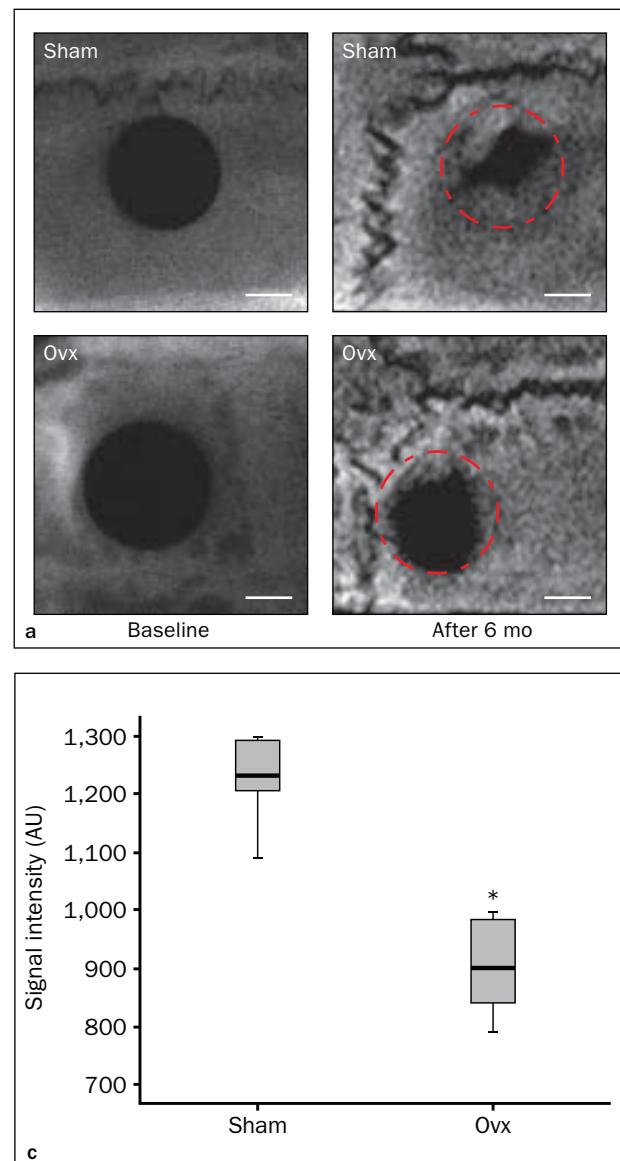
It is widely believed that osteoporosis is associated with a compromised regenerative capacity of bone, which may account for the clinical impairment seen with bone-regenerative approaches in osteoporotic models. This general belief is supported by clinical retrospective studies, which present weak evidence and do not provide any explanation or insights about the potential underlying mechanisms.³¹⁻³⁴ Accordingly, the assessment of bone regeneration in osteoporotic conditions is of particular clinical relevance.

In this study, sCSFs (3 mm in diameter) were established on the calvaria of 4-month-old Ovx and sham-operated animals (2 months after ovariectomy or sham surgery) and left to heal, unfilled, for 6 months. Assessment of bone regeneration was performed via radiographic, histologic, and histometric analyses. These surgically created defects have been used to evaluate the bone regeneration process following the establish-

Fig 4a Representative radiographic images of the sSCDs in sham and Ovx animals (left) at baseline and (right) after 6 months of healing (bar = 1 mm).

Fig 4b Densitometric analysis of the signal intensity within the ROI delimited in Fig 4a at 6 months. AU = arbitrary units.

Fig 4c Analysis of the regenerated area at the ROI delimited in Fig 4a at 6 months. *Significantly different versus the sham group.



ment of pathologic conditions or to assess the efficacy of various bone therapeutic approaches.²⁵ In this context, sCSDs have been effective to report a decreased bone regeneration capability in rodent models of diabetes,^{35,36} but no reports have been published regarding its use for bone regeneration in osteoporotic conditions.

The validity of the model of osteoporosis used in the present study was confirmed by the biochemical and structural changes that were verified following ovariectomy. This was established by the failure to detect ovarian tissue at the necropsy and the observation of atrophic uteri in the Ovx group, which showed significant weight differences versus the uteri of sham-operated animals. Moreover, Ovx animals showed a

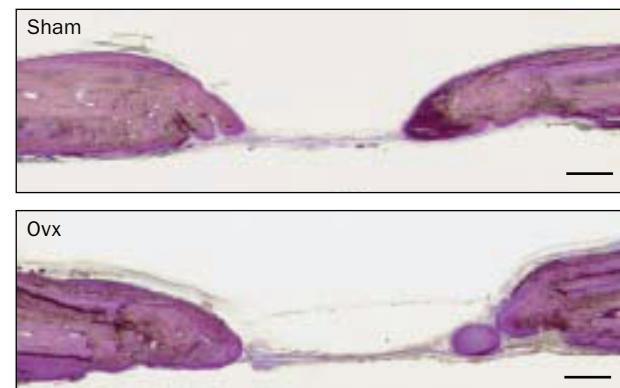


Fig 5 Low-magnification microphotographs of sham and Ovx calvarial sCSDs after 6 months of healing (toluidine blue; bar = 1 mm).

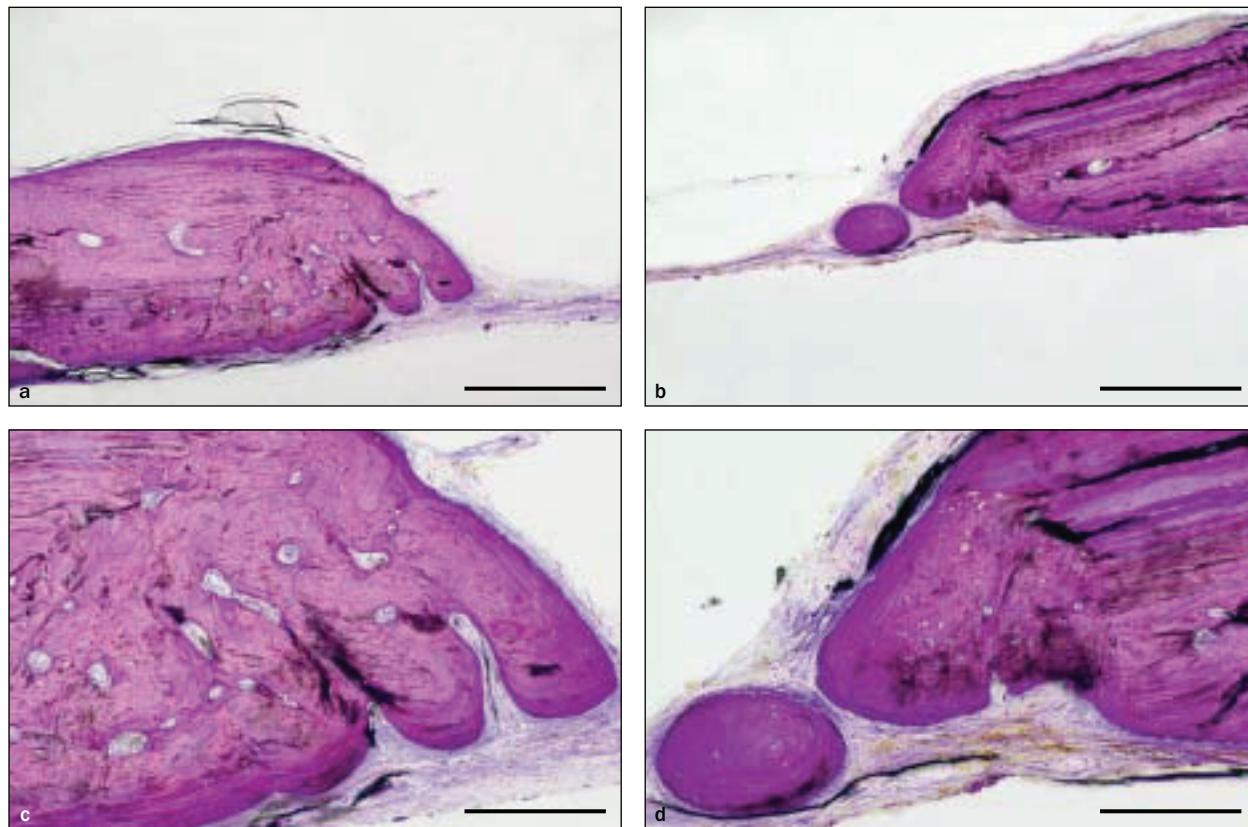


Fig 6 Photomicrographs of (a and c) sham and (b and d) Ovx calvarial sCSDs defects following 6 months of healing (toluidine blue; bars: top row, 500 µm, bottom row: 200 µm).

significant increase in body weight throughout the study period, when compared to the sham animals. This is in accordance with literature reports substantiating increased hyperphagia and augmented body weight associated with the ovariectomy-mediated disruption of the normal hypothalamic-pituitary-gonadal axis cycling in adult female rats.³⁷ Substantiating the efficacy of the ovarian ablation, plasma levels of estradiol were shown to be undetectable (by the test used) in the animals in the Ovx group. Skeletal alterations were also observed in animals submitted to ovariectomy. Radiographic analysis of the left tibiae revealed a decreased trabecular structure, especially in the proximal metaphysis. In addition to the established qualitative differences, quantitative assessment of the signal intensity by densitometric analysis showed significantly lower values in the Ovx group. This methodology has been shown to be a valid technique to determine bone mineral density, reflecting the status of the crystalline component of bone.³⁸ The attained tibial differences between Ovx and sham animals are in accordance with literature reports. Female rat ovariectomy has been shown to cause deterioration of the

three-dimensional trabecular microstructure, notably the structure model index and connectivity density, as assessed by microtomography of the proximal tibia.³⁹ Accordingly, a decrease in the trabecular bone mineral density of the tibia and associated morphologic changes in the Ovx rat have been reported by several authors, substantiating similarities between this animal model and the human condition of postmenopausal osteoporosis.⁴⁰⁻⁴²

Regarding the analysis of bone regeneration in calvaria sCSDs, conventional radiographic bone density, regenerated area assessment, and histologic and histometric analyses were used to address the intramembranous ossification process within the limits of the surgically created defects. Within the evaluated radiographic images, densitometric analysis and regenerated area assessment showed significant differences, namely a decreased amount of newly formed mineralized tissue in Ovx animals compared to sham animals. Accordingly, histologic analysis revealed reduced formation of new bone tissue extending centripetally from the margin of the defect into the center of the ROI in the Ovx animals compared to the sham animals.

These observations were confirmed by histometric analysis regarding the percentage of bone fill.

In the evaluated model, ovariectomy-induced osteoporosis seemed to impair the bone regeneration process in calvarial sCSDs. To the best of the authors' knowledge, the bone regeneration process per se, in osteoporotic conditions, has not been addressed previously in calvarial defects. Literature reports have typically focused on the evaluation of osteoporotic bone regeneration in the presence of biomaterials; nonetheless, conflicting results have been reported. Some authors substantiated an impaired process mediated by the osteoporotic condition^{9–11} while other studies observed no differences in biomaterial-mediated bone formation in osteoporotic and control animals.^{12–14} The differences in these results may be mostly likely related to the diversity of the used biomaterials—eg, ceramics, bioactive glasses, composites, and xenografts—as well as to the different experimental models. In either case, explanation or insights about the potential underlying mechanisms are broadly lacking. In this study, an evident reduction in new bone formation was established, and since no biomaterial was added to the regenerative milieu, the regenerative capabilities ought to be settled on the osteogenic potential of recruited precursor cells and/or the remodeling process.

The possibility of impaired bone formation in osteoporotic conditions has been addressed in a few studies. The evaluation of osteoporotic bone marrow-derived mesenchymal stem cell cultures revealed similar cellular size and morphology, as well as expression of similar cell surface antigens, compared to controls.⁴³ Nonetheless, osteoporotic-derived cell cultures differed: they had a lower growth rate and exhibited a deficient ability to differentiate into the osteogenic lineage, as evidenced by decreased ALP activity, type 1 collagen synthesis, and calcium phosphate deposition.^{43,44} Moreover, osteoporosis-associated estrogen deficiency seems to suppress the survival of osteocytes and impair the physiologic response of osteoblasts to mechanical stimuli, detection of microdamage, and repair of aged bone.^{45,46} Of additional relevance, a clinical report showed, through a histomorphometric analysis of iliac crest bone biopsy specimens, an inverse correlation between the cancellous apposition rate and the osteoid volume, with an increase in the proportion of adipose tissue present in the osteoporotic bone.⁴⁷ The cancellous apposition rate reflects osteoblastic activity, indicating that the increased volume of adipose tissue in the osteoporotic bone may be associated with the reduced bone formation. In accordance, osteoporotic-derived mesenchymal stem cell cultures have been shown to express an increased adipogenic potential compared to control cultures.⁴⁸ Overall, the data seem to support the postulated impairment of the bone formation process in osteoporotic conditions.

Additionally, excessive osteoclastic activity, which seems to lead to an imbalance in the bone remodeling process that favors bone resorption in osteoporosis, may also contribute to the decreased bone regeneration.^{49,50} Estrogen deficiency has been shown to enhance the production of pro-osteoclastogenetic cytokines (eg, tumor necrosis factor-alpha and receptor activator of nuclear factor kappa-B ligand) and increase the number of circulating osteoclastic precursors.⁵¹ The increased production of these cytokines may also substantiate the increased spontaneous osteoclastogenesis verified in women affected by postmenopausal osteoporosis.⁵² Moreover, osteoporotic conditions have been associated with an increased life span of mature osteoclasts.⁴⁵ Taken as a whole, the data seem to support an excessive bone resorption process in osteoporotic conditions, which may contribute to a disturbed equilibrium between bone formation and bone resorption.

CONCLUSIONS

Both impaired bone formation and disruption of the bone remodeling equilibrium seemed to converge to limit the bone regeneration process in this rat model of the human postmenopausal osteoporotic condition. The impairment of the intramembranous ossification process during the healing of calvarial subcritical-size defects in the reported model may suggest that selective bone regenerative strategies are required in osteoporotic patients.

ACKNOWLEDGMENTS

The authors reported no conflicts of interest related to this study.

REFERENCES

- Manolagas S, Jilka R. Bone marrow, cytokines, and bone remodeling. Emerging insights into the pathophysiology of osteoporosis. *N Engl J Med* 1995;332:305–311.
- Keen R. Burden of osteoporosis and fractures. *Curr Osteoporos Rep* 2003;1:66–70.
- Cole Z, Dennison E, Cooper C. Osteoporosis epidemiology update. *Curr Rheumatol Rep* 2008;10:92–96.
- Chrischilles E, Shireman T, Wallace R. Costs and health effects of osteoporotic fractures. *Bone* 1994;15:377–386.
- Burge R, Dawson-Hughes B, Solomon D, Wong J, King A, Tosteson A. Incidence and economic burden of osteoporosis-related fractures in the United States, 2005–2025. *J Bone Miner Res* 2007;22: 465–475.
- Namkung-Matthai H, Appleyard R, et al. Osteoporosis influences the early period of fracture healing in a rat osteoporotic model. *Bone* 2001;28:80–86.

7. Chao E, Inoue N, Koo T, Kim Y. Biomechanical considerations of fracture treatment and bone quality maintenance in elderly patients and patients with osteoporosis. *Clin Orthop Relat Res* 2004;425:12–25.
8. Giannoudis P, Tzioupis C, Almalki T, Buckley R. Fracture healing in osteoporotic fractures: Is it really different? A basic science perspective. *Injury* 2007;38(suppl 1):S90–99.
9. Fini M, Giavaresi G, Torricelli P, et al. Osteoporosis and biomaterial osteointegration. *Biomed Pharmacother* 2004;58:487–493.
10. Kim S, Kim S, Lim S, Bae C. Effects on bone formation in ovariectomized rats after implantation of tooth ash and plaster of Paris mixture. *J Oral Maxillofac Surg* 2004;62:852–857.
11. Ajduković Z, Najman S, Dordević L, et al. Repair of bone tissue affected by osteoporosis with hydroxyapatite-poly-L-lactide (HAp-PLLA) with and without blood plasma. *J Biomater Appl* 2005;20:179–190.
12. Hayashi K, Uenoyama K, Mashima T, Sugioka Y. Remodelling of bone around hydroxyapatite and titanium in experimental osteoporosis. *Biomaterials* 1994;15:11–16.
13. Fuegl A, Tangl S, Keibl C, Watzek G, Redl H, Gruber G. The impact of ovariectomy and hyperglycemia on graft consolidation in rat calvaria. *Clin Oral Implants Res* 2011 May;22(5):524–529. doi: 10.1111/j.1600-0501.2010.02048.x.
14. Turner A, Eckhoff D, Dewell R, Villanueva A, Aberman H. Peri-apatite-coated implants improve fixation in osteopenic bone. In: Proceedings from the 40th Annual Meeting of the Orthopaedic Research Society. New Orleans: The Orthopaedic Research Society, 1996:41.
15. Cancedda R, Giannoni P, Mastrogiammo M. A tissue engineering approach to bone repair in large animal models and in clinical practice. *Biomaterials* 2007;28:4240–4250.
16. Buma P, Schreurs W, Verdonschot N. Skeletal tissue engineering: From in vitro studies to large animal models. *Biomaterials* 2004;25:1487–1495.
17. Mooney MS, MI. Animal models for bone tissue engineering of critical-sized defects (CSDs), bone pathologies, and orthopedic disease states. In: Hollinger J, Einhorn T, Doll B, Sfeir C (eds). *Bone Tissue Engineering*. Boca Raton, FL: CRC Press, 2005:217–244.
18. Pearce A, Richards R, Milz S, Schneider E, Pearce S. Animal models for implant biomaterial research in bone: A review. *Eur Cell Mater* 2007;2:1–10.
19. Thompson D, Simmons H, Pirie C, Ke H. FDA Guidelines and animal models for osteoporosis. *Bone* 1995;17(4 suppl):125S–133S.
20. Turner A. Animal models of osteoporosis: Necessity and limitations. *Eur Cell Mater* 2001;22:66–81.
21. Wronski T, Cintrón M, Dann L. Temporal relationship between bone loss and increased bone turnover in ovariectomized rats. *Calcif Tissue Int* 1988;43:179–183.
22. Egermann M, Goldhahn J, Schneider E. Animal models for fracture treatment in osteoporosis. *Osteoporos Int* 2005;16(suppl 2):S129–138.
23. Lelovas P, Xanthos T, Thoma S, Lyritis G, Dontas I. The laboratory rat as an animal model for osteoporosis research. *Comp Med* 2008;58: 424–430.
24. Hollinger J, Kleinschmidt J. The critical size defect as an experimental model to test bone repair materials. *J Craniofac Surg* 1990;1:60–68.
25. Gomes P, Fernandes M. Rodent models in bone-related research: The relevance of calvarial defects in the assessment of bone regeneration strategies. *Lab Anim* 2010;45:14–24.
26. Schmitz J, Hollinger J. The critical size defect as an experimental model for craniomandibulofacial nonunions. *Clin Orthop Relat Res* 1986;205:299–308.
27. Pryor M, Susin C, Wiksjo U. Validity of radiographic evaluations of bone formation in a rat calvaria osteotomy defect model. *J Clin Periodontol* 2006;33:455–460.
28. Cooper G, Mooney M, Gosain A, Campbell P, Losee J, Huard J. Testing the critical size in calvarial bone defects: Revisiting the concept of a critical-size defect. *Plast Reconstr Surg* 2010;125:1685–1692.
29. Messora M, Nagata M, Dornelles R, et al. Bone healing in critical-size defects treated with platelet-rich plasma activated by two different methods. A histologic and histometric study in rat calvaria. *J Periodontal Res* 2008;43:723–729.
30. Messora M, Nagata M, Mariano R, et al. Bone healing in critical-size defects treated with platelet-rich plasma: A histologic and histometric study in rat calvaria. *J Periodontal Res* 2008;43:217–223.
31. Blomqvist J, Alberius P, Isaksson S, Linde A, Hansson B. Factors in implant integration failure after bone grafting: An osteometric and endocrinologic matched analysis. *Int J Oral Maxillofac Surg* 1996;25:63–68.
32. Schliephake H, Neukam F, Wichmann M. Survival analysis of endosteous implants in bone grafts used for the treatment of severe alveolar ridge atrophy. *J Oral Maxillofac Surg* 1997;55:1227–1233.
33. Izuka T, Smolka W, Hallermann W, Mericske-Stern R. Extensive augmentation of the alveolar ridge using autogenous calvarial split bone grafts for dental rehabilitation. *Clin Oral Implants Res* 2004;15: 607–615.
34. Toffler M. Osteotome-mediated sinus floor elevation: A clinical report. *Int J Oral Maxillofac Implants* 2004;19:266–273.
35. Shyng YC, Devlin H, Sloan P. The effect of streptozotocin-induced experimental diabetes mellitus on calvarial defect healing and bone turnover in the rat. *Int J Oral Maxillofac Surg* 2001 Feb;30(1):70–74.
36. Santana RB, Xu L, Chase HB, Amar S, Graves DT, Trackman PC. A role for advanced glycation end products in diminished bone healing in type 1 diabetes. *Diabetes* 2003 Jun;52(6):1502–1510.
37. Wade G, Gray J, Bartness T. Gonadal influences on adiposity. *Int J Obes* 1985;9(suppl 1):83–92.
38. Corday J, Schneider M, Belendez C, Ziegler W, Rahn B, Perren S. Effect of bone size, not density, on the stiffness of the proximal part of normal and osteoporotic human femora. *J Bone Miner Res* 1992;7(suppl 2):S437–444.
39. Ito M, Nishida A, Aoyagi K, Uetani M, Hayashi K, Kawase M. Effects of risedronate on trabecular microstructure and biomechanical properties in ovariectomized rat tibia. *Osteoporos Int* 2005;16:1042–1048.
40. Breen S, Millett A, Loveday B, Johnstone D, Waterton J. Regional analysis of bone mineral density in the distal femur and proximal tibia using peripheral quantitative computed tomography in the rat in vivo. *Calcif Tissue Int* 1996;58:449–453.
41. Laib A, Kumer J, Majumdar S, Lane N. The temporal changes of trabecular architecture in ovariectomized rats assessed by MicroCT. *Osteoporos Int* 2001;12:936–941.
42. Boyd S, Davison P, Müller R, Gasser J. Monitoring individual morphological changes over time in ovariectomized rats by in vivo micro-computed tomography. *Bone* 2006;39:854–862.
43. Rodríguez J, Garat S, Gajardo H, Pino A, Seitz G. Abnormal osteogenesis in osteoporotic patients is reflected by altered mesenchymal stem cells dynamics. *J Cell Biochem* 1999;75:414–423.
44. Rodríguez J, Montecinos L, Ríos S, Reyes P, Martínez J. Mesenchymal stem cells from osteoporotic patients produce a type I collagen-deficient extracellular matrix favoring adipogenic differentiation. *J Cell Biochem*. 2000;79:557–565.
45. Manolagas S. Birth and death of bone cells: Basic regulatory mechanisms and implications for the pathogenesis and treatment of osteoporosis. *Endocr Rev* 2000;21:115–137.
46. Stepan J, Alenfeld F, Boivin G, Feyen J, Lakatos P. Mechanisms of action of antiresorptive therapies of postmenopausal osteoporosis. *Endocr Regul* 2003;37:225–238.
47. Verma S, Rajaratnam J, Denton J, Hoyland J, Byers R. Adipocytic proportion of bone marrow is inversely related to bone formation in osteoporosis. *J Clin Pathol* 2002;55:693–698.
48. Astudillo P, Ríos S, Pastenes L, Pino A, Rodríguez J. Increased adipogenesis of osteoporotic human-mesenchymal stem cells (MSCs) characterizes by impaired leptin action. *J Cell Biochem* 2008;103: 1054–1065.
49. Boyle W, Simonet W, Lacey D. Osteoclast differentiation and activation. *Nature* 2003;423:337–342.
50. Wada T, Nakashima T, Hiroshi N, Penninger J. RANKL-RANK signaling in osteoclastogenesis and bone disease. *Trends Mol Med* 2006;12: 17–25.
51. D'Amelio P, Grimaldi A, Di Bella S, et al. Estrogen deficiency increases osteoclastogenesis up-regulating T cells activity: A key mechanism in osteoporosis. *Bone* 2008;43:92–100.
52. D'Amelio P, Grimaldi A, Pescarmona G, Tamone C, Roato I, Isaia G. Spontaneous osteoclast formation from peripheral blood mononuclear cells in postmenopausal osteoporosis. *FASEB J* 2005;19: 410–412.

Assessment of Leakage at the Implant-Abutment Connection Using a New Gas Flow Method

Marie-Alix Fauroux, DDS, MSc¹/Bernard Levallois, DDS, PhD²/
Jacques Yachouh, MD, PhD²/Jacques-Henri Torres, DDS, MD, PhD³

Purpose: The aim of this study was to evaluate, with a new gas flow technique, leakage at the implant/abutment junction in systems with four different connections. **Materials and Methods:** Five Bränemark System, five One Morse, five Intra-lock System, and five Ankylos Plus implants and abutments were used. A hole was drilled in the apex of each implant to allow gas to flow through the connection from negative to atmospheric pressure. The gas flow was calculated (slope of pressure decrease, in hPa.s^{-1}). Each connection was tested after both manual and key tightening. Statistical analysis was performed on a generalized linear model with repeated measurements. The significance level was set at $\alpha = .05$. **Results:** A global significant difference was observed between the various systems ($P = .0001$). After manual tightening, gas leakage was ($\text{Ln}[\text{hPa.s}^{-1}]$, means \pm standard deviations): One Morse: $0.20 (\pm 1.70)$; Bränemark System: $-4.56 (\pm 2.61)$; Intra-lock: $-4.31 (\pm 4.17)$; Ankylos Plus: $-7.59 (\pm 0.76)$. After key tightening, mean values were: One Morse: $-2.51 (\pm 2.72)$; Bränemark System: $-7.23 (\pm 1.01)$; Intra-lock: $-7.76 (\pm 0.50)$; Ankylos Plus: $-7.73 (\pm 0.62)$. **Conclusion:** This study confirms that gas flow is an appropriate method to assess connection leakage. Ankylos Plus connection leakage was very low when the assembly was tightened manually. Among conical connection systems, low (Ankylos Plus) and high (One Morse) leakage was observed. This gas flow study suggests, therefore, that connection design is not the most important parameter for implant/abutment connection leakage. INT J ORAL MAXILLOFAC IMPLANTS 2012;27:1409–1412

Key words: abutment, connection, dental implant, gas flow, implant-abutment interface, leakage

Most dental implant systems currently on the market consist of two parts: the implant itself and the abutment, which supports the prosthesis. It is desirable to use implant-abutment junctions that are impervious to bacterial contamination.¹ Leakage at the connection has already been tested by various means: microbial leakage at the implant-abutment interface was examined in both patients^{2–4} and in vitro^{5–11} (the latest studies focus on DNA hybridization¹²); color markers were placed between the implant and the abutment, and leakage was measured by spectro-

photometry^{13,14}; and, more recently, endotoxins were used instead of color markers.¹⁵ However, these techniques are insufficient to provide a quantitative and reproducible way to measure the leakage.

A quantitative, sensitive, and reproducible method using gas flow has been described to assess endodontic sealing.¹⁶ This technique, independent of water-wetting properties and not subjected to entrapped air bubbles,¹⁶ has been adapted to evaluate implant connection leakage.¹⁷ The gas flow method seems to be better than color marker techniques because it allows successive measurements without disconnecting the abutment from the implant. Moreover, statistical analysis in a crossover study is strengthened when the abutment is not detached. This new technique would therefore appear to be a simple, quantitative, reproducible, and practical in vitro technique to assess dental implant–abutment leakage and to compare leakage of different implant systems.¹⁷ The aim of the present study, therefore, was to compare leakage at the implant-abutment connection of various implant types with the gas flow method.

¹Université Montpellier 1, Montpellier, France.

²Assistant Professor, Université Montpellier 1, Montpellier, France.

³Professor, Université Montpellier 1, Montpellier, France.

Correspondence to: Prof Jacques-Henri Torres, UFR Odontologie, 545, avenue du Pr JL Viala, 34193 Montpellier cedex 5. Fax: +33-411-75-91-96. Email: jh.torres@univ-montp1.fr.

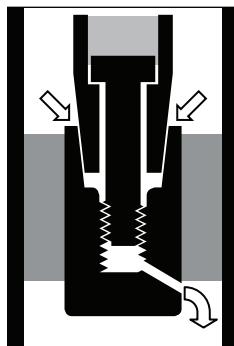


Fig 1 Implant embedded in epoxy glue (dark grey). The screw hole is sealed with wax (light grey). Arrows indicate nitrogen flow.

1. After manual tightening of the abutment;
2. After key tightening of the abutment according to the torque recommended by the manufacturers (Bränemark System, 35 Ncm; One Morse, 35 Ncm; Intra-lock, 30 Ncm; Ankylos Plus, 15 Ncm); and
3. After key tightening of the abutment and blockage of the implant-abutment connection with wax (as a negative test).

All final (negative) tests of the 20 implants were pooled to define a global control: the mean remaining leakage of the experimental setup. A previous published study¹⁷ indicated that, for a set of five implants, the method reproducibility was highly satisfactory: the observed standard deviation was about 10^{-3} hPa.s⁻¹, with a coefficient of variation of 1.3%. Therefore, based on these figures, to observe significant differences between implant systems, it was calculated that a small number of implants ($n = 5$) was necessary.

Statistical analyses were performed using SAS Software (version 9.2, SAS Institute) based on a "generalized linear model with repeated measures" using the PROC GLM routine. Pairwise comparisons were adjusted with the Benjamini correction. Since the measures did not follow a normal distribution, a logarithmic transformation was applied to normalize the distribution. The significance level was set at $\alpha = 0.05$.

To observe the microgap more closely, two implants (one each, One Morse and Ankylos Plus) were embedded in epoxy and cut along the longitudinal axis. After polishing and rinsing, the samples were placed on adhesive tape, fixed to a 5-cm-diameter plate, and examined with a FEI Quanta 200 FEG environmental scanning electron microscope (FEI Company) with accelerating voltage of 15.00 kV and a final water vapor pressure of 0.83 Torr. The secondary electron signal was focused to provide topographic contrast.

MATERIALS AND METHODS

Twenty samples of connections (implants and abutments) of four different brands (five assemblies each) were used:

1. Bränemark System (Mk III TiUnite Regular Platform), 4 mm diameter, 18 mm length (Nobel Biocare)
2. One Morse, 4.3 mm diameter, 12 mm length (One System Implant)
3. Intra-lock System (ref DT4015STI), 4 mm diameter, 15 mm length, with an internal conical connection (Intra-lock)
4. Ankylos Plus, 4.5 mm diameter, 14 mm length, internal conical connection (Dentsply Friadent)

A hole was drilled in the apical part of the screw cavity of all implants (Fig 1). The implants were then partially embedded in epoxy glue (Araldite 2012, Huntsman) and sealed in a glass tube, allowing free space around both the abutment connection and the hole. A standard straight abutment from the same manufacturer was attached to the implant (Fig 1). Wax (Purple wax, GC Europe) was used to block the screw hole.

The implants were positioned in an experimental chamber between atmospheric (P1) and negative (P2) nitrogen pressure. Gas flow was assessed by measuring the pressure difference between P1 and P2 with a differential pressure gauge (Testo 526). After a vacuum had been created, the valve was closed. The initial pressure difference was approximately 1,010 hPa. The pressure difference versus time was recorded. After an initial drop, a second sequence appeared as a straight line; therefore the nitrogen flow was no longer related to pressure difference, but only to the importance of leakage, according to Knudsen's law (for further detail, see Torres et al¹⁷). The slope of this line was measured.

For each implant specimen, nitrogen leakage was measured three times without disconnecting the abutment:

RESULTS

The mean stabilized slopes (\pm standard deviations) of nitrogen pressure decrease among the different systems were as follows ($\text{Ln}[\text{hPa.s}^{-1}]$). After manual tightening they were: One Morse: $0.20 (\pm 1.70)$, Bränemark System: $-4.56 (\pm 2.61)$, Intra-lock: $-4.31 (\pm 4.17)$, Ankylos Plus: $-7.59 (\pm 0.76)$. After key tightening, they were: One Morse: $-2.51 (\pm 2.72)$, Bränemark System: $-7.23 (\pm 1.01)$, Intra-lock: $-7.76 (\pm 0.50)$, Ankylos Plus, $-7.73 (\pm 0.62)$ (Fig 2).

No significant differences were noted between the four systems for the final negative test. The mean value ($e^{-8.01}$ hPa.s⁻¹) of this test (20 measurements) can be considered as a leak tightness reference. This value thus appears on Fig 2 as zero on the ordinate axis.

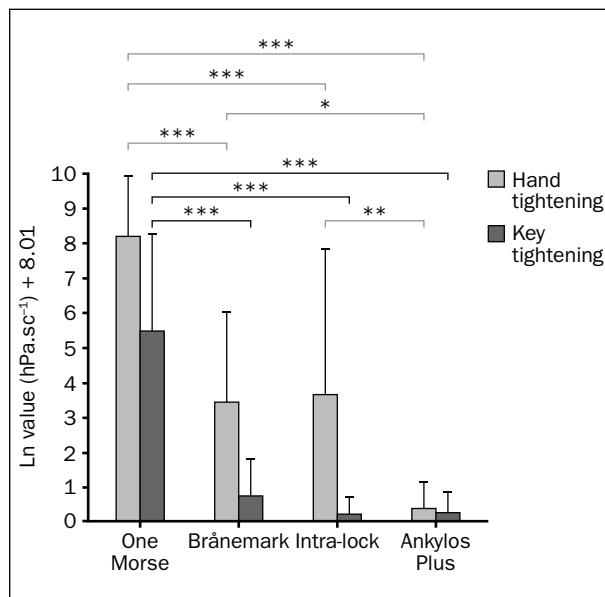


Fig 2 Mean nitrogen leakage in each group after hand tightening or key tightening (at torques recommended by the manufacturers). Mean values (\pm standard deviations) are shown after logarithmic transformation ($\ln[\text{hPa.s}^{-1}] + 8.01$) to ease reading. Complete leak tightness in the model (mean negative test value = $e^{-8.01}$ hPa.s $^{-1}$), was arbitrarily set to zero on the ordinate axis. Also, it is to be noted that the top of the y-axis was arbitrarily set to 10, whereas no maximal leakage value can be defined. * $P = .03$; ** $P = .001$; *** $P = .0001$.

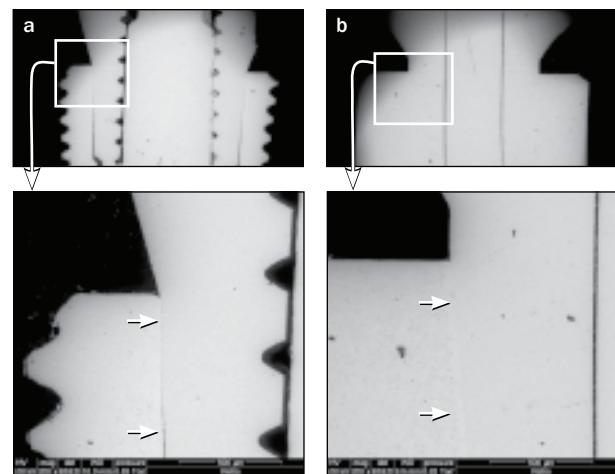


Fig 3 Electron microscope views of the two conical connection systems (a: One Morse; b: Ankylos Plus). The microgap (white arrows) is sharply visible in the One Morse connection, whereas it is difficult to distinguish in the Ankylos Plus connection.

A lower flow was observed after key tightening compared to hand tightening for Bränemark System ($P = .0014$) and One Morse ($P = .0004$) specimens. No significant differences between manual and key tightening were shown for Intra-lock ($P = .09$) and Ankylos Plus ($P = .09$) specimens.

Significant differences were observed globally between the various systems, both for manual ($P = .0001$) and for key ($P = .0001$) tightening. After manual tightening, all pair comparisons were significant, except for between the Bränemark and Intra-lock systems ($P = .80$). After key tightening, significant differences were observed between One Morse and each of the three other systems. The other pair comparisons were not significant.

The microscopic images of the two implants with a conical connection showed that the connection between the One Morse abutment and implant seems to feature a slight angular difference between the parts, resulting in a very small contact zone (Fig 3a). Conversely, for the Ankylos Plus system, the two parts were so well adapted that the line between the connection and the implant was difficult to observe (Fig 3b, white arrows).

DISCUSSION

This new technique using gas leakage provided precise physical and reproducible measures.¹⁷ This assay assessed only the overall leak tightness of the connection. The possible spaces around the implant collar that do not communicate with the inner part of the implant did not influence the result, although clinically, they can play a major role.

As already shown for One Morse implants with this technique,¹⁷ a lower flow was observed in the present study after key tightening compared to hand tightening for all implant types, although this was not significant for Intra-lock or for Ankylos Plus implants. Moreover, this difference was very small with Ankylos Plus: After manual tightening, the connection in this brand was noted to be already in the order of the values of key tightening. Indeed, the manufacturer recommends screwing the abutment with a lower torque (15 Ncm) compared with the three other systems (30 to 35 Ncm). The good results found for Ankylos Plus cannot be ascribed to its conical connection design only; indeed, another conical system (One Morse) showed the poorest results of all four systems. It is

therefore suggested that leakage is mainly caused by other factors that are more important than connection design. Although they were based on only one sample of each brand, the scanning electron images (Fig 3) were included mainly to illustrate the results and to propose a possible explanation, ie, the details of manufacturing could be essential.

Nowadays, the external connection of the Bränemark System is regarded as obsolete. However, in the present study, this system showed low leakage after key tightening (not significantly different from Intra-lock or Ankylos Plus). In fact, the authors hypothesize that a flat connection such as that in the Bränemark System can technically be machined to a correct tight result, and probably more easily than a conical connection.

Although this finding was not statistically significant, the gas leakage measured after key tightening was always greater than the leakage measured in (negative) control tests for every one of the 20 implants tested (data not shown). It is then likely that, within the four studied systems, implant connections are not completely tight, even after key tightening. This has also been observed with other in vitro methods.¹⁵ However, this finding can only have limited clinical relevance, for instance, if the microgap is remote from the bone (especially in the case of "platform switching" with the Ankylos Plus System) or if the microgap is smaller than the size of bacteria or endotoxins.¹⁵ However, the model used in this study cannot assess the size of the microgap.

The results of this in vitro gas leakage study cannot be extrapolated directly to clinical conditions. Indeed, under occlusal loading, it is likely that the mechanical stress of mastication would modify the implant-abutment connection. Further tests are therefore required to determine the connection leakage of various implant systems in different situations, such as insertion torque, chemical stress, or mechanical changes mimicking mastication.

CONCLUSION

This trial confirmed that gas flow is an appropriate method to assess connection leakage. The Ankylos Plus connection showed low leakage from manual tightening (it was already in the order of the values of key tightening). Among conical connection systems, completely different behaviors were observed: low leakage was seen with Ankylos Plus and much greater leakage was seen with One Morse. The results of the present study suggest that connection design is not the most important feature for implant-abutment leakage. Other factors could also be essential for minimizing leakage, such as manufacturing and engineering quality.

ACKNOWLEDGMENTS

The authors thank Dr Michael Mechali, Dr Olivier Romieu, and Dr Paul Tramini for their help with the gas flow measurements and statistical analysis. The authors reported no conflicts of interest related to this study.

REFERENCES

1. Oh TJ, Yoon J, Misch CE, Wang HL. The causes of early implant bone loss: Myth or science? *J Periodontol* 2002;73:322–333.
2. Persson LG, Lekholm U, Leonhardt A, Dahlin G, Lindhe J. Bacterial colonization on internal surfaces of Bränemark system implant components. *Clin Oral Implants Res* 1996;7:90–95.
3. Rimondini L, Marin C, Brunella F, Fini M. Internal contamination of a 2-component implant system after occlusal loading and provisionally luted reconstruction with or without a washer device. *J Periodontol* 2001;72:1652–1657.
4. Quirynen M, Alsaadi G, Pauwels M, Haffajee A, van Steenberghe D, Naert I. Microbiological and clinical outcomes and patient satisfaction for two treatment options in the edentulous lower jaw after 10 years of function. *Clin Oral Implants Res* 2005;16:277–287.
5. Quirynen M, Bollen CM, Eyssen H, van Steenberghe D. Microbial penetration along the implant components of the Bränemark system. An in vitro study. *Clin Oral Implants Res* 1994;5:239–244.
6. Steinebrunner L, Wolfart S, Bossmann K, Kern M. In vitro evaluation of bacterial leakage along the implant-abutment interface of different implant systems. *Int J Oral Maxillofac Implants* 2005;20:875–881.
7. Guindy JS, Besimo CE, Besimo R, Schiel H, Meyer J. Bacterial leakage into and from prefabricated screw-retained implant-borne crowns in vitro. *J Oral Rehabil* 1998;25:403–408.
8. Jansen VK, Conrads G, Richter EJ. Microbial leakage and marginal fit of the implant-abutment interface. *Int J Oral Maxillofac Implants* 1997;12:527–540.
9. Besimo CE, Guindy JS, Lewettag D, Meyer J. Prevention of bacterial leakage into and from prefabricated screw-retained crowns on implants in vitro. *Int J Oral Maxillofac Implants* 1999;14:654–660.
10. Piattelli A, Scarano A, Paolantonio M, et al. Fluids and microbial penetration in the internal part of cement-retained versus screw-retained implant-abutment connections. *J Periodontol* 2001;72:1146–1150.
11. Dibart S, Warbington M, Su MF, Skobe Z. In vitro evaluation of the implant-abutment bacterial seal: The locking taper system. *Int J Oral Maxillofac Implants* 2005;20:732–737.
12. do Nascimento C, Barbosa RE, Issa JP, Watanabe E, Ito IY, de Albuquerque RF Jr. Use of checkerboard DNA-DNA hybridization to evaluate the internal contamination of dental implants and comparison of bacterial leakage with cast or pre-machined abutments. *Clin Oral Implants Res* 2009;20:571–577.
13. Coelho PG, Sudack P, Suzuki M, Kurtz KS, Romanos GE, Silva NR. In vitro evaluation of the implant abutment connection sealing capability of different implant systems. *J Oral Rehabil* 2008;35:917–924.
14. Gross M, Abramovich I, Weiss EI. Microlleakage at the abutment-implant interface of osseointegrated implants: A comparative study. *Int J Oral Maxillofac Implants* 1999;14:94–100.
15. Harder S, Dimaczek B, Acil Y, Terheyden H, Freitag-Wolf S, Kern M. Molecular leakage at implant-abutment connection—In vitro investigation of tightness of internal conical implant-abutment connections against endotoxin penetration. *Clin Oral Investig* 2010;14:427–432.
16. Romieu OJ, Jacquot B, Callas-Etienne S, Dutilleul PY, Levallois B, Cuisinier FJ. Gas permeability: A new quantitative method to assess endodontic leakage. *Biomed Tech (Berl)* 2008;53:181–184.
17. Torres JH, Mechali M, Romieu O, et al. Development of a new quantitative gas permeability method for dental implant-abutment connection tightness assessment. *Biomed Eng Online* 2011;10:28.

The Effect of Covering Materials with an Open Wound in Alveolar Ridge Augmentation Using Beta-Tricalcium Phosphate: An Experimental Study in the Dog

Kenji Inomata, DDS¹/Eriko Marukawa, DDS, PhD²/Yukinobu Takahashi, DDS¹/Ken Omura, DDS, PhD³

Purpose: This study aimed to examine the effectiveness of a grafting technique using beta-tricalcium phosphate (β -TCP) covered with different materials in alveolar bone defects with dehiscences.

Materials

and Methods: In five beagle dogs, all premolars in the mandible were extracted bilaterally. After a 12-week healing period, two bone defects (length, 5 mm; width, 5 mm; depth, 7 mm) were created on each side of the mandible, and the buccal bone plate was resected. The four bone defects were randomly assigned to one of the following treatments: group 1, β -TCP alone (TCP group); group 2, β -TCP graft covered with collagen sponge (TCP+collagen group); group 3, β -TCP graft covered with free buccal mucosa (TCP+mucosa group); group 4, no treatment (control group). The microarchitecture of the regenerated bone was observed using microcomputed tomography, and the area of newly formed bone was measured. Specimens from each defect were selected and subjected to histologic and histomorphometric analysis; areas of newly formed bone and the ridge width were measured in the specimens.

Results:

Significant differences were found between the control group and all test groups. The median horizontal width of the ridge 2 mm from the top of the alveolar crest in the TCP+mucosa group was significantly greater than that of the TCP group. There was no significant difference between the TCP+mucosa and TCP+collagen groups in any measurement.

Conclusions: Application of β -TCP grafts to alveolar bone defects with dehiscence and covering of the open wound with free buccal mucosa or collagen sponge may be useful for ridge augmentation. Compared to no treatment or leaving the wound uncovered, these approaches resulted in more new bone formation and provided adequate horizontal mandibular width. *INT J ORAL MAXILLOFAC IMPLANTS* 2012;27:1413–1421

Key words: beta-tricalcium phosphate, canine mandible, open wound, ridge augmentation, socket preservation

Reduction of the original height and width of the alveolar bone generally occurs during healing after tooth extraction.^{1–3} Alveolar ridge resorption after tooth extraction in both jaws is significantly greater on the buccal aspect than on the lingual or palatal; therefore, the reduction in width of the alveolar ridge

is greater than the loss of height.^{4–6} Inadequate width of the alveolar ridge renders placement of dental implants difficult and impairs the long-term functional stability of the implant and the esthetic results after prosthodontic treatment. Therefore, augmentation of the alveolar ridge or socket preservation may be needed to optimize the success of implant placement in terms of both esthetics and function.

Augmentation of the alveolar socket at the time of tooth extraction (ie, socket preservation, ridge preservation) has been evaluated in several studies. Techniques for ridge preservation involving the use of hydroxyapatite in the form of root-shaped cones were introduced in the 1980s.^{7,8} Various methods using bone grafts or substitutes,^{9–15} with or without absorbable^{16,17} or nonabsorbable membranes,^{18–20} have been employed for ridge preservation after tooth extraction. Previously, bone grafts or substitutes required primary closure over the socket. However, this requirement increases surgical complexity, reduces the amount of keratinized gingiva, and disrupts the natural architecture of soft tissues in the area. As an alternative, the Bio-Col²¹ technique and socket seal surgery²² using a

¹Research Associate, Oral and Maxillofacial Surgery, Department of Oral Restoration, Division of Oral Health Science, Tokyo Medical and Dental University Graduate School, Japan.

²Assistant Professor, Oral and Maxillofacial Surgery, Department of Oral Restoration, Division of Oral Health Science, Tokyo Medical and Dental University Graduate School, Japan.

³Professor and Chairman, Oral and Maxillofacial Surgery, Department of Oral Restoration, Division of Oral Health Science, Tokyo Medical and Dental University Graduate School, Japan.

Correspondence to: Dr Eriko Marukawa, Oral and Maxillofacial Surgery, Department of Oral Restitution, Division of Oral Health Sciences, Tokyo Medical and Dental University Graduate School, 1-5-45 Yushima, Bunkyo-ku, Tokyo 113-8549, Japan. Fax: +81-3-5803-0199. Email: eriko.m.osur@tmd.ac.jp



Fig 1 Clinical photograph illustrating the two bone defects (length 5 mm, width 5 mm, depth 7 mm) on one side of the mandible.



Fig 2 (Left to right) Group 1 (TCP), group 2 (TCP+collagen), group 3 (TCP+mucosa), group 4 (no treatment/control).

free gingival graft and a modification of the technique that uses connective tissue²³ have been reported.

Clinicians have frequently explored the method of filling bone defects, such as alveolar postextraction sockets, with osteoconductive materials to preserve adequate bone volume.^{15,24,25} However, the use of grafting materials in fresh extraction sockets has been questioned, because it may interfere with the normal healing process.²⁶ Studies in humans using demineralized freeze-dried bone allografts, deproteinized bovine bone mineral, or bioactive glass have shown that graft particles, surrounded by connective tissue or woven bone in the alveolar sockets, may still be present 6 to 9 months following insertion.^{11,12,27}

Beta-tricalcium phosphate (β -TCP) is a bioabsorbable bone substitute that exhibits osteoconductivity. It has been used for bone regeneration in a variety of surgical procedures in both animal models^{28–31} and human trials.^{32–36} In a comparative histomorphometric study on different biomaterials in bone defects in miniature pig mandibles,³⁷ TCP showed the most promising results for biodegradation and substitution among other nonautologous graft materials such as coral-derived hydroxyapatite and demineralized freeze-dried bone allografts. A few studies have evaluated the use of β -TCP as a graft material to augment sockets or bone defects in the jaw.^{31,36}

As stated, various methods and graft materials for ridge preservation have been evaluated. According to Yeo and Ong,³⁸ socket preservation is not recommended in all extraction sites, but rather should be used on a case-by-case basis. They reported that the possibility of socket preservation depended on the type of defect that is present after tooth removal. It is difficult to preserve the alveolar ridge in the extraction socket of a tooth with dehiscence of the buccal or lingual wall.

The aim of the present study was to examine the effectiveness of β -TCP covered with collagen membrane or free buccal mucosa without primary closure in augmenting alveolar bone defects with dehiscence of the buccal wall in the canine mandible.

MATERIALS AND METHODS

Animals

Five healthy male beagle dogs, each approximately 5 years old and weighing 15 to 20 kg, were used in this study. All animal procedures were performed in accordance with the guidelines of Tokyo Medical and Dental University for the care and use of laboratory animals. The study protocol was approved by the Institutional Animal Care and Use Committee of Tokyo Medical and Dental University.

Surgical Procedures

The animals were anesthetized by intramuscular administration of ketamine hydrochloride (25 mg/kg; Veterinary Ketalar, Sankyo) and medetomidine hydrochloride (0.5 mg/kg; Domitor, Meiji Seika). A local anesthetic (lidocaine hydrochloride 2% with epinephrine 1:80,000 [Xylocaine, Dentsply Sankin]) was administered by infiltration. Initially, all premolars in the mandible (P1 to P4) were removed to create edentulous ridges. Twelve weeks after extraction, crestal incisions were made and full mucoperiosteal flaps were reflected. Two bone defects (length 5 mm, height 5 mm, depth 7 mm) were created on each side of the mandible, and the buccal bone plate was removed (Fig 1). Drilling was performed under sterile saline irrigation.

The four bone defects were randomly assigned to one of the following grafting treatments (Fig 2).

- Group 1: β -TCP grafting (TCP group, Fig 2a)
- Group 2: β -TCP graft covered with collagen sponge (TCP+collagen group, Fig 2b)
- Group 3: β -TCP graft covered with free buccal mucosa (TCP+mucosa group, Fig 2c)
- Group 4: No treatment (control group, Fig 2d)

The granules of the porous β -TCP (Osferion, Olympus Terumo Biomaterials) had a particle size of 0.5 to 1.5 mm, porosity of 75%, and a pore size of 100 to 400 μm . The defects were densely packed with the β -TCP,

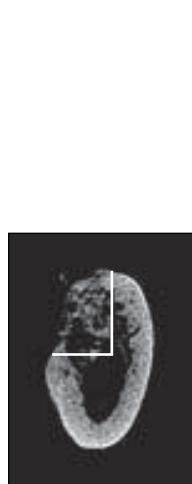


Fig 3 Cross-sectional scanning image obtained by micro-CT of the central portion in the regenerated bone defect. The white line represents the defect site (width 5 mm, depth 7 mm).

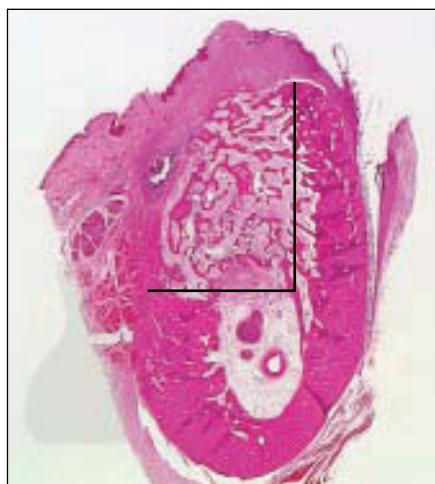


Fig 4 Photomicrograph of a buccolingual section at low magnification (hematoxylin-eosin). The black line represents the defect site (width 5 mm, depth 7 mm).

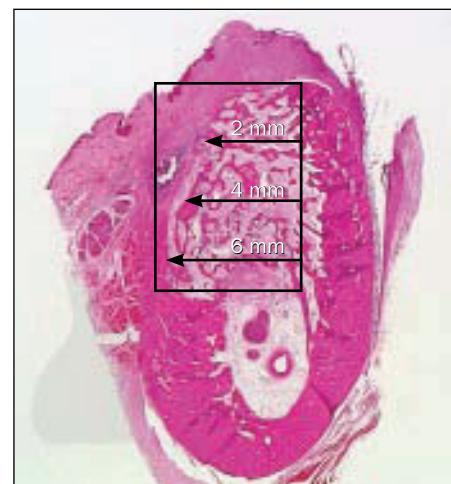


Fig 5 Mean horizontal width of the alveolar ridge measured at different levels. 2 mm = ridge width measured 2 mm from the top of the frame; 4 mm = ridge width measured 4 mm from the top of the frame; 6 mm = ridge width measured 6 mm from the top of the frame. The black frame represents the regenerated site (width 5 mm, depth 7 mm).

which was mixed with blood obtained from the surgical site. Four open wounds, which simulated extraction sockets, were made in all sites, and the gingiva above the defects was trimmed. At TCP+collagen sites (Fig 2b), the socket opening was additionally covered with a collagen sponge (Terudermis, Mesh Reinforced Type, Olympus Terumo Biomaterials), and a silicone membrane reinforced with polyester mesh was secured to the marginal gingiva of the extracted tooth with interrupted sutures. The membrane was used to prevent infection and control moisture flux (eg, exudates). At 14 days after surgery, the membrane was removed. At TCP+mucosa sites (Fig 2c), the socket opening was covered with a free buccal mucosa graft (3 mm thick and 5 mm in diameter), which was placed on top of the β-TCP, adapted, and sutured.

For 3 days after the operation, the animals received an intramuscular injection of 0.25 g cefazolin sodium hydrate, an antibiotic (Cefamezin alfa, Astellas), and butorphanol tartrate, an analgesic drug (Stadol injection, Bristol-Myers Squibb), one time daily. The animals were fed a soft diet throughout the study.

After a 12-week healing period, all animals were euthanized using an overdose of ketamine hydrochloride (30 mL intramuscular, 50 mg/mL; Veterinary Ketalar, Sankyo). Subsequently, the mandibles were block-resected, and the segments were immediately immersed in a 10% formaldehyde solution before histologic preparation.

Radiographic Analysis

The microarchitecture of the regenerated bone was observed using a microcomputed tomography (micro-CT) system (Scan Xmate-A090S; Comscantecno) operating at 70 kv and 20 μm. Two-dimensional coronal images of the bone specimens were taken using micro-CT. The size of the regenerated area (area of the new bone and β-TCP) of the defect site (width 5 mm, depth 7 mm) was calculated via image processing software (Scion Image, Scion) (Fig 3). The average area at three sites—namely midline, 1 mm mesial to midline, and 1 mm distal to midline—was used to compare the groups.

Histologic Analysis

The mandibles were sectioned through the midline area of each defect using a cutting-grinding system (Exakt). These harvested specimens were decalcified in hydrochloric acid (K-CX, Astellas), dehydrated in increasing concentrations of ethanol, embedded in paraffin, and cut into 4-μm sections in the buccolingual plane using a microtome (SM 2000R, Leica). The sections were then stained with hematoxylin and eosin and examined under a light microscope.

The area of newly formed bone (Fig 4) and the ridge widths at 2, 4, and 6 mm from the top of the established frame (Fig 5) of each specimen were measured and analyzed with image analysis software (Scion Image).

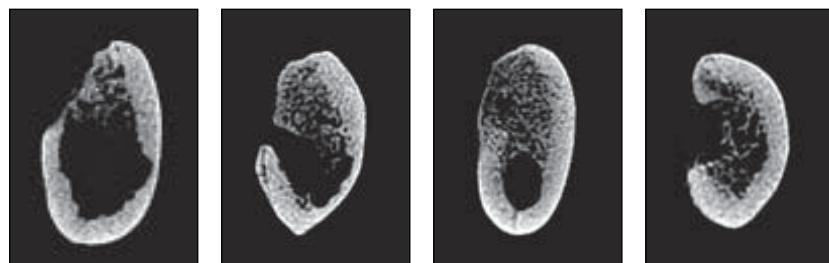


Fig 6 Cross-sectional micro-CT images of the midline area of each defect. (Left to right) Group 1 (TCP), group 2 (TCP+collagen), group 3 (TCP+mucosa), group 4 (no treatment/control).

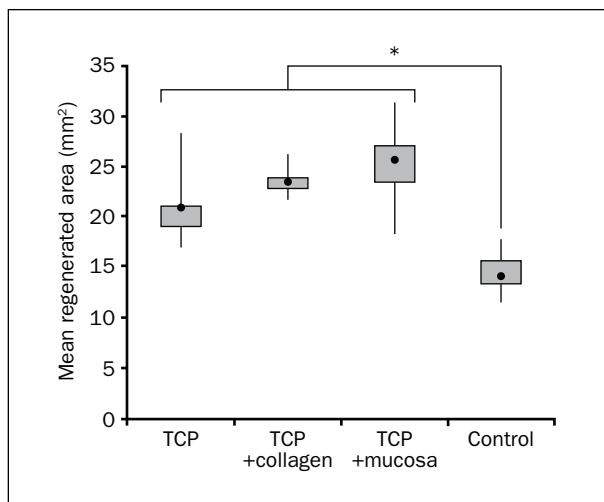


Fig 7 Mean regenerated area of the defect site measured by postoperative CT. Black dots indicate median values. *Statistically significant differences, $P < .05$.

Table 1 Mean Coronal Regenerated Area in Each Defect Site Determined by Postoperative CT

Site type	Coronal regenerated area (mm ²)
TCP	21.2 ± 4.3
TCP+collagen	23.6 ± 1.7
TCP+mucosa	25.4 ± 4.9
Control	14.5 ± 2.3

Statistical Analysis

Data analysis was performed using Microsoft Excel. The endpoint differences between the groups were analyzed using the Mann-Whitney U test ($P < .05$). The data were expressed as the means (\pm standard deviations) of five animals.

RESULTS

There were no clinical signs of infection during the healing process in any of the experimental groups. The sockets were completely covered with gingiva by 7 to 10 days after the operation. Extensive β -TCP leakage

was observed in group 1 sites, whereas slight leakage was observed in groups 2 and 3.

Radiographic Evaluation

The areas of new bone and remaining TCP in each group were examined for bone recovery after the operation (Fig 6). Twelve weeks after treatment, most of the TCP granules had resorbed. This indicated that TCP, which is highly radiopaque, had resorbed, and the resorbed areas were replaced with newly formed bone. In the experimental groups (groups 1 to 3), the hard tissue bridge was continuous with the buccal and lingual bone plates; however, in the control group, no hard tissue bridge was detected. In group 1, the augmented crest width was not sufficient, and the outline of the alveolar ridge showed edge contour. In the TCP+collagen and TCP+mucosa groups, the crest width had recovered to the contour of the original alveolar bone and the sites were filled with newly formed bone. The contour of the crest in the TCP+mucosa group was especially well augmented. CT results indicated a significant difference between the control group (14.5 ± 2.3 mm²) and the experimental groups (Fig 7, Table 1). The mean regenerated bone area was 21.2 ± 4.3 mm² in the TCP group, 23.6 ± 1.7 mm² in the TCP+collagen group, and 25.4 ± 4.9 mm² in the TCP+mucosa group (Table 1). However, there were no significant differences among the experimental groups.

Histologic Evaluation

Histologically, active new bone formation was noted in the experimental groups (Fig 8). New bone deposition was associated with residual TCP particles. In some samples of the TCP group, the TCP particles were not continuous with the regenerated woven bone, but they were undergoing resorption (Fig 9a). The particles were surrounded by inflammatory cells such as lymphocytes, and the alveolar bone crest still appeared irregular and rough. In the TCP+collagen group, no residual collagen was noted, and the grafted site was filled with new bone (Figs 8 and 9b). The bone trabeculae and bone marrow were still immature, although the contour of the alveolar bone crest had regained its original form (Fig 9b). In the TCP+mucosa group, the contour of the alveolar bone crest was well retained (Figs 8 and 9c). The trabecular structure was thin; however, the outer layer of the

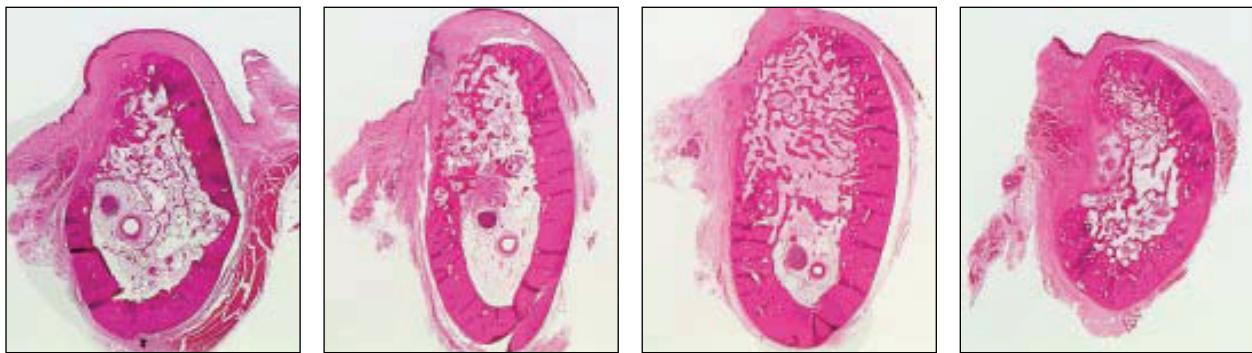


Fig 8 Specimens of each defect (in the buccolingual direction; stained with hematoxylin-eosin). (Left to right) Group 1 (TCP), group 2 (TCP+collagen), group 3 (TCP+mucosa), group 4 (no treatment/control).

Fig 9 Higher-magnification views of the defect region in each group (hematoxylin-eosin; original magnification $\times 40$). * = TCP particle; ★ = trabecula of bone; ▲ = inflammatory cells; ♦ = fat cells

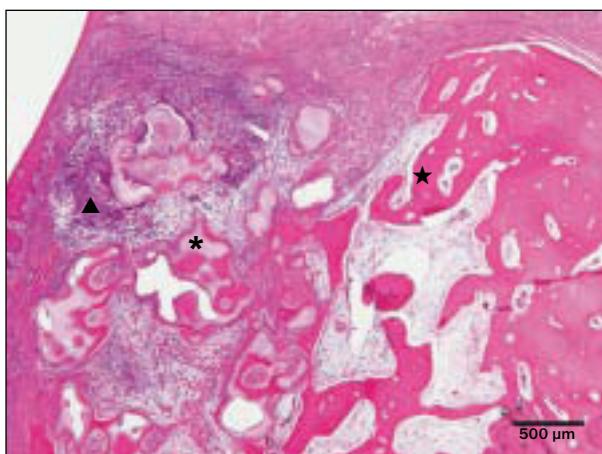


Fig 9a Group 1 site (TCP): Some TCP particles were not continuous with the bone, but they were undergoing resorption. The contour of the alveolar crest was still irregular and rough.

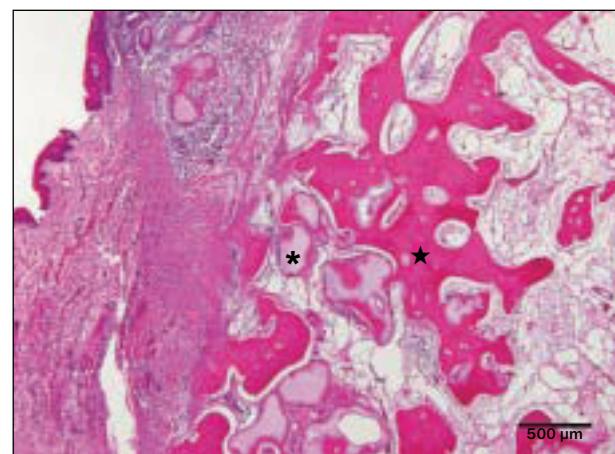


Fig 9b Group 2 site (TCP+collagen): The bone trabeculae were still immature and the process shows active bone formation.

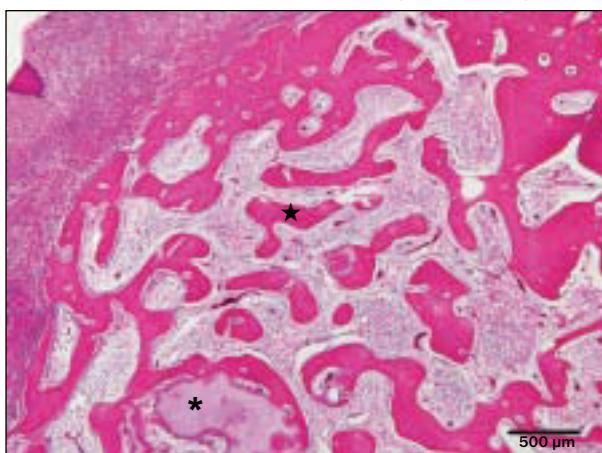


Fig 9c Group 3 site (TCP+mucosa): The bone trabeculae were still thin, but the contour of the alveolar crest was smooth and corticalization could be observed.

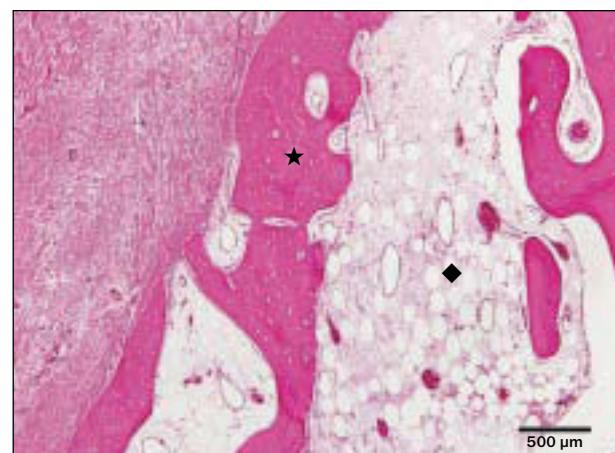


Fig 9d Group 4 site (no treatment/control): The bone trabeculae were mature. The formation of lamellar bone was observed and the fat cells were large and regular.

alveolar bone crest had started corticalization. In the control group, the crest width was not sufficient, and the outline of the buccal alveolar plate was depressed

and displayed epithelial invagination (Fig 8). However, the bone trabeculae were mature, lamellar bone had formed, and the fat cells were large and regular (Fig 9d).

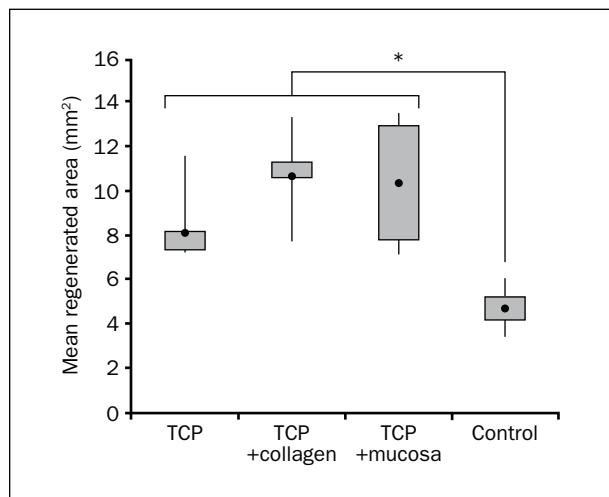


Fig 10 Mean area of newly formed bone in the defect site measured by histologic analysis. *Statistically significant differences, $P < .05$. White dots indicate median values.

Table 2 Mean Area of Newly Formed Bone Observed in the Specimens

Site type	Area (mm ²)
TCP	8.4 ± 1.8
TCP+collagen	10.9 ± 2.0
TCP+mucosa	10.5 ± 2.9
Control	4.8 ± 1.0

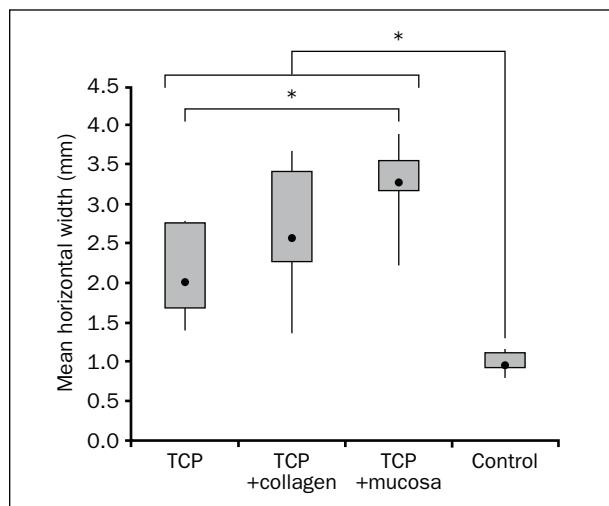


Fig 11 Mean horizontal width of the alveolar ridge 2 mm from the top of the frame (value 2 mm). Black dots indicate median values. *Statistically significant differences, $P < .05$.

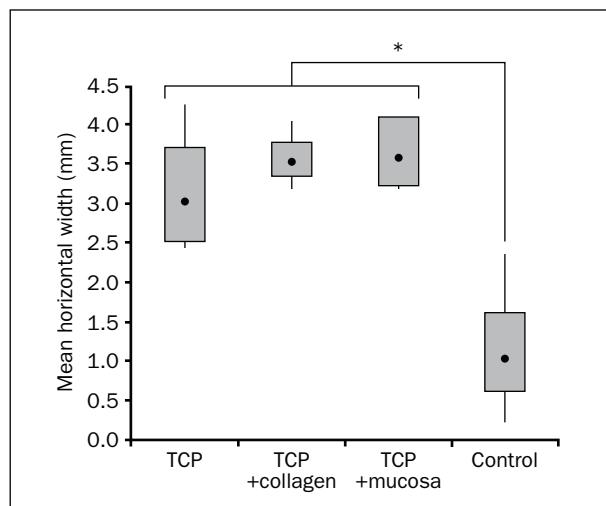


Fig 12 Mean horizontal width of the alveolar ridge 4 mm from the top of the frame (value 4 mm). Black dots indicate median values. *Statistically significant differences, $P < .05$.

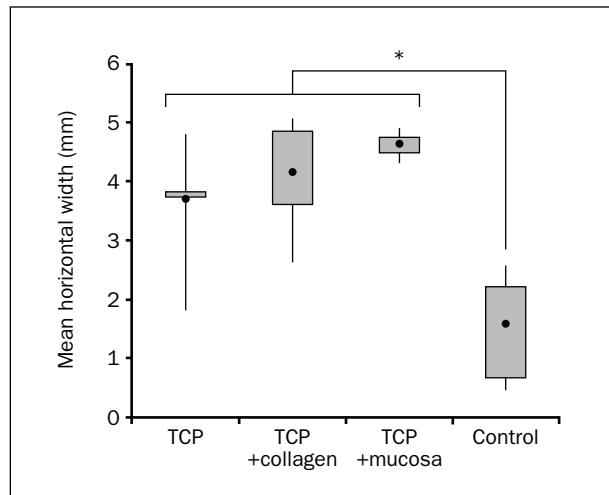


Fig 13 Mean horizontal width of the alveolar ridge 6 mm from the top of the frame (value 6 mm). Black dots indicate median values. *Statistically significant differences, $P < .05$.

The mean areas of the regenerated bone were $4.8 \pm 1.0 \text{ mm}^2$ in the control group, $8.4 \pm 1.8 \text{ mm}^2$ in the TCP group, $10.8 \pm 2.0 \text{ mm}^2$ in the TCP+collagen group, and $10.5 \pm 2.9 \text{ mm}^2$ in the TCP+mucosa group (Fig 10, Table 2). A significant difference was observed between the control group and all experimental groups ($P < .05$), but the differences between the experimental groups were not significant.

The horizontal width of the alveolar crest also differed significantly between the control group and the experimental groups (Figs 11 to 13). At all levels, the experimental groups, in the order of the largest to the smallest values, were as follows: TCP+mucosa group, TCP+collagen group, and TCP group (Table 3). At the 2-mm level, the mean width of the TCP+mucosa group differed significantly from that of the TCP group (Fig 11). At the 4-mm and 6-mm levels, there were no significant differences among the experimental groups (Figs 12 and 13).

Table 3 Mean Horizontal Ridge Width at 2 mm, 4 mm, and 6 mm

Site type	Defect level		
	2 mm	4 mm	6 mm
TCP	2.2 ± 0.6	3.2 ± 0.8	3.6 ± 1.1
TCP+collagen	2.6 ± 0.9	3.6 ± 0.4	4.2 ± 1.0
TCP+mucosa	3.2 ± 0.6	3.6 ± 0.5	4.6 ± 0.2
Control	1.0 ± 0.3	1.1 ± 0.9	1.5 ± 0.9

DISCUSSION

Alveolar ridge resorption is a process that occurs naturally after tooth extraction. The eventual shrinkage of the underlying edentulous ridge and overlying soft tissue often results in compromised prosthetic and esthetic outcomes. Most cases require reconstructive surgery to correct these ridge defects before prosthetic rehabilitation can be performed. Clinicians should include ridge preservation as part of their armamentarium of treatment options. When used appropriately, ridge preservation is a convenient and predictable procedure. The size and shape of the alveolar bone around the sockets at the time of extraction vary widely. The height, thickness, and number of bony walls around a tooth socket play significant roles in the final outcome.

A large number of experimental animal studies have evaluated socket preservation techniques using various materials. Autogenous bone grafts have osteogenic, osteoconductive, and osteoinductive properties and are widely recognized as the gold standard. Becker et al⁹ compared the effectiveness of application of autogenous bone with demineralized freeze-dried bone autografts in closed wounds and reported that autogenous bone grafts were superior. However, a minimally invasive technique is desirable in clinical practice, and few investigations have employed autogenous bone for socket preservation. Yeo and Ong³⁸ stated that allografts^{5,27} or xenografts^{11,12,14} demonstrated favorable ridge preservation; however, complete preservation of the alveolar contour was not documented.^{14,18} The results of these studies indicated that intrasocket grafts were unsuitable for achieving the ultimate goal of complete ridge preservation, but the authors were nevertheless able to reduce the amount of resorption compared with spontaneous healing. On the other hand, the principles of guided bone regeneration and soft tissue augmentation were applied to the extraction socket to build up the buccal aspect. Guided bone regeneration techniques using occlusive membranes^{39,40} and soft tissue augmentation using connective tissue

grafts⁴¹ have been reported to be effective and clinically successful. In a recent study of Araujo et al,³¹ a dog model was used to study healing of an extraction socket without dehiscence that had been grafted with Bio-Oss Collagen. The placement of Bio-Oss Collagen in the fresh extraction wound obviously delayed socket healing. However, a study published by Fickl et al⁴² showed that ridge preservation using Bio-Oss Collagen limited the buccal resorption in the horizontal dimension at 4 months after tooth extraction. Brkovic et al³⁶ reported management of a maxillary tooth extraction socket with an alveolar preservation technique involving placement of a cone of β-TCP combined with type 1 collagen without barrier membranes or flap surgery. Their report suggested that this technique prevented alveolar crest resorption after tooth extraction.

β-TCP has good biocompatibility and osteoconductive capacity.^{28,30,33–35} Its osteoconductive ability facilitates bone formation. Compared with other bone substitutes (eg, collagen scaffolds), β-TCP is characterized by precisely defined physical and chemocristalline properties, high level of purity, and uniformity of chemical composition, all of which render its biologic reactions reliably predictable.³⁵ Most of the graft particles present in the experimental sites were surrounded either by a dense provisional matrix or newly formed woven bone 3 months after tooth extraction. In β-TCP-grafted sites, the β-TCP particles were well integrated and continuous with the newly formed network of woven bone. In comparison with the nongrafted defects, large amounts of new mineralized bone were observed in the experimental sites after 3 months of healing (Table 2).

The present study in animals evaluated the use of β-TCP covered with different materials or left uncovered for alveolar ridge augmentation. All of the tested ridge augmentation techniques resulted in less contour reduction compared with the untreated defects in the control group. Both radiographic and histomorphometric analyses found significant differences in the newly formed bone area between the experimental groups in which β-TCP was used and the control group, which received no grafting material. The experimental groups showed wider alveolar processes than the control group. β-TCP would seem to have the potential to limit postoperative tissue shrinkage to a certain extent.

In the present study, buccal dehiscence-type bone defects were created at 3 months after tooth extraction. Surgically created defects may have a different healing pattern than chronic defects. The present animal experimental model, therefore, cannot be regarded as identical to a socket preservation study. However, it is difficult to re-create a buccal dehiscence-type of socket with severe resorption caused

by chronic infection. The authors examined the critical size of bone defect that could not heal in the canine mandible without treatment. Then, the bone defect size of the experimental model was decided from the result of preliminary experiments. Additionally, the gingiva over the sockets was trimmed to simulate an open wound. In the control group of this study, none of the sites showed a preserved alveolar ridge contour or sufficient horizontal width of the ridge to augment bone secondarily for dental implant placement.

The present study evaluated the use of β -TCP with covering materials as open wounds in ridge augmentation in an experimental dog model. Primary closure over β -TCP was not achieved in any of the groups in this study. Because primary closure requires releasing incisions or additional relieving of the flap, the authors avoided the use of primary closure in the surgical procedure; this maintained the attached gingiva and enhanced the esthetic outcome by retaining the mucogingival junction. On the other hand, Landsberg and Bichacho²² stated that primary closure and additional mechanical stability of the free graft materials might help prevent soft tissue collapse to an extent. In the present experiment, β -TCP was covered with a collagen sponge or free buccal mucosa. The histomorphometric measurements indicated that the dimension of the marginal portion (2 mm) of the extraction sites of the TCP group was significantly reduced compared to that seen in the TCP+mucosa group. Defect sites augmented with β -TCP and free buccal mucosa showed the most promising results from the histologic and histomorphometric perspectives. This result is in agreement with the findings of an experimental study by Fickl et al,⁴² in which the authors showed that stabilization of the extraction socket with a combination of Bio-Oss Collagen and a free gingival graft potentially limits the volume shrinkage that occurs after tooth extraction. The free gingival graft might help to hold the graft in place and prevent the soft tissue from collapsing. In the present experiment, the authors thought that the most promising results could be attributed to the free buccal mucosa maintaining the β -TCP and stabilizing the blood clot.

The relatively minimally invasive technique using β -TCP with a collagen sponge could be easily applied in clinical practice, but it did not prevent resorption of the alveolar crest width more effectively than did the free buccal mucosa. Histomorphometric analysis revealed that the mean area of newly formed bone and horizontal ridge width measurements at 2 mm, 4 mm, and 6 mm in the TCP+collagen group were not significantly different from the corresponding values of the TCP+mucosa group. Incorporation of β -TCP with a collagen sponge seems to reduce but not necessarily prevent postoperative contour shrinkage.

CONCLUSIONS

These results indicate that beta-tricalcium phosphate (β -TCP) covered with collagen sponge or free soft tissue in created bone defects was effective in ridge augmentation without primary closure. The results suggest that TCP graft covered with collagen or free soft tissue may be effective without primary closure when applied for socket preservation at dehiscence-type defects after tooth extraction. The conclusions of this study should be verified with additional studies of more rigorous design. Further clinical investigations should be conducted to evaluate the effectiveness of β -TCP with various covering materials in extraction sites.

ACKNOWLEDGMENTS

The authors gratefully thank Dr Naoto Ohbayashi for help with radiographic analyses. They also acknowledge Olympus Terumo Biomaterials for kindly donating the porous β -TCP. The authors reported no conflicts of interest related to this study.

REFERENCES

1. Amler MH. The time sequence of tissue regeneration in human extraction wounds. *Oral Surg Oral Med Oral Pathol* 1969;27:309–318.
2. Mecall RA, Rosenfeld AL. Influence of residual ridge resorption patterns on implant fixture placement and tooth position. *Int J Periodontics Restorative Dent* 1991;11:8–23.
3. Araújo MG, Lindhe J. Dimensional ridge alterations following tooth extraction. An experimental study in the dog. *J Clin Periodontol* 2005;32:212–218.
4. Amler MH, Johnson PL. Histological and histochemical investigation of human alveolar socket healing in undisturbed extraction wounds. *J Am Dent Assoc* 1960;61:32–44.
5. Isella JM, Greenwell H, Miller RL, et al. Ridge preservation with freeze-dried bone allograft and collagen membrane compared to extraction alone for implant site development: A clinical and histologic study in humans. *J Periodontol* 2003;74:990–999.
6. Pietrovski J, Massler M. Alveolar ridge resorption following tooth extraction. *J Prosthet Dent* 1967;17:21–27.
7. Quinn JH, Kent JN. Alveolar ridge maintenance with solid nonporous hydroxyapatite root implants. *Oral Surg Oral Med Oral Pathol* 1984;58:511–521.
8. Kentros GA, Filler SJ, Rothstein SS. Six month evaluation of particulate Durapatite in extraction sockets for the preservation of the alveolar ridge. *Implantologist* 1985;3:53–62.
9. Becker W, Becker BE, Caffesse R. A comparison of demineralized freeze-dried bone and autologous bone to induce bone formation in human extraction sockets. *J Periodontol* 1994;65:1128–1133.
10. Nemcovsky CE, Serfaty V. Alveolar ridge preservation following extraction of maxillary anterior teeth. Report on 23 consecutive cases. *J Periodontol* 1996;67:390–395.
11. Artzi Z, Tal H, Dayan D. Porous bovine bone mineral in healing of human extraction sockets. Part 1: Histomorphometric evaluations at 9 months. *J Periodontol* 2000;71:1015–1023.
12. Carmagnola D, Adriaens P, Berglundh T. Healing of human extraction socket filled with Bio-Oss. *Clin Oral Implants Res* 2003;14:137–143.
13. Sánder GK, Kainulainen VT, Queiroz JO, Carmichael RP, Oikarinen KS. Preservation of ridge dimensions following grafting with coral granules of 48 post-traumatic and post-extraction dento-alveolar defects. *Dent Traumatol* 2003;19:221–227.

14. Nevens M, Camelo M, De Paoli S, et al. A study of the fate of the buccal wall of extraction sockets of teeth with prominent roots. *Int J Periodontics Restorative Dent* 2006;26:19–29.
15. Nair PR, Schug J. Observation on healing of human tooth extraction sockets implanted with bioabsorbable polylactic-polyglycolic acids (PLGA) copolymer root replicas: A clinical, radiographic, and histologic follow-up report of 8 cases. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2004;97:559–569.
16. Lekovic V, Camargo PM, Klokkevold PR, et al. Preservation of alveolar bone in extraction sockets using bioabsorbable membranes. *J Periodontol* 1998;69:1044–1049.
17. Zubillaga G, Von Hagen S, Simon BI, Deasy MJ. Changes in alveolar bone height and width following post-extraction ridge augmentation using a fixed bioabsorbable membrane and demineralized freeze-dried bone osteoinductive graft. *J Periodontol* 2003;74: 965–975.
18. Lekovic V, Kenney EB, Weinlaender M, et al. A bone regenerative approach to alveolar ridge maintenance following tooth extraction. Report of 10 cases. *J Periodontol* 1997;67:390–395.
19. Hoffmann O, Bartee BK, Beaumont C, Kasaj A, Deli G, Zafiroopoulos GG. Alveolar bone preservation in extraction sockets using non-resorbable dPTFE membranes: A retrospective non-randomized study. *J Periodontol* 2008;79:1355–1369.
20. Barboza EP, Stutz B, Ferreira VF, Carvalho W. Guided bone regeneration using nonexpanded polytetrafluoroethylene membranes in preparation for dental implant placements—A report of 420 cases. *Implant Dent* 2010;19:2–7.
21. Sclar AG. Preserving alveolar ridge anatomy following tooth removal in conjunction with immediate implant placement. The Bio-Col technique. *Atlas Oral Maxillofac Surg Clin North Am* 1999;7:39–59.
22. Landsberg CJ, Bichacho N. A modified surgical/prosthetic approach for optimal single implant supported crown. Part I—The socket seal surgery. *Pract Periodontics Aesthet Dent* 1994;6:11–17.
23. Misch CE, Dietsh-Misch F, Misch CM. A modified socket seal surgery with composite graft approach. *J Oral Implantol* 1999;25:244–250.
24. Cardaropoli G, Araújo M, Hayacibara R, Sukekava F, Lindhe J. Healing of extraction sockets and surgically produced—augmented and non-augmented—defects in the alveolar ridge. An experimental study in the dog. *J Clin Periodontol* 2005;32:435–440.
25. Boix D, Weiss P, Gauthier O, et al. Injectable bone substitute to preserve alveolar ridge resorption after tooth extraction: A study in dog. *J Mater Sci Mater Med* 2006;17:1145–1152.
26. Becker W, Clokic C, Sennerby L, Urist MR, Becker BE. Histologic findings after implantation and evaluation of different grafting materials and titanium micro screws into extraction sockets: Case reports. *J Periodontol* 1998;69:414–421.
27. Froum S, Cho SC, Rosenberg E, Rohrer M, Tarnow D. Histological comparison of healing extraction sockets implanted with bioactive glass or demineralized freeze-dried bone allograft: A pilot study. *J Periodontol* 2002;73:94–102.
28. Artzi Z, Weinreb M, Givol N, Rohrer MD, Nemcovsky CE, Prasad HS. Biomaterial resorption rate and healing site morphology of inorganic bovine bone and beta-tricalcium phosphate in the canine: A 24-months longitudinal study and morphometric analysis. *Int J Oral Maxillofac Implants* 2004;19:357–368.
29. Chazono M, Tanaka T, Komaki H, Fujii K. Bone formation and biore-sorption after implantation of injectable beta-tricalcium phosphate granules-hyaluronate complex in rabbit bone defects. *J Biomed Mater Res A* 2004;70:542–549.
30. Kondo N, Ogose A, Tokunaga K. Bone formation and resorption of highly purified beta-tricalcium phosphate in rat female condyle. *Biomaterials* 2005;26:5600–5608.
31. Araújo MG, Lindhe J. Ridge preservation with the use of Bio-Oss Collagen: A 6-month study in the dog. *Clin Oral Implants Res* 2009; 20:433–440.
32. Zerbo IR, Bronckers AL, de Lange GL, van Beek GJ, Burger EH. Histology of human alveolar bone regeneration with a porous tricalcium phosphate. A report of two cases. *Clin Oral Implants Res* 2001;12: 379–384.
33. Ogose A, Hotta T, Kawashima H, et al. Comparison of hydroxyapatite and beta tricalcium phosphate as bone substitutes after excision of bone tumors. *J Biomed Mater Res B Appl Biomater* 2005;72:94–101.
34. Ogose A, Kondo N, Umezawa H, et al. Histological assessment in grafts of highly purified beta-tricalcium phosphate (OSferion) in human bones. *Biomaterials* 2006;27:1542–1549.
35. Horch HH, Sader R, Pautke C, Neff A, Deppe H, Kolk A. Synthetic, pure-phase beta-tricalcium phosphate ceramic granules (Cerasorb) for bone regeneration in the reconstructive surgery of the jaws. *Int J Oral Maxillofac Surg* 2006;35:708–713.
36. Brkovic BM, Prasad HS, Konandreas G, et al. Simple preservation of a maxillary extraction socket using beta-tricalcium phosphate with type I collagen: Preliminary clinical and histomorphometric observations. *J Can Dent Assoc* 2008;74:523–528.
37. Buser D, Hoffman B, Bernard JP, Lussi A, Mettler D, Schenk RK. Evaluation of filling materials in membrane-protected bone defects. A comparative histomorphometric study in the mandible of miniature pigs. *Clin Oral Implants Res* 1998;9:137–150.
38. Yeo AB, Ong MM. Principles and implications of site preservation for alveolar ridge development. *Singapore Dent J* 2004;26:15–20.
39. Esposito M, Grusovin MG, Worthington HV, Coulthard P. Interventions for replacing missing teeth: Bone augmentation techniques for dental implant treatment. *Cochrane Database Syst Rev* 2008; 16:CD003607.
40. Aghaloo TL, Moy PK. Which hard tissue augmentation techniques are the most successful in furnishing bony support for implant placement? *Int J Oral Maxillofac Implants* 2007;22(suppl):49–70.
41. Studer SP, Lehner C, Bucher A, Schärer P. Soft tissue correction of a single-tooth pontic space: A comparative quantitative volume assessment. *J Prosthet Dent* 2000;83:402–411.
42. Fickl S, Zuhri O, Wachtel H, Bolz W, Huerzeler MB. Hard tissue alterations after socket preservation: An experimental study in the beagle dog. *Clin Oral Implants Res* 2008;19:1111–1118.

The Effect of Impression Technique and Implant Angulation on the Impression Accuracy of External- and Internal-Connection Implants

Pavlos Mpikos, DDS, PhD¹/Nikolaos Kafantaris, DDS, PhD²/Dimitrios Tortopidis, DDS, PhD³/
Christos Galanis, PhD⁴/George Kaisarlis, PhD⁴/Petros Koidis, DDS, MSc, PhD⁵

Purpose: The purpose of this *in vitro* study was to investigate the effect of impression technique and implant angulation on the impression accuracy of external- and internal-connection implants using a novel experimental device. **Materials and Methods:** An experimental device was designed and fabricated to make *in vitro* impressions by means of open- and closed-tray techniques. Impressions of eight implants with two different connections (four external-hex and four internal-hex) at three angulations (0, 15, and 25 degrees) were made using a medium-consistency polyether material. Evaluation of implant impression accuracy was carried out by directly measuring the difference in coordinate values between the implant body/impression coping positioned on the base and the impression coping/laboratory analog positioned in the impression using a touch-probe coordinate measuring machine. Experimental data were analyzed by two-way analysis of variance. The significance level of all hypothesis testing procedures was set at $P < .05$. **Results:** The results showed that: (1) for implants with external connections, impression accuracy is not significantly affected by the impression technique, implant angulation, or their interaction; and (2) for implants with internal connections, impression accuracy is significantly affected only by implant angulation: Impression inaccuracy was greater at the 25-degree implant angulation. **Conclusions:** Within the limitations of this *in vitro* study, the open- and closed-tray techniques had no effect on the accuracy of multiple implant impressions. The interaction between impression technique and implant angulation was also not significant. However, implant angulation significantly affected the impression accuracy when implants with internal connections were used. INT J ORAL MAXILLOFAC IMPLANTS 2012;27:1422–1428

Key words: external-connection implants, implant angulation, impression accuracy, impressions, internal-connection implants

¹Research Associate, Department of Fixed Prosthesis and Implant Prosthodontics, School of Dentistry, Aristotle University of Thessaloniki, Thessaloniki, Greece.

²Professor Emeritus, School of Dentistry, Aristotle University of Thessaloniki, Thessaloniki, Greece.

³Assistant Professor, Department of Fixed Prosthesis and Implant Prosthodontics, School of Dentistry, Aristotle University of Thessaloniki, Thessaloniki, Greece.

⁴Research Associate, Section of Mechanical Design and Control Systems, School of Mechanical Engineering, National Technical University of Athens, Athens, Greece.

⁵Professor and Chairman, Department of Fixed Prosthesis and Implant Prosthodontics, School of Dentistry, Aristotle University of Thessaloniki, Thessaloniki, Greece.

Presented at the 33rd Annual Congress of European Prosthodontic Association, Innsbruck, Austria, October 1–3, 2009.

Submitted in partial fulfillment of the requirements for a PhD degree.

Correspondence to: Prof Petros Koidis, Department of Fixed Prosthesis and Implant Prosthodontics, School of Dentistry, Aristotle University of Thessaloniki, University Campus, Dentistry Building, GR 54124, Thessaloniki, Greece.
Fax: +30-2310-999676. Email: pkoidis@dent.auth.gr

Dental implants have become the treatment of choice in many situations where missing teeth require functional and esthetic replacements. Reproduction of the position and orientation of intraoral implants by means of an accurate impression in the definitive cast is the first step in achieving a passively fitting implant-supported prosthesis.^{1–3}

Several studies have examined the clinical variables affecting the accuracy of the implant impression, such as differing impression techniques,^{4,5} the use of different impression materials and trays,^{6,7} splinting or not splinting the implants,⁸ the relative implant angulations,^{9–11} and the lengths of impression coping connections.¹¹ The relevant scientific literature reveals many controversial issues regarding the accuracy of impressions using open-tray (pickup) and closed-tray (transfer) techniques in situations where three or more implants were placed.^{4,12–20} Most researchers have reported that the open-tray technique is more accurate and predictable than the closed-tray technique using

repositionable copings.^{12–16} Other authors, however, either found no significant differences between the two techniques or concluded that the closed-tray technique produced a more accurate definitive cast than the open-tray impression technique.^{10,17–20}

With regard to implants at various angulations, previous studies have found that impressions made in the presence of angulated implants were less accurate than those made with parallel implants.^{9,11,21,22} Interestingly, only a few investigations have compared the accuracy of implant impression techniques performed for external- and internal-connection implants, and these few have produced varying results.^{16,23–27}

In previous studies, the accuracy of the implant impressions was evaluated by measuring the differences in the relative positions and orientations of implants on the resulting definitive casts *in vitro*, without taking into account possible inaccuracies arising from dimensional changes in the dental stone during setting, the implant definitive cast technique, and the laboratory analog placement. Thus, the aim of the current *in vitro* study was to investigate the effect of impression technique, implant angulation, and their interaction on the accuracy of impressions of external-and internal-connection implants by using a novel experimental device that allowed direct measurement of the definitive impression. The research hypothesis was that the impression technique, implant angulation, and their interaction would have a significant effect on the accuracy of impressions made from either external- or internal-connection implants.

MATERIALS AND METHODS

Fabrication of the Experimental Device

For this study, a novel experimental device was designed and fabricated from solid aluminum, which was subsequently anodized. In the device, eight implants (four with external-hex connections and four with internal-hex connections; Dr Ihde Dental AG), each 4.1 mm in diameter and 13 mm in length, were mounted at angles of 0, 15, or 25 degrees relative to the horizontal matrix surface. The experimental device was designed to allow a clinical simulation of impression making by means of open- and closed-tray techniques in a standardized and reproducible manner. It comprised a base and an upper part.

The base of the device was a rectangular block with eight blind cylindric holes, each 5 mm in diameter and 15 mm deep, in its flat upper surface for mounting the eight implants (Fig 1). The eight implants were arranged in a semicircular formation on the base with angulations typical of teeth in the maxilla and sequentially numbered 1 to 8 (Fig 1). The external-connection

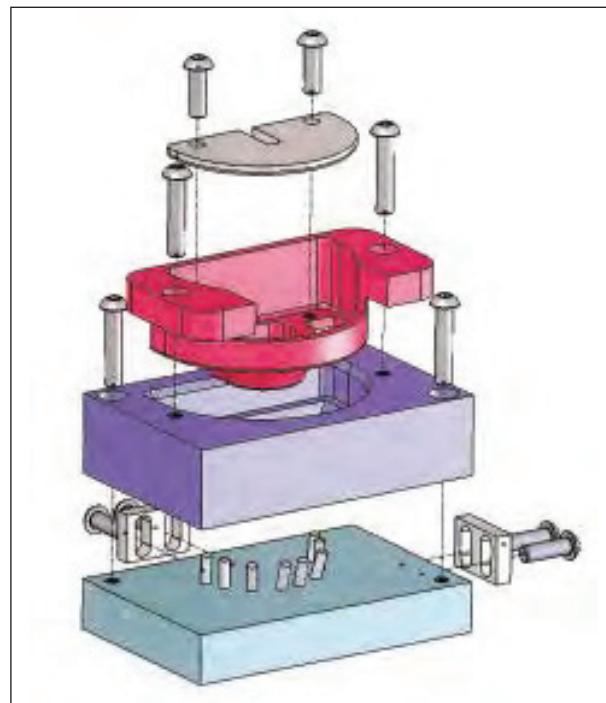


Fig 1 Schematic diagram of the experimental device with implant bodies secured to the base.

implants were placed in positions 1 to 4 on the left side, and the internal-connection implants were placed in positions 5 to 8 on the right side (all at 0, 15, or 25 degrees of angulation). The implant bodies were secured in the base component with autopolymerizing acrylic resin (Pattern Resin LS, GC Corporation). The base of the device had three plane surfaces, which were used as reference geometry (datum) features for the determination of the base reference system. These plane surfaces were finished to a high quality (International Organization for Standardization #4287:1997 surface roughness [Ra] = 1.8 μm). The base reference system allows the accurate determination of points in three-dimensional (3D) space and thus the position of all points in the impression.

The upper part of the device consisted of three separate components: an impression frame, a second component that fit inside the frame and allowed the simulation of an impression tray, and a cover plate that could be attached or removed according to the impression technique (open or closed tray). The components were connected together by set screws (Fig 1). The outer surfaces forming the upper reference planes were also finished to the same standard as the base (Ra = 1.8 μm) to form reference geometric (datum) features for the coordinate measuring machine (CMM) during the second series of measurements concerning the impression material itself.



Fig 2a Measurement of coordinates of the impression copings and implant bodies using the CMM.

Impression Procedures

In both experiments, the minimum required sample size was determined by means of an a priori power analysis using the GPower software (version 3.1, Franz Faul, Universität Kiel). Four impressions with impression copings were made with each of the two different techniques in a room with controlled temperature ($23^{\circ}\text{C} \pm 2^{\circ}\text{C}$) and a relative humidity of $50\% \pm 10\%$. Polyether impression material (Impregum, medium consistency, 3M ESPE) was used in accordance with the manufacturer's instructions. An automix machine (Pentamix 2, Automatic Mixing Unit, 3M ESPE) was used to standardize all mixtures. If the impression was made by means of the closed-tray technique, the impression copings were retained on the implants upon removal of the impression and had to be repositioned on their laboratory analogs in the corresponding holes. When the impression was made using the open-tray technique, the impression copings, which remained in the impression, had to be unscrewed before the impression could be removed from the base. The same torque setting (20 Ncm, standardized with a torque wrench) was used to tighten all the screws throughout the study. All procedures were performed by the same operator.

CMM Measurements

For the processing of the measurements, the CMM software (PC-DMIS, version 4.2, Wilcox Associates Inc) created a cylinder in 3D space of best fit of the measured cylindric parts. The coordinates of the long axis of this cylinder of any circular plane along this axis and the coordinates of the points on this axis that met the plane constituted the reference system for measurements of position and angulation. The relative difference in coordinate values of the cylinder before the impression (comprising the implant body and the impression coping on the base of the device) and the cylinder after the impression was made (comprising the impression

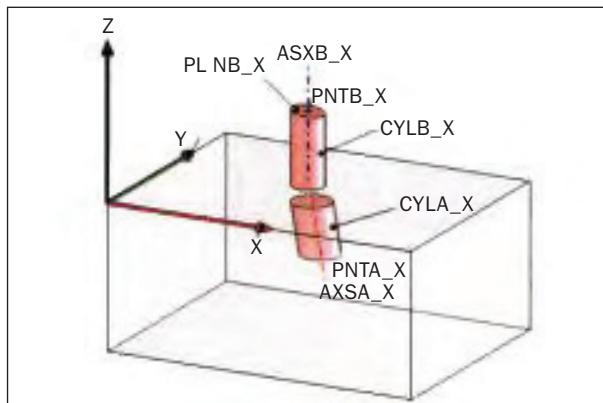


Fig 2b Schematic diagram showing the cylinders created from the CMM x, y, and z coordinate system adjusted to the base reference system.

coping and the laboratory analog within the setting impression material) was assessed in degrees by means of a Mistral 070705 (DEA, Brown & Sharpe) direct computer-controlled 3D CMM (Figs 2a and 2b).

The CMM accuracy performance specification, per International Organization for Standardization #10360-2, is $3.5 \mu\text{m}$ (maximum permissible volumetric error) for the computational manipulation and mathematical fitting of the 3D coordinate of selected points into geometric features (planes, cylinders, etc). The industry-standard Renishaw PH10M motorized head, in conjunction with a TP200 probe of 20 mm in length and a spherical tip with diameter of 1 mm, were used for the capture of the 3D coordinates of the required contact points. Measurements were made on eight different points of the outer surface of each implant system part according to the British Standards Institution #7172:1989. The deviation of the position and angulation of a solid body, such as an implant body/impression coping or laboratory analog/impression coping, was defined as the magnitude of its total translation and rotation from its initial state in 3D space to its final one, as an impression coping/laboratory analog.^{28,29} To calculate the total translation and the angular deviation of a specific reference point and axis respectively, computer-aided mechanical design software (SolidWorks, Dassault Systèmes SolidWorks) was used.

Measurement Procedure

The accurate measurements were made in a specially modulated laboratory space with a stable temperature ($20^{\circ}\text{C} \pm 1.5^{\circ}\text{C}/12$ hours; recorders of control: TESTO 175H2, s/n 20038973/408).

In the initial phase of the experiment, measurements were made to determine the machining tolerances of the components of the specific implant system, since these constituted a significant factor affecting the final impression accuracy and contributed to the total resultant distortion in implant impression. Mechanical parts

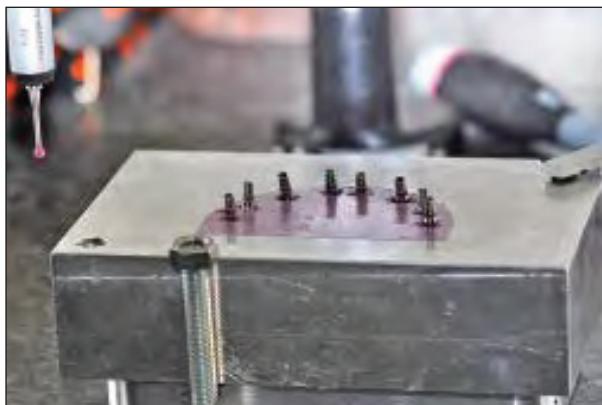


Fig 3a The base of the device was reversed on the measurement table of the CMM after the impression making, with the implant laboratory analogs projected from the impression material.

had to undergo machining and milling. The high precision of this procedure allowed the authors to consider as common the central axis of the connected cylindric bodies. During this phase, the implant bodies were attached in their position in the base component and secured.

The CMM was then calibrated. This was followed by the measurement of the coordinates CYLA_X (representing the implant body) and CYLB_X (representing the impression coping) and by the setup of the base reference system. The first measurement set concerned the measurement of the coordinate values of the eight assembled implants and impression copings fixed in the base of the device. The surfaces available for measurement were the planar face of the top of the impression coping PLNB_X and the cylindric surface of CYLA_X and CYLB_X (implant body and impression coping). At least six contact points were captured on each planar face and at least eight points were captured on each cylindric surface (Figs 2a and 2b).

After polymerization of the polyether, the upper part of the experimental device was manually removed from the base carrying the impression material (like a custom impression tray). The upper part of the device was reinstalled and reset, reversed, and repositioned on the measurement table of the CMM.

The second set of measurements concerned the positions of the eight assembled laboratory analogs CYLC_X and impression copings CYLB_X within the impression material. In this case, the surfaces available for measurement were the planar face at the bottom of the cylindric surface of the implant laboratory analog, PLNC_X, which protruded from the impression (Figs 3a and 3b).

In a computer-aided design environment, the coordinates of the cylinders were mathematically reversed so that they represented the new position of the impression coping following the procedure of impression taking. Thus, a third set of measurements was created involving the measurement of the relative changes in

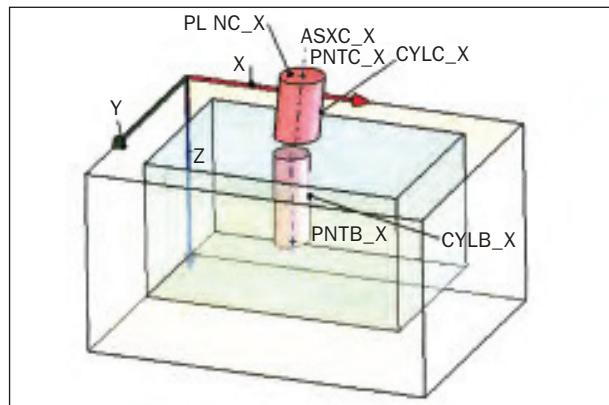


Fig 3b Diagram of the measured elements with the frame reference system.

position between the geometric features (planar and cylindric surfaces) of the implant bodies and those of its assembled coping or lab analog. This was performed for each of the eight assembled pairs used during the in vitro experimental procedure.

Using computer-aided design, the authors calculated the difference between the different implant positions (initial – final); this indicated the resultant positional distortion (x -, y -, and z -axes) that can be attributed to different impression techniques for the different implant connection geometries (external or internal) and the different axial angulations. After that, the computer mathematically turned the two cylinders to the degree of their highest congruence, having as a reference the common point of their axial intersection. The degree of divergence of congruence of the two cylinders gave the total deformation occurring in each case.

Statistical Analysis

Coordinate values in both types of implants (external and internal connections) were analyzed by two-way analysis of variance (ANOVA) according to the linear model, which included two factors between experimental units with interaction.

Specifically, the model involved the main effect of impression technique (factor A) with two levels (open or closed tray); the main effect of implant angulation (factor B) with three different orientations (0, 15, or 25 degrees) in four positions ($\theta_1, \theta_2, \theta_3, \theta_4$), respectively; and the interaction between the two factors (A \times B). For each of the eight factor combinations (two impression techniques \times four implant positions), four replications (impression cycles) were performed.

Comparisons of means were performed by the least significant difference (LSD) criterion.³⁰ The significance level for all hypothesis testing procedures was set at $P < .05$. All statistical analyses were conducted with SPSS software (version 17.0, IBM).

Table 1 Main Effect for Impression Technique

Impression technique	n	External-connection implants		Internal-connection implants		
		Mean	SD	Mean	SD	
Open tray	16	0.370	0.150	1.588	1.275	
Closed tray	16	0.557	0.392	1.402	1.486	
P value (LSD)	.209		.391			

SD = standard deviation.

Table 2 Main Effect for Implant Angulation

Implant angulation	n	External-connection implants		Internal-connection implants		
		Mean	SD	Mean	SD	
θ1	8	0.521	0.196	0.714	0.368	
θ2	8	0.438	0.255	0.739	0.409	
θ3	8	0.643	0.445	0.868	0.262	
θ4	8	0.354	0.158	3.660	0.851	
P value (LSD)	.296		.553			

SD = standard deviation.

Table 3 Interaction Effect for Impression Technique × Implant Angulation for External-Connection Implants

Impression technique/ implant angulation	n	Mean	SD	
Open tray				
θ1	4	0.390	0.147	
θ2	4	0.355	0.068	
θ3	4	0.518	0.034	
θ4	4	0.317	0.157	
Closed tray				
θ1	4	0.651	0.150	
θ2	4	0.521	0.359	
θ3	4	0.767	0.648	
θ4	4	0.391	0.173	
P value (LSD)	.468			

SD = standard deviation.

Table 4 Interaction Effect for Impression Technique × Implant Angulation for Internal-Connection Implants

Impression technique/ implant angulation	n	Mean	SD	
Open tray				
θ1	4	0.923	0.370	
θ2	4	0.964	0.286	
θ3	4	0.827	0.314	
θ4	4	3.640	0.563	
Closed tray				
θ1	4	0.505	0.251	
θ2	4	0.514	0.416	
θ3	4	0.908	0.239	
θ4	4	3.681	1.171	
P value (LSD)	.782			

SD = standard deviation.

RESULTS

For external-connection implant coordinate values, ANOVA revealed that: (1) the main effect of impression technique was not statistically significant ($F[1,24] = 3.43, P = .076$) (Table 1); (2) the main effect of implant angulation was not statistically significant ($F[3,24] = 2.60, P = .075$) (Table 2); and (3) the interaction between the two factors was not statistically significant ($F[3,24] = 0.18, P = .909$) (Table 3).

For internal-connection implant coordinate values, ANOVA revealed that: (1) the main effect of impression

technique was not statistically significant ($F[1,24] = 0.96, P = .337$) (Table 1); (2) the main effect of implant angulation was statistically significant ($F[3,24] = 58.13, P < .001$) (Table 2); and (3) the interaction between the two factors was not statistically significant ($F[3,24] = 0.57, P = .640$) (Table 4). For internal-connection implants, the impression inaccuracy was greater at 25 degrees of implant angulation, position θ4, compared with the other three positions (θ1, θ2, and θ3) with both impression techniques (Tables 2 and 4). In both cases, the differences between the corresponding mean values (θ4 versus θ1, θ2, or θ3) were greater than the critical LSD value.

DISCUSSION

The findings do not support the research hypothesis for external-connection implants; the impression technique, implant angulation, and their interaction had no effect on the accuracy of impressions ($P > .05$ for all effects) (Tables 1 to 3). In contrast, for internal-connection implants, the implant angulation had a significant effect on the impression accuracy ($P < .001$) (Tables 2 and 4).

Passive fit of an implant-retained prosthesis depends on the accuracy of the impression made.^{3,14} The accuracy of implant impressions is affected by various clinical variables related to the implants (eg, angulation, connection type) and the impression technique (eg, different direct or indirect techniques, impression tray, and splinting or no splinting of impression copings).⁴⁻¹⁶ In most previous studies, the accuracy of the implant impression was evaluated indirectly by measuring differences in the relative positions and orientations of implants on a typodont or a definitive cast in relation to the diagnostic cast.^{5,7, 9,11,16} The novel experimental device used in this study allowed impression making with either open-tray or closed-tray techniques. The relative difference in the positional accuracy between the implant body/impression coping on the base of the device and the impression coping/laboratory analog within the impression was therefore measured directly, using a CMM, without the use of a dental cast, thereby eliminating the possible inherent additional distortion caused by the laboratory fabrication of a cast. The pouring procedure can alter the positional relationship of the copings because of the expansion involved in the setting of the dental stone.

The findings of the present study contradict the results of previous studies that reported the superiority of the open-tray technique.¹²⁻¹⁶ In this investigation, no statistically significant differences concerning impression accuracy were detected between the open- and closed-tray techniques. These results are in accordance with the few studies focused on this subject.^{8,10,24,27} It should be emphasized that the cited studies used different evaluation methods and measurement devices for the positional changes of implant analogs, including a reflex microscope,⁸ a measuring stylus,¹⁰ strain gauges,^{24,27} or a profile projector,¹¹ and all used a definitive cast as the final reference point. This difference in findings is highly likely to be a result of the use of different components and study designs, all of which involved the use of a definitive dental cast, as opposed to the direct measurement technique used in the current study.

The different connection geometry between and within commercial implant systems may also affect the accuracy of impressions. Several studies^{1,2,23} have evaluated the accuracy of impression techniques with external-connection implants, and few studies have

examined the impression accuracy with internal-connection implants.^{16,27} The varying results among studies of external- and internal-connection implants are the consequence of employing different prosthetic connection mechanisms and measurement methods. Additionally, the results can probably be explained by the higher level of stress between impression material and impression copings that is created when an impression with impression copings is removed from internal-connection implants.

Angulated implants in the maxillary arch are common clinically because of anatomic limitations and esthetic considerations. It must be noted that impression accuracy measurements in the present study included eight implants dispersed in an arch similar to a maxilla. The results of this study showed that the main effect of implant angulation on impression accuracy was significant only for internal-connection implants. The effect was a result of the high relative differences in coordinate values between implant body/impression coping and impression coping/laboratory analog for an implant angulation of 25 degrees.

The results are in line with previous findings that stated that angulations of the implants may cause distortion of impressions, possibly because of the higher forces required for removal of the impression.^{9,11,21,22} Furthermore, it seems that the presence of angulated implants with internal connections had a significant effect on the accuracy of the experimental casts compared with the definitive casts owing to the distortion of the impression material.¹¹ However, other studies have shown that the axial angulation of two or three implants was not associated with inaccuracy in the impression.^{10,27} In cases of three or fewer implants, the angulation effect may be compensated by the elastic recovery of the impression material. If multiple implants dispersed along the dental arch are examined, the difference in angulation may be added to the linear distortion, resulting in overall increased distortion. The angulation effect on the accuracy of impressions may be heightened by an increased number of internal-connection implants because of the higher forces required to remove the impression tray after the impression material has set. Finally, the varying results among previous investigations of angulated implants may be a result of the employment of different numbers of implants, different prosthetic connection mechanisms, and different evaluation methods.

A possible limitation of the present study design was that the removal forces, and the consequent impression distortions in clinical practice, were considered to be different from those applied in the experimental conditions because of the different extent of dental undercuts in the novel experimental device and the resulting differences in removal forces. Further

studies addressing the much greater angulations commonly encountered in implant prosthodontics are required to evaluate the effect of connection geometry on implant impression accuracy. In addition, a comparison of dimensional differences in coordinate values between implant bodies/impression copings and impression copings/laboratory analogs should be also evaluated on definitive casts using the CMM.

CONCLUSIONS

Within the possible limitations of this study, the following conclusions were drawn:

1. The findings of this study suggested that, for external-connection implants, impression accuracy is not affected by the impression technique and implant angulations.
2. For internal-connection implants, although impression accuracy is not affected by the impression technique, it is significantly affected by implant angulations.
3. The interaction between impression technique and implant angulation was not significant in the accuracy of impressions for either external- or internal-connection implants.

ACKNOWLEDGMENTS

This study was partially supported by a grant from the General Secretariat for Research and Technology, Greek Ministry for Development (PENED 01-197). The authors express special thanks to Professor Emeritus N. Kafantaris for helpful assistance in aspects of the project including planning, support, and helpful comments. The authors also thank Professor Emeritus M. Sfantsikopoulos for providing laboratory equipment and helpful comments. The authors reported no conflicts of interest related to this study.

REFERENCES

1. Assif D, Fenton A, Zarb G, Schmitt A. Comparative accuracy of implant impression procedures. *Int J Periodontics Restorative Dent* 1992;12:112–121.
2. Assif D, Marshak B, Schmidt A. Accuracy of implant impression techniques. *Int J Oral Maxillofac Implants* 1996;11:216–222.
3. Taylor TD, Agar JR, Vogiatzi T. Implant prosthodontics: Current perspective and future directions. *Int J Oral Maxillofac Implants* 2000;15:66–75.
4. Carr AB. Comparison of impression techniques for a five-implant mandibular model. *Int J Oral Maxillofac Implants* 1991;6:448–455.
5. Vigolo P, Majzoub Z, Cordioli G. Evaluation of the accuracy of three techniques used for multiple implant abutment impressions. *J Prosthet Dent* 2003;89:186–192.
6. Burns J, Palmer R, Howe L, Wilson R. Accuracy of open tray implant impressions: An in vitro comparison of stock versus custom trays. *J Prosthet Dent* 2003;89:250–255.
7. Del'Acqua MA, Chavez AM, Amaral ALC, Compagnoni MA, De Assis Mollo F. Comparison of impression techniques and materials for an implant-supported prosthesis. *Int J Oral Maxillofac Implants* 2010;25:771–776.
8. Herbst D, Nel JC, Driessen CH, Becker PJ. Evaluation of impression accuracy for osseointegrated implant supported superstructures. *J Prosthet Dent* 2000;83:555–561.
9. Assuncao WG, Filho HG, Zaniquelli O. Evaluation of transfer impressions for osseointegrated implants at various angulations. *Implant Dent* 2004;13:358–366.
10. Conrad HJ, Pesun IJ, DeLong R, Hodges JS. Accuracy of two impression techniques with angulated implants. *J Prosthet Dent* 2007;97:349–356.
11. Sorrentino R, Gherlone EF, Calesini G, Zarone F. Effect of implant angulations, connection length, and impression material on the dimensional accuracy of implant impressions: An in vitro comparative study. *Clin Implant Dent Relat Res* 2010;12(suppl 1):e63–76.
12. Hsu CC, Millstein PL, Stein RS. A comparative analysis of the accuracy of implant transfer techniques. *J Prosthet Dent* 1993;69:588–593.
13. Barrett MG, De Rijk WG, Burgess JO. The accuracy of six impression techniques for osseointegrated implants. *J Prosthodont* 1993;2:75–82.
14. Phillips KM, Nicholls JI, Ma T, Rubenstein J. The accuracy of three implant impression techniques: A three-dimensional analysis. *Int J Oral Maxillofac Implants* 1994;9:533–540.
15. Del'Acqua MA, Arioli-Filho JN, Compagnoni MA, Mollo Fd A Jr. Accuracy of impression and pouring techniques for an implant-supported prosthesis. *Int J Oral Maxillofac Implants* 2008;23:226–236.
16. Lee YJ, Heo SJ, Koak JY, Kim SK. Accuracy of different impression techniques for internal-connection implants. *Int J Oral Maxillofac Implants* 2009;24:823–830.
17. Humphries RM, Yaman P, Bloem TJ. The accuracy of implant master casts constructed from transfer impressions. *Int J Oral Maxillofac Implants* 1990;5:331–336.
18. De La Cruz JE, Funkenbusch PD, Ercoli C, Moss ME, Graser GN, Tallents RH. Verification jig for implant-supported prostheses: A comparison of standard impressions with verification jigs made of different materials. *J Prosthet Dent* 2002;88:329–336.
19. Burawi G, Houston F, Byrne D, Claffey N. A comparison of the dimensional accuracy of the splinted and unsplinted impression techniques for the Bone-Lock implant system. *J Prosthet Dent* 1997;77:68–75.
20. Lee H, So JS, Hochstedler JL, Ercoli C. The accuracy of implant impressions: A systematic review. *J Prosthet Dent* 2008;100:285–291.
21. Carr AB, Master J. The accuracy of implant verification casts compared with casts produced from a rigid transfer coping technique. *J Prosthodont* 1996;5:248–252.
22. Assif D, Nissan J, Varsano I, Singer A. Accuracy of implant impression splinted techniques: Effect of splinting material. *Int J Oral Maxillofac Implants* 1999;14:885–888.
23. Spector MR, Donovan TE, Nicholls JI. An evaluation of impression techniques for osseointegrated implants. *J Prosthet Dent* 1990;63:444–447.
24. Naconeck MM, Teixeira ER, Shinkai RS, Frasca LC, Cervieri A. Evaluation of the accuracy of 3 transfer techniques for implant-supported prostheses with multiple abutments. *Int J Oral Maxillofac Implants* 2004;19:192–198.
25. Inturregui JA, Aquillino SA, Ryther JS, Lund PS. Evaluation of three impression techniques for osseointegrated oral implants. *J Prosthet Dent* 1993;69:503–509.
26. Carr AB. Comparison of impression techniques for a two-implant 15-degree divergent model. *Int J Oral Maxillofac Implants* 1992;7:468–475.
27. Choi JH, Lim YJ, Yim SH, Kim CW. Evaluation of the accuracy of implant-level impression techniques for internal-connection implant prostheses in parallel and divergent models. *Int J Oral Maxillofac Implants* 2007;22:761–768.
28. Nicholls JI. The measurement of distortion: Mathematical considerations. *J Prosthet Dent* 1978;39:339–343.
29. Phillips KM, Nicholls JI, Ma T, Rubenstein J. The accuracy of three implant impression techniques: A three-dimensional analysis. *Int J Oral Maxillofac Implants* 1994;9:533–540.
30. Toothaker L. Multiple Comparison Procedures. In: *Multiple Comparison Procedures*, ed. Toothaker L. Newbury Park, California: Sage Publications, 1993:40–43.

Efficacy and Predictability of Short Dental Implants (< 8 mm): A Critical Appraisal of the Recent Literature

Murali Srinivasan, BDS, MDS, MBA¹/Lydia Vazquez, MD, DMD²/Philippe Rieder, DMD³/Osvaldo Moraguez, DMD³/Jean-Pierre Bernard, MD, DMD, Prof Dr med dent⁴/Urs C. Belser, DMD, Prof Dr med dent⁵

Purpose: This review of literature was conducted to evaluate the predictability of treatment outcomes with short dental implants (SDI), ie, implants shorter than 8 mm. **Materials and Methods:** The review included studies, published between January 1990 and July 2011, that (1) involved SDI (< 8 mm) placed in human jaws, (2) had a minimum of 20 SDI in their analysis, (3) provided data on survival rates, and (4) reported a minimum observation period of at least 3 months after placement. **Results:** Forty-one studies fulfilled the above criteria; only 17 of these studies reported outcomes with microrough surface SDI. Six different lengths (4, 5, 6, 6.5, 7 and 7.5 mm) of microrough surface SDI with varying diameters (3.5 to 6 mm) were identified in the studies. A total of 1,828 microrough surface SDI were inserted and 45 failures were reported. Observation periods ranged from 3 months to 9 years. The reported survival rates for SDI ranged from 92.2% to 100%. From a total of 1,123 SDI inserted in specified jaw locations, failures were observed more often in the maxilla ($n = 297$, failed = 13) than in the mandible ($n = 826$, failed = 19). The review did not identify any correlation between implant diameter and survival for the microrough SDI. **Conclusions:** Microrough surface short implants (6 to 7.5 mm) appear to provide favorable survival rates and, therefore, can be predictably employed for simplification of implant therapy in situations of reduced alveolar heights in the posterior jaw segments. *INT J ORAL MAXILLOFAC IMPLANTS* 2012;27:1429–1437

Key words: dental implant, implant length (< 8 mm), literature review, short dental implants, treatment outcomes

Short dental implants were introduced for simplified placement in compromised alveolar situations to avoid interference with vital anatomical structures,

minimize surgical trauma and associated risks, and consequently reduce the morbidity of advanced surgical procedures.¹ Early descriptions in literature considered standard length implants as implants with intrabony lengths of 10 mm or more,² and short dental implants (SDI) as implants with less than 10 mm intrabony length.³ The currently accepted definition for short dental implants is "a device with ≤ 8 mm intrabony length."^{4,p47}

It has often been hypothesized that shorter implants have lower success rates than standard length fixtures. However, no distinct linear relationship between implant length and survival has been scientifically established.⁵ Standard length implants (≥ 10 mm) are quoted to represent a minimum length for predictable success because, hypothetically, a better distribution of functional forces throughout the entire length of the implant was assumed.⁶ However, these forces are demonstrated to be concentrated at the peri-implant crestal bone.⁷ There is evidence that implant length has minimal influence on the bone stress location, the intrabony implant displacement, and the implant component stress.^{8,9} It has also been suggested that longer implants are more prone to mechanical

¹ITI Scholar, Department of Fixed Prosthodontics and Occlusion, Department of Stomatology and Oral Surgery. Lecturer, Division of Gerodontology and Removable Prosthodontics, School of Dental Medicine, University of Geneva, Geneva, Switzerland.

²Head, Division of Maxillofacial and Dental Radiology, School of Dental Medicine, University of Geneva, Geneva, Switzerland.

³Lecturer, Department of Fixed Prosthodontics and Occlusion, School of Dental Medicine, University of Geneva, Geneva, Switzerland.

⁴Professor and Head, Department of Stomatology and Oral Surgery, School of Dental Medicine, University of Geneva, Geneva, Switzerland.

⁵Professor and Head, Department of Fixed Prosthodontics and Occlusion, School of Dental Medicine, University of Geneva, Geneva, Switzerland.

Correspondence to: Dr Murali Srinivasan, Department of Fixed Prosthodontics and Occlusion, School of Dental Medicine, University of Geneva, Rue Barthélémy-Menn 19, Geneva 1205, Switzerland. Email: murali.srinivasan@unige.ch

complications because of their rigidity, while SDI allow flexure within the bone inducing a stress breaking effect.¹⁰ Hence, it would appear that using SDI represents an overall prosthetic advantage in terms of long-term success in implant supported restorations.⁹ However, this hypothesis needs to be challenged by randomized controlled trials. Bone quality, or bone density, in the region of installation has also been reported to play a role in SDI survival, and the posterior maxilla has been cited as a region for frequent failures.^{11–15} Studies, however, do exist that demonstrate favorable success rates in this region.^{2,16,17}

Current literature classifies implants of 8-mm length as short implants. These have been associated with favorable success rates and high predictability, with reported survival rates of 96% to 100% (over a 3- to 7-year observation period).^{2,18–20} It is therefore natural to consider the use of 8-mm lengths as a routine treatment option and shift focus to lengths < 8 mm as "short implants." Few systematic reviews assessing the performance of SDI and their survival have been published to date.^{21–24} These have, however, included implants up to an intrabony length of 10 mm.^{21,23,24} Thus, the inclusion of longer implants in a short implant review may not effectively deliver a precise conclusion on predictability.

Therefore, the purpose of this review was to focus on evaluating the predictability of treatment outcomes with commercialized short implants of lengths < 8 mm by reviewing the available relevant publications. By excluding 8-mm implants from this analysis, the authors hypothesized to get a better insight on the clinically relevant predictability of SDI. Based on this assumption, a critical appraisal of the published data on such short implants (< 8 mm) placed in various edentulous segments of the jaws was undertaken to propose a well-defined rationale for the decision-making process when considering the installation of short implants in both compromised conditions or even routine situations.

MATERIALS AND METHODS

An electronic database search of the dental literature using PubMed was undertaken to identify all papers published in English between January 1990 and July 2011, using the following search terms individually and in different combinations: "short dental implants," "length," "studies on," "clinical studies," "prospective," "retrospective," "randomized," "survival and success rates," "dental implants," "treatment outcomes," "systematic review," "literature review," and "meta-analysis."

Selection of Studies

For inclusion in this review, the studies were required to (1) involve SDI (< 8 mm) placed in human arches,

(2) have a minimum number of 20 implants of the specified lengths in their analysis, (3) provide data on survival rates, and (4) report a minimum observation period of at least 3 months after placement.

Studies were excluded, if (1) implant length was not specified, or (2) complex surgical interventions and bone augmentation procedures were performed prior to implant placement.

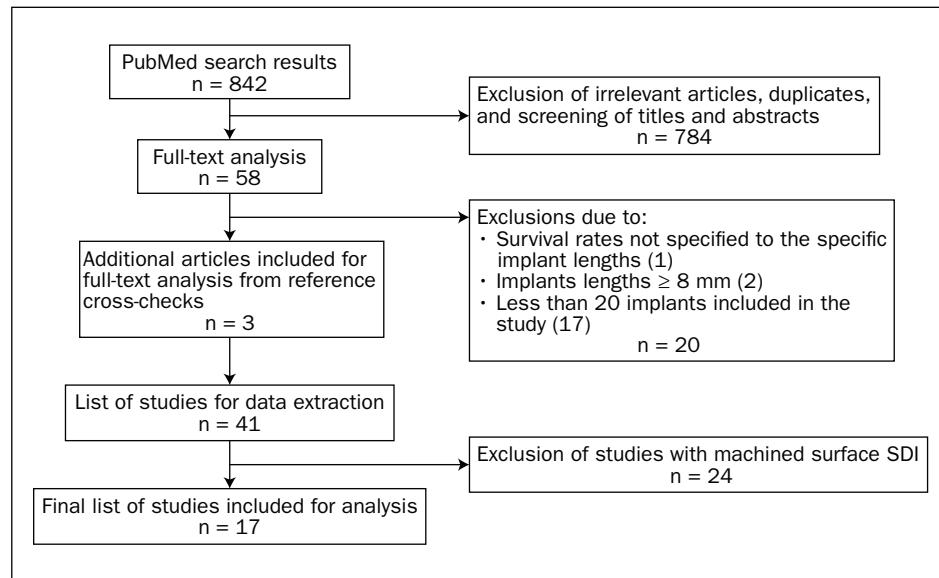
Since the available research on this topic is limited, it was decided to include, besides randomized clinical trials (RCTs) and systematic reviews of RCTs, case series studies, cohort studies, and case control studies. Publications were excluded if there was more than one study by the same researcher(s) conveying the same data. In such an instance, only the most recent study was included.

The database search strategy was devised and performed by the first author (MS). The abstracts of the searched articles were screened thoroughly by two reviewers (MS and PR). Full-text analyses were performed only on the short-listed articles based on the initial screening and on mutual agreement between the two reviewers. The data were extracted jointly by the two reviewers, and were subsequently rechecked and verified by a third reviewer (LV); any disagreement was solved by means of a consensus discussion presided over by a senior reviewer (JCB). The information was extracted from the selected publications, including name of author(s), journal, study type, implant length, surface characteristics, diameter of the implants, number of implants placed and failed, survival rates, and region of placement (if mentioned). A meta-analysis was planned for the extracted data.

RESULTS

The PubMed search yielded a total of 842 articles for the various combinations of the search terms mentioned in the methods section. The procedural aspects of the literature search and selection process are presented in Fig 1. From the screened titles and abstracts ($n = 842$), full-text analysis ($n = 58$), and reference crosschecks ($n = 3$), 41 publications qualified to be included in this study.^{1,17,19,25–61} However, studies reporting on machined surface implants were excluded from this review,^{1,17,25–35,39–44,47,48,52,62} and, finally, 17 quality studies reporting on microrough surface SDI were included for data extraction and interpretation (Table 1). Six lengths of implants < 8 mm (4, 5, 6, 6.5, 7, and 7.5 mm) were identified in this review. Different implant brands (eg, 3i, Astra-Tech, Bicon, BTI, Endopore, Nobel, RBM, Straumann) with varying diameters (3.5 to 6 mm) and surface characteristics (coated, porous, and microrough) were used in the selected studies.

Fig 1 Procedural flow of the literature search and selection process. SDI = short dental implants.



Most articles reported only a cumulative or an overall survival rate for the different lengths of implants investigated, while others did the same for different diameters. Some studies did not specify the region of installation of the implants (maxilla or mandible).^{37,42,44,46–49,51,52,56} The exact number of dropouts or the exact time of failure(s), specific to length, site, and observation time was not mentioned in many articles. Furthermore, the selected articles differed from each other in the following parameters: implant number, implant length, implant diameter, study design, statistical analysis, and observation time. Due to the heterogeneity amongst the studies, the originally planned meta-analysis was not possible and a comprehensively structured descriptive analysis was performed in this review.

Observed Time Period

The observed time periods, ranging from 3 months⁵⁵ to 9 years,⁵⁸ reported in the studies have been converted into years for convenience and uniformity.

Survival Rates with Respect to Implant Lengths

Survival rates reported for microrough surface SDI (placed = 1,828, failed = 45) ranged from 92.2% to 100% for an observation period of up to 9 years (Table 2).^{19,37,38,45,49,50,53,55,56,63} Three studies^{45,50,58} on 7-mm SDI and one study⁵⁶ on 6.5- and 7.5-mm SDI, reported 100% survival rates.

4-mm and 5-mm Lengths. A single study presented data on 4-mm-long SDI, that was a recent prospective multicenter study.⁶⁰ The study, based on 100 implants,

reported an implant survival rate of 92.3% over a 2-year period. A pilot study of a RCT on 5-mm SDI reported a 98.3% survival rate after 1 year.⁵⁹ This study reported on 60 SDI (5 mm × Ø 6 mm) that were placed in atrophic posterior maxillae and mandibles, with one failure in the maxilla before loading. Two other studies on 5-mm SDI reported 100% survival rates in a 1 to 9 year follow-up^{58,64}; but these were excluded from the review because of their small sample sizes.

6-mm Length. From all studies reviewed, a total of 639 microrough surface implants were inserted and from these only 18 failed, with overall survival rates of 92.2% to 98.5% (observed period of 1 to 8 years).^{19,37,38,51,53,57,61} The majority of the 6-mm SDI used were Straumann dental implants, comprising a total of 594 implants placed with only 15 failures (SLA = 302 placed, failed = 7; TPS = 292 placed, failed = 8).^{19,37,38,53,57,61}

7-mm Length. A total number of 758 microrough surface SDI of 7 mm length were placed in both arches and 19 implants failed. The survival rates reported in a total of nine studies ranged from 96.2% to 100% for an observed time of up to 9 years.^{19,45,46,49,50,54–56,58} Deporter et al⁴⁵ in a 3-year prospective study, presented a 100% survival rate for 7-mm sintered porous SDI (n = 32). Sohn et al,⁵⁸ in their retrospective study, also reported a 100% survival rate for 7-mm SDI (n = 30) in a 9-year follow-up period.

6.5-mm and 7.5-mm Lengths. Only one study supplied data in this category and reported a 100% survival rate over an observation period of 1 to 8 years.⁵⁶ More specifically, a total of 37 SDI of 6.5-mm length and 234 implants of 7.5-mm length were inserted.

Table 1 Overview of the Extracted Data on Microrough Surface Short Dental Implants (< 8 mm) from the Reviewed Studies

Study	Type of study	Restoration type	Follow-up period (y)	Implant surface (diameter in mm)	Number of		
					4 mm	Max	Man
						Max	SR%
Buser et al ³⁷	Prospective	Fixed/removable	1–8	TPS (4.1)	—	—	—
ten Bruggenkate et al ³⁸	Prospective	Fixed/overdentures	1–7	SLA (3.5, 4.1)	—	—	—
Deporter et al ⁴⁵	Retrospective	Fixed	3.02	Sintered porous (4.1, 5)	—	—	—
Davarpanah et al ⁴⁶	Prospective	Fixed/overdentures	1–5	Rough (3.75, 4, 5, 6)	—	—	—
Feldman et al ⁴⁹	Prospective	Fixed	2–5	Osseotite (3.75, 4)	—	—	—
Fugazzotto et al ⁵⁰	Retrospective	Fixed	1–7	SLA (4.1, 4.8)	—	—	—
Gentile et al ⁵¹	Retrospective	Fixed	1	Rough (5.7)	—	—	—
Arlin ⁵³	Retrospective	Fixed	1–5.4	SLA (4.1, 4.8)	—	—	—
Malo et al ⁵⁴	Retrospective	Fixed	1–5	TiUnite (3.75, 4)	—	—	—
Fugazzotto ¹⁹	Retrospective	Fixed	3.01	SLA (4.1, 4.8, WN)	—	—	—
Felice et al ⁵⁵	Prospective	Fixed	0.25–1	Nanotite (4.0)	—	—	—
Anitua and Orive ⁵⁶	Retrospective	Fixed/overdentures	1–8	BTI (3.75, 4, 4.5, 5, 5.5, 6)	—	—	—
Sohn et al ⁵⁸	Retrospective	Fixed	1–9	Sintered porous (4.1, 5)	—	—	—
Rossi et al ⁵⁷	Prospective	Fixed	2	SLA (4.1, 4.8)	—	—	—
Esposito et al ⁵⁹	Pilot study (RCT)	Fixed	1	RBM (6)	—	—	—
Van Assche et al ⁶¹	Prospective	Overdentures	2	SLActive (4.1)	—	—	—
Slotte et al ⁶⁰	Prospective	Fixed	2	SLActive (4.1)	0	100 (7)	92.3

Max = maxilla; Man = mandible; SR% = survival rate; WN = wide neck.

Table 2 Overview of Survival Rates of Microrough Surface Short Dental Implants in the Reviewed Studies

Implant length (mm)	No. of studies	Observation period (y)	Placed	Failed	Reported survival rate (%)
4	1	2	100	7	92.3
5	1	1	60	1	98.3
6	7	1–8	639	18	92.2–98.5
6.5	1	1–8	37	0	100
7	9	0.25–9	758	19	96.2–100
7.5	1	1–8	234	0	100
Total	17*	0.25–9	1,828	45	92.3–100

*Total number of reviewed studies.

Implant Diameter

Three of the 17 reviewed studies compared the impact of implant diameters and survival.^{19,46,58} In a study by Davarpanah et al,⁴⁶ an increase in failure rates corresponded to increasing implant diameters, irrespective of implant length. The study reported the highest failure rates (25%) for 6-mm-diameter implants. Fugazzotto¹⁹ reported survival rates of 99.2% for wide neck and

98.4% for standard neck configurations. Finally, Sohn et al⁵⁸ reported survival rates of 100% for both 5-mm and 4.1-mm diameters.

Location

Twelve studies specified the location of implant placement,^{19,38,45,50,53–55,57–61} reporting a total number of 1,123 SDI placed in different segments of the maxilla

implants placed (failed) length- and arch-wise with the reported survival rates															
5 mm			6 mm			6.5 mm			7 mm			7.5 mm			
Max	Man	SR%	Max	Man	SR%	Max	Man	SR%	Max	Man	SR%	Max	Man	SR%	
—	—	—	39	—	96.7	—	—	—	—	—	—	—	—	—	—
—	—	—	45 (6)	208 (1)	97.0	—	—	—	—	—	—	—	—	—	—
—	—	—	—	—	—	—	—	—	0	32 (0)	100.0	—	—	—	—
—	—	—	—	—	—	—	—	—	96 (4)	—	96.5	—	—	—	—
—	—	—	—	—	—	—	—	—	143 (5)	—	96.5	—	—	—	—
—	—	—	—	—	—	—	—	—	42 (0)	0	100.0	—	—	—	—
—	—	—	45 (3)	—	92.2	—	—	—	—	—	—	—	—	—	—
—	—	—	0	35 (2)	94.2	—	—	—	—	—	—	—	—	—	—
—	—	—	—	—	—	—	—	—	27 (3)	104 (2)	96.2	—	—	—	—
—	—	—	110 (1)	93 (2)	98.5	—	—	—	0	113 (2)	98.2	—	—	—	—
—	—	—	—	—	—	—	—	—	—	60 (2)	96.7	—	—	—	—
—	—	—	—	—	—	37 (0)	—	100	—	111 (1)	99.1	234 (0)	—	100.0	—
—	—	—	—	—	—	—	—	—	0	30 (0)	100.0	—	—	—	—
—	—	—	15 (2)	25	95.0	—	—	—	—	—	—	—	—	—	—
34 (1)	26 (0)	98.3	—	—	—	—	—	—	—	—	—	—	—	—	—
—	—	—	24 (1)	—	95.8	—	—	—	—	—	—	—	—	—	—
—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—

Table 3 Overview of Jaw-Wise Distribution of the Short Dental Implants in the Reviewed Studies

Implant length (mm)	No. of studies	Observation period (y)	Maxilla		Mandible	
			Placed	Failed	Placed	Failed
4	1	2	NA	NA	100	7
5	1	1	34	1	26	0
6	5	1–8	194	9	361	6
6.5	1	1–8	NA	NA	NA	NA
7	6	0.25–9	69	3	339	6
7.5	1	1–8	NA	NA	NA	NA
Total	17*	0.25–9	297	13	826	19

NA = no data available from the reviewed studies; *total number of reviewed studies.

and mandible. From this total, 297 implants were placed in the maxilla (13 failures) and 826 were inserted in the mandible, revealing 19 failures (Table 3). Most studies reported a higher number of implant failures in the maxilla,^{38,54,59,61} while Fugazzotto¹⁹ demonstrated higher failures in the mandible.

DISCUSSION

This comprehensive structured review scrutinized the clinical studies published from January 1990 through July 2011, while corresponding to strict inclusion and exclusion criteria. It primarily drew focus to implants of lengths less than 8 mm. The data obtained in this review are exclusively from peer-reviewed scientific journals

in English. The studies exhibited a broad diversity in terms of observation time, implant length, implant diameter, implant surface, location of installation, study design, and surgical protocol. Furthermore, the studies showed variations related to the cited text and tables, unspecified dropouts, specific time of failure with respect to specific length, method of statistical analysis, and reporting. These factors deemed it impossible to systematically compare the reviewed publications with one another; which was a similar finding in an earlier published review.²² Hence, the initially planned meta-analysis for the extracted data was not possible, and a descriptive, but nevertheless structured and methodologically sound, analysis was carried out in this review.

The authors observed that, although the studies were conducted with the focus of evaluating short length implants, the definition of "short length" varied in each study and ranged within a broad spectrum (4 to 11 mm). Although 8-mm length is considered short by the standards of current literature, its evaluation in this review was eliminated because the current-day survival rates for the 8-mm-length short implants are predictably high and comparable to those of standard implants.^{2,18-20} Hence, the present review focused on lengths shorter than 8 mm and the authors suggest redefining the term "short dental implant" as a dental implant with an intrabony length between 6 and 7.5 mm; and define "ultra-short dental implant" as an implant with an intrabony length of less than 6 mm.

This review identified considerable heterogeneity in the observation periods and in the sample sizes of the reviewed studies. A significant number of quality studies^{1,5,8,17,18,42,43,47,63-72} were excluded from this review because they had a sample size of less than 20 implants. An estimation of a proportion on small samples is unreliable and the chance of detecting a low or a high proportion is weak.⁷³ Hence, pooling studies with small sample sizes may underestimate the proportion of failures. It would also not be correct to pool all the studies analyzing implants with the same length and different surfaces because this may also further underestimate the failure rates. Therefore, studies with machined surface SDI were later decided to be excluded from this review, although they fulfilled the inclusion criteria and had adequate sample sizes.^{1,17,25-36,39-44,47,48,52,62} Furthermore, machined surface implants are obsolete in modern day implant practice, hence, including them in the analysis would not have provided a clinically relevant comparison.

A total of 17 studies on SDI with structured micro-rough surfaces were reviewed and revealed survival rates of 92.2% to 100%.^{19,37,38,45,46,49-51,53-61} The most recent study examined in this review was a 2-year prospective study on 4-mm long implants that reported a

survival rate of 92.3% over a 2-year period in severely atrophied posterior mandibles.⁶⁰ The study, however, strongly hypothesized on the need for extreme care during the surgery and meticulous planning of the prosthetic superstructure in terms of occlusion, so as to prevent implant overload and eventual implant loss. The results were said to be comparable with other short implant lengths (6 to 8.5 mm), and the success was predominantly attributed to the excellent implant stability at placement.

The occurrence of peri-implantitis in 16% of patients treated with machined-surface implants 9 to 14 years after loading has been documented.⁷⁴ A systematic review reported that the incidence of peri-implantitis is likely to be higher in implants with roughened surfaces at 3 years of loading when compared with machined-surface implants (risk ratio = 0.80; 95% CI: 0.67 to 0.96).⁷⁵ Implants with turned surfaces had a 20% reduction in risk of being affected by peri-implantitis. This may in fact be critical for survival in microrough SDI, especially with very short lengths (4 mm and 5 mm). It has been documented that untreated peri-implant mucositis, which may lead to progressive destruction of the peri-implant tissues and subsequently to peri-implantitis, ultimately may lead to implant failure.⁷⁶ With longer implants, this situation may still be manageable as the increased implant length provides better chances of survival. Hence, extreme care should be emphasized in maintaining the peri-implant bone levels while employing SDI of lengths < 6 mm. Clinical common sense and concerns relative to dimensional manufacturing limitations, peri-implantitis, technical complications relating to implant components, and, importantly, a lack of sufficient research restrict the use of such SDI (< 6 mm) to extreme clinical situations only.

The majority of studies included in this review have used SDI of 6-mm and 7-mm lengths. These dimensions seem to be the preferred choice of clinicians. Interestingly, the most commonly used 6 mm SDI was that of the Straumann Dental Implant System (Straumann AG).²² Studies on SLA surface 6-mm implants have been consistent with reported overall high survival rates between 94.2% and 100% for an observed period of 1 to 8 years.^{19,37,38,50,53,57,60,61}

Former studies suggest that the implant diameter is of more significance to the survival outcome than its length.^{77,78} Frequent failures were experienced with 5-mm diameter machined surface implants in comparison to the smaller diameters of 3.75 mm or 4.0 mm.⁴⁰ This increased failure rate may be attributed to the implant design, the bone quality at the site of placement, and the operator's learning curve. This review, however, did not identify such a correlation between implant diameters and implant survival in the microrough implants examined. In fact, this review identified

only three studies that had performed a comparison between implant diameters and failure rates.^{19,46,58} Davarpanah et al⁴⁶ reported higher failure rates for large diameter implants, while Fugazzotto¹⁹ reported better survival rates for wide neck configurations. Sohn et al⁵⁸ reported high survival rates for both standard (4.1 mm) and wide (5 mm) diameters of SDI. It should be underlined that data extracted from the studies on this topic were limited and inconclusive.

Bone quality and region of placement appear to play an important role in implant survival. In this review, the studies reported a marginally higher number of failures associated to SDI placed in the posterior maxilla.^{38,54,59,61} In comparison, the number of failures in the mandible was less. This could be explained by the fact that the shape of the jaw and bone density are governing factors that play an important role in the survival of implants.²⁶ Traditionally, the emphasis has been primarily placed on bone morphology or bone density as important factors in predicting implant success and survival, and comparisons between short and standard length implants have been made in this light.⁷⁹ However, it is important to note that this is not an appropriate assessment of the outcomes associated with the use of SDI, since in most studies SDI were usually placed under compromised situations. Unless studies have evaluated outcomes of SDI under normal alveolar conditions, superficial comparisons should not be made with standard length and/or longer implants.

Finally, very few RCTs relevant to the current topic were identified by this review. Thus, prospective clinical trials with standardized protocols and well-defined study parameters are needed to further assess treatment outcomes and predictability of SDI, especially with regard to shorter implants (< 6 mm).

CONCLUSIONS

The survival rates and treatment outcomes associated with short implants are dependent on multifactorial parameters, and cannot be determined by mere comparisons between the existing studies, which differ from one another. This structured review, however, provides sufficient evidence of the predictability of treatment outcomes with microrough surface SDI (< 8-mm lengths) in the treatment of partially and fully edentulous arches. Microrough surface implants with lengths in the range of 6 to 7.5 mm appear to provide favorable survival rates, and this fact may significantly contribute to the simplification of implant therapy, namely in posterior segments of the arches.

ACKNOWLEDGMENTS

The authors wish to express their gratitude to Dr Christophe Combescure, biostatistician, for his most valuable advice for the statistical analyses. The authors reported no conflicts of interest related to this study.

REFERENCES

- Renouard F, Nisand D. Short implants in the severely resorbed maxilla: A 2-year retrospective clinical study. *Clin Implant Dent Relat Res* 2005;7(suppl 1):S104–S110.
- Griffin TJ, Cheung WS. The use of short, wide implants in posterior areas with reduced bone height: A retrospective investigation. *J Prosthet Dent* 2004;92:139–144.
- Misch CE. Short dental implants: A literature review and rationale for use. *Dent Today* 2005;24:64–68.
- Renouard F, Nisand D. Impact of implant length and diameter on survival rates. *Clin Oral Implants Res* 2006;17(suppl 2):35–51.
- Wyatt CC, Zarb GA. Treatment outcomes of patients with implant-supported fixed partial prostheses. *Int J Oral Maxillofac Implants* 1998;13:204–211.
- Block MS, Delgado A, Fontenot MG. The effect of diameter and length of hydroxylapatite-coated dental implants on ultimate pullout force in dog alveolar bone. *J Oral Maxillofac Surg* 1990;48:174–178.
- Lum LB. A biomechanical rationale for the use of short implants. *J Oral Implantol* 1991;17:121–131.
- Ekfeldt A, Carlsson GE, Börjesson G. Clinical evaluation of single-tooth restorations supported by osseointegrated implants: A retrospective study. *Int J Oral Maxillofac Implants* 1994;9:179–183.
- Pierrissenard L, Renouard F, Renault P, Barquins M. Influence of implant length and bicortical anchorage on implant stress distribution. *Clin Implant Dent Relat Res* 2003;5:254–262.
- Morgan MJ, James DF, Pilliar RM. Fractures of the fixture component of an osseointegrated implant. *Int J Oral Maxillofac Implants* 1993;8:409–414.
- Cochran DL. A comparison of endosseous dental implant surfaces. *J Periodontol* 1999;70:1523–1539.
- Hagi D, Deporter DA, Pilliar RM, Arenovich T. A targeted review of study outcomes with short (< or = 7 mm) endosseous dental implants placed in partially edentulous patients. *J Periodontol* 2004;75:798–804.
- Jaffin RA, Berman CL. The excessive loss of Branemark fixtures in type IV bone: A 5-year analysis. *J Periodontol* 1991;62:2–4.
- Nedir R, Bischof M, Briaux JM, Beyer S, Szmukler-Moncler S, Bernard JP. A 7-year life table analysis from a prospective study on ITI implants with special emphasis on the use of short implants. Results from a private practice. *Clin Oral Implants Res* 2004;15:150–157.
- Roccuzzo M, Bunino M, Prioglio F, Bianchi SD. Early loading of sandblasted and acid-etched (SLA) implants: A prospective split-mouth comparative study. *Clin Oral Implants Res* 2001;12:572–578.
- Deporter DA, Todescan R, Caudry S. Simplifying management of the posterior maxilla using short, porous-surfaced dental implants and simultaneous indirect sinus elevation. *Int J Periodontics Restorative Dent* 2000;20:476–485.
- Tawil G, Younan R. Clinical evaluation of short, machined-surface implants followed for 12 to 92 months. *Int J Oral Maxillofac Implants* 2003;18:894–901.
- Bischof M, Nedir R, Abi Najm S, Szmukler-Moncler S, Samson J. A five-year life-table analysis on wide neck ITI implants with prosthetic evaluation and radiographic analysis: Results from a private practice. *Clin Oral Implants Res* 2006;17:512–520.
- Fugazzotto PA. Shorter implants in clinical practice: Rationale and treatment results. *Int J Oral Maxillofac Implants* 2008;23:487–496.
- Teixeira ER, Wadamoto M, Akagawa Y, Kimoto T. Clinical application of short hydroxylapatite-coated dental implants to the posterior mandible: A five-year survival study. *J Prosthet Dent* 1997;78:166–171.

21. Kotsovilis S, Fourmousis I, Karoussis IK, Bamia C. A systematic review and meta-analysis on the effect of implant length on the survival of rough-surface dental implants. *J Periodontol* 2009;80:1700–1718.
22. Neldam CA, Pinholt EM. State of the art of short dental implants: A systematic review of the literature. *Clin Implant Dent Relat Res* 2010 Oct 26 [epub ahead of print].
23. Pommer B, Sophie F, Willer J, Posch M, Watzek G, Tepper G. Impact of dental implant length on early failure rates: A meta-analysis of observational studies. *J Clin Periodontol* 2011;38:856–863.
24. Tellemans G, Raghoebar GM, Vissink A, den Hartog L, Slater JRRH, Meijer HJA. A systematic review of the prognosis of short (< 10 mm) dental implants placed in the partially edentulous patient. *J Clin Periodontol* 2011;38:667–676.
25. van Steenberghhe D, Lekholm U, Bolender C, et al. Applicability of osseointegrated oral implants in the rehabilitation of partial edentulism: A prospective multicenter study on 558 fixtures. *Int J Oral Maxillofac Implants* 1990;5:272–281.
26. Friberg B, Jemt T, Lekholm U. Early failures in 4,641 consecutively placed Bränemark dental implants: A study from stage 1 surgery to the connection of completed prostheses. *Int J Oral Maxillofac Implants* 1991;6:142–146.
27. Jemt T, Lindén B, Lekholm U. Failures and complications in 127 consecutively placed fixed partial prostheses supported by Bränemark implants: From prosthetic treatment to first annual checkup. *Int J Oral Maxillofac Implants* 1992;7:40–44.
28. Quirynen M, Naert I, van Steenberghhe D. Fixture design and overload influence marginal bone loss and fixture success in the Bränemark system. *Clin Oral Implants Res* 1992;3:104–111.
29. Bahat O. Treatment planning and placement of implants in the posterior maxillae: Report of 732 consecutive Nobelpharma implants. *Int J Oral Maxillofac Implants* 1993;8:151–161.
30. Jemt T. Implant treatment in resorbed edentulous upper jaws. A three year follow-up study on 70 patients. *Clin Oral Implants Res* 1993;4:187–194.
31. Jemt T, Lekholm U. Oral implant treatment in posterior partially edentulous jaws: A 5-year follow-up report. *Int J Oral Maxillofac Implants* 1993;8:635–640.
32. Nevins M, Langer B. Fixed implant-supported prostheses in the edentulous maxilla. A five-year follow-up report. *Int J Oral Maxillofac Implants* 1993;8:428–432.
33. Jemt T. Fixed implant-supported prostheses in the edentulous maxilla. A five-year follow-up report. *Clin Oral Implants Res* 1994;5:142–147.
34. Bränemark PI, Svensson B, van Steenberghhe D. Ten-year survival rates of fixed prostheses on four or six implants ad modum Bränemark in full edentulism. *Clin Oral Implants Res* 1995;6:227–231.
35. Higuchi KW, Folmer T, Kultje C. Implant survival rates in partially edentulous patients: A 3-year prospective multicenter study. *J Oral Maxillofac Surg* 1995;53:264–258.
36. Jemt T, Lekholm U. Implant treatment in edentulous maxillae: A 5-year follow-up report on patients with different degrees of jaw resorption. *Int J Oral Maxillofac Implants* 1995;10:303–311.
37. Buser D, Mericske-Stern R, Bernard JP, et al. Long-term evaluation of non-submerged ITI implants. Part 1: 8-year life table analysis of a prospective multi-center study with 2359 implants. *Clin Oral Implants Res* 1997;8:161–172.
38. ten Bruggenkate CM, Asikainen P, Foitzik C, Krekeler G, Sutter F. Short (6-mm) nonsubmerged dental implants: Results of a multicenter clinical trial of 1 to 7 years. *Int J Oral Maxillofac Implants* 1998;13:791–798.
39. Gunne J, Astrand P, Lindh T, Borg K, Olsson M. Tooth-implant and implant supported fixed partial dentures: A 10-year report. *Int J Prosthodont* 1999;12:216–221.
40. Ivanoff CJ, Gröndahl K, Sennerby L, Bergström C, Lekholm U. Influence of variations in implant diameters: A 3- to 5-year retrospective clinical report. *Int J Oral Maxillofac Implants* 1999;14:173–180.
41. Lekholm U, Gunne J, Henry P, et al. Survival of the Bränemark implant in partially edentulous jaws: A 10-year prospective multicenter study. *Int J Oral Maxillofac Implants* 1999;14:639–645.
42. Bahat O. Bränemark system implants in the posterior maxilla: Clinical study of 660 implants followed for 5 to 12 years. *Int J Oral Maxillofac Implants* 2000;15:646–653.
43. Friberg B, Gröndahl K, Lekholm U, Bränemark PI. Long-term follow-up of severely atrophic edentulous mandibles reconstructed with short Bränemark implants. *Clin Implant Dent Relat Res* 2000;2:184–189.
44. Winkler S, Morris HF, Ochi S. Implant survival to 36 months as related to length and diameter. *Ann Periodontol* 2000;5:22–31.
45. Deporter DA, Pilliar RM, Todescan R, Watson P, Pharoah M. Managing the posterior mandible of partially edentulous patients with short, porous-surfaced dental implants: Early data from a clinical trial. *Int J Oral Maxillofac Implants* 2001;16:653–658.
46. Davarpanah M, Martinez H, Etienne D, et al. A prospective multicenter evaluation of 1,583 3i implants: 1- to 5-year data. *Int J Oral Maxillofac Implants* 2002;17:820–828.
47. Naert I, Koutsikakis G, Duyck J, Quirynen M, Jacobs R, van Steenberghhe D. Biologic outcome of implant-supported restorations in the treatment of partial edentulism. Part I: A longitudinal clinical evaluation. *Clin Oral Implants Res* 2002;13:381–389.
48. Weng D, Jacobson Z, Tarnow D, et al. A prospective multicenter clinical trial of 3i machined-surface implants: Results after 6 years of follow-up. *Int J Oral Maxillofac Implants* 2003;18:417–423.
49. Feldman S, Boitel N, Weng D, Kohles SS, Stach RM. Five-year survival distributions of short-length (10 mm or less) machined-surfaced and Osseotite implants. *Clin Implant Dent Relat Res* 2004;6:16–23.
50. Fugazotto PA, Beagle JR, Ganeles J, Jaffin R, Vlassis J, Kumar A. Success and failure rates of 9 mm or shorter implants in the replacement of missing maxillary molars when restored with individual crowns: Preliminary results 0 to 84 months in function. A retrospective study. *J Periodontol* 2004;75:327–332.
51. Gentile MA, Chuang SK, Dodson TB. Survival estimates and risk factors for failure with 6 × 5.7-mm implants. *Int J Oral Maxillofac Implants* 2005;20:930–937.
52. Herrmann I, Lekholm U, Holm S, Kultje C. Evaluation of patient and implant characteristics as potential prognostic factors for oral implant failures. *Int J Oral Maxillofac Implants* 2005;20:220–230.
53. Arlin ML. Short dental implants as a treatment option: Results from an observational study in a single private practice. *Int J Oral Maxillofac Implants* 2006;21:769–776.
54. Maló P, de Araújo Nobre M, Rangert B. Short implants placed one-stage in maxillae and mandibles: A retrospective clinical study with 1 to 9 years of follow-up. *Clin Implant Dent Relat Res* 2007;9:15–21.
55. Felice P, Cannizzaro G, Checchi V, et al. Vertical bone augmentation versus 7-mm-long implants in posterior atrophic mandibles. Results of a randomised controlled clinical trial of up to 4 months after loading. *Eur J Oral Implantol* 2009;2:7–20.
56. Anitua E, Orive G. Short implants in maxillae and mandibles: A retrospective study with 1 to 8 years of follow-up. *J Periodontol* 2010;81:819–826.
57. Rossi F, Ricci E, Marchetti C, Lang NP, Botticelli D. Early loading of single crowns supported by 6-mm-long implants with a moderately rough surface: A prospective 2-year follow-up cohort study. *Clin Oral Implants Res* 2010;21:937–943.
58. Sohn DS, Kim WS, Lee WH, Jung HS, Shin IH. A retrospective study of sintered porous-surfaced dental implants in restoring the edentulous posterior mandible: Up to 9 years of functioning. *Implant Dent* 2010;19:409–418.
59. Esposito M, Pellegrino G, Pistilli R, Felice P. Rehabilitation of posterior atrophic edentulous jaws: Prostheses supported by 5 mm short implants or by longer implants in augmented bone? One-year results from a pilot randomised clinical trial. *Eur J Oral Implantol* 2011;4:21–30.
60. Slotte C, Grønningaeter A, Halmøy AM, et al. Four-millimeter implants supporting fixed partial dental prostheses in the severely resorbed posterior mandible: Two-year results. *Clin Implant Dent Relat Res* 2011;14(suppl 1):e46–58.
61. Van Assche N, Michels S, Quirynen M, Naert I. Extra short dental implants supporting an overdenture in the edentulous maxilla: A proof of concept. *Clin Oral Implants Res* 2012;23:567–576.
62. Naert I, Quirynen M, van Steenberghhe D, Darius P. A six-year prosthodontic study of 509 consecutively inserted implants for the treatment of partial edentulism. *J Prosthet Dent* 1992;67:236–245.
63. Testori T, Wiseman L, Woolfe S, Porter SS. A prospective multicenter clinical study of the Osseotite implant: Four-year interim report. *Int J Oral Maxillofac Implants* 2001;16:193–200.

64. Yi YS, Emanuel KM, Chuang SK. Short (5.0 × 5.0 mm) implant placements and restoration with integrated abutment crowns. *Implant Dent* 2011;20:125–130.
65. Becker W, Becker BE, Alsuwyed A, Al-Mubarak S. Long-term evaluation of 282 implants in maxillary and mandibular molar positions: A prospective study. *J Periodontol* 1999;70:896–901.
66. Brocard D, Barthet P, Baysse E, et al. A multicenter report on 1,022 consecutively placed ITI implants: A 7-year longitudinal study. *Int J Oral Maxillofac Implants* 2000;15:691–700.
67. Polizzi G, Grunder U, Goené R, et al. Immediate and delayed implant placement into extraction sockets: A 5-year report. *Clin Implant Dent Relat Res* 2000;2:93–99.
68. Mericske-Stern R, Grüter L, Rösch R, Mericske E. Clinical evaluation and prosthetic complications of single tooth replacements by non-submerged implants. *Clin Oral Implants Res* 2001;12:309–318.
69. Naert I, Koutsikakis G, Quirynen M, Duyck J, Steenberghe DV, Jacobs R. Biologic outcome of implant-supported restorations in the treatment of partial edentulism. Part 2: A longitudinal radiographic study. *Clin Oral Implants Res* 2002;13:390–395.
70. Pjetursson BE, Rast C, Bragger U, Schmidlin K, Zwahlen M, Lang NP. Maxillary sinus floor elevation using the (transalveolar) osteotome technique with or without grafting material. Part I: Implant survival and patients' perception. *Clin Oral Implants Res* 2009;20:667–676.
71. Etöz OA, Ulu M, Kesim B. Treatment of patient with Papillon-Lefevre syndrome with short dental implants: A case report. *Implant Dent* 2010;19:394–399.
72. Koo KT, Wikesjö UM, Park JY, et al. Evaluation of single-tooth implants in the second molar region: A 5-year life-table analysis of a retrospective study. *J Periodontol* 2010;81:1242–1249.
73. Combescure C, Courvoisier D, Haller G, Perneger TV. Meta-analysis of binary outcomes from two-by-two tables when the length of follow-up varies and hazards are proportional. *Stat Methods Med Res* 2010;20:531–540.
74. Roos-Jansäker AM, Lindahl C, Renvert H, Renvert S. Nine- to fourteen-year follow-up of implant treatment. Part II: Presence of peri-implant lesions. *J Clin Periodontol* 2006;33:290–295.
75. Esposito M, Murray-Curtis L, Grusovin MG, Coulthard P, Worthington HV. Interventions for replacing missing teeth: Different types of dental implants. *Cochrane Database Syst Rev* 2007 Oct 17;(4):CD003815.
76. Mombelli A. Prevention and therapy of peri-implant infections. In: Lang NP, Karring T, Lindhe J (eds). *Proceedings of the 3rd European Workshop on Periodontology Implant Dentistry*. Berlin: Quintessence, 1999:281–303.
77. Ivanoff CJ, Sennerby L, Johansson C, Rangert B, Lekholm U. Influence of implant diameters on the integration of screw implants. An experimental study in rabbits. *Int J Oral Maxillofac Surg* 1997;26:141–148.
78. Mahon JM, Norling BK, Phoenix RD. Effect of varying fixture width on stress and strain distribution associated with an implant stack system. *Implant Dent* 2000;9:310–320.
79. Lekholm U, Zarb GA. Patient selection and preparation. In: Branemark PI, Zarb GA, Albrektsson T (eds). *Tissue Integrated Prostheses: Osseointegration in Clinical Dentistry*. Chicago: Quintessence, 1985:199–209.

Reliability of Voxel Gray Values in Cone Beam Computed Tomography for Preoperative Implant Planning Assessment

Azin Parsa, DDS, MSc¹/Norliza Ibrahim, DDS, MSc²/Bassam Hassan, BDS, MSc, PhD³/
Alessandro Motroni, MS⁴/Paul van der Stelt, DDS, PhD⁵/Daniel Wismeijer, DDS, PhD⁶

Purpose: To assess the reliability of cone beam computed tomography (CBCT) voxel gray value measurements using Hounsfield units (HU) derived from multislice computed tomography (MSCT) as a clinical reference (gold standard). **Materials and Methods:** Ten partially edentulous human mandibular cadavers were scanned by two types of computed tomography (CT) modalities: multislice CT and cone beam CT. On MSCT scans, eight regions of interest (ROI) designating the site for preoperative implant placement were selected in each mandible. The datasets from both CT systems were matched using a three-dimensional (3D) registration algorithm. The mean voxel gray values of the region around the implant sites were compared between MSCT and CBCT. **Results:** Significant differences between the mean gray values obtained by CBCT and HU by MSCT were found. In all the selected ROIs, CBCT showed higher mean values than MSCT. A strong correlation ($R = 0.968$) between mean voxel gray values of CBCT and mean HU of MSCT was determined. **Conclusions:** Voxel gray values from CBCT deviate from actual HU units. However, a strong linear correlation exists, which may permit deriving actual HU units from CBCT using linear regression models. *INT J ORAL MAXILLOFAC IMPLANTS* 2012;27:1438–1442

Key words: accuracy, CBCT, cone beam computed tomography, Hounsfield unit

Bone density is one of the most important characteristics of bone quality. Assessing bone density prior to implant placement aids the practitioner in choosing a suitable implant site.¹ Several imaging modalities have

¹PhD candidate, Department of General and Specialized Dentistry, Section Oral and Maxillofacial Radiology, Academic Center for Dentistry Amsterdam (ACTA), Amsterdam, The Netherlands.

²PhD candidate, Department of General and Specialized Dentistry, Section Oral and Maxillofacial Radiology, Academic Center for Dentistry Amsterdam (ACTA), Amsterdam, The Netherlands. Lecturer Department of General Dental Practice and Oral & Maxillofacial Imaging, Faculty of Dentistry, University of Malaya, Kuala Lumpur, Malaysia.

³Assistant Professor, Department of General and Specialized Dentistry, Section Oral and Maxillofacial Radiology, Academic Center for Dentistry Amsterdam (ACTA), Amsterdam, The Netherlands.

⁴Bioimaging Specialist, AMIRG—Applied Medical Imaging Research Group, Milan, Italy.

⁵Professor, Department of General and Specialized Dentistry, Section Oral and Maxillofacial Radiology, Academic Center for Dentistry Amsterdam (ACTA), Amsterdam, The Netherlands.

⁶Professor, Department of Oral Implantology and Prosthodontics, Academic Center for Dentistry Amsterdam (ACTA), Amsterdam, The Netherlands.

Correspondence to: Dr Azin Parsa, Department of General and Specialized Dentistry, Section Oral and Maxillofacial Radiology, Academic Center for Dentistry Amsterdam (ACTA), Gustav Mahlerlaan 3004, 1081 LA Amsterdam, The Netherlands.
Email: a.parsa@acta.nl

been used to assess bone density including dual energy x-ray absorptiometry (DEXA),² digital image analysis of microradiographs,³ quantitative ultrasound (QUS),⁴ and computed tomography (CT).⁵ Of these imaging techniques, CT gained popularity in assessing bone density at the prospective implant bed. The concept was first introduced by Schwartz et al⁶ and has been in use more frequently ever since. In multislice CT (MSCT), calibrated Hounsfield units (HU) are obtained, which can be directly converted to bone density measurements. In the arches, bone density measurements derived from HU are highly reliable.^{7,8} However, numerous studies demonstrated higher radiation exposure risk for MSCT in comparison with other imaging modalities.^{9–12}

Cone beam computed tomography (CBCT), which emits a cone shaped x-ray beam, was introduced in the last decade in clinical dentistry. In comparison, CBCT has several advantages over MSCT in terms of increased accessibility to oral health specialists, more compact equipment, small footprint for the clinic, and relatively reduced scan costs. Additionally, lower radiation dose levels to the main organs of the head and neck region have been cited as one of the most important advantages of CBCT over MSCT.^{13–15} However, it has become recently well known that the effective dose from any CBCT device largely depends on the type of the machine and scan settings, including field of view (FOV), number of basis projections, and scan modes among other factors.¹⁶ Moreover, the latest generations of

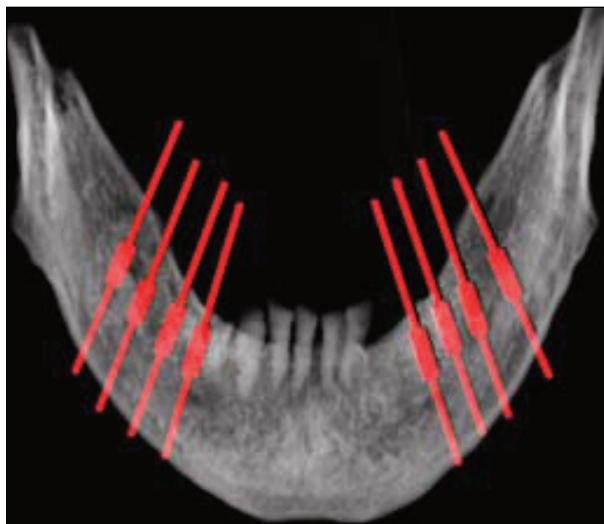


Fig 1 Three-dimensional reconstruction of the mandible with planning of implants.

MSCT offer low-dose “dental scan” modes, which can provide image quality and radiation dose levels comparable with large FOV CBCT scanners.¹⁷ Within any CBCT system, image quality and voxel gray values depend largely on FOV and scan setting selections.¹⁸ It is therefore inappropriate to automatically state that CBCT delivers much lower radiation doses than MSCT, irrespective of the machine or scan protocol used.¹⁹

Nevertheless, the aforementioned advantages of CBCT over MSCT remain substantial and for dental implant placement, CBCT is the modality of choice for preoperative assessment and postoperative diagnostic evaluation. Geometric accuracy was reported to be high for linear measurement so that bone height, width, and the proximity to relevant normal anatomical structures can be accurately measured.^{20–22} Furthermore, bone quality evaluated by CBCT was correlated with primary implant stability.^{23,24}

However, unlike single and multislice CT, CBCT does not represent the actual gray value expressed in HU.²⁵ Previous attempts to assess the reliability of this imaging modality in bone density measurements are noted in the literature. A large amount of scattered x-rays and artifacts have been mentioned as the reasons for unreliability of CBCT in evaluating bone mineral density.^{25–29} However, other studies showed a high correlation between MSCT and CBCT gray values suggesting that voxel values of CBCT can be used to estimate bone mineral density.^{30–34} Using micro-computed tomography (microCT) as the gold standard also established CBCT as a reliable tool to objectively determine bone density.³⁵ The aim of this study was to assess the reliability of CBCT (NewTom 5G) voxel gray value measurements using HU derived from MSCT as a clinical reference (gold standard).

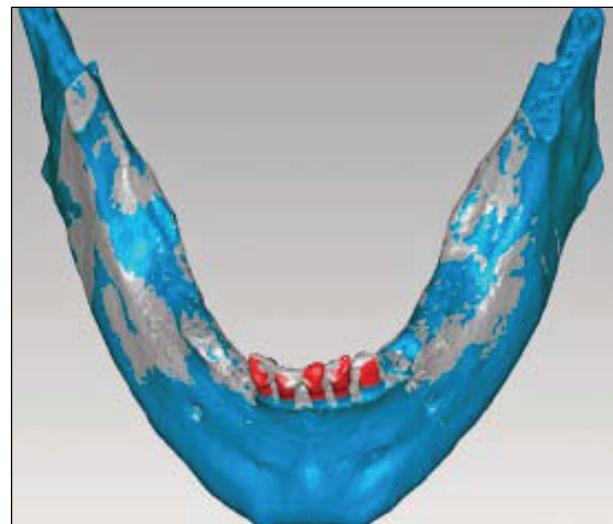


Fig 2 An example of the matching between MSCT and CBCT.

MATERIAL AND METHODS

Sample Preparation and Radiographic Evaluation

Ten partially edentulous human mandibular cadavers not identified by age, sex, or ethnic group were obtained from the functional anatomy department. The cadavers were sectioned at the midramus level and fixed in formaldehyde (formaldehyde, 74.79%; glycerol, 16.7%; alcohol, 8.3%; Fenol, 0.21%) and stored. A declaration was obtained from the functional anatomy department to use human remains material for research purposes. The mandibles were scanned by two types of CT modalities: MSCT (Philips, 120 kVp, 222 mA, 1.128 S, 0.67 mm³ isotropic voxel) and CBCT (NewTom 5G, 110 kVp, 0.57 mA, 5.4 S, 12 × 8 cm FOV, 0.150 mm³ isotropic voxel). In both CTs, the occlusal plane of each mandible was set perpendicular to the floor with zero gantry tilt.

CT Values Evaluation

The scans were converted to DICOM 3 format. The analysis of the data was performed using software (3Diagnosys 3.1, 3DIEMME). On MSCT scans, eight regions of interest (ROI) designating the site for preoperative implant placement were selected in each mandible. The selected ROIs were totally within the bone. Subsequently, four virtual implants in each left and right premolar region were manually placed (Fig 1). The datasets from both MSCT and CBCT were then matched using a volume-based three-dimensional (3D) registration algorithm to standardize the selection of ROI to ensure that the voxel value measurements between the two modalities were exactly from the same site (Fig 2). On the matched datasets, an area with 1 mm

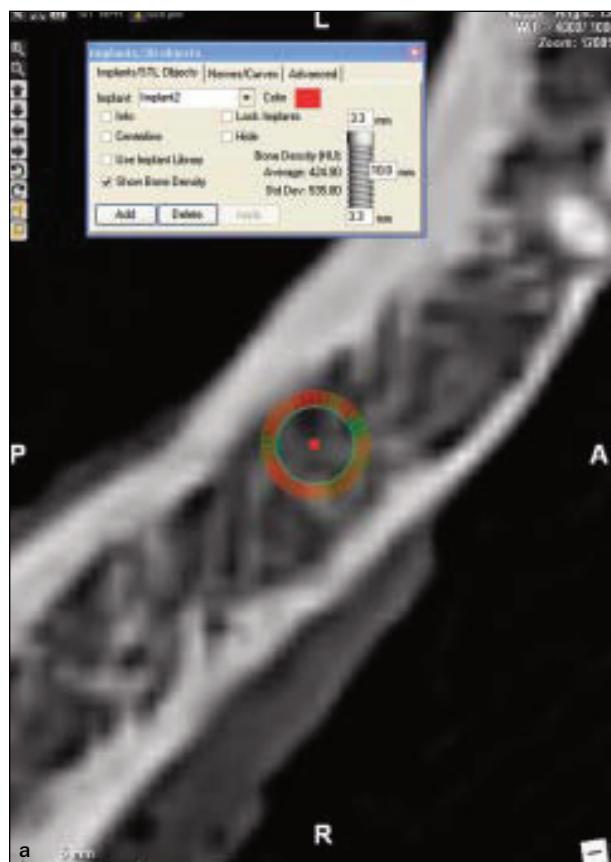


Fig 3 The position of the implant depicted on (a) axial and (b) cross-sectional reconstructed images.

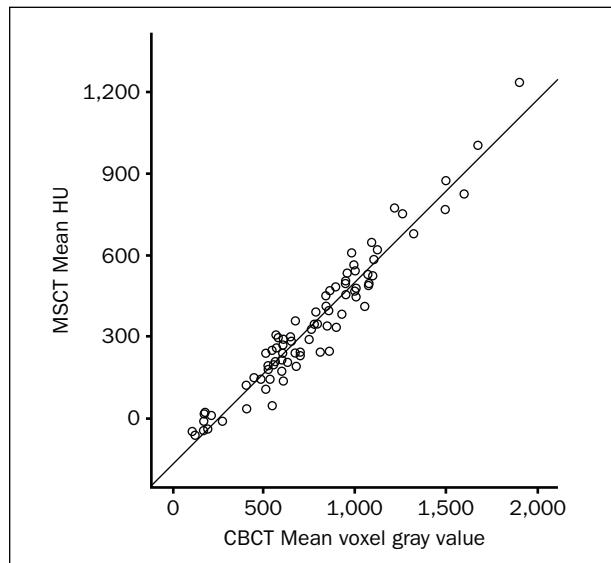
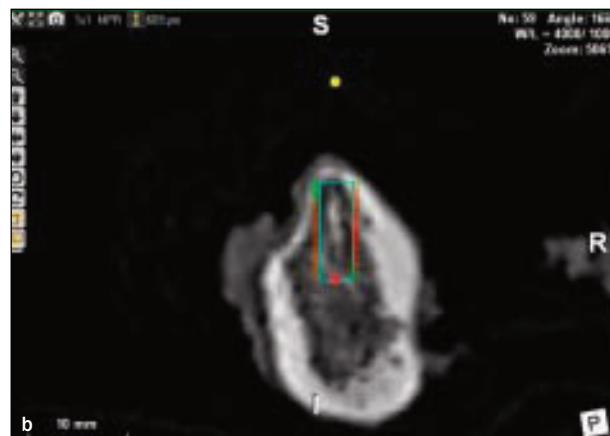


Fig 4 (left) Correlation between HU (MSCT) and mean gray values (CBCT). Linear regression analysis was performed and regression line was superimposed.

SPSS statistical software 18.0 (IBM). Linear regression analysis was used to relate the mean density measurements from both modalities.

RESULTS

The mean voxel gray values of the selected regions around the implant sites ranged from 109.76 to 1,901.84, with a mean of 773.28 (SD, 362.82) in CBCT. The mean HU of the same regions ranged from -61.52 to 1,236.10, with a mean of 348.25 (SD 252.04) in MSCT. Statistical analysis revealed significant differences between the mean gray values obtained by CBCT and the mean HU by MSCT ($P = .01$). In all selected implant sites, CBCT showed higher mean values than MSCT. Linear regression analysis between mean voxel gray values of CBCT and mean HU of MSCT revealed a strong correlation ($R = 0.968$), and the obtained regression equation was $HU = 0.67 \times \text{voxel gray value from CBCT} - 171.80$ (Fig 4).

thickness was selected around the implant sites (Fig 3). The voxel gray values of each hollow cylinder region around the implant sites were exported separately for MSCT and CBCT.

Data Analysis

The mean and standard deviation (SD) of exported gray values of each implant site were calculated using

DISCUSSION

The present ex vivo study showed a strong correlation between voxel gray values in CBCT with HU in MSCT; however, voxel gray values from CBCT deviate from actual HU units. This deviation arises from increased noise level, scattering, and artifacts specific to the scan technology. CBCT scanners operate at a lower kVp and mA in comparison with MSCT, resulting in a reduced signal-to-noise ratio.²⁷ Higher noise levels also cause more inconsistencies and introduce larger SDs in voxel gray values.^{28,36,37} Additionally, as the acquired volume in CBCT is proportionally larger than the highly collimated fan-beam MSCT, the influence these artifacts can produce is excessively exacerbated.^{27,29}

The performed regression analysis and superimposed regression line revealed the conversion formula from the voxel gray value of CBCT to the equivalent HU, which are representatives of bone mineral density. The negative HU values from MSCT may indicate the fat in trabecular spaces. In the present study, a fully automated and observer independent 3D matching algorithm was employed to ensure that both MSCT and CBCT measurements were exactly from the same site. The matching algorithm works on the iterative closest point (ICP) principle, which minimizes the distance between the two surfaces (CBCT and MSCT) by calibrating six-degree transformation parameters (three rotation and three translation).³⁸ Previous studies relied on observers to manually select the site of the measurements to assess voxel gray values between MSCT and CBCT.^{30–34} This approach, however, is less accurate and inevitably leads to discrepancies between the two modalities at the measurement sites.

It has been previously stated that CBCT does not represent the actual HU values in the reconstructed volume.^{25,26} CBCT image artifacts, including scattering, beam hardening, and heel effect, have been cited as the most important contributing factors.^{25,27} The amount of scattered radiation is higher in CBCT compared to MSCT, thus leading to increased noise levels and more inconsistencies in the voxel gray values.²⁷ In only one study were cadavers used to evaluate the bone density by CBCT, where the gray values from CBCT were correlated with objective (HU from MSCT) and subjective (Lekholm and Zarb classification bone density measures).^{30,39} A high correlation was found in the objective measurements. And while the authors observed an overall correlation between CBCT gray values and Lekholm and Zarb classification, the precision of this subjective correlation could not be established.

The present study was limited in that only one CBCT system with specific settings was used. The scan settings for other flat panel CBCT systems may widely vary. The exposure settings used (110 kVp, 0.57 mA,

5.4 S, 12 × 8 cm FOV) were typical for preoperative implant assessment of a patient with a bilateral edentulous mandible. The values obtained for the cadaver may deviate from the clinical situation. Due to time and labor constraints, it was not possible to include a larger sample size. Finally, the study was also limited in that surrounding anatomical structures, including the tongue and vertebra, were absent since standardizing the location of these structures in both modalities was rather cumbersome. As a result, artifacts resulting from structures placed outside the scan field were not simulated. It has been previously noted that artifacts resulting from partial sampling of objects outside the scan field could result in a deviation in the voxel gray values with CBCT.^{28,40}

CONCLUSIONS

With the limited sample used in this study, voxel gray values obtained from CBCT revealed a strong correlation with HU obtained from MSCT. However, due to image artifacts resulting from scattering, beam hardening, and heel effects, the voxel gray values from CBCT scans demonstrated a higher mean value and SD compared with HU from MSCT. More research is required using different CBCT scanners to evaluate the potential for deriving actual HU from CBCT through linear regression models.

ACKNOWLEDGMENTS

The authors would like to thank Dr Hans Verheij for his contribution in conducting the statistical analysis and Mr Patrick Schenkens for his support with the MSCT scans. The authors reported no conflicts of interest related to this study.

REFERENCES

- Tolstunov L. Dental implant success–failure analysis: A concept of implant vulnerability. *Implant Dent* 2006;15:341–346.
- Genant HK, Engelke K, Fuerst T, et al. Noninvasive assessment of bone mineral and structure: State of the art. *J Bone Miner Res* 1996; 11:707–730.
- Jager A, Radlanski RJ, Taufall D, Klein C, Steinhofel N, Doler W. Quantitative determination of alveolar bone density using digital image analysis of microradiographs. *Anat Anz* 1990;170:171–179.
- Hans D, Fuerst T, Uffmann M. Bone density and quality measurement using ultrasound. *Curr Opin Rheumatol* 1996;8:370–375.
- Schwarz MS, Rothman SL, Rhodes ML, Chafetz N. Computed tomography: Part I. Preoperative assessment of the mandible for endosseous implant surgery. *Int J Oral Maxillofac Implants* 1987;2:137–141.
- Schwarz MS, Rothman SL, Rhodes ML, Chafetz N. Computed tomography: Part II. Preoperative assessment of the maxilla for endosseous implant surgery. *Int J Oral Maxillofac Implants* 1987;2:143–148.
- Shapurian T, Damoulis PD, Reiser GM, Griffin TJ, Rand WM. Quantitative evaluation of bone density using the Hounsfield index. *Int J Oral Maxillofac Implants* 2006;21:290–297.

8. Shahlaie M, Gantes B, Schulz E, Riggs M, Crigger M. Bone density assessments of dental implant sites: 1. Quantitative computed tomography. *Int J Oral Maxillofac Implants* 2003;18:224–231.
9. Ekestubbe A, Thilander A, Gröndahl K, Gröndahl HG. Absorbed doses from computed tomography for dental implant surgery: Comparison with conventional tomography. *Dentomaxillofac Radiol* 1993;22:13–17.
10. Ekestubbe A, Thilander A, Gröndahl HG. Absorbed doses and energy imparted from tomography for dental implant installation. Spiral tomography using the Scanora technique compared with hypocycloidal tomography. *Dentomaxillofac Radiol* 1992;21:65–69.
11. Frederiksen NL, Benson BW, Sokolowski TW. Effective dose and risk assessment from computed tomography of the maxillofacial complex. *Dentomaxillofac Radiol* 1995;24:55–58.
12. Dula K, Mini R, van der Stelt PF, Lambrecht JT, Schneeberger P, Buser D. Hypothetical mortality risk associated with spiral computed tomography of the maxilla and mandible. *Eur J Oral Sci* 1996;104: 503–510.
13. Kau CH, Richmond S, Palomo JM, Hans MG. Three-dimensional cone beam computerized tomography in orthodontics. *J Orthod* 2005;32:282–293.
14. Carrafiello G, Dizionario M, Colli V, et al. Comparative study of jaws with multislice computed tomography and cone-beam computed tomography [in English, Italian]. *Radiol Med* 2010;115:600–611.
15. White SC. Cone-beam imaging in dentistry. *Health Phys* 2008;95:628–637.
16. Pauwels R, Beinsberger J, Collaert B, et al. Effective dose range for dental cone beam computed tomography scanners. *Eur J Radiol* 2012;81:267–271.
17. Suomalainen A, Kiljunen T, Käser Y, Peltola J, Kortesniemi M. Dosimetry and image quality of four dental cone beam computed tomography scanners compared with multislice computed tomography scanners. *Dentomaxillofac Radiol* 2009;38:367–378.
18. Mah P, Reeves TE, McDavid WD. Deriving Hounsfield units using grey levels in cone beam computed tomography. *Dentomaxillofac Radiol* 2010;39:323–335.
19. Hassan B, Nijkamp P, Verheij H, et al. Precision of identifying cephalometric landmarks with cone beam computed tomography *in vivo*. *Eur J Orthod* 2011 Mar 29 [epub ahead of print].
20. Naitoh M, Katsumata A, Mitsuya S, Kamemoto H, Ariji E. Measurement of mandibles with microfocus x-ray computerized tomography and compact computerized tomography for dental use. *Int J Oral Maxillofac Implants* 2004;19:239–246.
21. Lagravère MO, Carey J, Toogood RW, Major PW. Three-dimensional accuracy of measurements made with software on cone-beam computed tomography images. *Am J Orthod Dentofacial Orthop* 2008;134:112–116.
22. Lou L, Lagravère MO, Compton S, Major PW, Flores-Mir C. Accuracy of measurements and reliability of landmark identification with computed tomography (CT) techniques in the maxillofacial area: A systematic review. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2007;104:402–411.
23. Song YD, Jun SH, Kwon JJ. Correlation between bone quality evaluated by cone-beam computerized tomography and implant primary stability. *Int J Oral Maxillofac Implants* 2009;24:59–64.
24. Isoda K, Ayukawa Y, Tsukiyama Y, Sogo M, Matsushita Y, Koyano K. Relationship between the bone density estimated by cone-beam computed tomography and the primary stability of dental implants. *Clin Oral Implants Res* 2012;23:832–836.
25. Hua Y, Nackaerts O, Duyck J, Maes F, Jacobs R. Bone quality assessment based on cone beam computed tomography imaging. *Clin Oral Implants Res* 2009;20:767–771.
26. Yoo S, Yin FF. Dosimetric feasibility of cone-beam CT-based treatment planning compared to CT-based treatment planning. *Int J Radiat Oncol Biol Phys* 2006;66:1553–1561.
27. Schulze R, Heil U, Gross D, et al. Artefacts in CBCT: A review. *Dentomaxillofac Radiol* 2011;40:265–273.
28. Araki K, Okano T. The effect of surrounding conditions on pixel value of cone beam computed tomography. *Clin Oral Implants Res* 2011 Nov 17 [epub ahead of print].
29. Nackaerts O, Maes F, Yan H, Couto Souza P, Pauwels R, Jacobs R. Analysis of intensity variability in multislice and cone beam computed tomography. *Clin Oral Implants Res* 2011;22:873–879.
30. Aranyarachkul P, Caruso J, Gantes B, et al. Bone density assessments of dental implant sites: 2. Quantitative cone-beam computerized tomography. *Int J Oral Maxillofac Implants* 2005;20:416–424.
31. Naitoh M, Hirukawa A, Katsumata A, Ariji E. Evaluation of voxel values in mandibular cancellous bone: Relationship between cone-beam computed tomography and multislice helical computed tomography. *Clin Oral Implants Res* 2009;20:503–506.
32. Naitoh M, Hirukawa A, Katsumata A, Ariji E. Prospective study to estimate mandibular cancellous bone density using large-volume cone-beam computed tomography. *Clin Oral Implants Res* 2010;21:1309–1313.
33. Nomura Y, Watanabe H, Honda E, Kurabayashi T. Reliability of voxel values from cone-beam computed tomography for dental use in evaluating bone mineral density. *Clin Oral Implants Res* 2010;21: 558–562.
34. Lagravère MO, Fang Y, Carey J, Toogood RW, Packota GV, Major PW. Density conversion factor determined using a cone-beam computed tomography unit NewTom QR-DVT 9000. *Dentomaxillofac Radiol* 2006;35:407–409.
35. González-García R, Monje F. The reliability of cone-beam computed tomography to assess bone density at dental implant recipient sites: A histomorphometric analysis by micro-CT. *Clin Oral Implants Res* 2012 Jan 17 [epub ahead of print].
36. Rinkel J, Gerfault L, Estève F, Dinten JM. A new method for x-ray scatter correction: First assessment on a cone-beam CT experimental setup. *Phys Med Biol* 2007;52:4633–4652.
37. Maes F, Collignon A, Vandermeulen D, Marchal G, Suetens P. Multi-modality image registration by maximization of mutual information. *IEEE Trans Med Imaging* 1997;16:187–198.
38. Zhang Z. Iterative point matching for registration of free-form curves and surfaces. *Int J Comput Vis* 1994;13:119–152.
39. Lekholm U, Zarb GA. Patient selection and preparation. In: Brånemark P-I, Zarb GA, Albrektsson T (eds). *Tissue-integrated prostheses: Osseointegration in Clinical Dentistry*. Chicago: Quintessence; 1985: 199–209.
40. Katsumata A, Hirukawa A, Okumura S, et al. Relationship between density variability and imaging volume size in cone-beam computerized tomographic scanning of the maxillofacial region: An in vitro study. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2009;107: 420–425.

Effects of Systemic Zoledronic Acid Administration on Osseointegration of Hydroxyapatite-Coated and Resorbable Blast Material Surface Implants in Rabbit Models

Ferhan Yaman, DDS, PhD¹/Serkan Ağaçayak, DDS, PhD¹/Serhat Atılgan, DDS, PhD¹/Emre Benlidayı, DDS, PhD²/Musa Can Ucan, DDS, PhD¹/Behçet Erol, DDS, PhD³/Beyza Kaya, DDS, PhD³/Ahmet Gunay, DDS, PhD⁴/Sedat Guven, DDS, PhD⁵

Purpose: It is unknown whether zoledronic acid (ZA) interferes with initial bone healing at implant sites. The goal of this study was to examine the effects of systemic zoledronic acid administration on osseointegration of hydroxyapatite (HA)-coated and resorbable blast material surface (RBM) implants in rabbit models. **Materials and Methods:** Twenty-eight male New Zealand rabbits (aged 6 to 12 months) were used in this study. Rabbits were randomly assigned to four groups. In group A, HA-coated implants were placed in the right tibia of seven rabbits. In group B, RBM-surface implants were placed in the right tibia of seven rabbits. In group C, HA-coated implants were placed in seven rabbits with intravenous (IV) administration of ZA. Finally, in group D, RBM-surface implants were placed in seven rabbits with IV administration of ZA. For groups C and D, IV zoledronic acid (0.1 mg/kg) was performed monthly during the entire osseointegration period. All of the rabbits were sacrificed 12 weeks after the implantation, and tibial specimens were harvested. Histomorphometric bone-to-implant contact (BIC) analysis and the data were statistically analyzed. **Results:** The highest BIC percentage was detected in group D, with a mean value of $56.73\% \pm 1.85\%$, as compared with $45.80\% \pm 3.77\%$ in group C, $35.11\% \pm 0.76\%$ in group B, and $31.14\% \pm 1.04\%$ in group A. **Conclusions:** Histomorphometric analyses showed significant improvement in the osseointegration of implants in the RBM-surface ZA group compared with the HA-coated ZA group. The results of this study suggest that systemic ZA administration may improve osseointegration of titanium implants in bone. INT J ORAL MAXILLOFAC IMPLANTS 2012;27:1443–1447

Key words: histomorphometry, implant, zoledronic acid

Bisphosphonates are widely used as therapeutic agents in bone disorders, including cancer metastasis, due to their osteoclast inhibitory effect.^{1,2} Recent data shows that bisphosphonates may also induce bone-building by stimulating osteoblast activity.

Clinical observations, however, have revealed that bisphosphonates may cause necrosis in the oral cavity, which questions their usefulness in bone regeneration during the consolidation of implants.^{3,4}

Bisphosphonates are used for the treatment of osteoporosis, due to their inhibitory effects on osteoclast genesis and activity.^{5–7} Their side effects, however, represent an important limitation, especially in elderly patients.⁸ Furthermore, short-term zoledronic acid (ZA) treatment increases bone mineral density and the number of marrow clonogenic fibroblast progenitors after allogeneic stem cell transplantation.⁹ These data have raised questions as to the effects of chronic ZA treatment on osseointegration and bone structure.

To investigate this question, a novel *in vivo* experimental implant surface that allows the effect of systemic treatment has been developed by the present group of authors. This experiment includes hydroxyapatite (HA)-coated and resorbable blast material surface (RBM) implants.

¹Assistant Professor, Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, University of Dicle, Diyarbakir, Turkey.

²Assistant Professor, Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, University of Cukurova, Adana, Turkey.

³Professor, Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, University of Dicle, Diyarbakir, Turkey.

⁴Assistant Professor, Department of Periodontology, Faculty of Dentistry, University of Dicle, Diyarbakir, Turkey.

⁵Assistant Professor, Department of Prosthodontics Faculty of Dentistry, University of Dicle, Diyarbakir, Turkey.

Correspondence to: Asst Prof Dr Ferhan Yaman, Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, University of Dicle, 21280 Diyarbakir, Turkey. Email: dtferhan@hotmail.com

In the interface between alloplastic material and bone, HA surfaces have been known to degrade and in some instances separate, so the trend has changed to coatings with a roughened surface, which incidentally also shows a better and more rapid integration time. In addition, titanium alloy dental implants are more fracture resistant than grade one, two, or three, and in that regard it makes sense to choose them.¹⁰ During the last decade, numerous studies have been conducted to identify an enhanced surface feature to increase mechanical stability and bone-to-implant contact (BIC). Scientific evidence conclusively supports the idea that a roughened titanium implant surface provides significantly improved bone anchoring compared with a traditional machined titanium surface. The present study aimed to report the investigation of bone-to-implant contact with different coated implants following bisphosphonate treatment in a rabbit tibia model.

MATERIALS AND METHODS

Animal Procedures

Twenty-eight adult male New Zealand rabbits aged 6 to 12 months with a mean weight of 3 kg were included in this study. The rabbits were housed in individual cages with a circadian light rhythm of 12 hours. Standard pelleted laboratory chow and water ad libitum were available to the rabbits. All animal procedures were approved by the ethics committee and performed in compliance with the guidelines for the care and handling of experimental animals of the medical research center at Dicle University, Diyarbakir, Turkey.

Experimental Design

Dental implants (6.0 mm in length and 4.0 mm in diameter; BioLok) were used in this study. Implant designs were modified by the manufacturer. Rabbits were randomly assigned to one of four groups. In group A ($n = 7$), HA-coated implants were placed in the right tibia. In group B ($n = 7$), RBM surface implants were placed in the right tibia. In group C ($n = 7$), HA-coated implants were placed with intravenous ZA administration. Finally, in group D ($n = 7$), RBM surface implants were placed with IV zoledronic acid administration. For groups C and D, rabbits were administered ZA intravenously (0.1 mg/kg) once a month for a total of three doses. The dosage was higher than that given to humans (0.06 mg/kg or approximately 4 mg/month for a typical 70-kg healthy adult), but is safe for this animal model. Before implant surgery, the legs were shaved, washed, and decontaminated with an antiseptic iodine solution. Fascio-periosteal flaps were elevated in the medial surface of the proximal metaphysis of the tibia, and implant sites were prepared. Implant surgery was

carried out with rabbits under general anesthesia. General anesthesia was performed with intramuscular injection of 40 mg/kg of ketamine hydrochloride (Alfamine; EgeVet) and 5 mg/kg of xylazine (Alfazine; EgeVet). ZA administration was performed before implant surgery with an infusion pump. The authors administered 0.1 mg/kg of ZA (Zometa; Novartis) as a single intravenous infusion over a 10-minute period before implant surgery to the animals in groups C and D, whereas saline solution infusions (as placebo injections) were given to the animals in groups A and B. After this surgery, intravenous ZA was injected to groups C and D monthly. After implantation, the fascia and skin were closed in separate layers with resorbable sutures. Postoperative daily injections of 1 mg/kg of tramadol hydrochloride (Contramal; Abdi Ibrahim) and 50 mg/kg of cefazolin sodium (Cefamezine; Eczacibasi) were administered for 3 days. All of the subjects were sacrificed 12 weeks after the implantation by intravenous injection of 100 mg/kg of pentobarbital sodium (Pental; Bilim), and tibial specimens were harvested. Tibial specimens including the implants were removed by en bloc resection. The specimens were fixed in 10% buffered formalin, dehydrated in increasing concentrations of ethanol (70% to 99%) over a period of 10 days, and embedded in methylmethacrylate (Technovit 7200 VLC; Heraeus Kulzer). Fifty-micrometer-thick, undecalcified sections were prepared by use of a diamond-coated saw cutting and grinding system (Exakt). Sections were stained with toluidine blue, and digital images were obtained by a digital camera attached to a light microscope (Olympus DP 70; Olympus) at a magnification rate of 40 \times . The percentage of BIC at the lateral sides of the implants was calculated with image analysis software (ImageJ; National Institutes of Health). As defined, osseointegration is "the formation of a direct interface between an implant and bone, without intervening soft tissue."^{10,p228} An osseointegrated implant is defined as "an endosteal implant containing pores into which osteoblasts and supporting connective tissue can migrate."^{10,p229} No scar tissue, cartilage, or ligament fibers are present between the bone and implant surface. Traditionally, an implant is placed and then allowed to integrate for a period of 3 to 6 months.

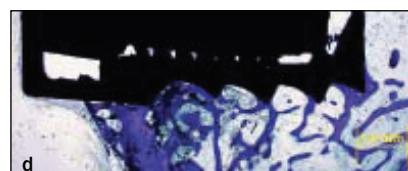
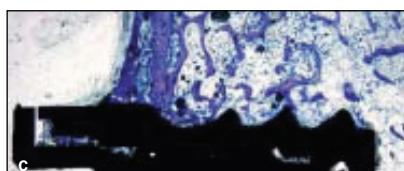
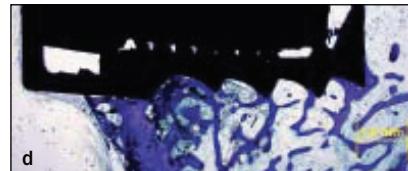
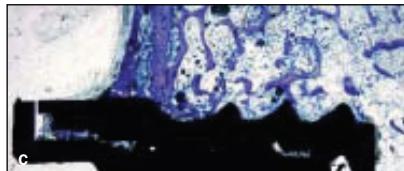
Because the surface at the bottom of the implants was a machined surface (implants were cut to a height of 6 mm during the manufacturing process), the apical surfaces were not included in the BIC calculations.

Statistical Analysis

Statistical analysis was performed with SPSS software, version 15 (IBM). The use of different drugs (ZA versus placebo) resulted in significant differences in the mean values of BIC between groups by two-way analysis of

Table 1 Descriptive Statistics

	Total	Minimum	Maximum	Mean	Standard deviation
Group A	7	29.46	32.56	31.14	1.04
Group B	7	33.97	36.41	35.11	0.76
Group C	7	38.34	49.21	45.80	3.77
Group D	7	54.28	59.21	56.73	1.85

Fig 1a Histologic views of HA-placebo (group A).**Fig 1b** Histologic views of RBM-placebo (group B).**Fig 1c** Histologic views of HA-ZA (group C).**Fig 1d** Histologic views of RBM-ZA (group D).**Table 2 Comparison Percentage of BIC**

	Group A (n = 7)	Group B (n = 7)	Group C (n = 7)	Group D (n = 7)	Total (n = 28)	P*
BIC (%) Mean \pm SD	31.14 \pm 1.04	35.11 \pm 0.76	45.80 \pm 3.77	56.73 \pm 1.85	42.19 \pm 10.35	.013 [†] .000 [‡] .000 [§] .000 [¶]

*Post hoc Tukey test.

[†]Comparison of A–B, [‡]Comparison A–C, [§]Comparison of B–C, [¶]Comparison of C–D ($P < .05$).

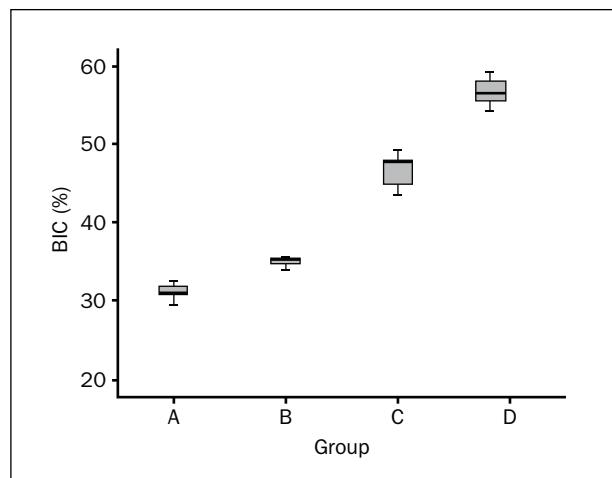
variance ($P < .001$). Post hoc Tukey HSD test was used to determine intragroup differences and two-way analysis of variance for intergroups.

RESULTS

Histomorphometric results of osseointegration in the groups are presented in Table 1. The highest BIC percentage was detected in group D, with a mean value of $56.73\% \pm 1.85\%$, compared with $45.80\% \pm 3.77\%$ in group C, $35.11\% \pm 0.76\%$ in group B, and $31.14\% \pm 1.04\%$ in group A (Fig 1). BIC in the experimental groups appeared better than in the placebo groups, and osseointegration in group D appeared better compared with the other groups (Fig 2).

Significant surface changes were observed in RBM values between groups by using HA-coated or RBM-coated implants ($P < .05$).

The post hoc Tukey HSD test BIC values of group C ($45.80 \pm 3.77\%$) had a significantly higher mean compared with group A ($31.14 \pm 1.04\%$) and group B ($35.11 \pm 0.76\%$) ($P < .001$) for each comparison (Table 2).

**Fig 2** Distribution of BIC percentage.

The mean BIC value of group D ($56.73 \pm 1.85\%$) was the highest compared with all other groups ($P < .001$) for each comparison.

DISCUSSION

Recent advances in dentistry have led to a rise in the use of dental implants, which have become less expensive and more widely available than ever before. The vast majority of dental implants used in the 21st century are placed within bone, and are known as root-form endosseous implants. The most fundamental principle for a successful implant procedure is osseointegration. Current researchers have focused on producing better osseointegration, therefore, many surface modifications of titanium implants have been developed to achieve this goal (machined, plasma-sprayed, grit blasted, and/or acid etched).

HA-coated implants exhibit osteoconductive properties as superior bone ingrowth has been found for HA-coated implants inserted with an initial gap into surrounding cancellous bone. Many studies (*in vivo* and *in vitro*) have shown that HA is osteoconductive and enhances the bone healing at the gaps between the bone and implant surface. Because HA is biocompatible and can bond with bone, it has been used to coat the surfaces of dental implants. HA-coated dental implants have been shown to accelerate surface bone apposition, thereby shortening the waiting period for dental implant restoration.^{11,12}

Another possibility for roughening titanium dental implants consists in using a biocompatible, osteoconductive, and resorbable blasting material. Calcium phosphates such as hydroxylapatite, beta-tricalcium phosphate, and mixtures have been considered as useful blasting materials. These materials are resorbable, leading to a clean, textured, pure titanium surface. Experimental studies have demonstrated a higher BIC with these surfaces when compared to machined surfaces. Experimental studies have demonstrated a BIC similar to that observed with other blasting surfaces when osseointegration is achieved.

In the present study, the RBM-surface implant groups (groups B and D) had a higher BIC percentage than HA-coated implant groups (groups A and C). Group D (intravenous ZA and RBM surface implants) had the highest BIC percentage of all groups.

Moreover, systemic drug therapy is used to achieve better osseointegration for implant procedures. Bisphosphonates are non-metabolized analogs of pyrophosphates that are often used to treat osteoporosis, Paget disease, metastatic osteolytic lesions associated with breast cancer, multiple myeloma, osteogenesis imperfect, and hypercalcemia associated with malignancies^{1–4} and, recently, intravenous bisphosphonates have also been advocated for the management of osteoporosis.^{5–7}

The improving effects of bisphosphonates on osteoblast proliferation, maturation, and differentiation have been shown. Im et al¹⁴ showed a significantly

increased osteoblastic cell number and enhanced gene expression of bone morphogenetic protein 2, type I collagen, and osteocalcin with alendronate and risedronate in cell cultures. Viereck et al¹⁵ studied the effects of pamidronate and zoledronate on osteoprotegerin messenger ribonucleic acid levels and protein production in primary human osteoblasts and suggested that enhancement of osteoprotegerin by bisphosphonates could be related to their stimulatory effects on osteoblastic differentiation. Fromigué and Body¹⁶ showed that ibandronate and zoledronate stimulated the proliferation of human osteoblast by up to 30%. Bobyn et al¹⁷ investigated the effect of ZA on bone ingrowth in an animal model in which porous tantalum implants were placed bilaterally within the ulnae of seven dogs. ZA in saline was administered via a single postoperative intravenous injection at a dose of 0.1 mg/kg. Individual islands of new bone formation within the implant pores were similar in number in placebo and treated groups, but were 69% larger in the ZA-treated group.

However, there have been concerns regarding the possible adverse effects of long-term therapy. Histomorphometric analysis of bone taken from patients receiving long-term bisphosphonates shows changes consistent with severely suppressed bone turnover, suggesting an adynamic bone disorder.¹⁸ These changes include reduction in osteoid thickness and volume, reduced osteoblastic/osteoclastic surface, and diminished bone matrix. Consequently, this may give rise to failure of microfracture repair and secondary mineralization with increased brittleness and deterioration of the bone biomechanical properties.¹⁹

Bisphosphonate-related osteonecrosis of the jaws (BRONJ) is a severe complication seen most frequently in patients on intravenous bisphosphonates treatment for malignant diseases. Osteonecrosis of the jaws (ONJ) or BRONJ was first reported by Marx in 2003.²⁰ This severe complication occurs most frequently in patients on intravenous bisphosphonates treatment for malignant diseases such as multiple myeloma or metastatic malignant disease, mainly breast cancer. Bisphosphonates prevent, reduce, and delay cancer-related skeletal complications.^{21,22}

Recently, it has been shown that treatment of patients with aminobisphosphonate following allogeneic bone marrow transplantation increased the frequency of colony forming mesenchymal preosteoblasts in bone marrow.²³ These results support the direct effect of bisphosphonates on bone-building osteoblasts and, thus, further reveal their potential dual effects.

In the authors' experiments, BIC increased three-fold following ZA treatment compared with placebo groups. Taking the native, BIC percentage as 100%,

the bone-to-implant contact of nontreated implant percentages were 31.14% for HA placebo group and 35.11% for RBM placebo group, while the bone-to-implant contacts reached 45.80% for the HA-ZA group and 56.73% for the RBM-ZA group.

CONCLUSION

The increased potency of ZA compared with other bisphosphonates makes it a logical choice to enhance net bone ingrowth. In the present study, the quantitative data on the bone islands that formed within the implant pores revealed that new bone formation and RBM-coated implant contact was better than HA-coated implants with administration of intravenous ZA once a month for a total of three doses. Also, the authors believe that RBM-coated implants and administration of ZA provides better osseointegration than other procedures.

ACKNOWLEDGMENT

The authors acknowledge institutional support and declare no potential conflicts of interests with respect to the authorship and/or publication of this article.

REFERENCES

- Michaelson MD, Smith MR. Bisphosphonates for treatment and prevention of bone metastases. *J Clin Oncol* 2005;23:8219–8223.
- Boissier S, Ferreras M, Peyruchaud O. Bisphosphonates inhibit breast and prostate carcinoma cell invasion, an early event in the formation of bone metastases. *Cancer Res* 2000;60:2949–2954.
- Merigo E, Manfredi M, Meleti M, Corradi D, Vescovi P. Jaw bone necrosis without previous dental extractions associated with the use of bisphosphonates (pamidronate and zoledronate). *J Oral Pathol* 2005;34:613–614.
- Farrugia MC, Summerlin DJ, Krowiak E, et al. Osteonecrosis of the mandible or maxilla associated with the use of new generation bisphosphonates. *Laryngoscope* 2006;116:115–120.
- Rodan GA, Martin TJ. Therapeutic approaches to bone diseases. *Science* 2000;289:1508–1514.
- van beek E, Lowik C, van der Pluijm G, Papapoulos S. The role of geranylgeranylation in bone resorption and its suppression by bisphosphonates in fetal bone explants in vitro: A clue to the mechanism of action of nitrogen-containing bisphosphonates. *J Bone Miner Res* 1999;14:722–729.
- Lee YP, Schwarz EM, Davies M, et al. Use of zoledronate to treat osteoblastic versus osteolytic lesions in a severe-combined-immuno-deficient mouse model. *Cancer Res* 2002;62: 5564–5570.
- Khosla S, Burr D, Cauley J, et al. Bisphosphonate-associated osteonecrosis of the jaw: Report of a task force of the American Society for Bone and Mineral Research. *J Bone Miner Res* 2007;22:1479–1491.
- Tauchmanová L, Ricci P, Serio B, et al. Short-term zoledronic acid treatment increases bone mineral density and marrow clonogenic fibroblast progenitors after allogeneic stem cell transplantation. *J Clin Endocrinol Metab* 2005;90:627–634.
- Bränemark PI, Zarb GA, Albrektsson T. Tissue-integrated prostheses. In: Bränemark PI, Zarb GA, Albrektsson T (eds). *Osseointegration in Clinical Dentistry*. Chicago: Quintessence, 1985:211–232.
- Kold S, Rahbek O, Vestermark M, Overgaard S, Soballe K. Bone compaction enhances fixation of weight-bearing hydroxyapatite-coated implants. *J Arthroplasty* 2006;21:263–270.
- Lee JJ, Rouhfar L, Beirne OR. Survival of hydroxyapatite-coated implants: A meta-analytic review. *J Oral Maxillofac Surg* 2000;58: 1372–1379.
- Guehennec LL, Soueidan A, Layrolle P, Amouriq Y. Surface treatments of titanium dental implants for rapid osseointegration. *Dent Mater* 2007;23:844–854.
- Im GI, Qureshi SA, Kenney J, et al. Osteoblast proliferation and maturation by bisphosphonates. *Biomaterials* 2004;25:4105–4115.
- Viereck V, Emons G, Lauck V, et al. Bisphosphonates pamidronate and zoledronic acid stimulate osteoprotegerin production by primary human osteoblasts. *Biochem Biophys Res Commun* 2002;291: 680–686.
- Fromigué O, Body JJ. Bisphosphonates influence the proliferation and the maturation of normal human osteoblasts. *J Endocrinol Invest* 2002;25:539–546.
- Bobyn JD, McKenzie K, Karabasz D, Krygier JJ, Tanzer M. Locally delivered bisphosphonate for enhancement of bone formation and implant fixation. *J Bone Joint Surg Am* 2009;91:23–31.
- Sayed-Noor AS, Sjoden G. Two femoral insufficiency fractures after long-term alendronate therapy. *Clin Orthop Relat Res* 2009;467: 1921–1926.
- Odvina CV, Zerwekh JE, Rao DS, Maalouf N, Gottschalk FA, Pak CY. Severely suppressed bone turnover: A potential complication of alendronate therapy. *J Clin Endocrinol Metab* 2005;90:1294–1301.
- Marx RE. Pamidronate (Aredia) and zoledronate (Zometa) induced avascular necrosis of the jaws: A growing epidemic. *J Oral Maxillofac Surg* 2003; 61:1115.
- Vescovi P, Campisi G, Fusco V, et al. Surgery-triggered and non surgery-triggered bisphosphonate-related osteonecrosis of the jaws (BRONJ): A retrospective analysis of 567 cases in an Italian multicenter study. *Oral Oncol* 2011;47:191–194.
- Bagan J, Scully C, Sabater V, Jimenez Y. Osteonecrosis of the jaws in patients treated with intravenous bisphosphonates (BRONJ): A concise update. *Oral Oncol* 2009;45:551–554.
- Shubayev VI, Bränemark R, Steinauer J, Myers RR. Titanium implants induce expression of matrix metalloproteinases in bone during osseointegration. *J Rehabil Res Dev* 2004;41:757–766.

Fracture Resistance of Crowns Cemented on Titanium and Zirconia Implant Abutments: A Comparison of Monolithic Versus Manually Veneered All-Ceramic Systems

Francisco Martínez-Rus, DDS, PhD¹/Alberto Ferreiroa, DDS²/
Mutlu Özcan, DDS, Dr Med Dent, PhD³/José F. Bartolomé, PhD⁴/Guillermo Pradés, DDS, PhD⁵

Purpose: To evaluate the fracture resistance of all-ceramic crowns cemented on titanium and zirconia implant abutments. **Material and Methods:** Customized implant abutments for maxillary right central incisors made of titanium (Ti) and zirconia (Zr) ($n = 60$, $n = 30$ per group) were fabricated for an internal connection implant system. All-ceramic crowns were fabricated for their corresponding implant abutments using the following systems ($n = 10$ per group): (1) monolithic computer-aided design/computer-assisted manufacture (CAD/CAM) lithium disilicate (MLD); (2) pressed lithium disilicate (PLD); (3) yttrium stabilized tetragonal zirconia polycrystal (YTZP). The frameworks of both PLD and YTZP systems were manually veneered with a fluorapatite-based ceramic. The crowns were adhesively cemented to their implant abutments and loaded to fracture in a universal testing machine (0.5 mm/minute). Data were analyzed using two-way analysis of variance (ANOVA) and Tukey's test ($\alpha = 0.05$). **Results:** Both the abutment material ($P = .0001$) and the ceramic crown system ($P = .028$) significantly affected the results. Interaction terms were not significant ($P = .598$). Ti-MLD (558.5 ± 35 N) showed the highest mean fracture resistance among all abutment-crown combinations ($340.3 \pm 62 - 495.9 \pm 53$ N) ($P < .05$). Both MLD and veneered ceramic systems in combination with Ti abutments ($558.5 \pm 35 - 495.9 \pm 53$ N) presented significantly higher values than with Zr abutments ($392.9 \pm 55 - 340.3 \pm 62$ N) ($P < .05$). MLD crown system showed significantly higher mean fracture resistance compared to manually veneered ones on both Ti and Zr abutments ($P < .05$). While Ti-MLD and Ti-PLD abutment-crown combinations failed only in the crowns without abutment fractures, Zr-YTZP combination failed exclusively in the abutment without crown fracture. Zr-MLD and Zr-PLD failed predominantly in both the abutment and the crown. Ti-YTZP showed only implant neck distortion. **Conclusions:** The highest fracture resistance was obtained with titanium abutments restored with MLD crowns, but the failure type was more favorable with Ti-YTZP combination. INT J ORAL MAXILLOFAC IMPLANTS 2012;27:1448–1455

Key words: CAD/CAM, lithium disilicate, monolithic crowns, pressed ceramics, titanium, YTZP

¹Associate Professor, Department of Buccofacial Prosthesis, Faculty of Odontology, University Complutense of Madrid, Madrid, Spain.

²Research Student, Department of Buccofacial Prosthesis, Faculty of Odontology, University Complutense of Madrid, Madrid, Spain.

³Professor, Head of Dental Materials Unit, University of Zürich, Center for Dental and Oral Medicine, Clinic for Fixed and Removable Prosthodontics and Dental Materials Science, Zurich, Switzerland.

⁴Researcher, Department of Biomaterials and Bioinspired Materials, Materials Science Institute of Madrid, Spanish Research Council, Madrid, Spain.

⁵Professor, Associate Dean, Department of Buccofacial Prosthesis, Faculty of Odontology, University Complutense of Madrid, Madrid, Spain.

Correspondence to: Prof Mutlu Özcan, Center for Dental and Oral Medicine, Clinic for Fixed and Removable Prosthodontics and Dental Materials Science, University of Zürich, Plattenstrasse 11, CH-8032, Zürich, Switzerland. Fax: +41-44-6344305. Email: mutluozcan@hotmail.com

Restoration of missing teeth in dentistry can be achieved with a variety of treatment options. In particular, restoration of the esthetic zone remains a challenge for clinicians. Although the least minimally invasive option is the application of resin-bonded fixed dental prostheses (FDP), their long-term survival rate is not predictable.^{1,2} On the other hand, the conventional full-coverage FDP requires the preparation of abutments that result in more tissue loss.

Clinical efficacy of osseointegrated implants for single-tooth replacement has been well documented.^{3–5} Several studies have demonstrated a high incidence of prosthetic complications associated with FDPs supported by implants such as screw or abutment loosening, screw or abutment fracture, or fractures in the framework or veneer parts of the FDPs.^{6–10}

Implant abutments are usually fabricated from commercially pure titanium due to its well-documented biocompatibility and mechanical properties.¹¹ Clinical

studies demonstrated excellent survival rates for fixed implant reconstructions supported by titanium abutments.^{10,12} Despite the numerous improvements in the fabrication and design of titanium abutments, their metallic color may still shine through the mucosa, impairing the esthetic outcome. Even when placed subgingivally, a dull gray background may give the soft tissue an unnatural bluish appearance. The presence of a gray gingival discoloration may also be partially attributed to a thin gingival tissue thickness around the abutment that is incapable of blocking reflective light from the metal abutment surface.^{13,14} Hence, although they are very stable from a biomechanical point of view, titanium abutments have limitations in esthetically delicate areas.

Especially in the anterior zone, the success of single-implant therapy is dictated by a number of factors that involve the appearance of the peri-implant soft tissues.¹⁵ The harmony of the crown-implant complex in terms of color and form with the mucosa and neighboring teeth is essential. In that respect, tooth-colored ceramic abutments such as yttrium tetragonal zirconia polycrystals (hereon, zirconia) have been proposed as an alternative material to titanium abutments. Zirconia has superior mechanical properties, presenting fracture resistance as high as 900 to 1,200 MPa.¹⁶ Zirconia abutments not only induce significantly less mucosal discoloration than metal abutments,¹³ but also yield to less bacterial adhesion than titanium.¹⁷ Moreover, the soft tissue integration of zirconia was found to be similar to that of titanium.^{11,12} However, not only implant abutments but also implant restoration materials should be considered during prosthetic treatment planning. Metal-ceramic FDPs are commonly indicated for implant-supported reconstructions. Since dental implants do not have periodontal ligament (PDL) interposed between the bone and implant surface that eliminates the special proprioceptive nerve endings, the sensitivity and mobility of natural dentition cannot be duplicated in endosseous implants.¹⁸ Therefore, in the absence of a neurosensory mechanism that adequately compensates for the PDL proprioception and compressibility, the stability of the prosthesis-implant complex is impaired resulting in FPD complications.

Recent developments in high strength ceramic materials and manufacturing techniques try to fulfill the expectations from both optical and biomechanical perspectives on implant reconstructions.¹⁹ Among the many options, in the late 1990s, lithium disilicate glass-ceramics ($\text{SiO}_2 - \text{Li}_2\text{O}$) was introduced to dentistry as a framework material. Its flexural strength ranges between 300 and 400 MPa and its fracture toughness between 2.8 and 3.5 MPa/m^{1/2}.²⁰ Lithium disilicate glass ceramics could be typically fabricated through a combination of the lost-wax and heat-pressed techniques

or milled with computer-aided design/computer-assisted manufacture (CAD/CAM) systems and used for the same indications. Using this material in conjunction with the pressed technique allows the dental technician to achieve better morphology and eliminate the purchase of CAD/CAM devices. Because of its high strength, this material offers versatile applications and can be used for the fabrication of monolithic crowns (chairside or labside) with subsequent staining and characterization. With lithium disilicate glass ceramics, limited information is available on artificial dies²¹ but no information is present on implants. In fact, one clinical study reported a 93% survival rate of three-unit FDPs using pressed lithium disilicate glass-ceramics up to 8 years²² but the survival of such ceramics on implant abutments is not known. Also, one of the most significant advances in this field has been the introduction of zirconia as a framework material that can be processed using CAD/CAM techniques. Compared to other all-ceramic systems, zirconia exhibits superior mechanical properties, owing to the transformation toughening mechanism.²³

Since the fracture resistance of lithium disilicate glass-ceramics is in general less than zirconia, higher fracture resistance could be anticipated with the latter on implant abutments. On the other hand, due to a delamination problem related to bilayered ceramic structures, monolithic ones are considered proper alternatives. Due to the ductility of metals, bending resistance could compensate for the fracture of the ceramic restoration. Thus, less fracture resistance could be expected from zirconia abutment-ceramic compared with titanium abutment-ceramic crown combinations.

The objectives of the present study were therefore to evaluate (1) the fracture resistance of titanium and zirconia implant abutments restored with monolithic CAD/CAM lithium disilicate, manually veneered pressable lithium disilicate, and manually veneered zirconia all-ceramic crowns, and (2) to identify the failure types. The tested hypotheses were that fracture resistance of crowns on titanium abutments would be higher than for the zirconia abutments, and that zirconia crowns would be more fracture resistant than lithium disilicate crowns.

MATERIALS AND METHODS

Sample Preparation

Sixty internal connection implants with a diameter of 4.1 mm and length of 12 mm (Straumann Standard Plus Implant) were obtained for this study. A clinical case was selected for the design of the master abutment with a height of 7 mm and taper of 6 degrees. This abutment was digitally designed for the patient's situation

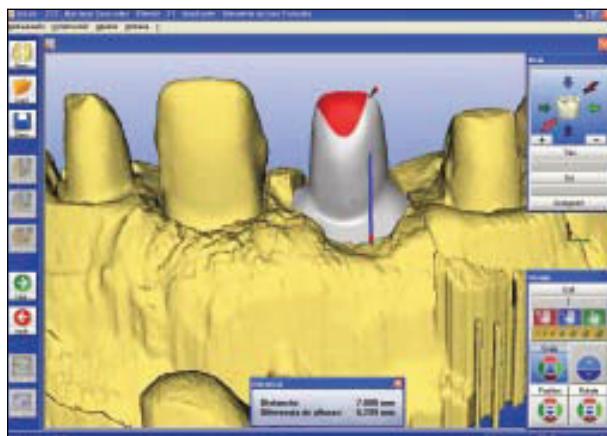


Fig 1 The digital design of the master abutment for the maxillary right central incisor using three-dimensional abutment fabrication software.

using three-dimensional abutment fabrication software (inLab 3D for Abutments, version 3.80, Sirona Dental Systems) (Fig 1).

The data generated were sent to the Straumann production center in Markkleeberg, Germany, for the construction of two groups of identical customized abutments ($n = 60$, 30 per abutment type), namely zirconia abutments (Straumann CARES Abutment Ceramic, Straumann) and titanium abutments (Straumann CARES Abutment Titanium, Straumann) (Fig 2).

The abutments were randomly divided into three subgroups ($n = 10$ per group) for the fabrication of all-ceramic crowns using the following systems: (1) monolithic CAD/CAM lithium disilicate (MLD; IPS e.max CAD, Ivoclar Vivadent); (2) heat-pressed lithium disilicate (PLD; IPS e.max Press); and (3) yttrium stabilized tetragonal zirconia polycrystal (YTZP; IPS e.max ZirCAD). Standardized maxillary central incisor crowns (height, 11 mm; mesiodistal width, 8.5 mm; wall thickness, 2 mm) were fabricated with the help of a silicone index. All ceramic crowns were fabricated according to their manufacturer's recommendations by one experienced dental technician.

Fully anatomically shaped MLD and YTZP frameworks were designed and milled with a CAD/CAM system (CEREC InLab, Sirona Dental Systems) from presintered blocks. After the milling procedure, MLD crowns and YTZP frameworks were sintered according to the manufacturer's guidelines. PLD frameworks (thickness, 0.6 mm) were fabricated using the heat-pressing technique. YTZP and PLD frameworks were then veneered manually using a fluorapatite veneering ceramic (IPS e.max Ceram, Ivoclar Vivadent).

Thereafter, all implants were embedded in special specimen holders using epoxy resin (Epoxicure Resin,

Buehler) with 3 mm of vertical distance from the most coronal bone-to-implant border to the top of the holder, simulating vertical bone resorption of 3 mm according to ISO Norm 14801.²⁴ The implants were placed in the center of the specimen holders and at an angle of 90 degrees to the horizontal plane. The embedding resin had a modulus of elasticity of approximately 12 GPa, which approximates that of human bone (18 GPa).²⁵ While the zirconia abutments were connected to the implants using secondary titanium abutments (SynOcta 1.5 mm, Straumann), the titanium abutments were directly connected to the implants. All abutments were torqued to 35 Ncm according to the manufacturer's recommendation using a torque control system (no. 046.049 Straumann). The screw cavities were filled with polytetrafluoroethylene (PTFE) tape and provisional restorative material (Fermit N, Ivoclar Vivadent).

To ensure maximum adhesion between the all-ceramic crowns and the abutments, the abutment surfaces of all groups and the inner surfaces of the zirconia crowns were air-abraded with Al_2O_3 particles (100 μm , 1 bar). The inner surfaces of lithium disilicate crowns were etched with 4.5% hydrofluoric acid (IPS Ceramic Etching Gel, Ivoclar Vivadent) for 20 seconds and rinsed thoroughly. Bonding areas of abutments and crowns were silanized (Monobond Plus, Ivoclar Vivadent) and the crowns were cemented using adhesive resin cement (Multilink Implant, Ivoclar Vivadent) according to the manufacturer's instructions. Finally, the restorations were stored at 37°C for 48 hours until testing.

Fracture Resistance Measurement and Failure Type Analysis

All specimens were mounted in a steel holder at an angle of 30 degrees in relation to the loading cell in the universal testing machine (Shimadzu AG-X Series, Shimadzu) (Fig 3). A piece of tin foil with a thickness of 0.5 mm was applied on the crowns. With this procedure, an even distribution of the load was achieved until fracture or deformation occurred. The load was applied at a crosshead speed of 0.5 mm/minute at the incisal edge according to ISO Norm 14801.²⁴ The fracture load was registered as soon as fracture load decreased by 10% of the maximum load (F_{max}). The fracture load was noted in Newton (N) calculated by the specific software (Trapezium X Software, Shimadzu).

After fracture resistance tests, the failure types were observed by two operators and categorized as follows: Score 1, complete crown fracture without abutment fracture; Score 2, only abutment fracture without any destruction in the crown; Score 3, screw fracture; Score 4, crown and abutment fracture; and Score 5, implant neck distortion.



Fig 2 Customized titanium and zirconia abutments for the maxillary right central incisor with identical dimension.



Fig 3 Representative photo of an implant with its abutment and the cemented crown mounted in the holder at the universal testing machine at an angle of 30 degrees in relation to the loading cell. To ensure an even distribution of the static forces, a tin foil (thickness, 0.5 mm) was placed on the crowns.

Table 1 Results of Two-way ANOVA ($\alpha = 0.05$)

Effect	df	Sum of squares	Mean square	F	P
Abutments	1	194011.1	194011.1	65.1	.0001*
All-ceramic crowns	2	23767.4	11883.7	3.9	.028*
Interaction	2	3110.9	1555.4	0.5	.598
Residue	54	101225.5	2977.2		
Total	59	350125.6			

Statistical Analysis

Statistical analysis was performed using SPSS 14.0 software for Windows (IBM). The data were submitted to two-way analysis of variance (ANOVA) with the fracture resistance as the dependent variable and the abutment type (two levels) and all-ceramic crown material (three levels) as independent variables. Multiple comparisons were made using Tukey's post hoc test. *P* values $< .05$ were considered to be statistically significant in all tests.

RESULTS

Both the abutment material ($P = .0001$) and the all-ceramic crown system ($P = .028$) significantly affected the results. Interaction terms were not significant ($P = .598$) (Table 1).

Ti-MLD (558.5 ± 35 N) showed the highest mean fracture resistance among all abutment–crown combinations (340.3 ± 62 – 495.9 ± 53 N) ($P < .05$) (Table 2, Fig 4). Both monolithic and veneered ceramic systems in com-

Table 2 Mean (Standard Deviation) Fracture Resistance Values (N) Recorded for the Experimental Groups

Abutment type	All-ceramic crown type		
	Monolithic CAD/CAM lithium disilicate (MLD)	Manually veneered pressable lithium disilicate (PLD)	Manually veneered zirconia (YTZP)
Titanium (Ti)	558.5 (35.2) ^a	482.2 (58.4) ^b	495.9 (53.4) ^c
Zirconia (Zr)	392.9 (55.3) ^d	363.0 (50.5) ^e	340.3 (61.8) ^e

*Same superscripts do not show significant differences in the column and row ($P < .05$).

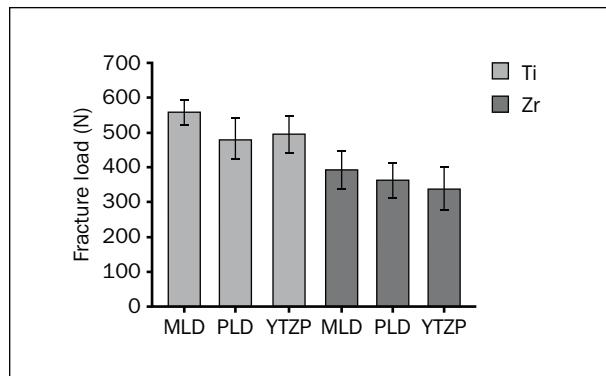


Fig 4 Mean fracture resistance (N) and standard deviations of all experimental groups.

bination with Ti abutments ($558.5 \pm 35 - 495.9 \pm 53$ N) presented significantly higher values than with Zr abutments ($392.9 \pm 55 - 340.3 \pm 62$ N) ($P < .05$). MLD crown system showed significantly higher mean fracture resistance compared to manually veneered ones on both Ti and Zr abutments ($P < .05$).

While Ti-MLD and Ti-PLD abutment–crown combinations failed only in the crowns without abutment fractures, Zr-YTZP combination failed exclusively in the abutment without crown fracture (Table 3). Zr-MLD and Zr-PLD failed predominantly in both the abutment and the crown. Ti-YTZP showed neither crown nor abutment fracture where only implant neck distortion was observed. In none of the samples was screw fracture observed.

DISCUSSION

This study evaluated the fracture resistance of titanium and zirconia implant abutments restored with monolithic CAD/CAM lithium disilicate, manually veneered pressable lithium disilicate, and manually veneered zirconia all-ceramic crowns. The results showed significantly higher fracture resistance values for all types of all-ceramic crown systems when they were cemented on the titanium abutments. Thus, the first hypothesis could be accepted. Since the mean fracture resistance of the monolithic lithium disilicate all-ceramic crowns

presented significantly higher results compared to the veneered lithium disilicate and zirconia ceramic systems, the second tested hypothesis was rejected.

The critical load of implanted-supported ceramic and metal abutments restored with all-ceramic crowns has been evaluated in previous studies, with the results ranging between 170 N and 1454 N.^{26–35} Yıldırım et al²⁷ investigated the fracture resistance of leucite reinforced heat-pressed glass ceramic (IPS Empress 1, Ivoclar Vivadent) crowns adhesively cemented on alumina and zirconia abutments on the external connection implants. Similar to the present study, in that study no artificial aging was practiced. The results showed significant differences between the mean fracture load of crowns cemented on alumina abutments (280 N) and those cemented on zirconia abutments (737 N). Although stronger ceramic systems were used compared to leucite reinforced ceramic, the mean fracture resistance of all-ceramic systems on zirconia abutments (340 to 393 N) in the present investigation was lower than those reported by Yıldırım et al.²⁷ This might be due to differences in the testing protocols. In this study, the implants were embedded in the epoxy resin molds simulating vertical bone loss of 3 mm, according to ISO Norm 14801,²⁴ whereas in the former investigation,²⁷ the implants were embedded in autopolymerizing composite up to the implant shoulder. Consequently, the loads applied in these two studies might have caused different lever arms. Furthermore, different to that study where external connection implants were used, in the present study internal connection implants with a neck height of 1.8 mm were used, possibly further increasing the bending moment.

The embedding parameters simulating vertical bone loss of 3 mm described in ISO Norm 14801²⁴ represents the worse-case scenario. In fact, marginal bone level can move apically following implantation to a relatively steady-state level in clinical practice, marginal bone loss > 3 mm are fortunately rare.³⁶ Therefore, this simulated bone loss can be considered excessive as it exposes the implant threads, making it more susceptible to early failure. It is possible that the results would have been different in this study if the implants had been placed at the nominal bone level, which requires further investigation.

Table 3 Distribution of Failure Types after Fracture Resistance Test

Failure types	Experimental groups					
	Ti-MLD	Ti-PLD	Ti-YTZP	Zr-MLD	Zr-PLD	Zr-YTZP
Score 1		10	10	0	0	0
Score 2		0	0	0	0	10
Score 3		0	0	0	0	0
Score 4		0	0	0	10	9
Score 5		0	0	10	0	0

Score 1 = complete crown fracture without abutment fracture; Score 2 = only abutment fracture without any destruction in the crown; Score 3 = screw fracture; Score 4 = crown and abutment fracture; Score 5 = implant neck distortion.

In another study³⁴ with similar testing conditions and the abutments (CARES), milled leucite reinforced glass-ceramic crowns adhesively cemented on zirconia abutments presented a mean fracture resistance value (283 N) lower than that reported by Yildirim et al.²⁷ Since stronger ceramics were used in the present study, the results were higher than that investigation.³⁴

Sundh and Sjögren³² evaluated the bending resistance of implant-supported titanium and zirconia abutments restored with all-ceramic copings. They reported that the bending resistance of the magnesia and yttrium stabilized zirconia ceramic specimens was equal or superior to that of the titanium control (> 300 N). These results are not in accordance with the present findings. The difference may be due to the mode of load application. In the present investigation, the fracture load was applied at 30 degrees to the long axis of the implants, whereas in the former study, the load was applied perpendicular to the long axis of the

specimens by means of a chisel-shaped steel blade, which probably aggravated the stress on the coping-implant assembly. Since the tests were performed on copings only, the lack of anatomical restoration might have also contributed to the differences between the two studies. According to Cho et al,²⁶ under vertical loading, the fracture resistance of restorations on titanium abutments was almost twice that of those on ceramic abutments. However, under oblique loading (45 degrees) no statistically significant differences in fracture resistance were seen between the restorations on titanium and ceramic abutments.²⁶

In the present investigation, no artificial aging or dynamic loading was applied to the test specimens that could be considered as the limitation of the study. Dynamic loading might lead to crack propagation in the ceramics and if it were involved, it could have affected the outcome of the study or ranking of the materials tested. Therefore, the results in its current form

could represent possible early clinical failures that may result not as a consequence of fatigue. Cyclic loading or thermo-mechanical fatigue conditions could reduce the fracture resistance of zirconia implant abutments significantly. Gehrke et al³⁰ reported decreased strength of zirconia abutments from 672 N without cyclic loading, to less than 405 N after 5,000,000 cyclic loading. In two other studies, the static fracture resistance of different implant-supported all-ceramic restorations was tested after chewing simulation.^{28,29} Ninety-six implants with an internal connection design received titanium, alumina, and zirconia abutments. All abutments were restored with alumina and zirconia all-ceramic crowns. The specimens were exposed to 1,200,000 cycles in a chewing simulator to simulate 5 years of clinical service. The median fracture loads after aging were 1251 N and 457 N for titanium abutment-zirconia crown and zirconia abutment-zirconia crown combinations, respectively. Although specimens in the present study were not aged, the results were surprisingly lower than those obtained by Att et al.^{28,29} Theoretically, the aging effect through environmental stresses could alter the metastable tetragonal crystalline phase of the YTZP-based ceramics. The consequences of this process are multiple and include surface degradation with grain pullout and microcracking and degradation in strength. Long-term exposure of zirconia ceramics to humidity and thermal cycling leads to a low-temperature degradation (LTD) of the material.²³ However, there is controversy over whether this would lead to a reduction in the fracture resistance of zirconia. Although it may be speculated that no water could seep into the implant body during chewing simulation,³⁵ the presence of water is necessary to initiate the LTD. Therefore, even though no aging was practiced in this study, the lower results may be explained on the grounds that in the above mentioned studies, the implants were placed at the nominal bone level. In the present study, the vertical bone loss of 3 mm together with the 1.8 mm implant neck resulted in the bone level almost 4.8 mm below the upper implant shoulder. All this makes a direct comparison difficult between studies on fracture resistance of implant supported reconstructions. Future studies should suggest some more standardization.

The fracture resistance results should also be coupled with the failure type analysis. The failure types were fairly uniform in each group. When monolithic or manually veneered lithium disilicate crowns were used on titanium abutments, only the crowns fractured. In bilayered ceramic structures, veneering ceramic is expected to fracture more frequent than the monolithic ones.³⁷ However, the exclusive crown fracture failure type in the monolithic crowns cemented on titanium abutments indicates that these ceramics do not pres-

ent advantages over bilayered ones even though the highest mean fracture resistance value was obtained with this ceramic. Due to lower load-bearing capacity of glass-ceramics than titanium, lithium disilicate crowns were identified as the weakest components in abutment-crown assemblies. From the clinical point of view, using glass-ceramic crowns on titanium abutments may not fulfil the esthetic requirements in the anterior region. Hence, the performance of lithium disilicate crowns on zirconia abutments may be of more relevance. In these groups, unfortunately both the crowns and their corresponding abutments showed fractures.

Among all testing groups, manually veneered zirconia on zirconia abutments failed exclusively in the abutments without any destruction in the crowns. The esthetic outcome would probably be better with zirconia abutments in combination with zirconia crowns. However, this failure type also indicates that the risk of zirconia abutment damage is more likely to occur. Interestingly, the same manually veneered zirconia crowns did not demonstrate any crown fractures on titanium abutments. In this group, no fractures of the crowns and the abutments but only implant neck distortions were observed. Since the translucency of zirconia ceramics are less than that of lithium disilicate ceramics, esthetic outcome on titanium abutments may be perhaps not perfect, but acceptable. Therefore, considering both the fracture resistance values and failure types, the most stable abutment-ceramic crown combination seem to be manually veneered zirconia on titanium abutments.

It is not always possible to extrapolate the findings of in vitro studies to clinical situations since the stresses and strains of dental restorations *in vivo* are complex. However, with the increasing number of implants, abutments, and ceramic systems in the dental market, in vitro studies may help ranking material combinations before they are experimented clinically. The tests were performed only in maxillary central incisors and the results may vary in posterior teeth due to morphological differences. Early and long-term clinical failure types in implant dentistry should be reported in more detail in order to verify the findings of in vitro studies.

CONCLUSION

Based on the results of the present study, overall titanium abutments showed better durability than zirconia abutments. Titanium abutments restored with monolithic lithium disilicate crowns presented the highest fracture resistance with complete crown fractures without abutment fractures. Titanium abutment-manually veneered zirconia crown combinations presented no crown fracture but only implant neck distortion.

ACKNOWLEDGMENTS

This investigation was partially supported by grant No. 320-2008 from the University Complutense of Madrid. The authors gratefully acknowledge Mr Javier Pérez (Técnica Dental Studio VP, Lugo, Spain) for the fabrication of the abutments and crowns. Furthermore, they thank the companies Straumann and Ivoclar Vivadent for the support of the study with implants, abutments, and ceramic ingots/blocks. The authors reported no conflicts of interest related to this study.

REFERENCES

- Creugers NH, Käyser AF, Van't Hof MA. A seven-and-a-half-year survival study of resin-bonded bridges. *J Dent Res* 1992;71:1822–1825.
- van Heumen CC, van Dijken JW, Tanner J, et al. Five-year survival of 3-unit fiber-reinforced composite fixed partial dentures in the anterior area. *Dent Mater* 2009;25:820–827.
- Romeo E, Lops D, Margutti E, Ghisolfi M, Chiapasco M, Vogel G. Long-term survival and success of oral implants in the treatment of full and partial arches: A 7-year prospective study with the ITI dental implant system. *Int J Oral Maxillofac Implants* 2004;19:247–259.
- Wagenberg B, Froum SJ. A retrospective study of 1925 consecutively placed immediate implants from 1988 to 2004. *Int J Oral Maxillofac Implants* 2006;21:71–80.
- Salinas TJ, Eckert SE. In patients requiring single-tooth replacement, what are the outcomes of implant- as compared to tooth-supported restorations? *Int J Oral Maxillofac Implants* 2007;22:71–95.
- Gunne J, Astrand P, Lindh T, Borg K, Olsson M. Tooth-implant and implant supported fixed partial dentures: A 10-year report. *Int J Prosthodont* 1999;12:216–221.
- Lekholm U, Gunne J, Henry P, et al. Survival of the Bränemark implant in partially edentulous jaws: A 10-year prospective multicenter study. *Int J Oral Maxillofac Implants* 1999;14:639–645.
- Gibbard LL, Zarb G. A 5-year prospective study of implant-supported single-tooth replacements. *J Can Dent Assoc* 2002;68:110–116.
- Brägger U, Karoussis I, Persson R, Pjetursson B, Salvi G, Lang N. Technical and biological complications/failures with single crowns and fixed partial dentures on implants: A 10-year prospective cohort study. *Clin Oral Implants Res* 2005;16:326–334.
- Kreissl ME, Gerds T, Muche R, Heydecke G, Strub JR. Technical complications of implant-supported fixed partial dentures in partially edentulous cases after an average observation period of 5 years. *Clin Oral Implants Res* 2007;18:720–726.
- Pjetursson BE, Lang NP. Prosthetic treatment planning on the basis of scientific evidence. *J Oral Rehabil* 2008;35:72–79.
- Cooper LF, Ellner S, Moriarty J, et al. Three-year evaluation of single-tooth implants restored 3 weeks after 1-stage surgery. *Int J Oral Maxillofac Implants* 2007;22:791–800.
- Jung RE, Sailer I, Hämmерle CH, Attin T, Schmidlin P. In vitro color changes of soft tissues caused by restorative materials. *Int J Periodontics Restorative Dent* 2007;27:251–257.
- Park SE, Da Silva JD, Weber HP, Ishikawa-Nagai S. Optical phenomenon of peri-implant soft tissue. Part I. Spectrophotometric assessment of natural tooth gingiva and peri-implant mucosa. *Clin Oral Implants Res* 2007;18:569–574.
- den Hartog L, Slater JJ, Vissink A, Meijer HJ, Raghoebar GM. Treatment outcome of immediate, early and conventional single-tooth implants in the aesthetic zone: A systematic review to survival, bone level, soft-tissue, aesthetics and patient satisfaction. *J Clin Periodontol* 2008;35:1073–1086.
- Manicone PF, Rossi Iommelli P, Raffaelli L. An overview of zirconia ceramics: Basic properties and clinical applications. *J Dent* 2007;35:819–826.
- Scarano A, Piattelli M, Caputi S, Favero GA, Piattelli A. Bacterial adhesion on commercially pure titanium and zirconium oxide disks: An in vivo human study. *J Periodontol* 2004;75:292–296.
- Gross MD. Occlusion in implant dentistry. A review of the literature of prosthetic determinants and current concepts. *Aust Dent J* 2008;53(suppl 1):60–68.
- Kohal RJ, Att W, Bächle M, Butz F. Ceramic abutments and ceramic oral implants. An update. *Periodontol 2000* 2008;47:224–243.
- Quinn JB, Sundar V, Lloyd IK. Influence of microstructure and chemistry on the fracture toughness of dental ceramics. *Dent Mater* 2003;19:603–611.
- Guess PC, Zavanelli RA, Silva NR, Bonfante EA, Coelho PG, Thompson VP. Monolithic CAD/CAM lithium disilicate versus veneered Y-TZP crowns: Comparison of failure modes and reliability after fatigue. *Int J Prosthodont* 2010;23:434–442.
- Wolfart S, Eschbach S, Scherer S, Kern M. Clinical outcome of three-unit lithium-disilicate glass-ceramic fixed dental prostheses: Up to 8 years results. *Dent Mater* 2009;25:63–71.
- Denry I, Kelly JR. State of the art of zirconia for dental applications. *Dent Mater* 2008;24:299–307.
- ISO Norm 14801. Dentistry – Implants – Dynamic fatigue test for endosseous dental implants. Genova, Switzerland: International Organization for Standardization, 2007.
- Burstein AH, Wright TM. Fundamental of orthopedic biomechanics. Baltimore, MD: Lippincott Williams & Wilkins, 1994.
- Cho HW, Dong JK, Jin TH, Oh SC, Lee HH, Lee JW. A study on the fracture strength of implant-supported restorations using milled ceramic abutments and all-ceramic crowns. *Int J Prosthodont* 2002;15:9–13.
- Yildirim M, Fischer H, Marx R, Edelhoff D. In vivo fracture resistance of implant-supported all-ceramic restorations. *J Prosthet Dent* 2003;90:325–331.
- Att W, Kurun S, Gerds T, Strub JR. Fracture resistance of single-tooth implant-supported all-ceramic restorations after exposure to the artificial mouth. *J Oral Rehabil* 2006;33:380–386.
- Att W, Kurun S, Gerds T, Strub JR. Fracture resistance of single-tooth implant-supported all-ceramic restorations: An in vitro study. *J Prosthet Dent* 2006;95:11–16.
- Gehrke P, Dhom G, Brunner J, Wolf D, Degidi M, Piattelli A. Zirconium implant abutments: Fracture strength and influence of cyclic loading on retaining-screw loosening. *Quintessence Int* 2006;37:19–26.
- Aramouni P, Zebouni E, Tashkandi E, Dib S, Salameh Z, Almas K. Fracture resistance and failure location of zirconium and metallic implant abutments. *J Contemp Dent Pract* 2008;9:41–48.
- Sundh A, Sjögren G. A study of the bending resistance of implant-supported reinforced alumina and machined zirconia abutments and copies. *Dent Mater* 2008;24:611–617.
- Kim S, Kim HI, Brewer JD, Monaco EA Jr. Comparison of fracture resistance of pressable metal ceramic custom implant abutments with CAD/CAM commercially fabricated zirconia implant abutments. *J Prosthet Dent* 2009;101:226–230.
- Sailer I, Sailer T, Stawarczyk B, Jung RE, Hämmärlie CH. In vitro study of the influence of the type of connection on the fracture load of zirconia abutments with internal and external implant-abutment connections. *Int J Oral Maxillofac Implants* 2009;24:850–858.
- Albrecht T, Kirsten A, Kappert HF, Fischer H. Fracture load of different crown systems on zirconia implant abutments. *Dent Mater* 2011;27:298–303.
- Laurell L, Lundgren D. Marginal bone level changes at dental implants after 5 years in function: A meta-analysis. *Clin Implant Dent Relat Res* 2011;13:19–28.
- Guazzato M, Proos K, Sara G, Swain MV. Strength, reliability, and mode of fracture of bilayered porcelain/core ceramics. *Int J Prosthodont* 2004;17:142–149.

Comparison of Heat Generation Between Internally Guided (Cannulated) Single Drill and Traditional Sequential Drilling With and Without a Drill Guide for Dental Implants

Scott E. Bulloch, DDS, MS¹/Russell G. Olsen, DPM²/Brandon Bulloch, BS³

Purpose: To determine whether a wire-guided single drill protocol could be utilized without causing an increase in bone temperature beyond those seen with the traditional techniques of sequential drilling with and without a drill guide. **Materials and Methods:** A bovine femoral bone model was used with thermocouples and infrared temperature measurements to record thermal increase of the bone and drills during implant site preparation. Two thermocouples, one on each side of the osteotomy, were placed 1 mm from the outer diameter of the final drill. Drilling was performed at a constant speed (2,100 rpm) and pressure (2 kg) under continuous room temperature irrigation. Infrared temperature measurements of each drill were taken immediately before and after drilling. The six study groups included standard sequential drilling protocols for 3.5-mm and 4.2-mm final drills with and without the use of a surgical guide, and cannulated single drill technique for 3.5-mm and 4.2-mm drills. Statistical analysis was performed using a Tukey post hoc one-way ANOVA test. $P < .05$ was determined to be significant. **Results:** No significant difference in thermal increase was found between single drill cannulated implant site preparation and sequential drilling with or without the use of a drill guide for the 3.5-mm or 4.2-mm drilling sequences, respectively. The thermal increase was found to be significantly less for the 4.2-mm single drill compared with the 3.5-mm sequential drill with surgical guide ($P = .046$). Infrared temperature measurement revealed no significant difference in drill temperatures throughout the study. **Conclusions:** Cannulated single drill technique does not cause an increase in bone temperature greater than that seen with standard sequential drilling with or without a surgical guide. *INT J ORAL MAXILLOFAC IMPLANTS* 2012;27:1456–1460

Key words: bone, cannulation, dental implants, drill guidance

Internal guidance using guide wires and cannulated drills has long been the preferred technique in many orthopedic procedures. This is especially true with regard to the more delicate and precise treatment of the smaller bones of the hands and feet.¹ This technology had previously not been adapted for use with the placement of dental implants. Cannulation as a general technique involves the placement of a guide wire such as a K-wire. This is most commonly done by drilling the wire into the bone in the desired location. Verification of location can then be accomplished radiographically. A drill with a hole through the entire length along the long axis and corresponding in size with the wire is then placed over the wire and drilling

is accomplished as the drill follows the wire into the bone. Although traditional sequential drilling can be done with a guide wire, one of the advantages of cannulation is that the wire provides sufficient stabilization of the drill to allow single-drill site preparation. In this manner, the final drill is the only drill used for the osteotomy, significantly shortening the necessary drilling time. Multiple studies from orthopedic and oral surgery literature demonstrate that bone heating is increased as drilling time increases.^{2–8}

Heat generation while drilling bone has long been recognized as a concern. Delayed healing as well as necrosis are among the complications associated with excessive drilling temperatures and duration. Motor speed, drill configuration and size, duration of drilling, irrigation techniques, use of surgical splints, along with many other factors, have been previously explored.^{2–12} This study is unique in its comparative evaluation of thermal increase using a cannulation technique compared with traditional sequential drilling for the placement of dental implants. This study did not specifically compare the total drilling time associated with each technique.

¹Oral and maxillofacial surgeon, private practice, St. George, Utah, USA.

²Podiatric surgeon, private practice, Cedar City, Utah.

³Student, laboratory assistant, Dixie State College, St. George, Utah, USA.

Correspondence to: Dr Scott E. Bulloch, 754 S Main #5, St. George, UT 84770, USA. Fax: 435-652-0138. Email: oms@infowest.com

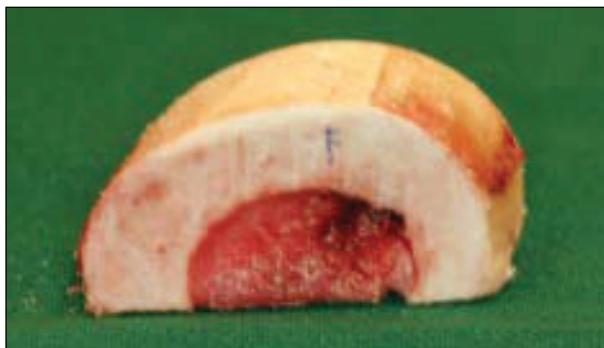


Fig 1 Bovine femoral bone segment.



Fig 2 Surgical guide.

MATERIALS AND METHODS

Uniform thickness bovine femoral cortical bone segments were used for this study (Fig 1). Bone segment use and sequence were randomized into one of six study groups as follows: Group A, sequential drilling up to 3.5 mm with the use of a surgical guide; Group B, sequential drilling up to 3.5 mm without the use of a surgical guide; Group C, 3.5-mm single cannulated drill; Group D, sequential drilling up to 4.2 mm with the use of a surgical guide; Group E, sequential drilling up to 4.2 mm without the use of a surgical guide; and Group F, 4.2-mm single cannulated drill (see Table 1). New drills manufactured by Straumann (Straumann USA) were used in this study. The cannulated drills were modified by the investigator for use with 0.8-mm guide wires. Sequential drill sizes consisted of 2.2 mm, 2.8 mm, 3.5 mm, and 4.2 mm when indicated. Groups A and D utilized the Straumann Surgical Guide kit (Straumann USA). The guide splint was fabricated using an acrylic disk that fit tightly around the individual guide sleeves (Fig 2). Red wax was used between the acrylic disc and the bone to simulate gingiva and to adapt the disk to the bone. In order to eliminate directional variations in drilling, a drill press was utilized for all drilling. Drilling was accomplished at a constant speed of 2,100 rpm, and a jig was fabricated to provide a constant 2-kg drilling pressure. Fifteen drilling sequences were completed for each group in random order for a total of 90 trials. Holes of 0.8 mm were drilled to a depth of 8 mm on both sides of the planned drilling site. These holes were positioned 1 mm outside the diameter of the final drill (5.5 mm apart for the 3.5-mm drilling sequences, and 6.2 mm apart for the 4.2-mm sequences). K type micro thermocouples (Omega Engineering) were placed into the holes and secured and sealed from moisture using silicone sealant (Fig 3). A handheld data logger (Omega HH147U) was used to collect constant

Table 1 Study Groups

Group

A	Three drill sequence of 2.2-mm, 2.8-mm, and 3.5-mm drills with guide splint
B	Three drill sequence of 2.2-mm, 2.8-mm, and 3.5-mm drills
C	Single 3.5-mm cannulated drill
D	Four drill sequence of 2.2-mm, 2.8-mm, 3.5-mm, and 4.2-mm drills with guide splint
E	Four drill sequence of 2.2-mm, 2.8-mm, 3.5-mm, and 4.2-mm drills
F	Single 4.2-mm cannulated drill

temperature data for both thermocouples (T1 and T2) which was recorded on a laptop computer throughout the study. Temperature change from predrilling (Start T1 and Start T2) to finish was collected for all drills in all sequences, and a maximum temperature was identified for each thermocouple (T1 Max, and T2 Max). Thermocouple readings were evaluated and the difference between the start and maximum temperatures were recorded as ΔT_1 and ΔT_2 . These two temperatures were averaged for each drill. Drilling sequences were evaluated by comparing the start temperatures (prior to the pilot drills) and the maximum temperature reached throughout the sequence. This provided a cumulative maximum temperature increase (cumulative T Max) for the sequence. An infrared temperature gun (Fluke 62 Mini IR Thermometer) was used to measure the starting and ending temperatures of each drill before and after drilling with irrigation. Irrigation consisted of room temperature water in a continuous flow with irrigation syringes. Cannulated drilling was accomplished by drilling a 0.032-inch (0.8 mm) wire into the bone. This was

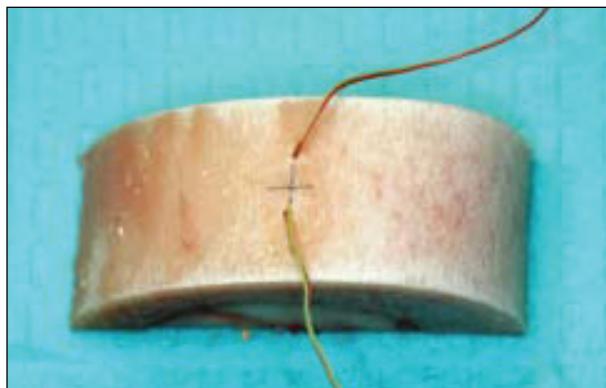


Fig 3 Microthermocouples in bone segment.

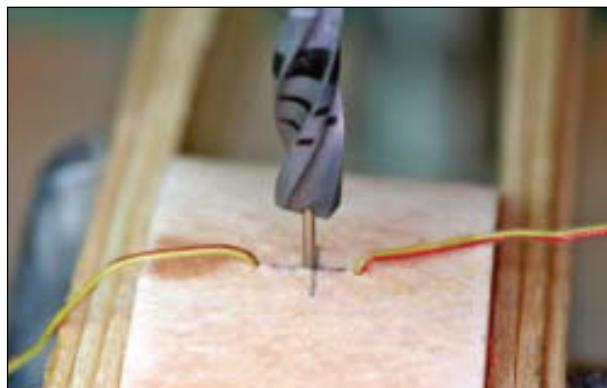


Fig 4 Cannulated implant drill and guide wire.

Table 2 Mean Maximum Temperature Increases (°C)

Group	Results
A	26.39*
B	23.3
C	23.69
D	21.84
E	22.94
F	14.77*

* Statistically significant

Table 4 Increase in Drill Temperature by Infrared Measurement (°C)

Group	Results
A	1.36
B	2.49
C	2.82
D	1.0
E	1.38
F	1.48

then followed by placing a 3.5- or 4.2-mm Straumann drill that had been modified by drilling a 0.032-inch hole through the long axis over the wire (Fig 4). All drilling sequences were taken to a depth of 10 mm. Statistical analysis was completed using a Tukey post hoc one-way ANOVA test.

RESULTS

The cumulative temperature increases in degrees Celsius were averaged for each of the six groups with the following results: Group A (3.5 guided sequence), 26.39; Group B (3.5 unguided sequence), 23.3; Group C (3.5 cannulated), 23.69; Group D (4.2 guided sequence),

Table 3 Combined Mean Temperature Increases by Category (°C)

Category	Groups	Mean increase
Guided	A and D	24.12
Unguided	B and E	23.12
Cannulated	C and F	19.23

21.84; Group E (4.2 unguided sequence), 22.94; and Group F (4.2 cannulated), 14.77 (Table 2). The combined averages for each technique were: guided sequence (groups A and D), 24.12; unguided sequence (groups B and E), 23.12; cannulated (groups C and F), 19.23 (Table 3). The difference between groups A and F was found to be statistically significant with $P = .046$. Infrared pre- and postreadings showed a minimal difference and were found not to be significant in any of the groups (Table 4). The start temperatures were noted to increase with each additional drill in a sequence indicating a tendency for bone to hold heat. The majority of the maximum temperature increases were noted with the pilot drills. The tendency was for a lower temperature increase with the larger diameter drills.

DISCUSSION

Wire guidance as a means of increasing drilling accuracy has been well established in various surgical disciplines. The effect of this technique on bone temperatures has not been previously evaluated compared with commonly used methods of bone drilling in preparation for placement of dental implants. Heat generation during drilling sequences has long been a known concern, and must be considered in the development of any placement technique.

Of interest is the fact that the largest temperature increase was noted with the use of the pilot drills during sequential drilling. Since all temperature measurements were taken beyond the extent of the final drills, this study refutes the concept that bone heating during the use of pilot drills is not significant because heated bone will be removed by subsequent drills. Possible explanations for this finding could include the fact that, at a constant pressure of 2 kg, the actual PSI at the drill tip would be many times greater for a 2.2-mm drill tip than for a 4.2-mm drill tip. Another possibility is that a smaller drill has smaller flute spaces which could restrict irrigation, thus decreasing its cooling effect. The difference in the mass of each drill is another potential factor since this could effect the heat storage or dissipation of each drill. Further investigation is needed to more thoroughly evaluate each potential factor. Of note also is the fact that, although necessary for standardization in this study, constant uniform pressure is seldom present in a clinical setting where pressure is generally lighter and variable.

The lack of significant variation in drill temperatures as measured by infrared temperature monitoring is most likely a measurement of the consistency of the irrigation cooling. An accurate measurement of drill heat increase in and of itself would require that the study be done without the use of irrigation.

Misir et al¹² demonstrated significantly higher heat generation with the use of surgical guide splints. This tendency was also seen in the present study, although the differences only reached statistical significance between groups A and F. This difference appears to be the result of a combination of increased drill size combined with the lack of a guide splint. The significance of each individual factor is thus unclear. This increased bone temperature was not seen with the use of wire guidance (cannulation).

Clinical Observations

Traditional drill guides most commonly guide the drills through the use of sleeves in a tissue borne splint. This approach has several inherent limitations. The splints generally block or limit the view of the surgical field.

Maintaining stability of the splint can be complex and difficult especially when drilling into narrow or angled bone is required. The need to reflect soft tissue, or perform bone grafting procedures renders many splint designs ineffective or inaccurate. Tissue punch techniques required by some guide splints can remove needed attached gingiva, thus compromising the final result. Nonguided techniques also have their challenges. Freehand placement leaves great room for operator error and misalignment. The technique of radiographically evaluating the placement of a pilot drill prior to further drilling can be useful; however, redirecting the misdirected pilot drill can be difficult due to the tendency for the drill to follow the path of the initial drill hole. Correct pilot drill angulation can be especially difficult to achieve in angled bone, such as fresh extraction sites, or in very narrow bone like a knife-edge ridge. Cannulation wire guidance has several advantages. Due to the sharp tip and small diameter of the guide wire, it can be more easily drilled into narrow or angled bone. Angulation errors can be corrected more easily due to a decreased tendency to follow previous holes. Wires can be placed with the use of a traditional guide splint, and then the splint is removed. At that time, the wires become a bone-borne rather than a tissue-borne guide, thus allowing for tissue reflection, bone grafting, etc, without loss of guidance accuracy. The operator has full unobstructed visualization of the surgical field throughout the drilling process. The depth of placement of the wires may be used as a guide for drilling depth with radiographic verification. Wires guide the drill tip with tremendous accuracy, thus eliminating any drill walk during drilling of narrow or angled bony walls. Parallelism or desired angle variations can be determined in the lab and accurately duplicated with the wires in the clinical setting. This, along with single drill implant site preparation, can significantly increase the accuracy of implant position and angulation while decreasing surgical time and bone trauma. The use of wire guidance requires technique modification and additional precautions when approaching vital structures, but is easily adaptable to most implant cases.

CONCLUSION

This study demonstrates that wire guidance with a single drill can be reliably performed without causing bone heating greater than that seen with standard drilling techniques under similar circumstances. Possibilities for implant site preparation, as well as the long term safety record of cannulation in orthopedic procedures, suggest that this is a technique that warrants further investigation.

ACKNOWLEDGMENT

Michael Hunter from Southern Utah University completed the statistical analysis. The authors reported no conflicts of interest related to this study.

REFERENCES

- Franssen BB, Schuurman AH, Van der Molen AM, Kon M. One century of Kirschner wires and Kirschner wire insertion techniques: A historical review. *Acta Orthop Belg* 2010;76:1–6.
- Fuchsberger A. Damaging temperature during the machining of bone [in German]. *Unfallchirurgie* 1988;14:173–183.
- Brisman DL. The effect of speed, pressure, and time on bone temperature during the drilling of implant sites. *Intl J Oral Maxillofac Implants* 1996;11:35–37.
- Abouzgia MB, James DF. Temperature rise during drilling through bone. *Intl J Oral Maxillofac Implants* 1997;12:342–343.
- Iyer S, Weiss C, Mehta A. Effects of drill speed on heat production and the rate and quality of bone formation in dental implant osteotomies. Part II: Relationship between drill speed and healing. *Intl J Prosthodont* 1997;10:536–540.
- Bachus KN, Rondina MT, Hutchinson DT. The effects of drilling force on cortical temperatures and their duration: An in vitro study. *Med Eng Phys* 2000;22:685–691.
- Augustin G, Davila S, Mihoci K, Udiljak T, Vedrina DS, Antabak A. Thermal osteonecrosis and bone drilling parameters revisited. *Arch Orthop Trauma Surg* 2008;128:71–77.
- Sharawy M, Misch CE, Weller N, Tehemar S. Heat generation during implant drilling: The significance of motor speed. *J Oral Maxillofac Surg* 2002;60:1160–1169.
- Yoshida K, Uoshima K, Oda K, Maeda T. Influence of heat stress to matrix on bone formation. *Clin Oral Implants Res* 2009;20:782–790.
- Bubeck KA, García-López J, Maranda LS. In vitro comparison of cortical bone temperature generation between traditional sequential drilling and a newly designed step drill in the equine third metacarpal bone. *Vet Comp Orthop Traumatol* 2009;22:442–447.
- Cordioli G, Majzoub Z. Heat generation during implant site preparation: An in vitro study. *Intl J Oral Maxillofac Implants* 1997;12:186–193.
- Misir AF, Sumer M, Yenisey M, Ergioğlu E. Effect of surgical drill guide on heat generation from implant drilling. *J Oral Maxillofac Surg* 2009;67:2663–2668.

Air Powder Abrasive Treatment as an Implant Surface Cleaning Method: A Literature Review

Ceylin S. Tastepe, DDS¹/Rien van Waas, DDS, PhD²/Yuelian Liu, DDS, PhD³/Daniel Wismeijer, DDS, PhD²

Objective: To evaluate the air powder abrasive treatment as an implant surface cleaning method for peri-implantitis based on the existing literature. **Materials and Methods:** A PubMed search was conducted to find articles that reported on air powder abrasive treatment as an implant surface cleaning method for peri-implantitis. The studies evaluated cleaning efficiency and surface change as a result of the method. Furthermore, cell response toward the air powder abrasive-treated discs, reosseointegration, and clinical outcome after treatment is also reported. **Results:** The PubMed search resulted in 27 articles meeting the inclusion criteria. In vitro cleaning efficiency of the method is reported to be high. The method resulted in minor surface changes on titanium specimens. Although the air powder abrasive-treated specimens showed sufficient levels of cell attachment and cell viability, the cell response decreased compared with sterile discs. Considerable reosseointegration between 39% and 46% and improved clinical parameters were reported after treatment when applied in combination with surgical treatment. The results of the treatment are influenced by the powder type used, the application time, and whether powder was applied surgically or nonsurgically. **Conclusion:** The in vivo data on air powder abrasive treatment as an implant surface cleaning method is not sufficient to draw definitive conclusions. However, in vitro results allow the clinician to consider the method as a promising option for implant surface cleaning in peri-implantitis treatment. INT J ORAL MAXILLOFAC IMPLANTS 2012;27:1461–1473

Key words: airflow, biofilm, implant surface, peri-implantitis

Peri-implantitis is an inflammatory process around an implant, characterized by soft tissue inflammation and loss of supporting marginal bone.¹ It has been associated with a predominantly gram-negative anaerobic microflora.² The microflora associated with peri-implantitis is similar to that associated with periodontal disease. Opportunistic periodontal pathogens such as *Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivalis*, *Bacteroides forsythus*, *Prevotella intermedia*, *Peptostreptococcus micros*, and *Fusobacterium nucleatum* have been identified in association with peri-implantitis in partially edentulous patients.^{3,4}

Few studies provide data on the prevalence of peri-implant diseases. Two studies reported the prevalence of peri-implantitis as 28% in at least 56% of subjects, and in 12% and 43% of implant sites.¹ However, general studies report percentages between 5% and 10%.^{5–7}

Several attempts have been made to find the optimum treatment for peri-implantitis. Treatment has to consist of the elimination of the infection and restoration of the original peri-implant condition, ie, to create conditions favorable to reosseointegration on the exposed implant surface. Reosseointegration is described as formation of new bone onto a previously biofilm-contaminated implant surface.⁸

Noninvasive (using antimicrobial and anti-inflammatory medicine), resective (removing the granulation tissue and decontaminating the implant surface), and regenerative (restoring the bone defect) treatments have been described in conjunction with various methods of additional surface cleaning and decontamination by chemical agents, mechanical devices, or laser applications or ultraviolet (UV) irradiation.^{9–13}

The air powder abrasive treatment is one of the mechanical methods described in the literature. It uses an abrasive powder brought into a stream of compressed air to clean or polish all kinds of surfaces by removing deposits or smoothing its texture.¹⁴ The air powder abrasive devices with different types of powders are commonly used for supra- and subgingival biofilm

¹Researcher, Department of Oral Implantology and Prosthetic Dentistry, Academic Centre for Dentistry Amsterdam (ACTA), Research Institute MOVE, VU University and University of Amsterdam, Amsterdam, The Netherlands.

²Professor, Department of Oral Implantology and Prosthetic Dentistry, Academic Centre for Dentistry Amsterdam (ACTA), Research Institute MOVE, VU University and University of Amsterdam, Amsterdam, The Netherlands.

³Assistant Professor, Department of Oral Implantology and Prosthetic Dentistry, Academic Centre for Dentistry Amsterdam (ACTA), Research Institute MOVE, VU University and University of Amsterdam, Amsterdam, The Netherlands.

Correspondence to: Dr Daniel Wismeijer, Academic Centre for Dentistry Amsterdam (ACTA), Gustav Mahlerlaan 3004, 1081 LA Amsterdam, The Netherlands. Fax: +31-(0)20-5980333. Email: D.Wismeijer@acta.nl

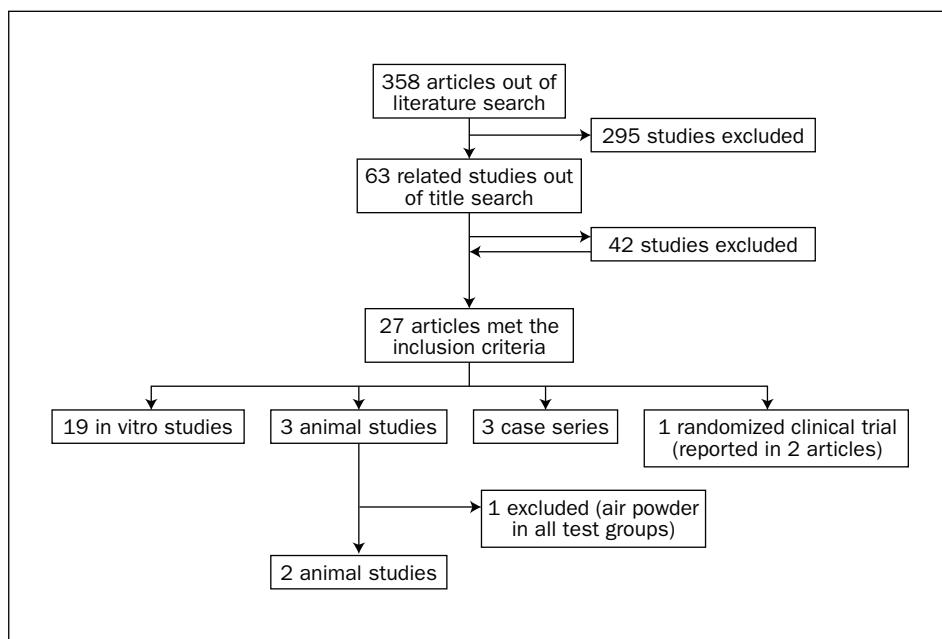


Fig 1 Flowchart of the selection of studies for review.

removal on teeth.¹⁵ Additionally, the same method is reportedly used for implant surface cleaning in combination with peri-implantitis treatment.

The aim of this review is to evaluate the air powder abrasive treatment as an implant surface cleaning method for peri-implantitis treatment with respect to the cleaning efficiency, the influence on the implant surface, and the clinical response, and to answer the question of whether it is possible to achieve reosseointegration following the treatment.

MATERIALS AND METHODS

A literature search was carried out in PubMed using the following key words: *Air powder abrasive OR Air polish* OR Mechanical cleaning implant OR Peri-implantitis air powder OR Peri-implantitis air powder abrasive OR implant surface air powder OR air abrasive OR air abrasive implant OR air abrasive implant surface OR air abrasive peri implantitis OR peri implantitis decontamination OR re osseointegration peri implantitis surface OR peri implantitis surface modification*. The database was searched for studies conducted in the period from 1955 until May 2011.

The inclusion criteria were: (1) articles in the English language; (2) articles that reported on the effect of air powder abrasive treatment on titanium implants, titanium abutments, titanium discs, or titanium platelets; (3) and *in vitro*, animal as well as human, studies.

The search resulted in 358 articles. After reviewing the titles and authors, 295 articles were excluded since they did not report on the effect of air powder abrasive treatment on titanium implants, discs, or abutments. Articles that could be related to the subject (63) were checked again through their abstracts and 36 of them did not meet the inclusion criteria; therefore, 27 articles were selected for review.

Among these 27 articles, 19 were *in vitro* studies, 3 were animal studies, 3 were case series, and 1 was a randomized clinical trial (reported in two articles). In one of the three animal studies, air powder abrasive treatment was used as a debridement method for all groups and the regenerative procedure was changed; therefore, this study was excluded for not exclusively reporting on the outcome of the air powder abrasive treatment.

In addition to these articles, six related studies were found during a manual search. However, all of these studies used air abrasive treatment as a standard debridement method to change the regenerative procedures in the test groups. The results do not report specifically on air powder abrasive treatment; therefore, these studies were not included.

The search of the database was performed independently by three different reviewers (CST, YL, and DW), first by title and abstract. In a second step, the full texts of the articles were read and papers fulfilling the inclusion criteria were chosen. Disagreements were resolved by discussion. All three reviewers agreed on the final articles selected (Fig 1).

The 27 remaining studies showed a variety in study design, application period, specimen type (implants, abutments, discs, platelets), and evaluation method (microbiologic, histologic, electron microscopy). They also differed in (1) treatment method (invasive or noninvasive); (2) powder types (sodium bicarbonate, amino acid glycine); (3) specimen types (implants [machined, TPS, HA, SAE implants], titanium discs, titanium abutments); (4) evaluation method (clinical, radiologic, histologic, microbiologic); and (5) evaluated aspects (cleaning efficiency, surface changes of the titanium, cell response).

Therefore, the studies were classified regarding the different aspects of the outcome of the air powder treatment on titanium specimens. Each aspect of the treatment is presented in tables under subtitles and the results were compared and analyzed. Since there was such broad variability among studies, a meta-analysis was not possible.

The studies were classified into five groups and presented separately in tables for each group. In presenting the results of the studies, only the information regarding the subject of the table is presented. Additional results on treatments other than air powder abrasive are not included in the tables.

Group Classification

Group 1: Cleaning Efficiency. In these studies, the cleaning efficiency of air powder abrasive treatment was evaluated with contaminated titanium implants, abutments, disks, or platelets. The specimens were contaminated with either bacteria endotoxin or biofilm and cleaned by air powder abrasive treatment afterwards. The residual bacteria or endotoxin were measured microbiologically and residual biofilm areas were measured by microscope.

Group 2: Surface Change. The surface of the titanium specimen before and after air powder abrasive application was monitored by scanning electron microscope. The change caused by the application was evaluated.

Group 3: Cell Response. Titanium surfaces were tested before and after air powder abrasive treatment in cell cultures to evaluate the osteoblast or fibroblast response to these surfaces. Cell attachment, proliferation, DNA activity, and cell viability were tested.

Group 4: Reosseointegration. These studies measured reosseointegration histologically or radiologically following air powder abrasive treatment on infected implants.

Group 5: Clinical Outcome. Clinical parameters like bleeding on probing, suppuration, and probing depth were measured in peri-implantitis patients who underwent air powder abrasive implant surface cleaning treatment.

RESULTS

Cleaning Efficiency

The cleaning efficiency of air powder abrasive treatment was evaluated by seven studies (six in vitro and one randomized clinical trial)^{16–22} (Table 1).

Two in vitro studies tested the removal of bacterial endotoxin from titanium specimens by several methods. Zablotsky et al¹⁶ reported significantly greater amounts of bacterial endotoxin removal with air powder abrasive treatment than citric acid, stannous fluoride, tetracycline HCl, chlorhexidine gluconate, hydrogen peroxide, chloramine T, sterile water, or a plastic sonic scaler tip. Dennison et al¹⁸ reported bacterial endotoxin removal at 98.8% from machined titanium surfaces, 84.2% from plasma sprayed surfaces, and 88.8% from HA-coated surfaces using air powder abrasive treatment. Three studies tested the removal of bacteria instead of endotoxin and all three reported 100% removal of the bacteria.^{18–20} Mouhyi et al²¹ applied air powder abrasive treatment to failed implants and reported efficient cleaning that resulted in a clean surface as observed by SEM.

A randomized clinical trial on this subject²² compared Er:YAG laser and air powder abrasive treatment by nonsurgical treatment. A total of 74 bacterial species were checked by pre- and posttreatment microbiologic samples. Although *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and *Staphylococcus anaerobius* were found at lower counts after 1 month, the treatment failed to reduce the bacterial counts at 6 months; however, this was a nonsurgical treatment based on studies included in the Consensus Report of the Sixth European Workshop on Periodontology. This conference concluded that nonsurgical therapy on peri-implantitis lesions is not effective. Additionally, to the authors' knowledge, no study reporting on the outcome of open surgical debridement with air powder treatment has been published.

According to these studies, in vitro cleaning efficiency of air powder abrasive treatment on titanium strips, disks, or implants is high. However, this result is not supported by the only clinical study that tested the method in a nonsurgical setup.³⁸ More clinical studies are needed to surgically test the treatment on implant surfaces.

Surface Change

Sixteen in vitro studies reported on the surface change of titanium implants, abutments, or disks following the air powder abrasive treatment^{17,19–21,23–34} (Table 2). Eight studies used titanium implants, four studies used titanium abutments, one study used both implants and abutments, one study used titanium platelets, and two studies used titanium disks. The application time, as well as the specimen types, differed among the studies.

Table 1 Studies Evaluating the Cleaning Efficiency of Air Powder Abrasive Treatment

Study (y)	Type	No. of specimens	Implant type	Decontamination method
Parham et al ¹⁷ (1989)	In vitro	28 implants	Plasma sprayed	1. Air powder abrasive (test) 2. Sterile water treated (control)
Zablotsky et al ¹⁶ (1992)	In vitro	9 titanium alloy test strips	Grit-blasted titanium alloy and hydroxylapatite-coated test strips	Grit blasted titanium alloy strips: 1. Citric acid 2. Stannous fluoride 3. Tetracycline HCl 4. Chlorhexidine gluconate 5. Hydrogen peroxide 6. Chloramine T 7. Sterile water 8. Plastic sonic scaler tip 9. Air powder abrasive unit Hydroxyapatite-coated strips: 1. Chloramine T 2. Citric acid 3. Burnished with sterile water on cotton pellets
Dennison et al ¹⁸ (1994)	In vitro	36 implants	Machined, plasma sprayed, hydroxylapatite-coated surfaces	1. Cotton pellet soaked in water 2. Citric acid solution 3. 0.12% chlorhexidine 4. Air powder abrasive
Augthun et al ¹⁹ (1998)	In vitro		Plasma sprayed; hydroxylapatite-coated implants; smooth titanium surface screws	1. Plastic curet 2. Metal curet 3. Diamond polishing device 4. Ultrasonic scaler 5. Air-powder-water spray with sodium hydrocarbonate 6. Chlorhexidine 0.1% solution rinse
Mouhyi et al ²¹ (1998)	In vitro	17 implants from 9 patients	Bränemark implants	1. Rinsing in absolute ethanol for 10 min 2. Cleaning in ultrasonic baths containing trichloroethylene and absolute ethanol, 10 min in each solution 3. Abrasive cleaning for 30 s 4. Cleaning in supersaturated citric acid for 30 s 5. Cleaning with continuous CO ₂ laser in dry conditions at 5 W for 10 s 6. Cleaning with continuous CO ₂ laser in wet conditions (saline) at 5 W for 10 s
Schwarz et al ²⁰ (2009)	In vitro	160 titanium disks; 48 hour biofilm	SAE surface	Air powder abrasive with amino acid glycine (three different types) or sodium bicarbonate (one type) powders; each sample received single as well as repeated treatment (20 s for both)
Persson et al ²² (2011)	Human	42 subjects		Nonsurgical treatment with: Group 1: Er:YAG laser Group 2: air abrasive subgingival polishing device

AIR = air powder abrasive; CA = citric acid solution; CHX = 0.12% chlorhexidine; SEM = scanning electron microscopy; TRI = trichloroethylene.

Although all studies evaluated surface change using SEM, there was no standard terminology or method to describe the level and character of surface change. The authors used subjective descriptions like "slight change" or "medium change;" therefore, the evaluations were not comparable. Still, the studies can be classified according to the specimen type used.

The studies on abutments reported minor surface alterations²³ or no change on the surface.²⁴ The character of the change was described as smoothing and rounding off the sharp machined grooves and obliterating the milling marks,^{25,26} obliterated metal tags, rounding of the edges,²⁷ or some surface pitting.²⁸

Other studies used implants with different surface properties as specimens. Four studies using plasma

spray-coated implants^{18,19,24,29} reported no perceptible differences or slight changes. The character of the change was reported as increased roughness of the surface³⁰ or coating removal.³¹

HA-coated implants were also tested. Coating removal on this surface as well as plasma-coated implants were reported,³¹ whereas others reported only a medium change in surface properties.¹⁹

Another type of implant used is the machined surface implant. Despite the fact that machined implants were reported to be more affected than plasma spray-coated implants,²⁷ studies reported no perceptible difference²⁹ or only the removal of the machining marks.²⁶ Mouhyi et al²¹ reported craters of 10 µm in diameter on machined surfaces.

Evaluation method	Results
SEM	100% removal of bacteria from the test group; 75% removal from control group
Residual lipopolysaccharide levels were measured by liquid scintillation spectrometry	For grit blasted titanium alloy strips, air-powder abrasive was significantly superior to other treatments For hydroxyapatite-coated surfaces, citric acid was superior when compared with the controls or chloramine T
Microbiologically	Machined implants, remaining amount of endotoxin: AIR < CA with AIR = water = CHX; Plasma-sprayed implants, remaining amount of endotoxin: water = CHX = CA AIR < water = CHX = CA; Hydroxyapatite implants: AIR = CA < water < CHX; Air powder abrasive most effective. Only hydroxyapatite coated surfaces can be treated equally with air abrasive and citric acid.
SEM	Only air powder abrasive treatment yielded a clean implant without damage to the surface
SEM and x-ray induced photoelectron spectroscopy	Cleaning of used implants in citric acid followed by rinsing with deionized water for 5 min followed by cleaning in ultrasonic baths with TRI and absolute ethanol gave the best results with regard to macroscopical appearance and surface composition
Residual biofilm	100% cleaning of the biofilm areas in all groups
Microbiological assessment	Both treatments failed to reduce the bacterial counts at 6 months

Two studies used sandblasted and acid-etched (SAE) surface titanium specimens.^{20,32} Kreisler et al³² reported microscopically visible changes and smoother surface and Schwarz et al²⁰ mentioned obvious alteration of the specific SAE surface morphology. In another study,³³ bioactive glass powder was applied on machined surfaces instead of conventional grit blasting to achieve a rough surface. Bioactive glass was distributed across the titanium surface and retained within fissures and roughened surface features.

The alterations were influenced by the application time. The studies that reported no perceptible difference on implant surface had an air abrasive treatment application time of less than 30 seconds.^{24,29,34} However, others³⁰ reported decreased roughness after a 2-second

application, and one study²⁷ reported rounding and removal of the machining grooves after a 5-second application. Chairay et al³⁴ reported that although a 5-second application did not induce deep changes, a 15-second application modified the specimen surfaces on machined and plasma spray-coated implants.

According to these studies, air powder abrasive treatment results in minor rounding of the sharp edges but does not create big surface changes. Most of these studies were done on older types of implants such as machined, plasma spray-coated, or HA-coated implants that are not commonly used today. However, implants that have been inserted can still develop peri-implantitis and, thus, may need treatment.

Table 2 Studies Evaluating the Surface Change of Titanium after Air Powder Abrasive Treatment

Study (y)	Type	Specimen type (no.)	Treatment method
Parham et al ¹⁷ (1989)	In vitro	28 plasma-sprayed implants	1. Air powder abrasive 2. Sterile water treated
Barnes et al ²⁹ (1991)	In vitro	4 machined, 4 plasma-sprayed, 4 highly-polished implants	Air abrasive treatment (10 s)
McCollum et al ²⁸ (1992)	In vitro	5.5 mm-abutments	1. Plastic scalers 2. Air powder abrasive system 30 seconds 3. Rubber cup polishing with pumice
Koka et al ²⁶ (1992)	In vitro	Bränemark titanium implants	Prophy jet and microprophy system for 90 s
Homiak et al ²⁵ (1992)	In vitro	5 new 10-mm titanium implant abutments	1. Metal scaler 2. Plastic scaler 3. Rubber cup 4. Rubber cup with tin oxide 5. Air powder abrasive (Cavi-Jet) (5 seconds-50 seconds) 2 phases, 1st: short, 2nd: long
Matarasso et al ³⁰ (1996)	In vitro	50 Straumann bonefit (plasma-spray) implants	1. Ultrasonic scaler 2. Plastic tip ultrasonic scaler 3. Stainless steel curette 4. Titanium curette 5. Teflon curette 6. Air powder abrasive (max air: 5 k/cm ² , max water: 2 k/cm ²) 1 to 2 s 7. Abrasive rubber cups 8. Polishing rubber cup and brush
Meschenmoser et al ²³ (1996)	In vitro	5 new titanium implant abutments	1. Steel curet 2. Prototype pure titanium curet 3. Air abrasive polishing system - 30 s 4. Ultrasonic system
Chairay et al ³⁴ (1997)	In vitro	4 machined, 4 plasma-sprayed; Both neck and body surfaces of the implants were analyzed	Air abrasive 5 s and 15 s
Brookshire et al ²⁷ (1997)	In vitro	Pure titanium and titanium alloy abutments	1. Gold alloy tipped scaler 2. High grade resin scaler 3. Graphite reinforced scaler 4. Air powder abrasive treatment 20 s 5. Rubber cup with tin oxide slurry
Mengel et al ²⁴ (1998)	In vitro	Titanium implants and abutments; plasma-sprayed implants; standard Bränemark implants	1. Titanium curettes 2. Gracey curettes 3. Plastic curettes 4. Plastic curettes 5. Rubber cups with Zircate prophy paste 6. Cavitron jet ultrasonic scaler 7. Air polishing nozzles with Prophy Jet cleaning powder (20-s pressure: 3 bars) 8. Dentsonic sonic scaler
Augthun et al ¹⁹ (1998)	In vitro	Plasma-sprayed, hydroxyapatite-coated implants; and smooth titanium surface screws	1. Plastic curettes 2. Metal curettes 3. Diamond polishing device, 4. Ultrasonic scaler 5. Air-powder-water spray with sodium hydrocarbonate solution 6. Chlorhexidine 0.1% solution rinse
Mouhyi et al ²¹ (1998)	In vitro	17 Bränemark implants from 9 patients	1. Rinsing in absolute ethanol for 10 min 2. Cleaning in ultrasonic baths containing trichloroethylene and absolute ethanol, 10 min in each solution 3. Abrasive cleaning for 30 s 4. Cleaning in supersaturated citric acid for 30 s 5. Cleaning with continuous CO ₂ laser in dry conditions at 5 W for 10 s 6. Cleaning with continuous CO ₂ laser in wet conditions (saline) at 5 W for 10 s
Kreisler et al ³² (2005)	In vitro	SAE surface titanium platelets	1. Er:YAG laser 2. Air powder abrasive with sodium bicarbonate

Evaluation method	Results
SEM	Slight changes in the surface topography, rounding of angles and edges of the plasma spray coating, and occasional surface pitting
SEM	No perceptible difference regarding surface integrity
SEM	Air powder abrasive largely obliterated the marks caused by milling and surface pitting; no roughening of the surface
SEM and EDS	Machining marks were completely removed by the Prophy Jet and partially removed by the Microprophy; both appeared smoother. A noncrystalline deposit was observed on the surface of the abutment cylinder exposed to the Microprophy, which was revealed to be sodium.
SEM and optical microscope	5-s air powder abrasive treatment rounded many of the sharp edges; 50-s caused further smoothing of the machined grooves
SEM and optical microscope laser profilometer analysis	Air powder abrasive (2 s in min and max) increased the roughness
SEM and confocal laser scanning microscope	All instruments caused surface alterations except the plastic curet
SEM	A single air abrasive treatment modified the exposed surfaces. The threaded neck surface of a machined group was least affected, whereas the body was the most altered. In the plasma-sprayed group surface, change was little. In all specimens, 5-s exposure did not induce deep changes in the surfaces, 15-s exposure modified all the specimen surfaces.
SEM	After 5-s exposure: slight rounding of the previously irregular edges of the metal tags After 20 s: the edges became even more rounded but no significant surface alteration was produced by the air powder abrasive system
SEM; optical laser profilometry	Cavitron jet airpolishing system left the implant surfaces unchanged; no visible change to the implant surfaces
SEM	Surface damage: air powder abrasive, chlorhexidine, and curettage with a plastic instrument caused little or no damage
SEM and x-ray induced photoelectron spectroscopy	Alteration of the surface topography, numerous craters (about 10 µm in diameter) were formed; powder particles were seen on the surface
SEM	Surface properties. Air powder abrasive: microscopically visible changes, smoother surface Er:YAG laser: no change

Table 2 Studies Evaluating the Surface Change of Titanium after Air Powder Abrasive Treatment (cont.)

Study (y)	Type	Specimen type (no.)	Treatment method
Ramaglia et al ³¹ (2006)	In vitro	7 HA-, 7 TPS-coated implants	1. Stainless steel curette 2. Plastic curette 3. Ultrasonic scaler tip 4. Air powder abrasive
Koller et al ³³ (2007)	In vitro	30 machined titanium disks	Grit blasting with bioactive glass
Schwarz et al ²⁰ (2009)	In vitro	160 SAE surface titanium disks; 48-hour biofilm	Air powder abrasive with amino acid glycine (three different types) or sodium bicarbonate (one type) powder; each sample received single as well as repeated treatment (20 s for both)

SEM = scanning electron microscopy; EDS = energy-dispersive x-ray spectroscopy; SAE = sandblasted acid-etched; HA = hydroxyapatite; TPS = titanium plasma spray.

Table 3 Studies Evaluating the Cell Response Toward the Air Powder Abrasive Treated Titanium Disks

Study (y)	Type	Specimen type (no.)	Treatment method
Parham et al ¹⁷ (1989)	In vitro	28 plasma-sprayed implants	1. Air powder abrasive with sodium bicarbonate 2. Sterile water treated
Augthun et al ¹⁹ (1998)	In vitro	6 plasma-sprayed; 6 hydroxyapatite-coated implants; 6 smooth titanium surface screws	1. Plastic curette 2. Metal curette 3. Diamond polishing device 4. Ultrasonic scaler 5. Air-powder-water spray with sodium hydrocarbonate solution 6. Chlorhexidine 0.1% solution rinse
Shibli et al ³⁵ (2003)	In vitro	26 sterile abutments	1. Prophy Jet with sodium bicarbonate for 30 s
Kreisler et al ³² (2005)	In vitro	SAE surface titanium platelets	1. Er:YAG laser 2. Air powder abrasive with sodium bicarbonate
Schwarz et al ²⁰ (2009)	In vitro	SAE surface titanium discs	1. Air powder abrasive with sodium bicarbonate 2. Air powder abrasive with amino acid glycine (distance: 1 mm to 2 mm; angle: 30 to 90 degrees) 3. Control: noncontaminated, nontreated

SAE = sandblasted acid-etched.

Cell Response

Five in vitro studies evaluated the cell response toward air powder-treated titanium by cell attachment and viability tests^{17,19,20,32,35} (Table 3). Four studies applied air powder-abrasive treatment on contaminated specimens and one study applied air powder-abrasive treatment directly on sterile titanium abutments.

Cell attachment tests showed that the number of attached cells on the air powder abrasive-treated specimens is slightly lower but not significantly different than sterile, untreated control specimens or water treated controls.^{18,19,32} However, others^{20,35} reported a significant decrease in the number of cells attached and lower mitochondrial activity.

The cell morphology was reported to be unaffected³⁵ and uniform attachment was observed on the disks.^{18,19}

Another parameter evaluated was cell proliferation and it was reported to be higher in the air powder abrasive-treated group compared with the laser-treated group.³²

Cell activity was compared between disks that were treated by air powder abrasive treatment with sodium bicarbonate and amino acid glycine powder.²⁰ Both groups showed significantly lower activity than sterile discs. However, sodium carbonate resulted in significantly higher values than amino acid glycine.

According to these results, cell response to air powder abrasive-treated disks decreased compared with sterile non-treated disks and was influenced by the type of powder used. However, the results did demonstrate sufficient levels of cell attachment and cell viability.

Reosseointegration

Two animal studies reported reosseointegration amounts following peri-implantitis therapy with air powder abrasive treatment^{36,37} (Table 4). In one study, 64 implants were placed in eight monkeys and ligature induced peri-implantitis was created.³⁶ Afterwards, implants were treated with different decontamination

Evaluation method	Results
SEM and profilometry	All methods showed changes related to the implant coating material; coating removal and decreasing of surface roughness; air powder abrasive and plastic curette induce less implant surface alterations
SEM residual abrasive	The roughness attained compares favorably with currently used implant designs Bioactive glass was distributed across the titanium surface and retained within fissures and roughened surface features
SEM	Surface morphology. Sodium bicarbonate powder: obvious alteration of the specific surface morphology, irregular grooves, and pits appeared to be unchanged, the sharp-edged elevations were markedly flattened Aminoacidglycine: did not result in specific surface alterations

Results
The mean numbers of attached fibroblasts was not statistically significant between test and control groups; uniform attachment over the entire implant surface
Percentage of vital cells was nearly same as control; good cell spreading was observed; mostly vital cells were found on implants sprayed with the air powder abrasive
Cell morphology was not affected by air powder abrasive treatment (no significant difference); number of cells was significantly higher in control group than test group
Cell growth was not significantly different than sterile specimens for both laser- and air powder abrasive-treated specimens; cell proliferation on air powder abrasive group was the highest
Mitochondrial activity is significantly higher in control group followed by sodium bicarbonate, which is significantly higher than amino acid glycine

methods with open surgical debridement. Among four different treatments, one group was treated with air powder abrasive and another with air powder abrasive plus citric acid. All groups showed almost complete bone fill, whereas the reosseointegration (proportion of the implant "surface" within defect covered by regenerated bone) was on average 39% to 46% for all groups. Reosseointegration was not dependent upon surface treatment.

A similar study was done with six dogs and 60 implants.³⁷ One group was treated with air powder abrasive, a second with carbon dioxide laser, and a third group with a combination of these two treatments. During surgery, one fourth of the implants received membranes. The results were evaluated with radiographs and histologic sections. The mean depth of the defects was 1.70 mm. According to radiologic results, bone fill was smallest in the air powder abrasive therapy group and larger in the laser and laser plus air powder abrasive groups. The mean bone gain on

radiographs was 0.48 mm for air abrasive treatment, 1.20 mm for laser treatment, and 0.70 mm for combination treatment. However, the histometric analyses of the histologic sections of the same samples showed no statistical difference between groups. The histometry mean bone gain in the air powder abrasive treatment group was 0.64 mm; in the laser group, 0.62 mm; and in the combination treatment group, 0.75 mm. More preferable results occurred with membrane-treated implants and some reosseointegration was observed in all groups.

According to these two studies, air powder abrasive treatment does not produce any additional beneficial or detrimental effects on reosseointegration. However, not enough studies exist to make a definitive conclusion on this subject.

Clinical Outcome

Air powder abrasive treatment can be employed in peri-implantitis therapy either with open surgical

Table 4 Studies Evaluating Reosseointegration Following Air Powder Abrasive Treatment

Study (y)	Implant no. and type	Test groups
Deppe et al ³⁷ (2001)	6 dogs; 60 TPS implants	Group 1: air powder abrasive Group 2: CO ₂ laser Group 3: Prophy Jet and CO ₂ laser; each group consisted of four hemimandibles, three received one nonresorbable membrane, whereas the fourth did not
Schou et al ³⁶ (2003)	8 monkeys; 64 TPS implants	Group 1: air powder abrasive unit plus citric acid Group 2: air powder abrasive unit Group 3: gauze soaked in saline plus citric acid Group 4: gauze soaked alternately in chlorhexidine and saline All groups: autogenous bone and ePTFE membrane Antibiotic: systemic metronidazole, systemic ampicilin

TPS = titanium plasma spray.

Table 5 Studies Evaluating the Clinical Response Following the Air Powder Abrasive Treatment

Study (y)	No. of implants	Decontamination method
Duarte et al ³⁹ (2009)	10 healthy control; 10 mucositis; 20 peri-implantitis	Mucositis group: mechanical debridement with air powder abrasive and resin curettes Peri-implantitis group: open surgical debridement using air powder abrasive and resin curettes
de Mendonca et al ⁴⁰ (2009)	10 patients; 10 implants	Flap elevation plus resin curettes plus air powder abrasive with sodium bicarbonate
Maximo et al ⁴¹ (2009)	35 subjects: 10 healthy; 12 mucositis; 13 peri-implantitis Implant type: Brānemark system	Peri-implantitis treatment: flap elevation plus Teflon curettes plus air abrasive sodium carbonate air powder
Renvert et al ³⁸ (2011)	42 subjects; 100 implants (70 machined; 30 medium rough)	No surgical operation: Group 1: air powder abrasive device nozzle was placed in the pocket, used for approximately 15 s Group 2: Er:YAG laser at an energy level of 100 mJ/pulse and 10 Hz (12.7 J/cm ²)

debridement or subgingivally without raising the flap. Four studies on air powder abrasive treatment with surgery were found in the literature^{38–41} (Table 5). One randomized clinical trial compared Er:YAG laser and air powder abrasive in noninvasive peri-implantitis treatment.³⁸ Microbiological results⁴¹ and clinical outcome³⁹ were reported in two articles. Three case series^{39–41} reported the outcome of open surgical treatment with air

powder abrasive treatment. All case series reported significant improvement in all clinical parameters such as marginal bleeding, bleeding on probing, suppuration, and probing depth after both 3 and 12 months.^{39–41} The studies that used air powder abrasive treatment nonsurgically, without raising the flap, reported limited improvement. One study³⁸ reported a slight reduction in probing pocket depth, frequency of suppuration, and

Observation period	Evaluation method	Results
4 mo	Histologic	Radiology: laser groups showed significantly more bone-to-implant apposition and laser alone was significantly better than laser combo. All measurements considered entire defects. Histology: without membranes; group 1 demonstrated minimal new bone regeneration; groups 2 and 3 showed large amounts of rapidly formed bone; all groups showed some reosseointegration. With membranes: better results in all groups. Histometric evaluation: no statistical difference between groups for bone gain.
6 mo	Histologic and radiographic results	Almost complete bone regeneration and considerable reosseointegration were obtained irrespective of the method applied; a mean bone-to-implant contact of 39% to 46% was observed within the defects

Observation period	Evaluation method	Results
3 mo	Clinical observation: interleukin (IL)-4, -10, -12 TNF- α osteoprotegerin and peri-implant crevicular fluid were measured by enzyme-linked immunosorbent assay	Significant improvement in all clinical parameters for mucositis and peri-implantitis. TNF- α levels were significantly reduced achieving the same level as the healthy group at 3 mo.
3 and 12 mo	Clinical parameters and TNF- α levels	Clinical parameters were significantly improved at 3 and 12 months. TNF- α levels decreased from 3 to 12 mo after therapy. Significantly positive correlations were found between TNF- α and bleeding on probing and probing depth.
3 mo	Clinical parameters and microbiologic counts	Clinical parameters were reduced significantly; microbiological counts also decreased significantly after treatment
6 mo	Clinical and radiographic assessment	Both methods resulted in a reduction of probing pocket depth, the frequency of suppuration, and bleeding at implants but there was no significant difference between the groups; overall clinical improvement was limited. Alveolar bone change failed to demonstrate differences between baseline and 6 mo.

bleeding but did not reach the healthy level and another²² reported that clinical improvements were limited.

It can be concluded that air powder abrasive cleaning as an implant surface cleaning method may result in improved clinical parameters as long as it is used in combination with surgical treatment. However, noninvasive use of air powder abrasive treatment does not show significant improvement.

DISCUSSION

Considering air powder abrasive treatment as an implant surface treatment method, there are several aspects to be evaluated. Safety is as important as efficiency since the method will be used subgingivally and on the specific surface of a titanium implant. Because of this fact, several in vitro studies were performed

before the method was clinically applied. Although these in vitro studies provide a general idea on the method, they should be supported by future in vivo studies.

All in vitro studies on the cleaning efficiency of air powder abrasive treatment reported consistent results. Although the studies varied in design (different implant types, endotoxin contamination or intraoral keeping, SEM observation or light microscope, staining or no staining), the cleaning efficiency of the method always resulted in high values ranging between 85% and 100%.^{16–20} However, the only clinical study on this subject reports low bacterial reduction at 2 months and no reduction at 6 months.²² The reason that the in vivo result is not in agreement with in vitro studies could be due to the different application methods. In this randomized clinical trial, air powder abrasive was applied without raising the flap. This makes it difficult or perhaps impossible for the powder to reach the implant surface. Additionally, nonsurgical therapy on peri-implantitis lesions was already concluded to be ineffective.¹ Therefore, this study may not be enough to draw conclusions on the efficiency of air powder abrasive therapy since the unsuccessful reduction of bacterial counts could be due to nonsurgical therapy.

Another concern about air powder abrasive treatment is the possible damage that it may cause on the implant surface. According to the in vitro studies, slight to medium change is observed on the treated surfaces.^{19,20,25,28,29,31,32,34} However, there is no standard evaluation method to report the level of damage. The results have to be reported in a subjective way. This makes it difficult to compare studies and draw conclusions. However, descriptions of the damage are similar in all studies reporting small craters, rounding, or the removal of sharp edges. Since no dramatically big changes were reported, the method could be considered safe in this respect.

The effect of the treated surface on reosseointegration is evaluated by cell response in a number of studies.^{18–20,32,35} The results show that cell response changes depending on application time and powder type.²⁰ It can be concluded that the residual powder particles on the titanium surface may influence the cell response. Thus, the cell response may be improved by using biocompatible powders.

Reosseointegration following air powder abrasive treatment was tested in animal studies. The amount of reosseointegration observed was not significantly different than other cleaning methods.^{22,37} However, clinicians need to keep in mind that reosseointegration is very difficult to achieve. In order to have a good level of reosseointegration, the original peri-implant condition should be restored.⁴² Because contamination of the implant surface results in a lowering of the surface

free energy,⁴³ the chance of bone growing into contact with the titanium surface is low.⁴⁴ No treatment method has been described in the literature to be predictable in achieving sufficient reosseointegration.

Although there are hardly any studies reporting on the clinical outcome of air powder abrasive treatment, available studies report improved clinical parameters following the treatment.^{39–41} However, the method should be applied directly on the implant surface after raising the flap. Nonsurgical treatment does not result in significant improvements.³⁸ At this point, the complications that can be caused by this method need to be considered. Abrasion in the soft tissue and air emphysema may be seen following application. Air emphysema is reported following tooth cleaning or implant maintenance with air powder abrasive treatment with sodium bicarbonate.^{45–48} However, in other studies,^{14,15} amino acid glycine, a softer powder specially developed for subgingival applications, was used on 74 patients subgingivally with a lower air pressure. No case of air emphysema was seen in these studies.

CONCLUSION

Air powder abrasive treatment gives promising results. The method should be improved for it to be used safely on implant surfaces. If the modified air powder abrasive treatment is gentle enough not to harm the bone and soft tissue, as well as efficient enough to remove all deposits, the amount of reosseointegration following treatment could be increased.

ACKNOWLEDGMENTS

The authors reported no conflicts of interest related to this study.

REFERENCES

1. Lindhe J, Meyle J, Group D of European Workshop on Periodontology. Peri-implant diseases. Consensus Report of the Sixth European Workshop on Periodontology. *J Clin Periodontol* 2008;35(suppl):282–285.
2. Mombelli A, Lang NP. The diagnosis and treatment of peri-implantitis. *Periodontol* 2000 1998;17:63–76.
3. Quirynen M, Vogels R, Peeters W, van Steenberghe D, Naert I, Haffajee A. Dynamics of initial subgingival colonization of “pristine” peri-implant pockets. *Clin Oral Implants Res* 2006;17:25–37.
4. van Winkelhoff AJ, Goené RJ, Benschop C, Folmer T. Early colonization of dental implants by putative periodontal pathogens in partially edentulous patients. *Clin Oral Implants Res* 2000;11:511–520.
5. Salinas T, Eckert S. Implant-supported single crowns predictably survive to five years with limited complications. *J Evid Based Dent Pract* 2010;10:56–57.
6. Aglietta M, Siciliano VI, Zwahlen M, et al. A systematic review of the survival and complication rates of implant supported fixed dental prostheses with cantilever extensions after an observation period of at least 5 years. *Clin Oral Implants Res* 2009;20:441–451.

7. Triplett RG, Andrews JA, Hallmon WW. Management of peri-implantitis. *Oral Maxillofac Surg Clin North Am* 2003;15:129–138.
8. Renvert S, Polyzois I, Maguire R. Re-osseointegration on previously contaminated surfaces: A systematic review. *Clin Oral Implants Res* 2009;20:216–227.
9. Wetzel AC, Vlassis J, Caffesse RG, Hämerle CH, Lang NP. Attempts to obtain re-osseointegration following experimental peri-implantitis in dogs. *Clin Oral Implants Res* 1999;10:111–119.
10. Romanos G, Ko HH, Froum S, Tarnow D. The use of CO(2) laser in the treatment of peri-implantitis. *Photomed Laser Surg* 2009;27:381–386.
11. Sawase T, Jimbo R, Wennerberg A, Suketa N, Tanaka Y, Atsuta M. A novel characteristic of porous titanium oxide implants. *Clin Oral Implants Res* 2007;18:680–685.
12. Suzuki T, Hori N, Att W, et al. Ultraviolet treatment overcomes time-related degrading bioactivity of titanium. *Tissue Eng Part A* 2009;15:3679–3688.
13. Aita H, Att W, Ueno T, et al. Ultraviolet light-mediated photofunctionalization of titanium to promote human mesenchymal stem cell migration, attachment, proliferation and differentiation. *Acta Biomater* 2009;5:3247–3257.
14. Moëne R, Décailliet F, Andersen E, Mombelli A. Subgingival plaque removal using a new air-polishing device. *J Periodontol* 2010;81:79–88.
15. Petersilka GJ, Tunkel J, Barakos K, Heinecke A, Häberlein I, Flemmig TF. (2003) Subgingival plaque removal at interdental sites using a low-abrasive air polishing powder. *J Periodontol* 2003;74:307–311.
16. Zablotsky MH, Diedrich DL, Meffert RM. Detoxification of endotoxin-contaminated titanium and hydroxyapatite-coated surfaces utilizing various chemotherapeutic and mechanical modalities. *Implant Dent* 1992;1:154–158.
17. Parham PL Jr, Cobb CM, French AA, Love JW, Drisko CL, Kilroy WJ. Effects of an air-powder abrasive system on plasma-sprayed titanium implant surfaces: An in vitro evaluation. *J Oral Implantol* 1989;15:78–86.
18. Dennison DK, Huerzeler MB, Quinones C, Caffesse RG. Contaminated implant surfaces: An in vitro comparison of implant surface coating and treatment modalities for decontamination. *J Periodontol* 1994;65:942–948.
19. Augthun M, Tinschert J, Huber A. In vitro studies on the effect of cleaning methods on different implant surfaces. *J Periodontol* 1998;69:857–864.
20. Schwarz F, Ferrari D, Popovski K, Hartig B, Becker J. Influence of different air-abrasive powders on cell viability at biologically contaminated titanium dental implants surfaces. *J Biomed Mater Res B Appl Biomater* 2009;88:83–91.
21. Mouhyi J, Sennerby L, Pireaux JJ, Dourou N, Nammour S, Van Reck J. An XPS and SEM evaluation of six chemical and physical techniques for cleaning of contaminated titanium implants. *Clin Oral Implants Res* 1998;9:185–194.
22. Persson GR, Roos Jansåker AM, Lindahl C, Renvert S. Microbiologic results after non surgical erbium-doped:yttrium, aluminum, and garnet laser or air-abrasive treatment of peri-implantitis: A randomized clinical trial. *J Periodontol* 2011;82:1267–1278.
23. Meschenmoser A, d'Hoedt B, Meyle J, et al. Effects of various hygiene procedures on the surface characteristics of titanium abutments. *J Periodontol* 1996;67:229–235.
24. Mengel R, Buns CE, Mengel C, Flores-de-Jacoby L. An in vitro study of the treatment of implant surfaces with different instruments. *Int J Oral Maxillofac Implants* 1998;13:91–96.
25. Homiak AW, Cook PA, DeBoer J. Effect of hygiene instrumentation on titanium abutments: A scanning electron microscopy study. *J Prosthet Dent* 1992;67:364–369.
26. Koka S, Han J, Razzoog ME, Bloem TJ. The effects of two air-powder abrasive prophylaxis systems on the surface of machined titanium: A pilot study. *Implant Dent* 1992;1:259–265.
27. Brookshire FV, Nagy WW, Dhur VB, Ziebert GJ, Chada S. The qualitative effects of various types of hygiene instrumentation on commercially pure titanium and titanium alloy implant abutments: An in vitro and scanning electron microscope study. *J Prosthet Dent* 1997;78:286–294.
28. McCollum J, O'Neal RB, Brennan WA, Van Dyke TE, Horner JA. The effect of titanium implant abutment surface irregularities on plaque accumulation in vivo. *J Periodontol* 1992;63:802–805.
29. Barnes CM, Fleming LS, Mueninghoff LA. SEM evaluation of the in-vitro effects of an air-abrasive system on various implant surfaces. *Int J Oral Maxillofac Implants* 1991;6:463–469.
30. Matarasso S, Quaremba G, Coraggio F, Vaia E, Cafiero C, Lang NP. Maintenance of implants: An in vitro study of titanium implant surface modifications subsequent to the application of different prophylaxis procedures. *Clin Oral Implants Res* 1996;7:64–72.
31. Ramaglia L, di Lauro AE, Morgese F, Squillace A. Profilometric and standard error of the mean analysis of rough implant surfaces treated with different instrumentations. *Implant Dent* 2006;15:77–82.
32. Kreisler M, Kohnen W, Christoffers AB, et al. In vitro evaluation of the biocompatibility of contaminated implant surfaces treated with an Er:YAG laser and an air powder system. *Clin Oral Implants Res* 2005;16:36–43.
33. Koller G, Cook RJ, Thompson ID, Watson TF, Di Silvio L. Surface modification of titanium implants using bioactive glasses with air abrasion technologies. *J Mater Sci Mater Med* 2007;18:2291–2296.
34. Chairay JP, Boulekabache H, Jean A, Soyer A, Bouchard P. Scanning electron microscopic evaluation of the effects of an air-abrasive system on dental implants: A comparative in vitro study between machined and plasma-sprayed titanium surfaces. *J Periodontol* 1997;68:1215–1222.
35. Shibli JA, Silverio KG, Martins MC, Marcantonio júnior E, Rossa júnior C. Effect of air-powder system on titanium surface on fibroblast adhesion and morphology. *Implant Dent* 2003;12:81–86.
36. Schou S, Holmstrup P, Jørgensen T, et al. Implant surface preparation in the surgical treatment of experimental peri-implantitis with autogenous bone graft and ePTFE membrane in cynomolgus monkeys. *Clin Oral Implants Res* 2003;14:412–422.
37. Deppe H, Horch HH, Henke J, Donath K. Per-implant care of ailing implants with the carbon dioxide laser. *Int J Oral Maxillofac Implants* 2001;16:659–667.
38. Renvert S, Lindahl C, Roos Jansåker AM, Persson GR. Treatment of peri-implantitis using an Er:YAG laser or an air-abrasive device: A randomized clinical trial. *J Clin Periodontol* 2011;38:65–73.
39. Duarte PM, de Mendonça AC, Máximo MB, Santos VR, Bastos MF, Nociti FH. Effect of anti-infective mechanical therapy on clinical parameters and cytokine levels in human peri-implant diseases. *J Periodontol* 2009;80:234–243.
40. de Mendonça AC, Santos VR, César-Neto JB, Duarte PM. Tumor necrosis factor-alpha levels after surgical anti-infective mechanical therapy for peri-implantitis: A 12-month follow-up. *J Periodontol* 2009;80:693–699.
41. Máximo MB, de Mendonça AC, Renata Santos V, Figueiredo LC, Feres M, Duarte PM. Short-term clinical and microbiological evaluations of peri-implant diseases before and after mechanical anti-infective therapies. *Clin Oral Implants Res* 2009;20:99–108.
42. Baron M, Haas R, Dörnbudak O, Watzek G. Experimentally induced peri-implantitis: A review of different treatment methods described in the literature. *Int J Oral Maxillofac Implants* 2000;15:533–544.
43. Bair RE, Meyer AE. Implant surface preparation. *Int J Oral Maxillofac Implants* 1988;3:9–20.
44. Kubies D, Himmlová L, Riedel T, et al. The interaction of osteoblasts with bone-implant materials: 1. The effect of physicochemical surface properties of implant materials. *Physiol Res* 2011;60:95–111.
45. Van de Velde E, Thielens P, Schautteet H, Vanclooster R. Subcutaneous emphysema of the oral floor during cleaning of a bridge fixed on an IMZ implant. Case report [in French]. *Rev Belge Med Dent* (1984) 1991;46:64–71.
46. Bergendal T, Forsgren L, Kvist S, Löwstedt E. The effect of an air-abrasive instrument on soft and hard tissues around osseointegrated implants. A case report. *Swed Dent J* 1990;14:219–223.
47. Finlayson RS, Stevens FD. Subcutaneous facial emphysema secondary to use of the Cavi-Jet. *J Periodontol* 1988;59:315–317.
48. Liebenberg WH, Crawford BJ. Subcutaneous, orbital, and mediastinal emphysema secondary to the use of an air-abrasive device. *Quintessence Int* 1997;28:31–38.

Biotribological Behavior of Two Retrieved Implant Abutment Screws after Long-Term Use In Vivo

Youssef S. Al Jabbari, BBS, MS, PhD¹/Raymond A. Fournelle, PhD²/
Spiros Zinelis, PhD³/Anthony M. Iacopino, DMD, PhD⁴

Purpose: To evaluate the effect of functional cyclic loading on two retrieved abutment screws used with single implant supporting cement-retained porcelain-fused-to-metal crowns by characterizing the structure, properties, and biotribologic behavior after long-term use in vivo. **Materials and Methods:** Two abutment screws were retrieved from the same patient and same implant at two different times. An external hex implant was used to replace a missing central incisor. A traumatic incident occurred 9 months after insertion and displaced the implant palatally by bending the screw. A second, similar incident occurred 31 months after insertion. In both cases, the abutment screws were retrieved and subjected to thorough nondestructive and destructive testing.

Results: Light and scanning electron microscopic examinations revealed very minimal surface deterioration of the thread profile for the first screw (in service for 9 months) and demonstrated advanced metal adhesive wear in the form of galling for the second screw (in service for 31 months). The galling led to moderate thinning of the thread profile. Both screws were composed of Au-based alloy, where the microstructure of the matrix consisted of homogeneous equiaxed fine grains with two different second phase particles. **Conclusion:** It appears that the occurrence of adhesive wear on abutment screws in the form of galling is highly related to the length of in-service time in the mouth. This biotribologic behavior was inevitable and considered to be a normal consequence of long-term use in vivo. Metallurgic analysis indicated that both screws were identical in terms of composition and microstructure. INT J ORAL MAXILLOFAC IMPLANTS 2012;27:1474–1480

Key words: abutment screw, adhesive wear, biotribological behavior, galling, retrieval analysis, thread wear

The treatment of partially edentulous patients with implants was originally adapted from the treatment of fully edentulous patients. Currently, this type of therapy is very common because of its predictability and high success rate.^{1,2} Clinical management of pa-

tients missing a single tooth utilizing an implant is now commonplace and arguably the treatment of choice if teeth adjacent to the edentulous space are caries free and periodontally sound.

A high survival rate was reported in a recent systematic review for implant-supported single crowns, and the survival rate after 5 years of function was 94.5%.³ This high survival rate may be compromised by biologic and mechanical complications involving implants and prosthetic components. Abutment screw loosening is considered an attributing and/or precipitating factor for screw and/or implant fracture.⁴ The incidence of abutment and/or prosthetic screw loosening was reported to be 12.7% for implant-supported single crowns while screw fracture was 0.35% (a rare complication).³ In cement-retained implant-supported single crowns, screw loosening may require only screw retightening (assuming provisional cement was utilized), while screw fracture may require more sophisticated and expensive intervention.⁵ It has been suggested that implant abutment screw loosening and/or fracture can be minimized by tightening the screw to the recommended torque value by the manufacturer.⁶ Proper torque will assure optimal preload delivery, thus, the correct clamping force will be achieved to hold the crown to the implant.^{7,8}

¹Dental Biomaterials Research and Development Chair, Assistant Professor, College of Dentistry, King Saud University, Riyadh, Saudi Arabia.

²Professor, Department of Mechanical and Industrial Engineering, School of Engineering, Marquette University, Milwaukee, Wisconsin, USA.

³Assistant Professor, Department of Dental Biomaterials, School of Dentistry, University of Athens, Athens, Greece; Dental Biomaterials Research and Development Chair, College of Dentistry, King Saud University, Riyadh, Saudi Arabia.

⁴Professor, Department of Restorative Dentistry, Faculty of Dentistry, University of Manitoba, Winnipeg, Manitoba, Canada.

Correspondence to: Dr Youssef S. Al Jabbari, Director, Dental Biomaterials Research and Development Chair, Department of Prosthetic Dental Sciences, College of Dentistry, King Saud University, PO Box 60169, Riyadh 11545, Saudi Arabia. Fax: +966 1 4679015. Email: yaljabbari@ksu.edu.sa

This article was presented at the 18th International Conference on Wear of Materials (WOM-2011), April 3–7, 2011, Philadelphia, Pennsylvania, USA, abstract no. 0614.

Screws may become loose and the preload value reduced as a result of (1) improper torque; (2) chewing patterns and/or loads; or (3) surface microroughness and/or asperities of the threads (settling effect or short-term relaxation).^{7,9} However, the exact mechanism of screw loosening is not fully understood, and therefore adequate design guidelines to avoid loosening are not yet available.¹⁰ It has been proposed that preload is not the only factor influencing the stability of two clamped joints.¹¹ In a recent *in vivo* retrieval analysis study performed on prosthetic retaining screws utilized with fixed-detachable hybrid prostheses, the importance of finding optimal preload has been questioned because, to date, there have been no long-term *in vivo* studies regarding optimal preload values. Additionally, there is a lack of evidence that screw loosening is solely a result of improper preload.⁵ The study introduced a phenomenon called "long-term relaxation of the implant screw" resulting from long-term use *in vivo*. The proposed phenomenon occurs as a result of continual adhesive wear between female/male threads until the wear reaches an advanced stage called metal galling. Galling will minimize the intimate contact of screw threads, thus minimizing the preload value.⁵ Galling has been defined as "a form of surface damage arising between sliding solids, distinguished by macroscopic, usually localized, roughening and creation of protrusions above the original surface. It often includes plastic flow, or materials transfer, or both".¹²

The aim of this study was to evaluate the effect of long-term use *in vivo* on two retrieved abutment screws utilized with cement-retained and implant-supported single porcelain-fused to-metal (PFM) crowns.

MATERIALS AND METHODS

Samples Collection

Two abutment screws (Fig 1) were retrieved from the same patient and same implant at two different times. The 21-year-old male patient was a skier and lost his maxillary right central incisor due to trauma. The missing incisor was replaced by utilizing a regular plate form (3.75 mm) machined implant with external hex from Nobel Biocare (formerly Bränemark). Additionally, a UCLA implant abutment was utilized to fabricate a custom abutment cast from a noble metal alloy. The final cement-retained and implant-supported PFM crown was delivered to the patient after achieving proper occlusion, adequate esthetics, and patient satisfaction. After 9 months of insertion, a traumatic incident occurred when the patient was skiing; the ski hit the PFM crown, displacing the crown palatally by bending the abutment screw. A very similar scenario occurred 31 months after insertion of a replacement PFM



Fig 1 The two retrieved abutment screws.

crown. In both instances, the cemented PFM crowns were sacrificed and the two abutment screws were retrieved. There had been no damage to either the custom abutment or the external hex of the implant. The retrieved abutment screws were ultrasonically cleaned and stored in small plastic vials containing methanol before they were subjected to thorough nondestructive and destructive testing. In this study, the first retrieved abutment screw (in service for 9 months) was designated screw no. 1 and the second retrieved abutment screw (in service for 31 months) was designated as screw no. 2.

Nondestructive Testing

For nondestructive testing, a low power stereomicroscope (MZS-TR Model, Meiji Techno) and a scanning electron microscope (SEM) (JEOL JSM 35, JEOL USA) were operated according to manufacturer instructions. The SEM was operated at 25 kV in the high vacuum mode using secondary electron imaging (SEI). Both stereomicroscope and SEM were used to observe thread wear occurrence as a result of long-term use *in vivo*. Additionally, they were used to detect any fracture occurrence (fatigue) resulting from long-term use *in vivo* and/or trauma. Both abutment screws were comprehensively examined under SEM by rotating them 180 degrees between observations.

Destructive Testing

For destructive testing, metallographic specimens of the tested abutment screws were fabricated according to previously suggested protocol.¹³ The screws were positioned on their sides in the middle of plastic mould mounting cups (Buehler Sample-Kup; Buehler). Next, a properly mixed epoxicure resin (Buehler) was poured into the mould and allowed to set for 8 hours

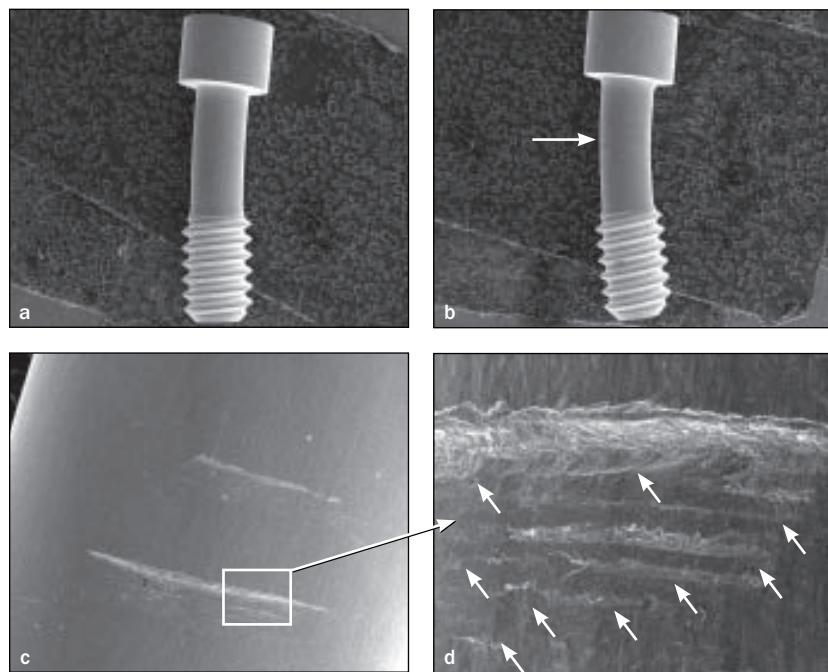


Fig 2 SEM micrographs (a) and (b) of the two retrieved abutment screws showing the bend located mainly at the shank area. The severity of the bend was greater for screw no. 2, as shown in (c). Note the severe plastic deformation of the shank area on screw no. 2 appearing as two short white lines (arrow). (c) and (d) are higher magnification of the shank area for screw no. 2 showing severe form of plastic deformation as a result of a significant impact load value with no crack formation. Arrows in (d) show smaller plastic deformation.

in a desiccator, partially evacuated to assure air bubble removal. The resin blocks with the embedded screws were then sectioned and ground with silicon carbide abrasive (80 to 600 grit) until the middle of the longitudinal section of the screws was reached. The final polishing and etching of the exposed metal surface of the screws was achieved with polishing compounds (9 to 0.25 μm) and immersion of the specimens in a freshly prepared solution of 45% hydrochloric acid, 25% nitric acid, and 30% tap water for 15 seconds.

To qualitatively determine the overall phase and chemical composition of the retrieved abutment screws, the prepared and etched specimens were examined using a light microscope (MPE3, Olympus Optical) and SEM/energy-dispersive x-ray spectroscopy (EDS) microanalysis. The EDS microanalysis was performed on the SEM using an x-ray analyzer (Tracor Northern Series II, Tracor Northern) with a Li drifted Si detector and a Be window. Spectra were obtained with the microscope operated at 25 kV with dead time being held to less than 20%. Spectra characteristics of the overall microstructures were obtained from area scans at $\times 100$. Spectra characteristics of the matrix phase were obtained with area scans, while spectra from second phase particles were obtained by spot analysis. Additionally, overall mean Vickers hardness (VH) of the screws no. 1 and 2 was determined with a microhardness tester (Buehler Micromet 5101, Buehler) at a load of 500 gm and an application time of 10 seconds. Hardness was determined for each screw at five measurements involving multiple microstructural grains for each depth. To identify any

statistically significant differences between mean values of the VH for the two abutment screws, a Student *t* test was performed at $P < .05$.

RESULTS

Light and SEM Observations

Light and SEM of screws no. 1 and 2 demonstrated significant screw bending located mainly on the shank area. The bend on screw no. 2 was more severe than screw no. 1, indicating a greater impact force for the second traumatic incident (Figs 2a and 2b). Under low SEM magnification, two small white lines were observed on the shank area for screw no. 2. Higher SEM magnification, as shown in Figs 2c and 2d, indicated that those white lines, as well as multiple smaller lines, were due to severe inhomogeneous plastic deformation with no sign of cracking and/or fracture.

SEM revealed minimal surface metal wear and/or thread profile deterioration for screw no. 1. Under higher magnifications of the threaded portion of screw no. 1, the crest of the threads, upper and lower flanks, and root of the threads were almost intact. This was true for the upper, middle, and bottom parts of the threaded portion (Fig 3). According to a previously proposed classification for thread wear or deterioration utilizing the SEM,⁵ screw no. 2 demonstrated moderate thread profile deterioration as a result of adhesive wear. The advanced adhesive wear in the form of galling involved upper and lower flanks of the entire

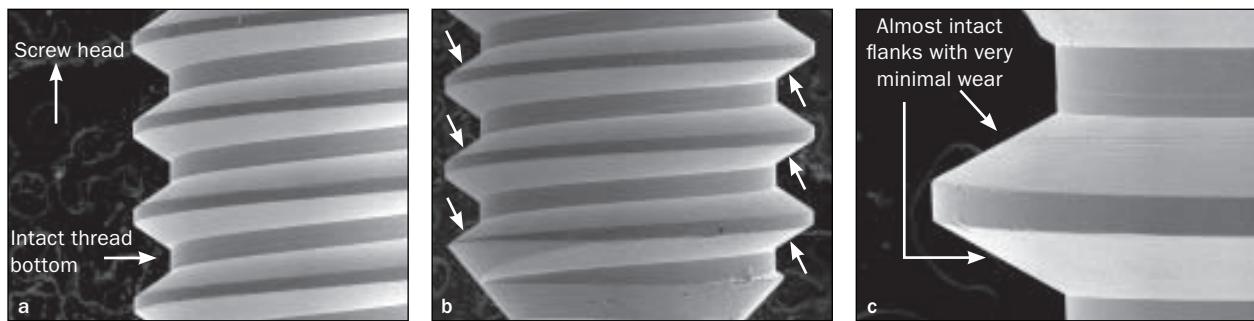
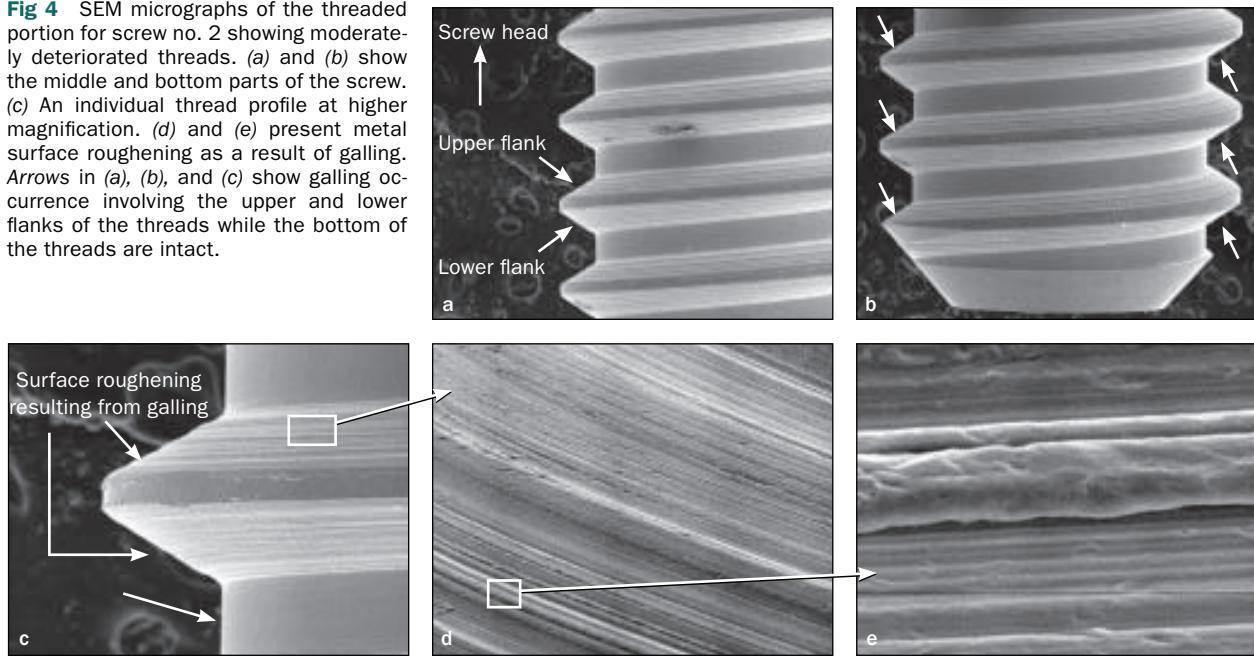


Fig 3 SEM micrographs of the threaded portion for screw no. 1 showing no significant adhesive wear occurrence or thread profile deterioration. (a) and (b) show the middle and bottom parts of the screw. (c) An individual thread profile at higher magnification. Arrows in (a) and (b) show no galling occurrence involving the upper and lower flanks of the threads.

Fig 4 SEM micrographs of the threaded portion for screw no. 2 showing moderately deteriorated threads. (a) and (b) show the middle and bottom parts of the screw. (c) An individual thread profile at higher magnification. (d) and (e) present metal surface roughening as a result of galling. Arrows in (a), (b), and (c) show galling occurrence involving the upper and lower flanks of the threads while the bottom of the threads are intact.



threaded portion of the screw (Fig 4). At higher SEM magnifications, the galled metal surface of the screw was associated with surface roughening (Figs 4d and 4e). For both the no. 1 and 2 screws, the bottom portion and related threads had no plastic deformation indicating great passivity of fit which is expected for a single-implant supported restoration.

Metallographic Observations Before and After Etching

After polishing but before etching, the longitudinal sections of both screws revealed second phase particles parallel to the long axis of the screws as shown in Fig 5a. More second phase particles were observed in screw no. 2 than in screw no. 1. At high magnification with bright field illumination, observation of the etched longitudinal surface of the screws showed that the microstructure exhibited, in addition to the second

phase observed in the as-polished specimens, a matrix of equiaxed grains with another second phase aligned parallel to the axis of the screws (Figs 5b through 5d). This provided the screws with a "textured" appearance at low magnification (Fig 5b). The microstructure suggests that the screws were machined from wire that had been cold or hot drawn and subsequently annealed. The appearance of undistorted elongated second phase particles in thread areas with no deformations indicates that the threads of the two abutment screws were formed by machining "machine threading."

EDS Microanalysis and Microhardness Measurements

After etching, three EDS spectra were obtained from three different regions (the matrix and both second phases). The obtained spectra were essentially the same for both abutment screws in terms of peaks

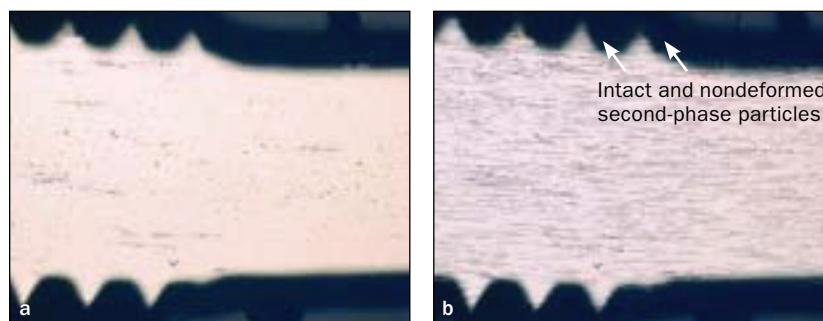


Fig 5 High- and low-magnification light micrographs of the longitudinal section for screw no. 2. (a) Before etching revealing second-phase particles parallel to long axis of the screw. (b), (c), and (d) After etching revealing “textured” appearance of the screw at low magnification and a matrix of equiaxed grains with two different second-phase particles aligned parallel to the long axis of the screw at higher magnification.

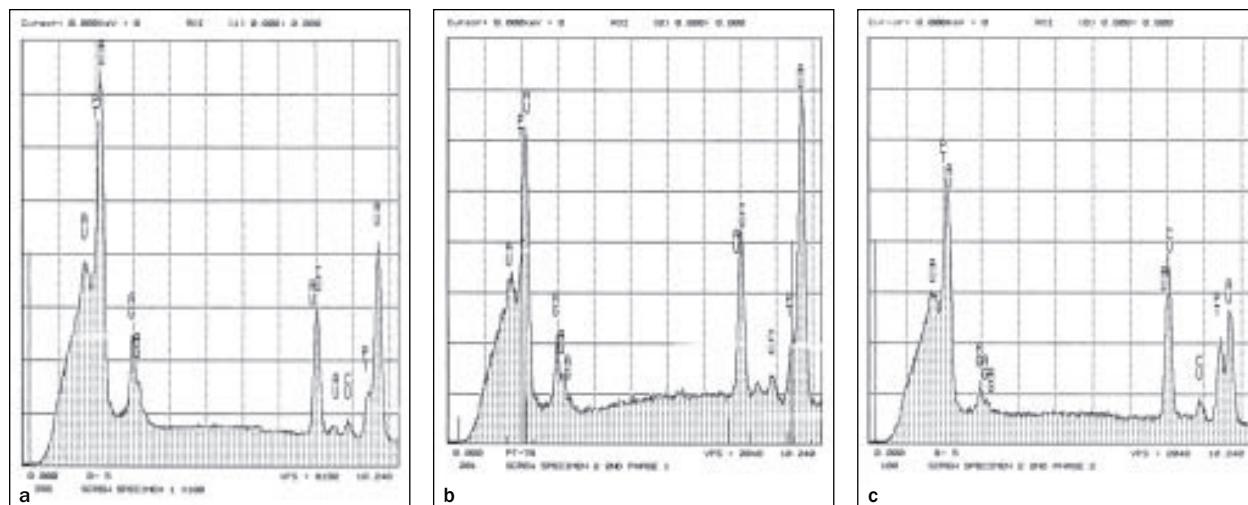
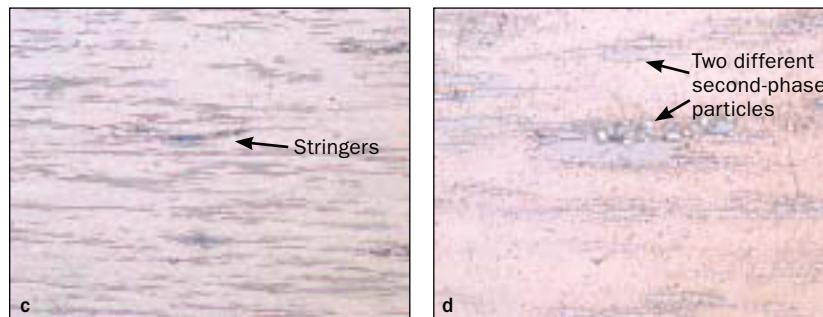


Fig 6 (a) EDS spectrum for the overall structure of abutment screw no. 1. (b) EDS spectrum for second-phase particles observed in the as-polished specimen before etching and identified as stringers. (c) EDS spectrum for second-phase particles observed after etching, which appeared as gray particles.

present and their intensities. The matrix spectra were similar to the overall spectrum shown in Fig 6a. Both screws were mainly composed of Au with Pt, Cu, and Ag. The spectra shown in Fig 6b were obtained from the second phase and identified as stringers in the as-polished specimen before etching. The spectra indicate that the screw alloys are alloys of Au, Ag, Cu, and Pt with Au and Ag being the major constituents. The spectrum of the second phase, which was revealed by etching as a gray phase, was richer in Pt and Cu (Fig 6c). The overall mean VH values of abutment screws no. 1 and 2 were 282 ± 7.3 and 292 ± 7.8 , respectively, with no statistically significant difference ($P > .05$).

DISCUSSION

This failure analysis study is the first *in vivo* study reporting biotribologic behavior for two implant abutment screws used with a single-implant supporting cement-retained PFM crown. Tribology has been defined as the science concerned with the design, friction, lubrication, and wear of contacting surfaces that move in relative to one another.¹⁴ Biotribology represents all aspects of tribology in relation to biologic systems.¹⁴ In the present study, the observed advanced adhesive wear in the form of galling is comparable to previously reported adhesive wear involving prosthetic retaining screws used

with fixed removable hybrid prostheses.⁵ However, the previously reported galling, which involved prosthetic screws, was observed on upper and lower flanks and on the bottom of the screw threads, whereas in this study, the galling involved only the upper and lower flanks of each thread of abutment screw no. 2, keeping the bottom of the threads intact. This could be related to the magnitude of the applied occlusal forces. In hybrid prostheses, greater force is expected because of the existence of posterior occlusion and posterior cantilever.

The occurrence of galling is normally considered an undesired tribologic behavior resulting from an adhesive junction between two metal surfaces combined with a sliding motion, leading to local plastic deformation and ductile rupture at the contact region.¹⁵ Galling begins with a pure sliding motion between two mating metal surfaces, and as sliding continues, wear marks develop on the sliding surfaces due to local adhesive wear; further sliding will lead to progressively coarser wear marks and roughening.^{16,17} This may explain the mechanism of roughening observed on Figs 3d and 3e.

Despite the sample size in the present study being very low, the analysis provided some useful and significant information. Although both screws were utilized on the same patient and same implant by the same treating prosthodontist and manufactured from the same materials, they behaved differently intraorally. It appears that the adhesive wear occurrence on abutment screws was highly related to the in-service time period. Abutment screws demonstrated no sign of wear and an intact thread profile within the first year in service. However, advanced stage adhesive wear (galling) with moderately deteriorated thread profile occurred after 2.5 years in service. This can be considered an alarming finding for clinicians because adverse effects of adhesive wear may range from thread disengagement and preload loss to fatigue failure.^{5,13} Compared to previous findings,⁵ it can be suggested that wear of abutment screws in the single implant and crown is slow and gradual but advances with time. This may explain the previously reported high rate of screw loosening (12.7%) in single-implant supported crowns.³ Additionally, this may explain and reinforce previous opinions regarding gradual preload loss for screws and fasteners under tilted cyclic loading.^{10,18–21} A previous study suggested that the failure of a clamped joint occurs initially by subjecting the joint to an external repeated load that gradually leads to “preload erosion,” and with additional tilted loading, slippage between the threads will occur leading to preload reduction.¹⁰ In the present study, the observed galling that was proportional to the period of in-service time can be an assumed trigger and/or influential guide to “preload erosion.”

Although it is important to confirm the proposed biotribologic behavior with a future study involving a larger sample size, retorquing could be recommended for an abutment screw that has been in service for 2 years in order to maintain the original delivered preload at the time of prosthesis insertion. This reinforces a previously suggested conclusion that, instead of finding an optimal preload, it is more important to maintain the original preload value.⁵ It is important to clarify that, in the present study, both screws were torqued according to manufacturer instructions utilizing the manufacturer’s torquing wrench.

There may be questions related to whether internal (female) threads of the implant fixture develop some adhesive wear and galling. At present, there is no definitive answer. There are many factors related to wear and galling, including type of load, contact area, hardness of mating metal, finish, coefficient of friction, and metal and/or alloy microstructure.^{11,22–28} It is anticipated that galling occurrence on the internal threads of the implant fixture may be minimal since it has been previously proposed that surface wear is inversely proportional to hardness.^{11,25} Thus, harder surfaces and/or materials will wear softer surfaces and/or materials and, as determined in this study, the retrieved abutment screws were made from gold-based alloys providing reduced hardness compared to the internal threads of the implant which were made from titanium alloys. However, other studies found no obvious relationship between wear and hardness; harder materials did not resist wear and galling.^{26,28} For example, the coefficient of friction between mating metals was found to be related to wear rate and galling occurrence while, at the same time, the coefficient of friction had no relationship to hardness.

In the present study, the failure of the abutment screws was distortion failure rather than fracture. Normally, fracture is associated with material separation while the abutment screws had geometric changes that prevented them from functioning properly. The geometric-induced failure resulted from stress induced material yielding. Since the beginning of the implant era, the abutment and/or prosthetic screws are designed to be the weakest link within the entire implant system and prosthetic component apparatus.^{29,30} The present study confirmed how important this concept is and manufacturers and clinicians should continue making implant screws the weakest link in the design of fail-safe mechanisms. This is more important when a prosthesis is subjected to an overload or a severe impact load. In this study, the patient received his third PFM crown 7 years ago and has had no problems related to the implant and/or surrounding bone. Manufacturing abutment screws from annealed gold-based alloy allows them to be more ductile, thus the screws

absorbed the larger load of traumatic impact forces which resulted in their bending. Accordingly, this minimized the load transmitted to the implant and the surrounding bone (this would not have occurred if the abutment screws had been strong and rigid, sharing similar mechanical properties with the implant).

Microstructural and EDS analyses suggested that both abutment screws had a face-centered cubic single phase solid solution matrix of Au, Pt, Cu, and Ag, which is in agreement with previous studies that attempted to evaluate prosthetic retaining screws metallurgically.^{13,31}

CONCLUSIONS

It appears that the occurrence of adhesive wear on abutment screws in the form of galling is highly related to the length of in-service time in the mouth. This biotribologic behavior was inevitable and considered to be a normal consequence of long-term use *in vivo*. Metallurgical analysis indicated that both screws were identical in terms of composition and microstructure.

ACKNOWLEDGMENT

The authors wish to thank the Research Group Program for funding this project. This study was funded by research grant no. RGP-VPP-206 from Research Group Program, Deanship of Scientific Research, King Saud University, Riyadh, Saudi Arabia. The authors also thank Professor Kenneth Waliszewski, treating prosthodontist, at the Marquette University School of Dentistry. The authors reported no conflicts of interest related to this study.

REFERENCES

- Naert I, Koutsikakis G, Duyck J, Quirynen M, Jacobs R, van Steenberghe D. Biologic outcome of implant-supported restorations in the treatment of parial edentulism. Part I: A longitudinal clinical evaluation. *Clin Oral Implants Res* 2002;13:381–389.
- Naert I, Koutsikakis G, Duyck J, Quirynen M, Jacobs R, van Steenberghe D. Biologic outcome of implant-supported restorations in the treatment of parial edentulism. Part 2: A longitudinal radiographic study. *Clin Oral Implants Res* 2002;13:390–395.
- Jung R, Pjetursson B, Gläuser R, Zembic A, Zwahlen M, Lang N. A systemic review of the 5-years survival and complication rates of implant-supported single crowns. *Clin Oral Implants Res* 2008;19: 119–130.
- Conrad H, Schulte J, Vallee M. Fractures related to occlusal overload with single posterior implants: A clinical report. *J Prosthet Dent* 2008;99:251–256.
- Al Jabbari YS, Fournelle R, Ziebert G, Toth J, Iacopino AM. Mechanical behavior and failure analysis of prosthetic retaining screws after long-term use *in vivo*. Part 1: Characterization of adhesive wear and structure of retaining screws. *J Prosthodont* 2008;17:168–180.
- Haack JE, Sakaguchi RL, Sun T, Coffey JP. Elongation and preload stress in dental implant abutment screws. *Int J Oral Maxillofac Implants* 1995;10:529–536.
- Jorneus L, Jemt T, Carlsson L. Load and design of screw joints for single crowns supported by osseointegrated implants. *Int J Oral Maxillofac Implants* 1992;7:353–359.
- Burguete RL, Johns RB, King T, Patterson EA. Tightening characteristics for screwed joints in osseointegrated dental implants. *J Prosthet Dent* 1994;71:592–599.
- Sakaguchi RL, Borgersen SE. Nonlinear contact analysis of preload in dental implant screws. *Int J Oral Maxillofac Implants* 1995;10:295–302.
- Pai NG, Hess DP. Experimental study of loosening threaded fastener due to dynamic shear loads. *J Sound Vib* 2002;253:585–602.
- Bickford JH. An Introduction to the Design and Behavior of Bolted Joints, ed 3. New York: Marcel Dekker, 1995.
- American Society for Testing and Materials. Standard G40-98b, Standard Terminology Relating to Wear and Erosion. West Conshohocken, PA: ASTM, 1999.
- Al Jabbari YS, Fournelle R, Ziebert G, Toth J, Iacopino AM. Mechanical behavior and failure analysis of prosthetic retaining screws after long-term use *in vivo*. Part 2: Metallurgical and microhardness testing. *J Prosthodont* 2008;17:181–191.
- Neu C, Komvopoulos K, Reddi H. The interface of functional biotribology and regenerative medicine in synovial joints. *Tissue Eng Part B Rev* 2008;14:235–247.
- Wiklund U, Hutchings IM. Investigation of surface treatments for galling protection of titanium alloys. *Wear* 2001;251:1034–1041.
- van der Heide E, Schipper DJ. Galling initiation due to frictional heating. *Wear* 2003;254:1127–1133.
- Gård A, Krakhmalev PV, Bergström J. Wear mechanisms in deep drawing of carbon steel—Correlation to laboratory testing. *Tribotest* 2008;14:1–9.
- Tsuge T, Hagiwara Y. Influence of lateral-oblique cyclic loading on abutment screw loosening of internal and external hexagon implants. *Dent Mater* 2009;28:373–381.
- Rangert BR, Sullivan RM, Jemt TM. Load factor control for implants in the posterior partially edentulous segment. *Int J Oral Maxillofac Implants* 1997;12:360–370.
- Rangert B, Krog PH, Langer B, Van Roekel N. Bending overload and implant fracture: A retrospective clinical analysis. *Int J Oral Maxillofac Implants* 1995;10:326–334.
- Haas R, Mensdorff-Pouilly N, Mailath G, Watzek G. Bränemark single tooth implants: A preliminary report of 76 implants. *J Prosthet Dent* 1995;73:274–279.
- Williams S, Stewart TD, Ingham E, Stone MH, Fisher J. Effect of swing phase load conditions on the wear of metal-on-metal hip joints. *J Bone Joint Surg Br* 2005;87B(suppl 8):228.
- Goto H, Amamoto Y. Effect of varying load on wear resistance of carbon steel under unduplicated conditions. *Wear* 2003;254:1256–1266.
- Ameen HA, Hassan KS, Mubarak E. Effect of loads, sliding speeds, and time on the rate for wear of different materials. *Am J Sci Ind Res* 2011;2:99–106.
- Bressan JD, Daros DP, Sokolowski A, Mesquita RA, Barbosa CA. Influence of hardness on the wear resistance of 17-4 PH stainless steel evaluated by the pin-on-disc testing. *J Mater Process Technol* 2008;205:353–359.
- Varano R, Bobyn JD, Medley JB, Yue S. The effect of microstructure on the wear of cobalt-based alloys used in metal-on-metal hip implants. *Proc Inst Mech Eng H* 2006;220:145–159.
- Wieleba W. The statistical correlation of the coefficient of friction and wear rate of PTFE composites with steel counterface roughness and hardness. *Wear* 2002;252:719–729.
- Yuanyuan Li, Ngai TL. Grain refinement and microstructural effect on mechanical and tribological behavior of Ti and Be modified aluminium bronze. *J Mater Sci* 1996;31:5333–5338.
- Zarb GA, Schmitt A. The longitudinal clinical effectiveness of osseointegrated dental implants: The Toronto study. Part III: Problems and complications encountered. *J Prosthet Dent* 1990;64:185–194.
- Rangert B, Jemt T, Joreous L. Forces and moments on Bränemark implants. *Int J Oral Maxillofac Implants* 1989;4:241–247.
- Rambhai KS, Nagy WW, Fournelle RA, Dhuru VB. Defects in hexed gold prosthetic screws: A metallographic and tensile analysis. *J Prosthet Dent* 2002;87:30–39.

Localized Bone Augmentation with Cortical Bone Blocks Tented over Different Particulate Bone Substitutes: A Retrospective Study

Arash Khojasteh, DMD¹/Hossein Behnia, DMD, MS²/Yadollah Soleymani Shayesteh, DDS, MS³/Golnaz Morad, DDS⁴/Marzieh Alikhasi, DDS, MS⁵

Purpose: To assess the efficacy of a block tenting technique for reconstruction of vertical or horizontal alveolar ridge defects. **Materials and Methods:** Patients who underwent a block tenting graft technique between 2005 and 2010 were analyzed retrospectively. Intraoral bone blocks (ramus, chin, or tuberosity) or allogeneic blocks were fixed at 4 mm from the deficient area, and the gap was filled with bone substitutes, with or without plasma rich in growth factors (PRGF). Implants were placed simultaneously or 4 to 5 months postgrafting. Patient demographic information, amount of width/height augmentation after 4 to 5 months of healing, complications, and contributing factors were gathered and analyzed. **Results:** One hundred two patients were enrolled. Among the horizontal augmentations, the greatest width increase was achieved in the anterior maxilla (4.31 ± 0.93 mm). The average height increase in the vertically augmented regions was greatest in the posterior maxilla (5.75 ± 2.22 mm). Mean horizontal augmentation was the greatest with ramus (3.65 ± 0.65 mm) and allogeneic materials (3.97 ± 0.79 mm). The greatest vertical gain was achieved with tuberosity blocks (4.25 ± 3.06 mm) and a combination of allogeneic/autogenous bone particles (3.90 ± 1.05 mm). Application of PRGF showed no appreciable effect. The most common primary complications of surgery were hematoma and inflammation. The most common complication in the anterior maxilla was hematoma. Inflammation was the most common complication associated with ramus grafts, while hematoma occurred most often in cases with chin and tuberosity grafts. Total graft failure occurred in 13 patients, mainly associated with the allogeneic blocks. Most patients were followed for 11 to 38 months. Five of 237 inserted implants failed to osseointegrate. **Conclusion:** The block tenting technique might be effective for localized ridge augmentation and may reduce the amount of autograft required from donor sites. INT J ORAL MAXILLOFAC IMPLANTS 2012;27:1481–1493

Key words: allogeneic bone graft, alveolar ridge augmentation, autogenous bone graft, guided bone regeneration, tenting technique

¹Assistant Professor and Director of Basic Science Research, Department of Oral and Maxillofacial Surgery, Dental Research Center, Faculty of Dentistry, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

²Professor and Chairman, Department of Oral and Maxillofacial Surgery, Dental Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

³Associate Professor, Department of Periodontics, Faculty of Dentistry, Tehran University of Medical Sciences, Tehran, Iran.

⁴Research Fellow, Dental Research Center, Faculty of Dentistry, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

⁵Associate Professor, Dental Research Center, Dental Implant Research Center, Dental Laser Research Center, Department of Prosthodontics, Tehran University of Medical Sciences, Tehran, Iran

Correspondence to: Dr Arash Khojasteh, Department of Oral and Maxillofacial Surgery, Dental Research Center, Faculty of Dentistry, Shahid Beheshti University of Medical Sciences, Daneshjou Boulevard, Evin, Tehran, Iran, P.O. 19839. Fax: +98-21-88507688. Email: arashkhojasteh@yahoo.com

In many cases of complete or partial edentulism, the optimal dental implant rehabilitation might be unachievable without restoring the lost volume of an atrophic alveolar ridge. Endeavors to replace the resorbed bone with a bone graft, either autogenous or nonautogenous, have provided favorable results.^{1,2} Autogenous bone, still known as the best option for bone grafting, can be harvested from both extraoral and intraoral donor sites.³ The latter typically resorbs less at the recipient site by virtue of its thicker cortical compartment and greater revascularization. In addition, the less complicated surgical procedure for graft harvesting makes intraoral grafts more desirable. Unavailability in large amounts is considered the major drawback of intraoral donor sites when extensive reconstruction is required.^{3–6} The practicality of alveolar ridge augmentation via grafting procedures depends not only on the choice of bone graft but is also affected

by the grafting method that is employed. The concept of guided bone regeneration (GBR) for the treatment of bone defects has been practiced since the 1980s.^{7,8} During this time, a variety of modifications have been developed to improve the outcome of this technique, including coapplication of GBR with onlay bone grafting.^{8,9} In a review of the literature, the average reported amounts of bone augmentation associated with GBR in vertical and horizontal deficiencies were 3.5 mm and 4.2 mm, respectively.¹ Dahlin et al presented a novel GBR model for bone augmentation, in which implants were inserted in a protruding position and simultaneously covered with barrier membranes. Formation and stabilization of blood clot within the space created under the membrane was assumed to be sufficient for bone regeneration.¹⁰ The success of this technique was confirmed by other animal studies^{11–13} and human reports.^{14–17} Potential membrane collapse was a matter of concern, which was prevented by using bone grafts beneath the membrane in other experiments.^{18,19} The aforementioned tenting model was further altered to be suitable for ridge augmentation prior to implant placement.²⁰ A three-dimensional method for vertical bone augmentation was first introduced by Khoury and Khoury.²¹ Thin mandibular bone blocks were used to reconstruct the buccal and palatal (lingual) walls of vertical defects, and the intervening space was filled with particulate autogenous bone. The concept of combining bone blocks and particulate bone material was implemented in a tenting design by Le et al.⁵ Application of compacted particulate allograft material under dense cortical bone blocks made it possible for clinicians to perform long-span alveolar ridge reconstruction with limited sources of intraoral bone. In the current retrospective study, a similar tenting concept was evaluated in 102 augmentation procedures. Intraoral autogenous bone blocks of different sources or blocks of allogeneic bone were tented over horizontal or vertical ridge defects, creating a “secured healing space,” which was filled with different types of particulate bone substitutes. The merit of mixing particulate bone materials with plasma rich in growth factors (PRGF) was also appraised.

MATERIALS AND METHODS

Patients

Data from patients who had undergone alveolar ridge augmentation via bone grafting during the period between 2005 and 2010 were collected to be analyzed. In all included cases, indication for bone augmentation prior to implant treatment was determined based on measurements performed preoperatively on computed tomography (CT) scans. Horizontal bone deficiency

was defined as a horizontal dimension less than 4 mm (measured at the crest of the ridge). Vertical bone deficiency was defined as a ridge that was too short to insert 8-mm dental implants while maintaining a 2-mm distance to the critical anatomic structures and/or a 2- to 3-mm distance to the cementoenamel junction of the adjacent teeth. The presence of poor physical status, ie, a classification of 4 according to the American Society of Anesthesiologists,²² was an exclusion factor. Patients who smoked at least 10 cigarettes per day were also excluded from the study. Data extracted from files included demographic information, alterations in bone width and bone height, and any concomitant complications, as well as contributing factors such as the source of intraoral bone blocks, type of bone substitutes, initial bone width and height of the recipient site, use of PRGF in the grafting procedure, and time of implantation.

Surgical Procedure

All patients received premedication with 500 mg amoxicillin (Tehran Chemie) or 300 mg clindamycin if allergic to penicillin, 400 mg ibuprofen (Rouz Darou), and 0.5 mg of dexamethasone (Iran Hormone). All surgeries were performed by a single surgeon with patients under local anesthesia (lidocaine 2% with adrenaline 1:100,000). Prior to graft harvesting, the edentulous areas were fully exposed by retracting full-thickness mucoperiosteal flaps through midcrestal incisions. In cases of partial edentulism, crestal incisions were extended as sulcular incisions to the teeth adjacent to the edentulous ridge.

Block Bone Harvesting and Graft Preparation.

When the ramus was chosen as the donor site for augmentation of the posterior mandibular ridge, access was provided by extending the midcrestal incision on the atrophic alveolar ridge over the external oblique ridge. When areas other than the posterior mandible were to be reconstructed with ramal bone graft, a single incision was made over the external oblique ridge to expose the donor site. Vertical and horizontal osteotomies limited to the cortical bone were performed using a fissure bur under copious irrigation with saline. Extreme care was made to avoid injury to the inferior alveolar nerve. The outlined graft was subsequently levered and disengaged from its bed by means of careful application of a chisel. The size of the obtained bone segments depended on the extent of the area to be reconstructed (Fig 1). To harvest bone grafts from the chin, in cases of partial edentulism in the anterior mandible, access to this donor site was achieved through crestal incisions with sulcular extensions combined with vertical releasing incisions, and the mucoperiosteal flap was further retracted to expose the symphyseal area. When teeth were present



Fig 1 Thin cortical bone harvested from the lateral body of the ramus. The bone block extended from the proximal end of the external oblique ridge anteriorly to the coronoid notch posteriorly.



Fig 2 Tenting the ramal cortical plate over the deficient posterior mandibular ridge. The crest was perforated to enhance vascularization of the particulate bone substitute within the secured healing space.



Fig 3 The secured healing space filled with the allogeneic bone materials. The outer bony osteogenic membrane was secured with three microscrews and the space was filled with the particulate bone substitute. The blood coagulum held the material within the healing space.

Fig 4 (Left) Mixture of the PRGF with the bone substitute can work as a network to hold the material within the healing space, hence facilitating the surgery.



Fig 5 (Right) The lateral ramus bone block was tented over the deficient ridge concomitant with implant placement and was stabilized with two microscrews.



in the anterior mandible, a mucoperiosteal incision 15 mm from the mucogingival junction was used. Grafts were harvested from a safe region between the mental foramina using burs and chisels. When the maxillary tuberosity was the donor site of choice for reconstruction of the atrophic edentulous posterior maxilla, a crestal incision was extended posteriorly with an approximately 4-mm-long vertical incision. When teeth were present in this area, the incision was begun distal to the distalmost tooth. A bone block was subsequently harvested from the exposed enlarged tuberosity. If intraoral bone harvesting was not a possible option, blocks of allogeneic bone (AlloOss, ACE Surgical Supply) were chosen to augment the atrophic ridge.

Grafting Procedure. Harvested grafts were properly adapted to the recipient site, and any sharp edges on the blocks were trimmed with a large round bur. Fixation screw holes were created in at least three sites on the lateral surface of the bone block using a drill (Jeil). The cortical surface of the recipient bone was also perforated to expedite vascularization of the area to be regenerated. The bone block(s) were placed at least 3 to 4 mm from the vertically deficient site or buccal to the lateral surface of horizontally deficient ridge. Fixation microscrews (Jeil, 10 to 12 mm in length) were tightened while a periosteal elevator was placed between the bone block and the recipient site to maintain the

desired distance (Fig 2). Particulate bone substitute materials were used to fill the gap between the graft and the recipient site. Allogeneic (AlloOss, ACE Surgical Supply), xenogeneic (Bio-Oss, Geistlich), monophasic synthetic (tricalcium phosphate, Cerasorb, Curasan), or biphasic synthetic (hydroxyapatite/tricalcium phosphate, Atlantic) materials were used (Fig 3). In some cases, the substitutes were mixed with PRGF to encourage a better outcome (Fig 4). To obtain PRGF, 30 mL of blood was drawn from the patient and was collected in citrated tubes. The blood sample was centrifuged (GAC Medical) at 480g for 8 minutes at room temperature. The uppermost half of the separated plasma, ie, the platelet-poor plasma, was collected with a pipette. To prepare the platelet-rich fibrin membrane, the lower half of the plasma, immediately above the blood cell phase, was transferred to a separate tube. To activate the platelets and boost the release of growth factors, the tube was supplemented with 50 μ L of 10% calcium chloride for each 1-mL unit of plasma. After 20 minutes at room temperature, the resultant preparation was mixed with the bone substitute. In some cases of horizontal augmentation, implants were inserted simultaneously (Fig 5). Suitable dental implants were placed in the deficient ridge to provide acceptable primary stability. Afterward, the grafting procedure was completed as explained to cover the exposed parts of

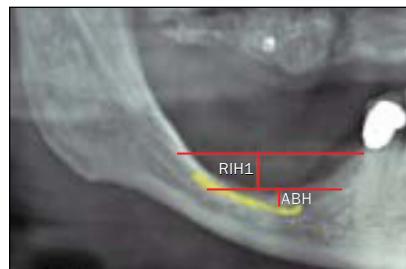


Fig 6a Measurement of the available bone height (ABH) and the required increase in height (RIH) in the posterior mandible.

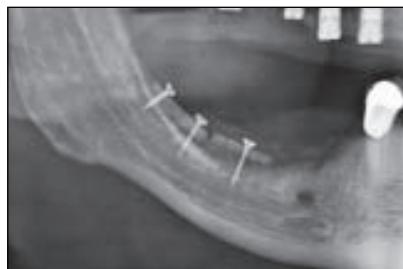


Fig 6b Radiographic evaluation of a patient at 4 months postsurgery demonstrated stable bone height and opacification of the secured healing space.



Fig 6c Implants were placed in the new regenerated bone in the posterior mandible. The outer cortical layer provided primary stability for the implants, and the new bone in the secured healing space can remodel gradually. The microscrews can remain in place until the implants are uncovered.

the implants. The flaps were subsequently closed with continuous horizontal mattress sutures (5-0 Vicryl, Ethicon Inc). Whenever necessary, a periosteal releasing incision in the buccal flap or detachment of the mylohyoid muscle from the lingual surface was used to ensure tension-free closure of the flap.

Follow-up Protocol

Postoperative medications included amoxicillin 500 mg (three times per day for 7 days; clindamycin 300 mg two times a day for allergic patients); appropriate analgesics (ibuprofen 400 mg alone or with acetaminophen codeine 300/10 mg, for moderate and severe pain, respectively); as well as a single intramuscular injection of 8 mg dexamethasone (Alborz Darou) and 75 mg diclofenac (Troge Medical). Patients were instructed to use chlorhexidine mouthwash 0.2% (Behsa Pharmaceutical) for a week beginning the day after surgery. Sutures were removed after 10 to 14 days.

During the first month after surgery, follow-up examinations were performed biweekly; these continued at 1-month intervals for 4 to 5 months. Following this period of graft consolidation, dental implants were inserted submerged at the augmented site or, in case of simultaneous implant placement, the second surgery for implant exposure was performed. A two-stage implant placement procedure was employed in all patients. Intervals for post-implant placement follow-up examinations within the first year were managed as described earlier. Thereafter, patients were examined every 6 months.

Measurement of Bone Gain. The initial bone width (BW1) of narrow ridges was measured intrasurgically at the time of augmentation using a caliper (Hilbro; precise to 0.1 mm). During the second surgery for implant placement or implant exposure in simultaneous cases,

a second measurement of the ridge width (BW2) was performed with the same device. Both measurements were recorded at the crest of the ridge.

Because of the diversity of criteria describing the ideal bone height for proper implant placement in different sites, to attain homogenous records, a special factor was defined, designated as required increase in height (RIH) (Figs 6a to 6c). In all sites, a minimum of 10 mm from critical anatomical structures (nasal floor in the anterior maxilla, floor of the sinus in the posterior maxilla, border of the anterior mandible, and inferior alveolar nerve canal in the posterior mandible) was required for safety reasons. In cases of partial edentulism in anterior areas, a 2- to 3-mm distance between the level of bone and the cementoenamel junction of the adjacent teeth was necessary for an esthetically acceptable outcome. RIH signified the required amount of bone gain to achieve the adequate vertical dimension and was recorded in panoramic radiographs at the time of augmentation (RIH1) and at the time of implant placement (RIH2). Radiographic magnification was estimated from the actual length and the radiographic length of dental implants and was considered in bone height measurements. Because both radiographs for measuring RIH1 and RIH2 were obtained at the same radiology center with the same device, the calculated magnifications in the second panoramic radiographs were applied to the first radiographic measurements (RIH1) and subtracted by computer software (Image-Pro Plus, Media Cybernetics). Increases in BW and bone height (BH) were assessed by calculating the difference between the two measurements.

Assessment of Complications. Patients were assessed for complications during the follow-up period. Evidence of transudation within the first 2 weeks postsurgery and at the time of suture removal was recorded

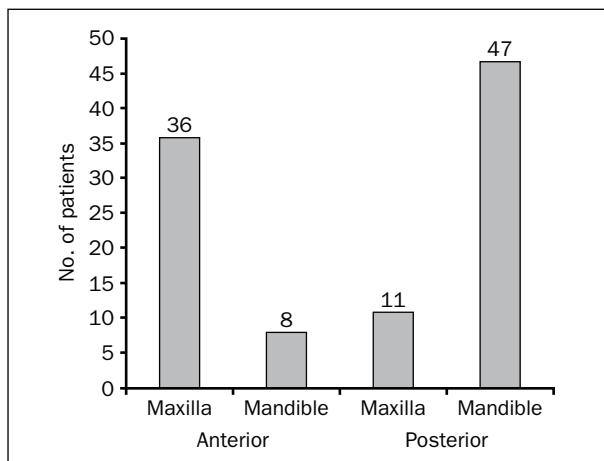


Fig 7 Case distribution based on the site of reconstruction. The block tenting technique was implemented most frequently in the posterior mandible and the anterior maxilla.

as inflammation. Discharge of pus from the surgical site indicated infection. Hematoma formation was investigated during the first 2 weeks postsurgery by direct evaluation of the surgical area for ecchymosis on the mucosa or skin. The presence of neuropathic signs and symptoms such as alteration or loss of sensation was regarded as paresthesia. Exposure of the graft within the first 4 weeks after surgery was classified as early graft exposure, while occurrence of this complication after 4 weeks was classified as delayed graft exposure. Mobility and loss of the grafted bone block were recorded as graft failure. Lack of osseointegration leading to mobile implants indicated implant failure.

Statistical Analysis

All data were analyzed using the Statistical Package for Social Sciences (SPSS software, version 14.0, IBM). Descriptive statistical analysis included means with standard deviations and frequencies, for continuous and discrete variables, respectively. Significance was determined with the independent *t* test, with statistical significance indicated by a *P* value less than or equal to .05.

RESULTS

This retrospective study included 102 patients aged 20 to 73 years (mean age, 52.4 years). Forty-eight patients were men and 54 were women. The systemic condition encountered most often (11 patients) was controlled diabetes mellitus (fasting blood sugar in the range of 120 to 130 mg/dL). In the other 91 patients, no remarkable systemic condition was diagnosed. Smoking habits, as defined previously, were only present in nine.

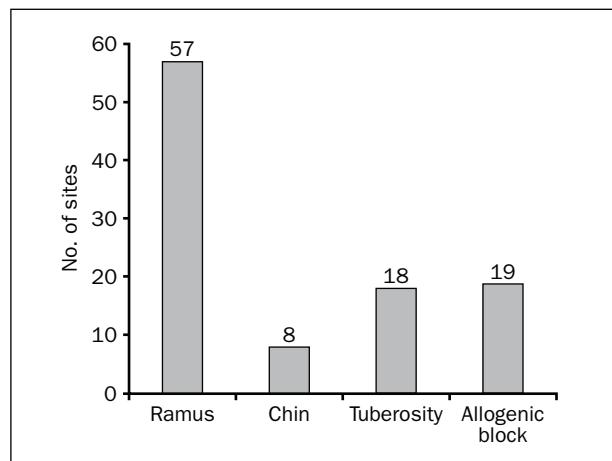


Fig 8 Distribution of the different types of bone blocks tented over the ridge defects. The ramus was the most common intraoral donor site chosen in this study.

Table 1 Distribution of the Different Types of Bone Blocks Based on the Recipient Site (No. of Cases)

Donor site	Anterior		Posterior	
	Maxilla	Mandible	Maxilla	Mandible
Ramus	12	–	1	44
Chin	–	6	–	2
Tuberosity	12	–	6	–
Allogeneic	12	2	4	1

A combination of bone blocks and particulate bone materials were arranged in a tenting fashion to augment deficient ridges. Based on the area of reconstruction, the largest group of patients ($n = 47$) was reconstructed in the posterior mandible (Fig 7). The majority of utilized bone blocks were harvested from intraoral donor sites (83 patients), with the mandibular ramus being the most common donor site ($n = 57$) (Fig 8). The main donor sites of choice for augmentation of posterior mandible, anterior mandible, and maxilla were ramus, chin, and tuberosity, respectively. The distribution of the different types of bone blocks based on the recipient site is demonstrated in Table 1. The distribution of the different kinds of particulate bone substitute materials in the secured healing space is depicted in Fig 9; as shown, the most commonly employed bone substitute was particulate allogeneic bone (AlloOss).

Dental implants were also used for rehabilitation of the augmented edentulous area. In 17 patients, this was performed simultaneously with horizontal bone

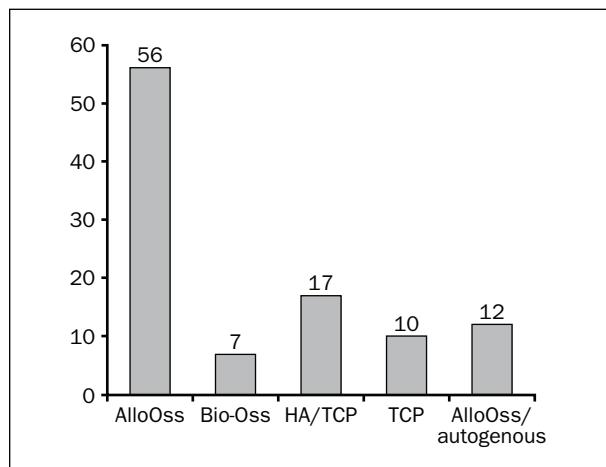


Fig 9 Distribution of the different types of bone substitutes used to fill the secured healing space. AlloOss was the most commonly employed bone substitute in this study. HA = hydroxyapatite; TCP = tricalcium phosphate.

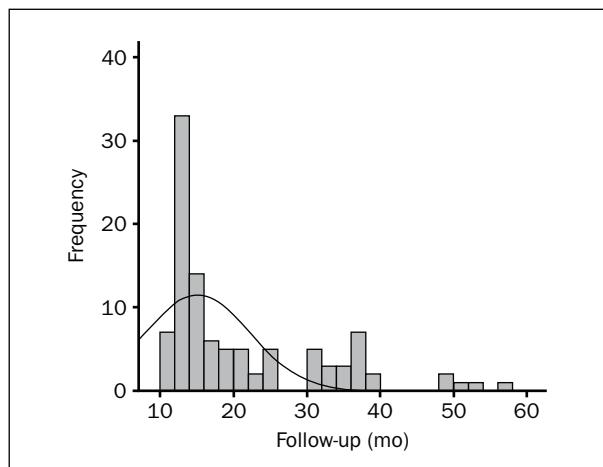


Fig 10 Histogram and normal curve of patients distribution based on the follow-up period.

Table 2 Amount of Horizontal and Vertical Augmentation (in mm) in the Different Areas of the Arches

	Anterior		Posterior	
	Maxilla	Mandible	Maxilla	Mandible
Horizontal cases	27	8	7	23
BW1				
Mean	2.10 ± 0.63	2.42 ± 0.53	2.20 ± 0.63	2.05 ± 0.47
Min	1.20	1.50	1.00	1.00
Max	3.50	3.00	3.00	3.50
BW2				
Mean	6.41 ± 0.74	5.35 ± 0.85	5.90 ± 0.63	5.90 ± 0.3
Min	2.00	4.00	4.40	2.80
Max	7.05	6.00	6.30	6.20
Mean increase in BW	4.31 ± 0.93	2.94 ± 0.79	3.70 ± 0.38	3.85 ± 0.56
Vertical cases	9	–	4	24
RIH1				
Mean	5.56 ± 2.38	–	7.5 ± 2.64	5.85 ± 1.3
Min	3.00	–	5.00	2.00
Max	10.00	–	10.00	9.00
RIH2				
Mean	2.31 ± 1.03	–	1.75 ± 0.96	2.25 ± 1.05
Min	1.00	–	1.00	1.10
Max	4.00	–	3.00	3.50
Mean increase in BH	3.25 ± 3.07	–	5.75 ± 2.22	3.6 ± 1.7

augmentation; in the remaining 85 patients, the implants were inserted following a 4- to 5-month graft consolidation period. All patients were followed for a minimum of 11 months following bone augmentation surgery. The longest follow-up time was 56 months (average follow-up, 20.3 ± 10.9 months). Most patients in this study were followed successfully for 11 to 38 months (Fig 10).

Bone Augmentation Data

Sixty-five patients required horizontal augmentation, while vertical augmentation was performed in 37 patients. All areas of the arch incorporated both horizontal and vertical augmentation except for the anterior mandible, which included only horizontally deficient cases. Alterations in horizontal dimension were measured intrasurgically prior to bone augmentation and

Table 3 Amount of Bone Augmentation and Frequency of Complications with Respect to Graft Type

	Ramus	Chin	Tuberosity	Allogeneic block
Mean increase in BW (mm)	3.65 ± 0.65 (n = 32)	2.94 ± 0.79 (n = 8)	3.30 ± 1.05 (n = 10)	2.88 ± 0.85 (n = 15)
Mean increase in BH (mm)	3.94 ± 2.1 (n = 25)	—	4.25 ± 3.06 (n = 8)	3.02 ± 1.7 (n = 4)
Complications				
Inflammation	22	3	8	4
Early graft exposure	5	2	0	2
Delayed graft exposure	6	0	0	6
Hematoma	17	6	12	6
Paresthesia	17	3	0	0
Infection	5	0	0	1
Graft failure	5	0	1	7
Implant failure	1	0	1	3

Table 4 Amount of Bone Augmentation and Frequency of Complications with Respect to Bone Substitute

	AlloOss	Bio-Oss	HA/TCP	TCP	AlloOss/ autogenous
Mean increase in BW (mm)	3.97 ± 0.79 (n = 37)	2.88 ± 0.55 (n = 5)	3.55 ± 0.98 (n = 10)	2.60 ± 0.65 (n = 5)	3.42 ± 0.58 (n = 8)
Mean increase in BH (mm)	3.66 ± 1.87 (n = 19)	2.90 ± 0.35 (n = 2)	2.55 ± 1.1 (n = 7)	2.60 ± 1.06 (n = 5)	3.90 ± 1.05 (n = 4)
Complications					
Inflammation	18	3	8	3	5
Early graft exposure	6	1	2	0	0
Delayed graft exposure	6	2	2	1	1
Infection	3	1	2	0	0
Graft failure	10	1	2	0	0

at the time of implant placement. When the amount of bone augmentation was calculated, cases with graft failure were excluded. The greatest increase in bone width was achieved in the anterior maxilla (mean, 4.31 ± 0.93 mm). The greatest (vertical) increase was seen in the posterior maxilla (mean, 5.75 ± 2.22 mm). Table 2 provides detailed information regarding the amount of augmentation in different areas of the arch. The amount of alveolar ridge augmentation achieved with different types of bone blocks and bone substitutes is presented in Tables 3 and 4, respectively. In 44 patients, particulate bone materials were mixed with PRGF (Table 5). However, its use did not significantly affect the amount of bone gain ($P > .05$).

Complications and Corresponding Management

The two most common complications that occurred following surgery were early inflammation ($n = 41$) and hematoma formation ($n = 37$) (Fig 11). In six patients diagnosed with infection, the area was irrigated with saline solution. Oral hygiene instruction was also provided. Clindamycin 300 mg (taken two times per day for 7 days) and chlorhexidine gel 0.2% (Perio-Kin, applied two times per day at the infected site) were

Table 5 Amount of Bone Augmentation and Frequency of Complications With and Without PRGF

	With PRGF	Without PRGF
Mean increase in BW	3.85 ± 0.68 (n = 28)	3.11 ± 0.86 (n = 38)
Mean increase in BH	3.95 ± 2.5 (n = 16)	3.74 ± 2.07 (n = 20)
Complications		
Inflammation	17	20
Early graft exposure	3	6
Delayed graft exposure	4	8
Graft failure	5	8

prescribed. Graft exposure (early and delayed) was documented in 21 cases. However, these complications did not necessarily result in graft mobility and failure. In both situations, oral hygiene instructions were given and application of chlorhexidine gel to the grafted area was prescribed. Early graft exposure was treated with proper irrigation and resuturing of the dehisced incision; however, in cases of delayed graft exposure, at the time of reopening for implant insertion, the

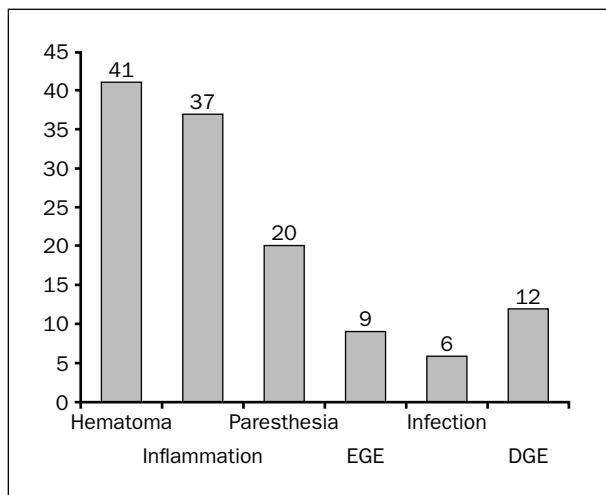


Fig 11 Frequency of complications associated with alveolar ridge augmentation via the tenting bone grafting technique. DGE = delayed graft exposure; EGE = early graft exposure.

ridge was trimmed so that acceptable tension-free closure could be obtained. Overall, graft failure occurred in 13 cases; these were treated with a second bone grafting procedure. The greatest numbers of complications were documented for the posterior mandible and the anterior maxilla, respectively (Table 6). The major complication associated with tuberosity block harvesting was hematoma (12 of 18 patients), whereas inflammation was the most common complication in sites augmented with ramal bone grafts (22 of 57 patients). Table 3 includes the frequencies of complications based upon different sources of bone blocks. The frequency of complications was also evaluated based upon the type of bone substitutes (Table 4) or the use of PRGF (Table 5).

Because of the lack of normal distribution of patients with respect to the duration of follow-up, the implant failure rate might have been affected as the only variable that was appraised during the whole follow-up period. Hence, outliers for the follow-up variable were identified (four cases) with statistical software (SPSS), and the implant failure rate was calculated with those cases omitted. The result was 2.1% (5 of 237 implants).

DISCUSSION

In the attempts to improve upon the options currently available for reconstruction of atrophic arches, a wide range of grafting techniques has been introduced. Feasible alternatives might differ based on the area to be reconstructed as well as the type of deficiency.^{1,23} In this retrospective study, secured healing spaces created by tenting bone blocks over the deficient ridges were filled with different particulate bone substitutes

Table 6 Frequency of Complications Based on the Recipient Site

Complication	Anterior		Posterior	
	Maxilla	Mandible	Maxilla	Mandible
Inflammation	18	2	2	15
Early graft exposure	4	1	1	3
Delayed graft exposure	3	0	2	7
Hematoma	21	3	2	15
Paresthesia	0	2	0	18
Infection	1	0	1	4
Graft failure	5	1	2	5
Implant failure	4	0	1	0

to augment the alveolar bone. This "tenting" technique was employed in different areas of the arch to restore horizontal or vertical deficiencies. Eighty-nine of 102 cases were treated successfully, with no evidence of graft failure. Only 2.1% of the inserted implants showed mobility and were documented as failures.

Introductory tenting models incorporated non-submerged implants tented with barrier membranes.^{10–12,14,15} In animal studies evaluating bone formation around protruding implants covered with reinforced expanded polytetrafluoroethylene (e-PTFE) membranes, a mean supracrestal bone gain of 1.9 mm¹¹ and 57.42% bone fill¹² have been reported. In human research using e-PTFE membranes to treat vertical deficiencies around implants, 3 to 4 mm of vertical bone gain have been achieved.^{15,16} In parallel with the earliest tenting studies, Khouri and Khouri introduced a three-dimensional reconstruction technique for vertical bone grafting.²¹ The buccal and lingual (palatal) walls or the occlusal wall of the defective area were reconstructed using cortical bone blocks, and the residual space was filled with particulate autogenous bone. The underlying premise of this approach was to benefit from the strength of cortical blocks and the greater ability of particulate bone to revascularize. A mean vertical increase of 7.8 mm was obtained. The resorption within the first year post-grafting was 10% to 15%.²¹ The augmentation procedure evaluated in the present study also incorporated a combination of block and particulate bone grafts, although this was done in a tenting arrangement. A comparable method was previously presented by Le et al; autogenous bone blocks were tented over particulate material to enhance the bone width of large-span edentulous areas.⁵ Although the exact amount of

bone gain was not reported, in all 10 patients included in the study, sufficient bone volume was achieved for implant placement after 4 to 5 months. Also, the bone level around the implants remained stable during the average 22-month follow-up period.

According to the results of the present study, in 65 cases of horizontal augmentation, the mean amount of width enhancement was in the range of 2.94 ± 0.79 mm to 4.31 ± 0.93 mm, depending on location. The anterior maxilla showed the greatest increase in bone width. Onlay bone block grafting, with a mean bone gain of 4.5 mm, was introduced as the most predictable method for treating narrow ridges.¹ However, considerable graft resorption following vertical augmentation with this method calls its predictability into question.^{24,25} A retrospective study evaluated volume alterations of onlay autogenous grafts after implant placement. Mean volume resorption was between 35% and 51%.²⁶

Thirty-seven cases of vertical ridge augmentation were also included in this study. The average vertical bone gain was 3.25 ± 3.07 mm to 5.75 ± 2.22 mm, depending on location. It should be pointed out that more precise results would have been achieved if the vertical measurements had been performed on CT scans. However, a CT scan at the time of implant placement seemed to be unnecessary for all patients and hence not ethical. Therefore, this retrospective study used the available panoramic radiographs, and the amount of magnification was taken into consideration. The average vertical bone gain with other grafting methods has been reported to be 4.5 mm.¹ According to the data analysis of this study, the greatest vertical bone augmentation was obtained in the posterior maxilla (5.75 ± 2.22 mm). Given the assumption that graft resorption in the posterior maxilla is less pronounced than in other sites,^{21,26} this finding might be a result of the smaller change in volume.

Onlay bone grafts were utilized in a study by Rocuzzo et al²⁷ to enhance the vertical dimension of edentulous areas. The average vertical augmentation was 5.5 mm at the time of bone grafting and resorbed to 3.6 mm after 4 to 6 months. Necrosis of the outer layer of bone grafts was reported in a few cases. It was hypothesized that revascularization of the graft might have been impeded by the cortical nature of block bone grafts.²⁷ Considering the important effect of revascularization on graft integration,⁴ the use of bone blocks for the restoration of extreme deficiencies might be quite challenging, as the increased distance between the outer surface of the bone graft and the recipient bone will probably weaken the vascularization, hence jeopardizing the graft.²⁸ This issue might not be as significant when augmentation is performed using particulate bone grafts with a higher vascular-

ization potential.⁴ In the present study, application of particulate bone substitutes to attain a part of the required augmentation probably improved the vascularization of the reconstructed area, resulting in greater osteogenesis compared to onlay block methods in which the entire deficiency is reconstructed with block bone grafts. At the same time, the overlying bone blocks offered protection for the particulate material. Onlay graft resorption is believed to be a shortcoming of two-stage procedures by some authors.²⁹ Lessening the time interval between grafting and implant placement increases the amount of available bone at the time of implant insertion.³⁰ However, there is controversy regarding whether simultaneous implant placement diminishes the amount of graft resorption. In a 10-year prospective study by Verhoeven et al, which evaluated onlay bone grafting with simultaneous implant placement, grafts resorbed by 50%.³¹ Implants were placed concurrent with grafting in only 17 patients in the present study, since the authors believed that the possibility of graft exposure might increase with simultaneous implant placement.

GBR principles have been applied by several authors to diminish the postsurgical resorption associated with onlay grafting.¹ Antoun et al treated localized horizontal defects using intraoral autogenous bone blocks.³² Utilization of a membrane in the test group significantly decreased the amount of resorption within a 6-month follow-up period. Satisfactory results were also obtained when restoring localized vertical deficiencies with intraoral bone blocks and overlying titanium mesh.²⁷ Notably less postsurgical resorption after 4 to 6 months was recorded for the test group (13.5%) compared to the control group, in which no titanium mesh was used (34.5%). Conversely, in a study of Heberer et al, more extensive augmentations were performed with onlay iliac bone grafts. Graft coverage with either periosteum or a resorbable membrane led to comparable results.³³ In the present study, no membrane was used to cover the augmented sites. It was hypothesized that the outer cortical surface of bone blocks, along with the inner osteoblastic layer of the periosteum, would be sufficient to inhibit graft resorption. It should be noted that since the authors did not measure the amount of augmentation immediately after bone grafting, the amount of resorption could not be determined. The possibility of membrane exposure and the resultant compromised healing hamper broad application of this technique. The more extensive the area to be reconstructed, the greater the risk of membrane exposure will be. Therefore, GBR might only be appropriate for localized augmentations.^{34,35} Nevertheless, the use of particulate bone grafts to restore vertically deficient ridges is possible with the support of a membrane.^{36,37} This is of utmost importance when

the advantages of particulate materials over bone blocks, such as rapid vascularization and consolidation, are taken into consideration.³⁸ A combination of bone blocks and particulate bone substitutes in the demonstrated tenting technique decreased the need to harvest large volumes of bone blocks, allowing the authors to use intraoral donor sites exclusively. Furthermore, harvested bone grafts with a certain volume could be used to reconstruct more extensive deficiencies. It is generally believed that less resorption occurs in grafts harvested from intraoral donor sites compared to extraoral grafts.^{4,5} In addition, approximation of donor tissue to the recipient area, as well as elimination of the hospitalization that is often mandatory for extraoral bone harvesting, makes intraoral donor sites a superior option for graft-mediated alveolar ridge augmentation. This might be true when the procedure is not hindered by quantitative limitation of attainable intraoral bone grafts.^{3,5,6,39}

Implants placed following intraoral graft-mediated augmentation have demonstrated high survival rates and minimal marginal bone loss.⁴⁰ Two of the five failed implants in the present patients were inserted in integrated intraoral grafts; the other three were related to allogeneic blocks, which were used in only 19 of 102 procedures.

With unilateral harvest of bone blocks from the ramus, an edentulous area spanning up to four teeth might be reconstructed.⁴¹ Aiming to benefit from the high density of cortical ramus bone, many studies have used blocks of this bone graft to reconstruct vertical^{27,39,42,43} and/or horizontal deficiencies.^{5,44,45} When ramal block bone grafts were covered with titanium mesh, the mean vertical augmentation was 4.8 mm, while it reached only 3.6 mm without titanium mesh.²⁷ Acocella et al also made meticulous bone gain measurements following horizontal augmentation with ramus bone blocks. After a 3- to 9-month healing period, the average bone width enhancement was 4 mm.⁴⁵ The results of the present study were roughly comparable to that experiment. In 57 patients, the lateral ramus was chosen as the donor site, mainly for augmentation of the posterior mandible. The mean increase in bone width was 3.65 ± 0.65 mm, which was greater than that seen with bone blocks. This might be a result of the highly cortical nature of ramus bone grafts resisting resorption. It is worth mentioning, though, that this type of graft might prolong neovascularization, hence increasing the necessary healing time.⁴⁵ The most common complication reported with graft harvesting from the ramus is inferior alveolar nerve damage.³⁹ In 17 of the 57 patients for whom bone grafts were harvested from the ramus, paresthesia ensued. However, signs and symptoms were alleviated gradually and disappeared completely within 6 months in all

but one patient. With the use of the more conservative harvesting method presented by Hwang et al, the possibility of nerve damage might be decreased, although the volume of bone graft obtained with this technique might not be sufficient for extensive reconstructions.³⁹ Apart from the hematoma formation in 17 ramus cases, additional complications that have been reported with ramus bone harvesting, such as donor site incision dehiscence, were not seen in the current study. Furthermore, trismus, another reported complication,³ was not measured.

Overall, the complications associated with the ramus as a donor site seem to be fewer than those related to graft harvest from chin.^{45–48} Augmentations through utilization of corticocancellous bone blocks from the chin have been performed successfully.^{49–53} Kaufman and Wang reported up to 5 mm of vertical bone gain with symphyseal bone cores.⁵⁴ Eight patients in the current study received a chin bone graft and only for horizontal augmentation. Bone width was increased by an average of 2.94 ± 0.79 mm. The major complication was hematoma formation (six of eight patients), followed by inflammation and paresthesia, which were encountered in three patients. Some studies have reported a lower incidence of paresthesia compared to the present findings.⁴⁷ However, subjective assessment of paresthesia in a study by Raghoobar et al revealed a 43% incidence of this complication.⁴⁸ Conceivably, subjective appraisal apart from objective evaluation might be an explanation for the high occurrence of paresthesia documented in the present sample.

The maxillary tuberosity was the other intraoral donor site selected (18 patients). This site poses several advantages over the ramus and chin, namely, simplicity of bone harvest and minimal nerve injury.⁵⁵ However, because it possesses a thin cortical compartment, along with marrow spaces and adipose tissue, the tuberosity might not be an appropriate donor site for some patients.⁵⁶ Surprisingly, the greatest vertical bone gain (4.25 ± 3.06 mm) among the different bone blocks was achieved with this type of bone graft. Harvesting block bone grafts from this site is a more recent development. Localized horizontal augmentation was accomplished in the reported cases. Nevertheless, the presence of a large and bulky tuberosity is a prerequisite that limits the application of this kind of bone graft.⁵⁵

Whenever intraoral bone harvesting was unachievable, blocks of allogeneic bone were used. Allografts have been widely advocated to make up for the disadvantages of autogenous bone harvesting, such as patient morbidity and the costly and time-consuming nature of the procedure.^{57,58} Keith et al performed a 3-year clinical evaluation of 37 patients treated with block allografts; 8.5% of the grafts failed, mostly within

the first year.⁵⁹ According to a review by Waasdorp and Reynolds, most studies have reported a high short-term implant survival rate with allografts.⁶⁰ In contrast, the present authors observed a relatively high incidence of graft (7 of 19 patients) and implant (3 patients) failure with the use of allogeneic bone blocks. This absence of graft consolidation and implant osseointegration highlights a concern about the lack of osteoinductivity in allogeneic bone, which has, to date, prevented the absolute replacement of autografts with allografts. Nevertheless, allografts have provided favorable results in most experiments.^{59,61–65} Its efficacy in vertical bone augmentation has been demonstrated to be comparable to that of autogenous bone.⁵⁷

In addition, the application of particulate allogeneic bone with^{20,57,66} or without a membrane^{67,68} has been shown to improve ridge volume auspiciously. In 56 patients in this study, the secured healing space was filled with particulate allogeneic bone substitute (AlloOss). The mean increase of 3.97 ± 0.79 mm in bone width reported with this bone material is more or less consistent with a study of Feuille et al, in which the application of mineralized freeze-dried bone allograft covered with an e-PTFE barrier led to an average of 3.2 mm of bone gain.⁶⁶ Other bone substitutes included in this study were Bio-Oss, tricalcium phosphate, and biphasic hydroxyapatite/tricalcium phosphate. There is a large amount of literature regarding the application of these particulate materials in maxillofacial reconstruction, particularly in sinus augmentation.⁶⁹ In a total of 12 patients, AlloOss was mixed with particulate autogenous bone; this resulted in the greatest vertical bone gain among all the implemented bone substitutes (3.90 ± 1.05 mm). This finding was expected because of the inherent osteogenic capacities of autogenous bone.

The beneficial role of growth factors administered in conjunction with bone augmentation procedures has been widely supported.^{69–71} PRGF, a platelet-rich preparation, comprises a relatively high concentration of pivotal growth factors for bone regeneration.^{72,73} Anitua and colleagues have successfully used this formulation along with different augmentation procedures.^{74,75} In 44 patients in the current study, PRGF was added to the bone substitutes, with minimal effect on bone augmentation. In agreement with this result, Molina-Minano et al observed no significant positive effect on bone formation when PRGF was applied with or without autogenous bone particles in a rabbit tibia bone defect model.⁷⁶

It is important to distinguish the effects of confounding factors on the final results of the study. A restricted appraisal of identified confounding factors is a consequence of the retrospective nature of this study. Undoubtedly, more reliable results could be achieved if the patients had been matched in this respect.

CONCLUSION

Within the aforementioned limitations, it was concluded that tenting fixed block bone grafts over particulate bone substitutes might serve as a successful alternative to conventional methods of localized bone augmentation. It is worth noting that, because of the unequal distribution of cases among most variables, an explicit comparison could not be made in the current study. However, it seems that a combination of ramus block bone with a mixture of allogeneic/autogenous particulate bone can contribute to more promising results. Controlled clinical trials are warranted to confirm this conclusion.

ACKNOWLEDGMENTS

The authors reported no conflicts of interest related to this study.

REFERENCES

- Jensen SS, Terheyden H. Bone augmentation procedures in localized defects in the alveolar ridge: Clinical results with different bone grafts and bone-substitute materials. *Int J Oral Maxillofac Implants* 2009;24(suppl):218–236.
- Barker D, Walls AW, Meechan JG. Ridge augmentation using mandibular tori. *Br Dent J* 2001;190:474–476.
- Brener D. The mandibular ramus donor site. *Aust Dent J* 2006;51: 187–190.
- Barone A, Covani U. Maxillary alveolar ridge reconstruction with nonvascularized autogenous block bone: Clinical results. *J Oral Maxillofac Surg* 2007;65:2039–2046.
- Le B, Burstein J, Sedghizadeh PP. Cortical tenting grafting technique in the severely atrophic alveolar ridge for implant site preparation. *Implant Dent* 2008;17:40–50.
- Schwartz-Arad D, Levin L. Intraoral autogenous block onlay bone grafting for extensive reconstruction of atrophic maxillary alveolar ridges. *J Periodontol* 2005;76:636–641.
- Dahlin C, Linde A, Gottlow J, Nyman S. Healing of bone defects by guided tissue regeneration. *Plast Reconstr Surg* 1988;81:672–676.
- Retzepi M, Donos N. Guided bone regeneration: Biological principle and therapeutic applications. *Clin Oral Implants Res* 2010;21:567–576.
- Buser D, Dula K, Hirt HP, Schenk RK. Lateral ridge augmentation using autografts and barrier membranes: A clinical study with 40 partially edentulous patients. *J Oral Maxillofac Surg* 1996;54:420–432.
- Dahlin C, Sennerby L, Lekholm U, Linde A, Nyman S. Generation of new bone around titanium implants using a membrane technique: An experimental study in rabbits. *Int J Oral Maxillofac Implants* 1989;4:19–25.
- Jovanovic SA, Schenk RK, Orsini M, Kenney EB. Supracrestal bone formation around dental implants: an experimental dog study. *Int J Oral Maxillofac Implants* 1995;10:23–31.
- Simion M, Fontana F, Rasperini G, Maiorana C. Vertical ridge augmentation by expanded-polytetrafluoroethylene membrane and a combination of intraoral autogenous bone graft and deproteinized anorganic bovine bone (Bio-Oss). *Clin Oral Implants Res* 2007;18: 620–629.
- de Macedo NL, do Socorro Ferreira Monteiro A, de Macedo LG. Vertical bone augmentation using a polytetrafluoroethylene nonporous barrier for osseointegrated implants partially inserted in tibiae of rabbits. *Implant Dent* 2009;18:182–191.

14. Dahlin C, Lekholm U, Linde A. Membrane-induced bone augmentation at titanium implants. A report on ten fixtures followed from 1 to 3 years after loading. *Int J Periodontics Restorative Dent* 1991;11: 273–281.
15. Cornelini R, Cangini F, Covani U, Andreana S. Simultaneous implant placement and vertical ridge augmentation with a titanium-reinforced membrane: A case report. *Int J Oral Maxillofac Implants* 2000;15:883–888.
16. Simion M, Trisi P, Piattelli A. Vertical ridge augmentation using a membrane technique associated with osseointegrated implants. *Int J Periodontics Restorative Dent* 1994;14:496–511.
17. Simon Bl, Chiang TF, Drew HJ. Alternative to the gold standard for alveolar ridge augmentation: Tenting screw technology. *Quintessence Int* 2010;41:379–386.
18. von Arx T, Kurt B. Implant placement and simultaneous ridge augmentation using autogenous bone and a micro titanium mesh: A prospective clinical study with 20 implants. *Clin Oral Implants Res* 1999;10:24–33.
19. Boronat A, Carrillo C, Penarrocha M, Pennarocha M. Dental implants placed simultaneously with bone grafts in horizontal defects: A clinical retrospective study with 37 patients. *Int J Oral Maxillofac Implants* 2010;25:189–196.
20. Le B, Rohrer MD, Prasad HS. Screw “tent-pole” grafting technique for reconstruction of large vertical alveolar ridge defects using human mineralized allograft for implant site preparation. *J Oral Maxillofac Surg* 2010;68:428–435.
21. Khoury F, Khoury C. Mandibular bone block grafts: Diagnosis, instrumentation, harvesting techniques and surgical procedures. In: Khoury F, Antoun H, Missika P (eds). *Bone Augmentation in Oral Implantology*. Chicago: Quintessence, 2007:169–199.
22. Maloney WJ, Weinberg MA. Implementation of the American Society of Anesthesiologists Physical Status classification system in periodontal practice. *J Periodontol* 2008;79:1124–1126.
23. McAllister BS, Haghghiati K. Bone augmentation techniques. *J Periodontol* 2007;78:377–396.
24. Vermeeren JL, Wismeijer D, van Waas MA. One-step reconstruction of the severely resorbed mandible with onlay bone grafts and endosteal implants. A 5-year follow-up. *Int J Oral Maxillofac Surg* 1996;25:112–115.
25. Pelo S, Boniello R, Gasparini G, Longobardi G, Amoroso PF. Horizontal and vertical ridge augmentation for implant placement in the aesthetic zone. *Int J Oral Maxillofac Surg* 2007;36:944–948.
26. Sbordone L, Toti P, Menchini-Fabris GB, Sbordone C, Piombino P, Guidetti F. Volume changes of autogenous bone grafts after alveolar ridge augmentation of atrophic maxillae and mandibles. *Int J Oral Maxillofac Surg* 2009;38:1059–1065.
27. Rocuzzo M, Ramieri G, Bunino M, Berrone S. Autogenous bone graft alone or associated with titanium mesh for vertical alveolar ridge augmentation: A controlled clinical trial. *Clin Oral Implants Res* 2007;18:286–294.
28. Moghadam HG. Vertical and horizontal bone augmentation with the intraoral autogenous J-graft. *Implant Dent* 2009;18:230–238.
29. Felice P, Pistilli R, Lizio G, Pellegrino G, Nisii A, Marchetti C. Inlay versus onlay iliac bone grafting in atrophic posterior mandible: A prospective controlled clinical trial for the comparison of two techniques. *Clin Implant Dent Relat Res* 2009;11(suppl 1):e69–82.
30. Bell RB, Blakey GH, White RP, Hillebrand DG, Molina A. Staged reconstruction of the severely atrophic mandible with autogenous bone graft and endosteal implants. *J Oral Maxillofac Surg* 2002;60: 1135–1141.
31. Verhoeven JW, Cune MS, Ruijter J. Permucosal implants combined with iliac crest onlay grafts used in extreme atrophy of the mandible: Long-term results of a prospective study. *Clin Oral Implants Res* 2006;17:58–66.
32. Antoun H, Sitbon JM, Martinez H, Missika P. A prospective randomized study comparing two techniques of bone augmentation: Onlay graft alone or associated with a membrane. *Clin Oral Implants Res* 2001;12:632–639.
33. Heberer S, Ruhe B, Krekeler L, Schink T, Nelson JJ, Nelson K. A prospective randomized split-mouth study comparing iliac onlay grafts in atrophied edentulous patients: Covered with periosteum or a bioresorbable membrane. *Clin Oral Implants Res* 2009;20:319–326.
34. Chiapasco M, Abati S, Romeo E, Vogel G. Clinical outcome of autogenous bone blocks or guided bone regeneration with e-PTFE membranes for the reconstruction of narrow edentulous ridges. *Clin Oral Implants Res* 1999;10:278–288.
35. Capelli M. Autogenous bone graft from the mandibular ramus: A technique for bone augmentation. *Int J Periodontics Restorative Dent* 2003;23:277–285.
36. Urban IA, Jovanovic SA, Lozada JL. Vertical ridge augmentation using guided bone regeneration (GBR) in three clinical scenarios prior to implant placement: A retrospective study of 35 patients 12 to 72 months after loading. *Int J Oral Maxillofac Implants* 2009;24: 502–510.
37. Langer B, Langer L, Sullivan RM. Vertical ridge augmentation procedure using guided bone regeneration, demineralized freeze-dried bone allograft, and miniscrews: 4- to 13-year observations on loaded implants. *Int J Periodontics Restorative Dent* 2010;30:227–235.
38. Louis PJ, Gutta R, Said-Al-Naief N, Bartolucci AA. Reconstruction of the maxilla and mandible with particulate bone graft and titanium mesh for implant placement. *J Oral Maxillofac Surg* 2008;66:235–245.
39. Hwang KG, Shim KS, Yang SM, Park CJ. Partial-thickness cortical bone graft from the mandibular ramus: A non-invasive harvesting technique. *J Periodontol* 2008;79:941–944.
40. Levin L, Nitzan D, Schwartz-Arad D. Success of dental implants placed in intraoral block bone grafts. *J Periodontol* 2007;78:18–21.
41. Misch CM. Use of the mandibular ramus as a donor site for onlay bone grafting. *J Oral Implantol* 2000;26:42–49.
42. Rocuzzo M, Ramieri G, Spada MC, Bianchi SD, Berrone S. Vertical alveolar ridge augmentation by means of a titanium mesh and autogenous bone grafts. *Clin Oral Implants Res* 2004;15:73–81.
43. Vassos DM. Ramus graft and 1-stage implant placement: A case report. *J Oral Implantol* 2005;31:192–196.
44. Cordaro L, Amade DS, Cordaro M. Clinical results of alveolar ridge augmentation with mandibular block bone grafts in partially edentulous patients prior to implant placement. *Clin Oral Implants Res* 2002;13:103–111.
45. Acocella A, Bertolai R, Colafranceschi M, Sacco R. Clinical, histological and histomorphometric evaluation of the healing of mandibular ramus bone block grafts for alveolar ridge augmentation before implant placement. *J Craniomaxillofac Surg* 2010;38:222–230.
46. Sbordone L, Menchini-Fabris GB, Toti P, Sbordone C, Califano L, Guidetti F. Clinical survey of neurosensory side-effects of mandibular parasympyseal bone harvesting. *Int J Oral Maxillofac Surg* 2009; 38:139–145.
47. Joshi A. An investigation of post-operative morbidity following chin graft surgery. *Br Dent J* 2004;196:215–218.
48. Raghoobar GM, Louwerse C, Kalk WW, Vissink A. Morbidity of chin bone harvesting. *Clin Oral Implants Res* 2001;12:503–507.
49. Dortbudak O, Haas R, Bernhart T, Mailath-Pokorny G. Inlay autograft of intra-membranous bone for lateral alveolar ridge augmentation: A new surgical technique. *J Oral Rehabil* 2002;29:835–841.
50. Meijndert L, Raghoobar GM, Schupbach P, Meijer HJ, Vissink A. Bone quality at the implant site after reconstruction of a local defect of the maxillary anterior ridge with chin bone or deproteinised cancellous bovine bone. *Int J Oral Maxillofac Surg* 2005;34:877–884.
51. Meijndert L, Raghoobar GM, Meijer HJ, Vissink A. Clinical and radiographic characteristics of single-tooth replacements preceded by local ridge augmentation: A prospective randomized clinical trial. *Clin Oral Implants Res* 2008;19:1295–1303.
52. Schwartz-Arad D, Levin L. Symphysis revisited: Clinical and histologic evaluation of newly formed bone and reharvesting potential of previously used symphyseal donor sites for onlay bone grafting. *J Periodontol* 2009;80:865—869.
53. Stevens MR, Emam HA, Alaily ME, Sharawy M. Implant bone rings. One-stage three-dimensional bone transplant technique: A case report. *J Oral Implantol* 2010;36:69–74.
54. Kaufman E, Wang PD. Localized vertical maxillary ridge augmentation using symphyseal bone cores: A technique and case report. *Int J Oral Maxillofac Implants* 2003;18:293–298.
55. Tolstunov L. Maxillary tuberosity block bone graft: Innovative technique and case report. *J Oral Maxillofac Surg* 2009;67:1723–1729.
56. Gapski R, Satheesh K, Cobb CM. Histomorphometric analysis of bone density in the maxillary tuberosity of cadavers: A pilot study. *J Periodontol* 2006;77:1085–1090.

57. Fontana F, Santoro F, Maiorana C, Iezzi G, Piattelli A, Simion M. Clinical and histologic evaluation of allogeneic bone matrix versus autogenous bone chips associated with titanium-reinforced e-PTFE membrane for vertical ridge augmentation: A prospective pilot study. *Int J Oral Maxillofac Implants* 2008;23:1003–1012.
58. Barone A, Varanini P, Orlando B, Tonelli P, Covani U. Deep-frozen allogeneic onlay bone grafts for reconstruction of atrophic maxillary alveolar ridges: A preliminary study. *J Oral Maxillofac Surg* 2009;67:1300–1306.
59. Keith JD Jr, Petrungaro P, Leonetti JA, et al. Clinical and histologic evaluation of a mineralized block allograft: Results from the developmental period (2001–2004). *Int J Periodontics Restorative Dent* 2006;26:321–327.
60. Waasdorp J, Reynolds MA. Allogeneic bone onlay grafts for alveolar ridge augmentation: A systematic review. *Int J Oral Maxillofac Implants* 2010;25:525–531.
61. Lyford RH, Mills MP, Knapp CI, Scheyer ET, Mellonig JT. Clinical evaluation of freeze-dried block allografts for alveolar ridge augmentation: A case series. *Int J Periodontics Restorative Dent* 2003;23:417–425.
62. Keith JD Jr. Localized ridge augmentation with a block allograft followed by secondary implant placement: A case report. *Int J Periodontics Restorative Dent* 2004;24:11–17.
63. Petrungaro PS, Amar S. Localized ridge augmentation with allogenic block grafts prior to implant placement: Case reports and histologic evaluations. *Implant Dent* 2005;14:139–148.
64. Wallace S, Gellin R. Clinical evaluation of a cancellous block allograft for ridge augmentation and implant placement: A case report. *Implant Dent* 2008;17:151–158.
65. Morelli T, Neiva R, Wang HL. Human histology of allogeneic block grafts for alveolar ridge augmentation: Case report. *Int J Periodontics Restorative Dent* 2009;29:649–656.
66. Feuille F, Knapp CI, Brunsvold MA, Mellonig JT. Clinical and histologic evaluation of bone-replacement grafts in the treatment of localized alveolar ridge defects. Part 1: Mineralized freeze-dried bone allograft. *Int J Periodontics Restorative Dent* 2003;23:29–35.
67. Block MS, Degen M. Horizontal ridge augmentation using human mineralized particulate bone: Preliminary results. *J Oral Maxillofac Surg* 2004;62:67–72.
68. Nevins ML, Camelo M, Nevins M, et al. Minimally invasive alveolar ridge augmentation procedure (tunneling technique) using rhPDGF-BB in combination with three matrices: A case series. *Int J Periodontics Restorative Dent* 2009;29:371–383.
69. Hallman M, Thor A. Bone substitutes and growth factors as an alternative/complement to autogenous bone for grafting in implant dentistry. *Periodontol 2000* 2008;47:172–192.
70. Boyapati L, Wang HL. The role of platelet-rich plasma in sinus augmentation: A critical review. *Implant Dent* 2006;15:160–170.
71. Wikesjö UM, Huang YH, Polimeni G, Qahash M. Bone morphogenic proteins: A realistic alternative to bone grafting for alveolar reconstruction. *Oral Maxillofac Surg Clin North Am* 2007;19:535–551.
72. Chen FM, Zhang J, Zhang M, An Y, Chen F, Wu ZF. A review on endogenous regenerative technology in periodontal regenerative medicine. *Biomaterials* 2010;31:7892–7927.
73. Anitua E, Sanchez M, Orive G, Andia I. The potential impact of the preparation rich in growth factors (PRGF) in different medical fields. *Biomaterials* 2007;28:4551–4560.
74. Anitua E, Orive G, Pla R, Roman P, Serrano V, Andia I. The effects of PRGF on bone regeneration and on titanium implant osseointegration in goats: A histologic and histomorphometric study. *J Biomed Mater Res A* 2009;91:158–165.
75. Anitua E, Prado R, Orive G. A lateral approach for sinus elevation using PRGF technology. *Clin Implant Dent Relat Res* 2009;11(suppl 1):e23–31.
76. Molina-Minano F, Lopez-Jornet P, Camacho-Alonso F, Vicente-Ortega V. Plasma rich in growth factors and bone formation: a radiological and histomorphometric study in New Zealand rabbits. *Braz Oral Res* 2009;23:275–280.

Bone Response to Submerged Implants in Organ Transplant Patients: A Prospective Controlled Study

Lucio Montebugnoli, MD, DDS¹/Mattia Venturi, DDS²/Fabio Cervellati, DDS²

Purpose: To compare the short-term outcome of dental implant therapy in a group of organ transplant patients with that of a control group. **Materials and Methods:** The study population included consecutive organ transplant patients and consecutive normal (healthy) subjects as controls. Two films were taken of all patients: one at baseline (implant placement) and one after 3 months of healing. All radiographs were analyzed twice (15 days apart) blindly by two independent trained radiologists. Crestal bone level (CBL) was measured, defined as the perpendicular distance from the reference point on the implant to the first visible apical bone-to-implant contact. **Results:** The study population included 10 organ transplant patients (eight hearts, two livers) and 10 control patients, who received 20 and 12 submerged dental implants, respectively. At the 3-month follow-up visit, no implants showed any exposed cover screws. CBL increased in both groups, without any significant difference between the groups (CBL increased from 0.08 ± 0.09 mm to 0.28 ± 0.20 mm in transplant patients and from 0.11 ± 0.16 mm to 0.42 ± 0.32 mm in controls). Multiple analysis of variance showed that the mean bone loss of 0.21 ± 0.18 mm observed in the group of transplant patients was not statistically different from that (0.32 ± 0.25 mm) seen in the control group and was not influenced by any of the variables considered. **Conclusions:** The present pilot study seems to indicate that the bone response around submerged dental implants in immunocompromised organ transplant patients does not differ from that observed in control patients and that this particular population of patients may be successfully rehabilitated with dental implants. *INT J ORAL MAXILLOFAC IMPLANTS* 2012;27:1494–1500

Key words: crestal bone loss, dental implants, longitudinal study, organ transplants, osseointegration

Survival rates following solid-organ transplantation have improved greatly during the past 2 decades, and patients with transplanted organs are represented increasingly often in the general population.¹ A large proportion of these patients need to be orally rehabilitated as a consequence of the mandatory removal of all compromised teeth before the transplantation to reduce postoperative mortality and morbidity caused by infectious diseases.² The endosseous implant is acknowledged as a standard of care for the rehabilitation of edentulous or partially edentulous patients, and the placement of titanium implants in the arches of transplant patients should be considered as an option in oral rehabilitation.

The success of osseointegration depends on the state of the host bone and its healing capacity. However, the immunosuppressive treatment that follows organ transplantation has been demonstrated to have a negative effect upon bone mineral metabolism.^{3,4} Marked suppression of osteoblast-mediated bone formation and inhibition of osteoblast synthetic function are effects of immunosuppressive treatment that are clearly supported by the literature. It is also known that a significant increase in bone resorption contributes to the alteration in bone metabolism. In fact, osteoporosis is one of the most frequently reported side effects in allogeneic organ transplantation, and the use of cyclosporine and other immunosuppressive drugs such as glucocorticoids is generally considered to be its cause.^{5–7}

Despite the great abundance of data about the effects of immunosuppressive regimens on bone demineralization in transplanted patients, there is a lack of data about the bone response to dental implants in these patients, and, to the best of the authors' knowledge, no controlled study has yet been conducted in humans. Two case reports involving humans have been published (both in human liver-transplant patients),

¹Professor, Department of Oral Science, University of Bologna, Italy.

²Researcher, Department of Oral Science, University of Bologna, Italy.

Correspondence to: Dr Lucio Montebugnoli, Department of Oral Science, University of Bologna, Via S. Vitale 59, 40125 Bologna, Italy. Fax: +390-51225208. Email: lucio.montebugnoli@unibo.it

and both reported successful rehabilitation with dental implants at 5 and 10 years, respectively.^{8,9}

Some controlled studies have been conducted in animals, but with contradictory results concerning the influence of immunosuppressive treatment on bone healing around titanium implants. Duarte et al^{10,11} reported a lack of any influence of cyclosporine on bone density adjacent to the titanium implant surface in rabbits, while Sakakura et al reported a negative effect on bone healing around dental implants in rabbits.¹²⁻¹⁴

The present study is the first prospective and controlled study in humans aiming to evaluate the bone response around dental implants during healing in a group of organ transplant patients and to compare this with the bone response around implants in a control group.

MATERIALS AND METHODS

The study population consecutively included organ transplant patients and normal subjects as controls who had requested oral rehabilitation with at least one implant.

The following inclusion criteria were used:

- Age between 30 and 75 years
- Sufficient amount of bone in the recipient site to host implants with a diameter of at least 3.5 mm and a length of at least 8 mm
- Implant sites that were completely healed (for at least 1 year after extraction), without any sign of infection
- Absence of oral lesions, periodontitis, or gingival overgrowth
- Organ transplantation at least 2 years previous

Patients were excluded from the study if any of the following criteria existed:

- Previous irradiation of the head and neck region
- Alcohol or drug abuse or psychiatric disorders that made it difficult to obtain informed consent
- Severe bruxism or clenching habits
- Heavy smoking (> 10 cigarettes/day)

The study was designed in accordance with the Helsinki Declaration of 2008.¹⁵ Approval for the study was obtained from the Ethical Review Committee of the University of Bologna, Italy (no. CE09037, November 5, 2009). In addition to an intraoral clinical examination, panoramic radiographs and computed tomography were performed on all patients to screen for bony pathoses and determine the amount of bone present to facilitate the selection of the appropriate implant sizes.

Each participant received one or more dental implants to rehabilitate an edentulous gap using a two-stage surgical protocol. All implants were placed by the same surgeon according to the same protocol and without any guided bone regeneration or any other augmentation procedure. Bone quality and quantity at each implant site were assessed according to the Lekholm and Zarb classification.¹⁶ Following implant placement, the patients were provided with home care maintenance instructions and mouth rinses (chlorhexidine 0.20%, Dentosan, Johnson and Johnson, three times a day for 1 week) as an adjunctive treatment to routine oral hygiene. Sutures were removed after 10 days. After a healing period of 3 months, stage-two surgery was carried out to connect the abutments to the implants.

Standardized radiographs were taken at baseline (stage-one surgery) and at the time of stage-two surgery immediately before the abutments were connected, with the film parallel and the x-ray beam perpendicular to the implant by using individually fabricated repositionable film holders. Radiographs (Kodak Insight IP-21, Eastman Kodak Company) were exposed using an x-ray machine (Castellini XSafe 70, Castellini) set at 70 kV and 8 mA. The films were processed immediately after exposure in an automatic processor (DL 26, Dürr Dental) that was calibrated daily.

In all patients, films were taken at baseline and again immediately before abutment connection. The radiographs were scanned with a slide scanner (Epson Perfection V750 Pro) with a resolution of 968 dpi and a magnification factor of $\times 20$. Dedicated image analysis software (UTHSCSA Image Tool, version 3.00 for Windows, University of Texas Health Science Center) was used to perform the measurements. The known diameters and lengths of the implants were used to calibrate the measurements. All radiographs (baseline and abutment connection) were blindly analyzed twice (15 days apart) by two independent trained radiologists.

Crestal bone levels (CBL) were defined as the perpendicular distance from the reference point on the implant (the top of the rough portion of the implant collar) to the first visible apical bone-to-implant contact.¹⁷ The distance from the reference point to the bone level was recorded both mesially and distally and then averaged for each implant. Each single value of CBL was considered as the mean of eight single observations (two radiographs each read twice by two observers).

The validity and error of the methods (measurement precision) were evaluated for intraobserver (precision of each observer) and interobserver (comparison between observers) variability. Intraobserver variability was determined separately for the two observers and as a mean of the two, either by comparing

the readings of the first and second radiographs or by comparing the first and second readings obtained by each observer 15 days apart. Interobserver variability was determined by comparing all radiographic readings obtained by the two observers. The variability was expressed as mean difference (\pm standard deviation [SD]) and maximum and minimum differences between readings.

The primary endpoint with respect to efficacy was the CBL 3 months after implant placement. The results were expressed as time-related variations in CBL and in bone loss.

Statistical Analysis

After it was determined that the standardized skewness and standardized kurtosis were within the ranges expected for normally distributed data, a generalized linear model was fitted, and analysis of variance (ANOVA) for repeated measures with a split-plot design was performed to evaluate differences between patients (transplants vs controls), time-related variations in CBL (3 months vs baseline), and the interaction between patients and time-related variations in CBL. The Bonferroni *t* test was applied as a multiple-comparison *t* test for significance.

Multiple-comparison ANOVA was used to evaluate the presence of any significant effect on bone loss of a series of variables. These included age, gender, smoking habits, bone density, implant diameter and length, implant location (anterior vs posterior, maxilla vs mandible), and transplants vs controls.

One-way ANOVA was used to evaluate the presence of any significant difference in the mean bone loss considering the interaction between single/multiple implants and therapy with or without corticosteroids and the interaction between implant location and therapy with or without corticosteroids.

Chi-square analysis was used to evaluate the presence of any significant difference in the between-group distribution with regard to age (cutoff 54 years), gender, implant position (maxilla vs mandible and anterior vs posterior), bone density, and implant diameter or length.

RESULTS

The study population included 10 consecutive organ transplant patients (eight hearts, two livers; eight men and two women aged 35 to 72 years; mean age, 57.6 ± 15.8) and 10 consecutive normal subjects as controls (nine men and one woman aged 41 to 64 years; mean age, 50.1 ± 7.0) who had requested oral rehabilitation with at least one implant. Table 1 shows the features of the population. No statistically significant difference was found in the between-group distri-

Table 1 Features of the Study Population

Patient	Age (y)	Gender	Smokers	Bone density
Transplant group				
1	58	M	No	3
2	68	M	No	2
3	38	M	No	2
4	68	M	No	3
5	59	M	Yes	2
6	35	M	No	3
7	72	M	No	2
8	75	M	No	2
9	35	F	No	2
10	68	F	Yes	3
Control group				
1	54	M	No	3
2	49	M	Yes	3
3	41	M	No	3
4	55	M	No	2
5	41	M	No	2
6	64	M	No	2
7	47	M	No	2
8	54	M	No	3
9	48	M	No	3
10	47	F	Yes	2

*FDI tooth-numbering system.

bution regarding age (cutoff 54 years), gender, implant position (maxilla vs mandible and anterior vs posterior), bone density, implant diameter, or implant length.

In all patients, standard tapered implants with anodized surfaces (NobelReplace Tapered Groovy, Nobel Biocare) were used. Thirty-two implants were placed, 20 in the transplant patients and 12 in the control patients.

The between-radiographs intraobserver variability (256 readings) was 0.01 ± 0.08 mm with a range

Transplanted organ/immunosuppressive treatment	Implant diameter × length (mm)	Implant location*	Bone loss (mm)
Heart; cyclosporine 125 mg/d, prednisone 12.5 mg/d	3.5 × 8	15	0.04
Heart; cyclosporine 150 mg/d, prednisone 5 mg/d	3.5 × 10 4.3 × 10	34 35	0.30 0.29
Heart; cyclosporine 200 mg/d, prednisone 12.5 mg/d	4.3 × 13	14	0.76
Liver; sirolimus 3 mg/d, no corticosteroids	3.5 × 10 4.3 × 13 4.3 × 13 3.5 × 10 4.3 × 13 4.3 × 10	11 13 15 21 23 25	0.16 0.42 0.18 0.43 0.04 0.05
Liver; cyclosporine 75 mg/d, no corticosteroids	3.5 × 10 3.5 × 10 3.5 × 10	11 13 21	0.07 0.04 0.18
Heart; cyclosporine 200 mg/die, prednisone 5 mg/d	3.5 × 10	15	0.29
Heart; cyclosporine 100 mg/d, prednisone 7.5 mg/d	3.5 × 10 4.3 × 10	12 22	0.02 0.12
Heart; cyclosporine 75 mg/d, no corticosteroids	4.3 × 8 4.3 × 8	45 46	0.43 0.08
Heart; tacrolimus 5 mg/d, no corticosteroids	4.3 × 8	37	0.03
Heart; cyclosporine 100 mg/d, no corticosteroids	3.5 × 8	13	0.24
<hr/>			
N/A	3.5 × 10 4.3 × 10	15 25	0.33 0.42
N/A	3.5 × 8	25	0.01
N/A	3.5 × 10 3.5 × 10	11 21	0.18 0.22
N/A	3.5 × 8	36	0.64
N/A	4.3 × 8	35	0.36
N/A	3.5 × 8	45	0.88
N/A	4.3 × 10	36	0.41
N/A	3.5 × 10	25	0.16
N/A	4.3 × 8	16	0.10
N/A	3.5 × 10	36	0.09

Table 2 Within-Observer and Between-Observer Differences in Radiographic CBL Readings

	Within-observer differences		Between-observer differences	
	Observer 1, between-Rx difference	Observer 2, between-Rx difference	Observer 1, time-related difference	Observer 2, time-related difference
No. of readings	128	128	256	256
Mean difference ± SD	0.013 ± 0.10 mm	0.011 ± 0.07 mm	0.034 ± 0.12 mm	0.037 ± 0.15 mm
Minimum	-0.21 mm	-0.15 mm	-0.46 mm	-0.71 mm
Maximum	0.44 mm	0.33 mm	0.48 mm	0.55 mm

of -0.21 to 0.44 mm. The time-related (15 days apart) intraobserver variability considering both observers (512 readings) was 0.04 ± 0.13 mm, with a range of -0.71 to 0.55 mm. The interobserver variability

considering both moments (128 readings) was 0.06 ± 0.16 mm, with a range of -0.34 to 0.92 mm. The precision of the methods for the two observers is reported in Table 2.

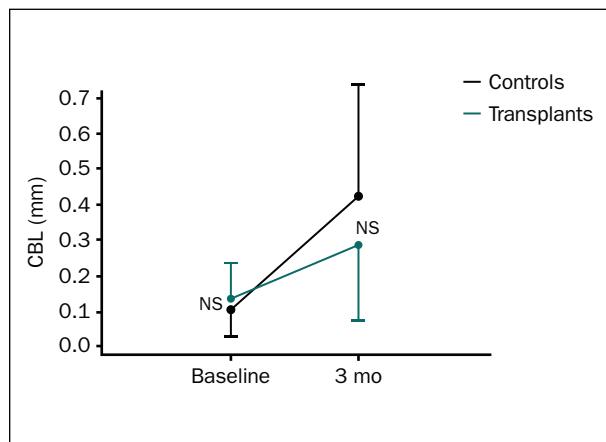


Fig 1 ANOVA for repeated measures with split-plot design showing CBL variation in the two groups of transplants and in controls. A significant time-related increase in CBL was found within both groups, but there was no significant difference between groups.

At the 3-month follow-up visit, no implant cover screws were exposed. In both groups, all implants were stable at re-entry and no implants were lost during the healing period. CBL increased from 0.08 ± 0.09 mm to 0.28 ± 0.20 mm in the transplant group and from 0.11 ± 0.16 mm to 0.42 ± 0.32 mm in the group of controls. Repeated-measures ANOVA with split-plot design showed that the time-related increase was statistically significant ($F = 41.6$; $P < .01$) within both groups, but there was no significant difference between groups ($F = 1.9$; NS) (Fig 1). A mean bone loss of 0.21 ± 0.18 mm (range, 0.02 to 0.74 mm) was observed in the transplant patients, compared to a mean bone loss of 0.32 ± 0.25 mm (range, 0.01 to 0.88 mm) in the control patients.

Multiple-comparison ANOVA did not show any statistically significant between-group differences. Nor was there any significant relationship between bone loss and all considered variables (age, gender, smoking habits, bone density, implant diameter and length, and implant location).

In particular, the results of one-way ANOVA did not show any significant difference in the mean bone loss between patients ($n = 2$) with single implants and those with multiple implants ($n = 3$ patients with 11 implants) who were taking corticosteroids, and between patients with single implants ($n = 3$ patients) or multiple implants ($n = 2$ patients with 4 implants) who were not taking corticosteroids (0.13 ± 0.15 mm, 0.19 ± 0.16 mm, 0.36 ± 0.36 mm, 0.18 ± 0.14 mm, respectively; $F = .79$ NS). Further, considering the interaction between implant location and therapy with or without corticosteroids, the results did not show any significant between-group statistically significant differences, although very little bone loss was observed in one transplant patient (no. 7) who was taking corticosteroids and had two implants located in the anterior maxilla.

DISCUSSION

The present study has shown very good bone healing around oral implants in all the transplant patients. No implants were lost, and no cover screws were even minimally exposed. Furthermore, the bone loss during the first 3 months was not statistically significantly different from that of the control group—in fact, it was actually less than that seen in the control subjects. Within the limitations of the study (namely, the small population), the mean bone loss did not seem to be influenced by the location of the implants, the presence of single or multiple implants, or the consumption of corticosteroids.

Because of the small size of the study population, great care was taken to standardize a design that could provide reliable comparisons of the data obtained in the two groups of patients. The composition of the two study groups was homogenous, with no statistically significant between-group differences for any of the variables considered. The study protocol was the same for the two groups and included the same operator, the same type of implants, and the same blinded examiners for the radiographic evaluation.

Great care was also paid to the precision of CBL assessments. Radiographs were taken at each examination, and all were blindly examined twice by two radiologists 15 days apart. The intra- and interobserver variability was low and similar to that usually reported in the literature.^{18–21} The precision of each CBL measurement was increased²² by considering each single value of CBL as the mean of eight single observations (two radiographs read two times by two observers).

The short-term mean bone loss of 0.21 mm in the transplant patients should be considered a very good result, not only because the value did not differ significantly from that of the control patients but also because it is similar to values found in the literature

for healthy subjects. Short-term bone loss values of 0.18 mm, 0.21 mm, and 0.1 mm were documented in normal subjects by Kim et al,²³ Bratu et al,²⁴ and Nickenig et al,²⁵ respectively, and similar data were also been reported in beagle dogs in studies by Abrahamsson et al,²⁶ who observed a bone loss of 0.23 mm at 3 months after surgery, and by Cochran et al,²⁷ who measured a mean bone loss of 0.52 mm.

These data seem to suggest that short-term success of dental implant therapy might not be influenced by the long-term immunosuppressive regimen that is typically associated with organ transplantation, although many studies have shown that the immunosuppressants in organ transplants affect short-term and long-term bone metabolism and that osteoporosis is one of the most common side effects in organ transplant patients.^{3,4}

Glucocorticoids have been demonstrated to have significant direct skeletal effects on bone metabolism consisting of decreases in osteoblast replication, differentiation, and life span, as well as the inhibition of many cytokines that cause profound reductions in bone formation (with less prominent effects on bone resorption). Moreover, the indirect effects of these drugs may worsen bone metabolism by decreasing gonadal function and reducing calcium transport in the gastrointestinal tract, kidneys, and parathyroids.⁶

The introduction of newer agents, including cyclosporine, tacrolimus, and, more recently, rapamycin and daclizumab, has reduced the need for high doses of glucocorticoids and, in some cases, enabled adoption of steroid-free regimens. However, calcineurin inhibitors are not devoid of effects on bone metabolism, and, in fact, have been demonstrated to regulate both osteoblast and osteoclast differentiation.^{28,29} Cyclosporine, in addition to its effects on the immune system, increases bone turnover, resulting in higher resorption versus the bone formation rate and probably leading to the high percentage of osteoporosis among transplant patients.³⁰⁻³² Tacrolimus has been documented to have similar, but less pronounced, effects as cyclosporine.^{33,34} Both drugs additionally reduce renal function and increase parathyroid hormone secretion.⁴ Similar or more negative effects on bone metabolism have been reported for other agents frequently associated with the immunosuppressive therapy used to control hypertension,^{35,36} such as nifedipine. Despite the great abundance of data concerning the relationship between immunosuppressive therapy and bone demineralization in patients with organ transplants, there is a lack of data about the bone response around dental implants placed in these patients.

A negative effect of immunosuppressive therapy on bone healing around dental implants was first suggested by Sakakura et al¹²⁻¹⁴ following the results of

their studies in rabbits. A short-term lower removal torque and lower percentage of bone contact of implants inserted in rabbits undergoing cyclosporine therapy was reported by the authors in 2003.¹² Later, the same authors using the same animal model demonstrated that cyclosporine administration impaired mechanical retention and bone quality, even around well-integrated dental implants.^{13,14}

Conflicting results were obtained by Duarte et al,^{10,11} who demonstrated that short-term administration of cyclosporine and nifedipine in rabbits did not affect bone-to-implant contact, nor did it significantly influence the proportion of mineralized bone (bone density) lateral to the titanium implant surface, although a significant decrease in bone area around the implants was observed.

In humans, only two case reports have documented a positive outcome in organ transplant patients. The first case report refers to a 71-year-old man who had undergone liver transplantation 10 years before and had received two interforaminal implants in the edentulous mandible 1 year after transplantation. At 10 years, all peri-implant parameters were within normal ranges, and only moderate vertical bone loss was detected.⁸ The second case report refers to a 45-year-old man treated with 11 dental implants 1 year after liver transplantation, who showed stable osseointegration with moderate vertical bone loss 5 years after implant placement.⁹

The preliminary results of this first prospective, controlled study in humans are in line with the aforementioned case reports. All organ transplant patients who were followed in the study experienced good bone healing around all implants, at least in the short term. Further studies are being conducted to determine whether similar good results can be confirmed in the long term.

CONCLUSIONS

Within the limitations of the study, the present data suggest that: (1) the bone response around submerged dental implants in immunocompromised organ transplant patients does not differ from that observed in control patients and (2) patients with organ transplants may be successfully rehabilitated with dental implants.

ACKNOWLEDGMENTS

The authors are grateful to Nobel Biocare for supplying the implants. The authors reported no conflicts of interest related to this study.

REFERENCES

1. Taylor DO, Edwards LB, Aurora P, et al. Registry of the International Society for Heart and Lung Transplantation: Twenty-fifth official adult heart transplant report 2008. *J Heart Lung Transplant* 2008; 27:943–956.
2. Sanromán Budíño B, Vázquez Martul E, Pérgola Díaz S, Veiga Barreiro A, Carro Rey E, Mosquera Reboredo J. Autopsy-determined causes of death in solid organ transplant recipients. *Transplant Proc* 2004;36:787–789.
3. Kulak CA, Borba VZ, Kulak JJ Jr, Shane E. Transplantation osteoporosis. *Arq Bras Endocrinol Metabol* 2006;50:783–792.
4. Stein E, Ebeling P, Shane E. Post-transplantation osteoporosis. *Endocrinol Metab Clin North Am* 2007;36:937–963.
5. Shane E, Mancini D, Aaronson K, et al. Bone mass, vitamin D deficiency, and hyperparathyroidism in congestive heart failure. *Am J Med* 1997;103:197–207.
6. Van Staa TP. The pathogenesis, epidemiology and management of glucocorticoid-induced osteoporosis. *Calcif Tissue Int* 2006;79: 129–137.
7. Cohen A, Addonizio LJ, Lamour JM, et al. Osteoporosis in adult survivors of adolescent cardiac transplantation may be related to hyperparathyroidism, mild renal insufficiency, and increased bone turnover. *J Heart Lung Transplant* 2005;24:696–702.
8. Heckmann SM, Heckmann JG, Linke JJ, Hohenberger W, Mombelli A. Implant therapy following liver transplantation: Clinical and microbiological results after 10 years. *J Periodontol* 2004;75:909–913.
9. Gu L, Wang Q, Yu YC. Eleven dental implants placed in a liver transplantation patient: A case report and 5-year clinical evaluation. *Chin Med J* 2011;124:472–475.
10. Duarte PM, Nogueira Filho GR, Sallum EA, de Toledo S, Sallum AW, Nociti FH Jr. The effect of an immunosuppressive therapy and its withdrawal on bone healing around titanium implants. A histometric study in rabbits. *J Periodontol* 2001;72:1391–1397.
11. Duarte PM, Nogueira Filho GR, Sallum EA, Sallum AW, Nociti FH Jr. Short-term immunosuppressive therapy does not affect the density of the pre-existing bone around titanium implants placed in rabbits. *Pesqui Odontol Bras* 2003;17:362–366.
12. Sakakura CE, Margonar R, Holzhausen M, Nociti FH Jr, Alba RC Jr, Marcantonio E Jr. Influence of cyclosporin A therapy on bone healing around titanium implants: A histometric and biomechanical study in rabbits. *J Periodontol* 2003;74:976–981.
13. Sakakura CE, Margonar R, Sartori R, Morais JA, Marcantonio E Jr. The influence of cyclosporin A on mechanical retention of dental implants previously integrated to the bone: A study in rabbits. *J Periodontol* 2006;77:2059–2062.
14. Sakakura CE, Marcantonio E Jr, Wenzel A, Scaf G. Influence of cyclosporin A on quality of bone around integrated dental implants: A radiographic study in rabbits. *Clin Oral Implants Res* 2007;18:34–39.
15. Williams JR. The Declaration of Helsinki and public health. *Bull World Health Organ* 2008;86:650–651.
16. Lekholm U, Zarb GA. Patient selection and preparation. In: Brånemark PI, Zarb GA, Albrektsson T (eds). *Tissue-Integrated Prostheses: Osseointegration in Clinical Dentistry*. Chicago: Quintessence, 1985: 199–209.
17. Blanes RJ, Bernard JP, Blanes ZM, Belser UC. A 10-year prospective study of ITI dental implants placed in the posterior region. I: Clinical and radiographic results. *Clin Oral Implants Res* 2007;18:699–706.
18. Chang M, Wennström JL. Peri-implant soft tissue and bone crest alterations at fixed dental prostheses: A 3-year prospective study. *Clin Oral Implants Res* 2010;21:527–534.
19. Brägger U, Häfeli U, Huber B, Hämmeter CH, Lang NP. Evaluation of postsurgical crestal bone levels adjacent to non-submerged dental implants. *Clin Oral Implants Res* 1998;9:218–224.
20. Wennström JL, Ekestubbe A, Gröndahl K, Karlsson S, Lindhe J. Oral rehabilitation with implant-supported fixed partial dentures in periodontitis-susceptible subjects. A 5-year prospective study. *J Clin Periodontol* 2004;31:713–724.
21. Sakka S, Al-ani Z, Kasioumis T, Worthington H, Coulthard P. Inter-examiner and intra-examiner reliability of the measurement of marginal bone loss around oral implants. *Implant Dent* 2005;14:386–388.
22. Gröndahl K, Sundén S, Gröndahl HG. Inter- and intraobserver variability in radiographic bone level assessment at Bränemark fixtures. *Clin Oral Implants Res* 1998;9:243–250.
23. Kim TH, Lee DW, Kim CK, Park KH, Moon IS. Influence of early cover screw exposure on crestal bone loss around implants: Intraindividual comparison of bone level at exposed and non-exposed implants. *J Periodontol* 2009;80:933–939.
24. Bratu EA, Tandlich M, Shapira L. A rough surface implant neck with microthreads reduces the amount of marginal bone loss: A prospective clinical study. *Clin Oral Implants Res* 2009;20:827–832.
25. Nickenig HJ, Wichmann M, Schlegel KA, Nkenke E, Eitner S. Radiographic evaluation of marginal bone levels adjacent to parallel-screw cylinder machined-neck implants and rough-surfaced microthreaded implants using digitized panoramic radiographs. *Clin Oral Implants Res* 2009;20:550–554.
26. Abrahamsson I, Berglundh T, Moon IS, Lindhe J. Peri-implant tissues at submerged and non-submerged titanium implants. *J Clin Periodontol* 1999;26:600–607.
27. Cochran DL, Nummikoski PV, Higginbottom FL, Hermann JS, Makins SR, Buser D. Evaluation of an endosseous titanium implant with a sandblasted and acid-etched surface in the canine mandible: Radiographic results. *Clin Oral Implants Res* 1996;7:240–252.
28. Sun L, Blair HC, Peng Y, et al. Calcineurin regulates bone formation by the osteoblast. *Proc Natl Acad Sci U S A* 2005;102:17130–17135.
29. Sun L, Peng Y, Zaidi N, et al. Evidence that calcineurin is required for the genesis of bone-resorbing osteoclasts. *Am J Physiol Renal Physiol* 2007;292:F285–291.
30. Guo CY, Johnson A, Locke TJ, Eastell R. Mechanisms of bone loss after cardiac transplantation. *Bone* 1998;22:267–271.
31. McDonald JA, Dunstan CR, Dilworth P, et al. Bone loss after liver transplantation. *Hepatology* 1991;14:613–619.
32. Cueto-Manzano AM, Konel S, Hutchison AJ, et al. Bone loss in long-term renal transplantation: Histopathology and densitometry analysis. *Kidney Int* 1999;55:2021–2029.
33. Goffin E, Devogelaer JP, Lalaoui A, et al. Tacrolimus and low-dose steroid immunosuppression preserves bone mass after renal transplantation. *Transpl Int* 2002;15:73–80.
34. Monegal A, Navasa M, Guañabens N, et al. Bone mass and mineral metabolism in liver transplant patients treated with FK506 or cyclosporine A. *Calcif Tissue Int* 2001;68:83–86.
35. Duriez J, Flautre B, Blary MC, Hardouin P. Effects of the calcium channel blocker nifedipine on epiphyseal growth plate and bone turnover: A study in rabbit. *Calcif Tissue Int* 1993;52:120–124.
36. Ritchie CK, Maercklein PB, Fitzpatrick LA. Direct effect of calcium channel antagonists on osteoclast function: Alterations in bone resorption and intracellular calcium concentrations. *Endocrinology* 1994;135:996–1003.

Use of 8-mm and 9-mm Implants in Atrophic Alveolar Ridges: 10-Year Results

Christian Mertens, DDS¹/Amelie Meyer-Bäumer, DDS²/Hannes Kappel, DDS¹/Jürgen Hoffmann, MD, DDS, PhD³/Helmut G. Steveling, DDS⁴

Purpose: The use of short implants can reduce the need for augmentative procedures prior to implant placement and, thus, morbidity and treatment time for patients with severely atrophied alveolar ridges. However, the inevitably less favorable crown-to-implant ratio is often associated with higher implant failure rates and greater marginal bone loss. The aim of this study was to evaluate the long-term survival and success rates of short implants in severely atrophic alveolar ridges retaining restorations on these short implants only.

Materials and Methods: In this study, 8-mm and 9-mm implants were inserted in atrophic alveolar ridges according to the manufacturer's protocol for the respective bone quality and loaded after 3 months of healing. Prosthetic restorations were supported only by short implants (not in combination with longer implants). After a mean observation period of 10.1 years (\pm 1.9 years), all patients were re-examined clinically and radiographically. **Results:** In this study, fifty-two 8-mm and 9-mm implants were placed in 14 patients. After 10.1 years, no implants and suprastructure had been lost. A mean marginal bone loss of 0.3 mm (\pm 0.4 mm) was recorded. According to the Albrektsson criteria, all implants were successful; with respect to the more rigorous Karoussis et al criteria, four implants failed. **Conclusions:** The results of this long-term study suggest that the use of short implants results in marginal bone resorption and failure rates similar to those for longer implants. The higher crown-to-implant ratio did not seem to have any negative influence on implant success in this study. INT J ORAL MAXILLOFAC IMPLANTS 2012;27:1501–1508

Key words: bone atrophy, dental implants, implant success, implant survival

Endosseous dental implants have become a highly predictable treatment option for completely and partially edentulous patients. After tooth loss, severe atrophy of the alveolar ridges is quite common in patients with a history of periodontitis or in patients whose edentulism is of long duration. Especially in the posterior region, the applicability of dental implants may be limited because of insufficient alveolar ridge

height caused by bone resorption. This results in a closer proximity to adjacent anatomical structures (eg, the inferior alveolar nerve, the sinus floor). In these cases, advanced surgical procedures, such as vertical bone grafting, are often performed to allow the placement of longer implants.^{1–3} Other alternatives, such as alveolar nerve transpositions, are accompanied by high rates of complications.² On the other hand, the use of shorter implants can reduce the need for augmentative procedures and thus diminish morbidity and treatment time for patients.

A review by Esposito et al⁴ compared the results of vertical ridge augmentation procedures to those of the insertion of short dental implants. The vertically augmented group experienced a higher implant failure rate and statistically significantly more complications. Therefore, the authors concluded that short implants appear to be a superior alternative to vertical bone grafting.⁴ Other authors, however, often associate the resulting poor crown-to-implant ratio of short implants with higher implant failure rates and higher marginal bone loss. Winkler et al documented a survival rate of 74.4% for 7-mm implants over 3 years.⁵ Herrmann et al presented similar results, with a survival rate of 78.2%.⁶

¹Clinician, Department of Oral and Maxillofacial Surgery, University Hospital Heidelberg, Heidelberg, Germany.

²Clinician, Section of Periodontology, Department of Conservative Dentistry, University Hospital Heidelberg, Heidelberg, Germany.

³Professor and Chairman, Department of Oral and Maxillofacial Surgery, University Hospital Heidelberg, Heidelberg, Germany.

⁴Clinician, Private Practice, Gernsbach, Germany.

Correspondence to: Dr Christian Mertens, Department of Oral and Maxillofacial Surgery, University Hospital Heidelberg, Im Neuenheimer Feld 400, 69120 Heidelberg, Germany.
Fax: +49-6221-56-4222.
Email: christian.mertens@med.uni-heidelberg.de

Many other studies demonstrated higher failure rates. In contrast, other studies showed similar survival rates for short and longer implants.^{7,8} A further group of studies reported that implant length did not influence survival rates.^{9–11} In addition, other factors seem to influence implant survival. With respect to implant surface topography, machined implants show significantly higher rates of implant failure than those with rough surfaces. Furthermore, adapted surgical protocols can have positive effects on implant survival.^{12,13}

The aim of this retrospective study was to evaluate long-term survival rates and bone level alterations around short implants that acted as sole support for prostheses. Furthermore, parameters determining implant prognosis, such as peri-implant bleeding on probing, probing depth, and radiographic marginal bone levels, were assessed over a period of 10 years.

MATERIALS AND METHODS

Patients

All included patients had been referred to the Department of Oral and Maxillofacial Surgery, University Hospital Heidelberg, for implant treatment between 1998 and 1999. The study was conducted in accordance with the principles of the Declaration of Helsinki. In addition, the Ethics Committee for clinical studies of the Medical Faculty of the Heidelberg University had reviewed and approved the study protocol, and informed consent was obtained from each patient.

All patients had to fulfill the following inclusion criteria:

- Atrophic edentulous or partially edentulous ridges (Class III and IV according to Cawood and Howell¹⁴) with at least 8 mm of residual bone height prior to implant placement
- Sufficient denture in the opposing arch providing for good occlusion
- Suprastructures retained exclusively by short implants

Exclusion criteria were:

- Untreated periodontal diseases
- Caries
- Insufficient oral hygiene
- Previous radiation therapy and systemic disorders potentially affecting the outcome of the implant therapy (eg, uncontrolled diabetes mellitus, current chemotherapy, pregnancy)

Patients with treated periodontal diseases, smoking habits, or clenching/parafunctional habits were not excluded.

Implants were defined as short if they were 9 mm or shorter.^{15–17} Short implants were not splinted together with longer implants. Single crowns, splinted crowns, and partial and complete dentures were included if they were supported solely by short implants. The implants under examination were used for all indications.

Implant Treatment

After clinical and radiographic examinations, the patients were scheduled for implant placement. Implant surgery was performed by one experienced surgeon under local anesthesia using a two-stage surgical approach. The implants had a moderately rough titanium-blasted surface (TiOblast, Astra Tech) and were screw-shaped and parallel-walled. The implants differed in diameter (3.5/4.0/4.5 mm) and in effective length (8 and 9 mm), depending on the bone dimension at each site. The drilling protocol was performed according to the manufacturer's specifications and was adapted to bone quality. The insertion depth of the implants was determined by the surrounding bone; the implant neck was placed flush with the alveolar ridge.

After surgery, patients were advised not to wear any removable dentures for 1 week. A chlorhexidine mouth rinse was prescribed for use two times per day. No antibiotics were prescribed before or after implant placement. Sutures were removed after 7 days. When the patients began to use their dentures again, any pressure from the denture base on the implant region was relieved. The healing period was 3 months for both maxillary and mandibular implants.

All prosthetic rehabilitations were performed by the same prosthodontist and were constructed to enable patients to maintain optimal oral hygiene. Therefore, reconstructions in the molar and premolar regions were mainly screw retained. Hygiene instructions, including the use of interdental brushes and flossing technique, were given to each patient.

Clinical Examinations

Patients were followed up yearly. Clinical parameters such as the Mombelli et al Modified Plaque Index and Sulcus Bleeding Index were determined.¹⁸ Peri-implant pocket depths were measured at four sides per implant (mesial, distal, vestibular, and oral). Furthermore, in cases of screw-retained suprastructures, the mobility of each individual implant was tested manually after the restorations were removed. Occlusion was monitored and hygiene instructions were given to the patients.

Radiographic Examination

At the time of placement of the definitive reconstruction, intraoral radiographs were obtained (baseline). Additional radiographs were acquired at the annual follow-up visits. To ensure standardization, all periapical

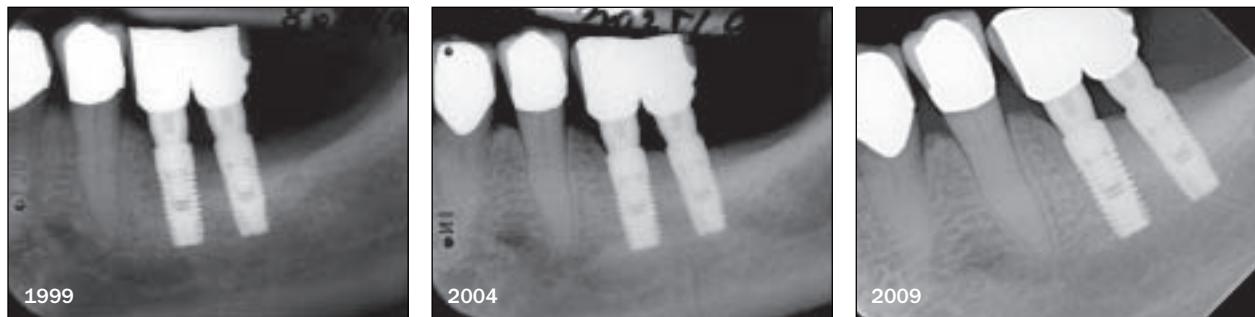


Fig 1 Radiographic follow-up after 10 years (diameter 3.5 mm, length 9 mm).

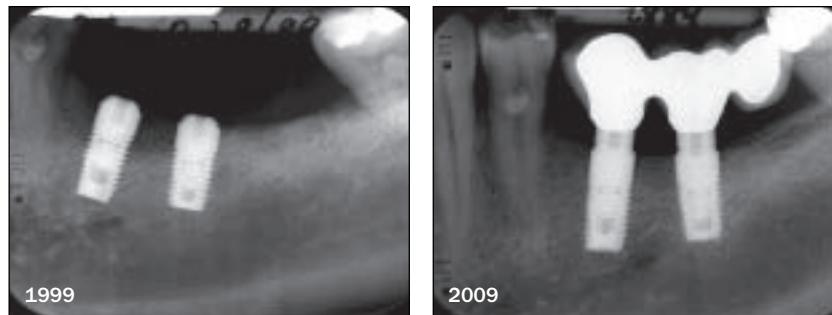


Fig 2 Radiographic follow-up after 10 years (diameter 4.0 mm, lengths 9 and 8 mm).

radiographs were taken with the long-cone technique and using a film holder (Figs 1 and 2). The distance between the implant shoulder and the first visible bone-to-implant contact was assessed at the mesial and distal aspects of the implant using the Friacomp DentalOffice software program (Version 2.5, Friadent). The linear dimensions of the digitized images were calibrated to take into account anatomic magnification and distortions in the films. This was achieved by setting the scale in the image to the known distance between the implant threads. All radiographs were analyzed by the same independent radiologist, who had not previously been actively involved in this study. Any apparent bone gain was recorded as zero bone loss.

Success Criteria

The Albrektsson et al¹⁹ radiographic success criteria were applied to determine the success or failure of an implant. That is, an implant was considered successful if the marginal bone loss was 1 mm or less during the first year after insertion of the prosthesis and no greater than 0.2 mm in every following year of function and if no signs of peri-implant radiolucency were apparent.

Furthermore, the more stringent success criteria of Karoussis et al²⁰ were applied, since these additionally

include soft tissue parameters, such as probing depths and bleeding on probing. To be defined as successful, the following requirements had to be met:

1. Absence of mobility
2. Absence of persistent subjective complaints (pain, foreign-body sensation, and/or dysesthesia)
3. No probing pocket depth > 5 mm
4. No probing pocket depth = 5 mm with bleeding on probing
5. Absence of continuous radiolucency around the implant
6. Vertical bone loss not to exceed 0.2 mm annually after the first year of function

Data Analysis

Statistical analysis was performed using SPSS (version 18, IBM) and SAS (version 9, SAS Institute) software. Only exact statistical methods were applied ('SPSS module', 'Exact Tests'). Arithmetic means, medians, percentiles, standard deviations (SDs), and cumulative frequencies were calculated for descriptive purposes. The main outcome parameter was implant survival; the secondary outcome variable was implant success according to the criteria of Albrektsson et al¹⁹ and Karoussis et al.²⁰

Table 1 Implant Distribution

	Total	Maxilla	Mandible
Sex	52	16	36
Female	42	31	11
Male	10	5	5
Location			
Anterior	10	1	9
Posterior	42	15	27
Implant length			
8 mm	13	1	12
9 mm	39	15	24
Implant diameter			
3.5 mm	35	9	26
4.0 mm	13	3	10
4.5 mm	4	4	0
Suprastructure			
Full-arch restoration	12	0	12
Screw-retained partial denture	9	0	9
Interconnected crowns	18	4	14
Single crown	13	12	1

Table 2 Scores for Clinical Parameters (n = 52 Implants)

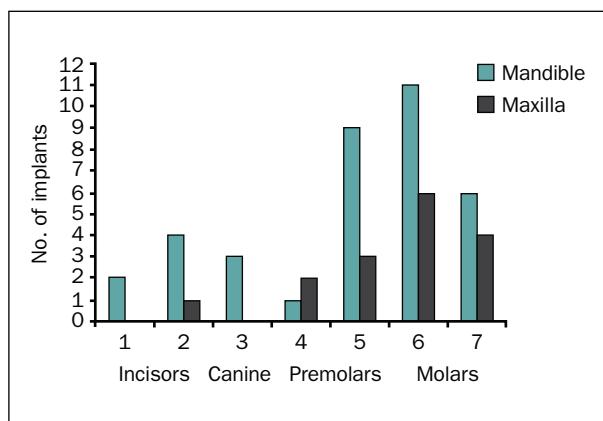
	No. of implants	%
Probing depth		
3 mm	43	82.7
4 mm	5	9.6
5 mm	3	5.8
6 mm	1	1.9
Plaque*		
Score 0	20	38.5
Score 1	23	44.2
Score 2	9	17.3
Score 3	0	0
Bleeding*		
Score 0	40	76.9
Score 1	12	23.1
Score 2	0	0
Score 3	0	0

*According to Mombelli et al.¹⁸

RESULTS

Patients

Fifty-two dental implants were placed in 14 patients (11 women, 3 men). The mean age of patients at implant surgery was 57.9 years (SD 8.9 years; range, 37.3 to 71.5 years). Mean follow-up time was 10.1 years

**Fig 3** Distribution of placed implants according to position in the jaw.

(SD 1.9 years; range, 9.5 to 12 years). Twelve of the 14 patients were observed for at least 9 years. One patient died during the study period (after 6 years and 9 months), and another did not appear for follow-up examinations after 6 years.

Thirty-six implants were placed in the mandible and 16 in the maxilla. Forty-two implants were placed in posterior regions (ie, premolar/molar areas) and 10 were placed in the anterior arches (Table 1). The distribution of implants with respect to jaw positions is depicted in Fig 3.

Clinical Examination

Measurement of the peri-implant Plaque Index showed good oral hygiene for 82.7% of the implants at the last follow-up visit (grades 0 and 1; Table 2). At 23.1% of the implants, peri-implant bleeding could be provoked but was predominantly weak. A maximum periodontal probing depth of less than 4 mm was recorded for 82.7% of all implants, and a maximum of 6 mm was found at only 1.9% of the implants. No implants were lost during the observation period, resulting in a survival rate of 100%.

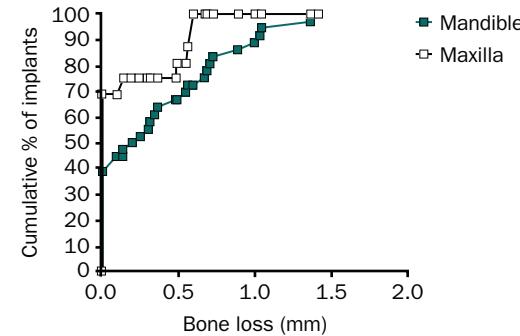
Bone Loss and Implant Success

After a mean observation period of 10.1 years, an average marginal bone loss of 0.3 mm (SD 0.5 mm; range, 0 to 1.4 mm) was recorded. Bone loss on the mesial and distal surfaces did not differ significantly: 0.24 mm (SD 0.45 mm) and 0.36 mm (SD 0.52 mm), respectively. Almost half of all implants (48%) showed no marginal bone loss, and 12 implants (23%) showed a loss of less than 0.5 mm of marginal bone (Table 3). Marginal bone loss was greater in the mandible (0.37 mm; SD 0.54 mm) than in the maxilla (0.15 mm, SD 0.3 mm; Fig 4). Screw-retained reconstructions showed an average

Table 3 Distribution of Bone-Level Changes from Baseline to 10 Years

Bone loss	No. (%) of implants (n = 52)
0 mm	25 (48%)
< 0.5 mm	12 (23%)
0.5–1 mm	10 (19%)
1–1.5 mm	5 (10%)
>1.5 mm	0 (0%)

Mean 0.3 mm, SD 0.4 mm, range 0–1.4 mm, median 0.1 mm.

**Fig 4** Average (mesial + distal) bone loss and cumulative distribution.

marginal bone loss of 0.36 mm (SD 0.57 mm), whereas cemented reconstructions showed less bone loss (mean of 0.14 mm).

According to the Albrektsson et al¹⁹ criteria, all implants were successful. Under the more stringent success criteria of Karoussis et al,²⁰ four implants failed.

Prosthetic Treatment and Success

After a healing period of 3 months, patients received their definitive rehabilitation from the same prosthodontist. All 52 implants supported fixed reconstructions. Twelve implants supported two screw-retained full-arch restorations in the mandible. Nine implants supported four screw-retained partial dentures in the mandible, whereas 13 implants were loaded with cemented single crowns and 18 implants supported splinted interconnected crowns (Table 1). In all, 36 implants had screw-retained suprastructures and 16 implants had cement-retained restorations.

No reconstructions had to be replaced. Thus, the survival rate of the prosthetic rehabilitations was 100% at the end of the observation period. After the screw-retained rehabilitations were removed at the 10-year follow-up appointment, no signs of clinical mobility or abutment loosening could be documented. Ceramic chipping had occurred in two cases only.

DISCUSSION

The use of long implants was recommended for many years to reduce marginal bone loss and to increase implant survival.^{21,22} It was assumed that longer implants would offer greater predictability than shorter implants. However, since the introduction of rough

implant surfaces, the success rates of short and longer implants have become similar.^{13,23} In addition, a high implant-to-crown ratio was assumed to have a negative biologic effect on crestal bone loss.²⁴ Overloading as a result of higher bone stress was believed to lead to bone atrophy and greater marginal bone loss.^{22,25,26} However, a systemic review by Blanes found that implant-to-crown ratios did not influence marginal bone loss.²⁷ One article even reported less marginal bone loss with higher crown-to-implant ratios.²⁸

The results of the presented data are in accordance with recent studies on short implants,^{29–31} whereas older studies often described higher implant failure rates and higher marginal bone loss for short versus longer implants.^{5,6} The high survival rate of 100% and low marginal bone loss of 0.3 mm of short dental implants placed in various clinical situations in this long-term follow-up analysis are outcomes that are comparable to those reported for longer implants from the same manufacturer for the same observation period.^{32–34} Also, in a recent review that compared the survival of short and conventional implants, no significant differences between totally and partially edentulous patients could be demonstrated.¹⁶ Although there are some long-term studies on short implants, to the authors' knowledge, there are no long-term studies over a period of 10 years of short implants as the sole support for prosthetic reconstructions. Therefore, the success and survival rates of those short implants were assessed in the present study.

The use of short implants is well documented from a biomechanical point of view. Multiple finite element analysis studies have proven that the highest stress concentrations in bone occur in the crestal region of an implant, whereas very little stress is transferred to

the apical portion.³⁵ Increased implant length can decrease the stress around the implant neck only in a very minor way.^{36,37} Perrinard et al even stated that, independent of implant length, bone stress was virtually constant.³⁸ However, implant stress increased significantly with implant length and bicortical anchorage. Ivanoff et al also observed that implants with bicortical anchorage failed almost four times more often than those with monocortical anchorage.³⁹

According to recent reviews, the success of short implants is dependent upon multiple factors. For example, the implant surface structure is important. Therefore, all included implants in this study had a moderately rough surface, which has been found to achieve higher bone-to-implant contact. Furthermore, an increase in diameter could also help minimize complications.^{15,40} While all implants in this study were short, their diameters varied. However, a short implant with a wide diameter provides an increased implant surface area, which then results in a higher bone-to-implant contact area. This could make a short implant comparable to a longer implant with a smaller diameter.

Another influencing factor is the individual bone quality; different site preparation is required depending on the specific bone quality to ensure primary stability. Therefore, the survival and success of short implants placed in severely resorbed jaws should not be compared with those of longer implants placed in adequate native bone but rather with the outcome of implants placed in grafted sites. This is because the treatment alternatives to short implants are complex bone grafting procedures, such as vertical ridge augmentation (eg, distraction osteogenesis, onlay grafts, sinus floor augmentation), or alveolar nerve transposition. These operations are often associated with higher morbidity for the patient and less favorable implant survival and success rates.³ Versus longer implants placed in augmented bone, short implants also have the advantage that they are retained by native bone only. This bone is more reliable than bone, eg, from the iliac crest.⁴ Depending upon the amount of residual bone still available, implants placed in grafted bone may be retained solely by the softer iliac crest bone graft. Such grafts are often associated with significantly higher implant failure and complication rates.⁴

The very good outcome of the short implants in this study could be a result of splinting the implants. Most implants in this study were reconstructed with an interconnected suprastructure to provide additional stability. Bergqvist et al reported that stress levels in the bone tissue surrounding splinted implants were markedly lower than stress levels surrounding uncoupled implants by a factor of nearly 9.⁴¹ Also, the number of implants placed and splinting of short implants to longer implants can influence implant survival.^{15,25}

To eliminate the possible positive influence of longer implants in this study, however, only reconstructions with short implants exclusively were included.

The long study observation period of 10 years resulted in highly reliable data, despite the fact that the number of implants was limited. To increase the homogeneity and significance of the data, only patients with suprastructures solely retained by short implants were observed. Patients with suprastructures retained by short implants as well as longer implants (implants at least 10 mm long) were not included. Also, only implants with rough surfaces from the same manufacturer were inserted.

A comparison of the present evaluation of short implants inserted in atrophied bone with results of the placement of long implants in similar bone could have increased the value of the study. Thus, the inclusion of an adequate control group in this research would have been beneficial. The defined inclusion criteria, however, focused the evaluation of patients with a degree of atrophy, which—without prior bone augmentation—permitted the insertion of short implants only. Therefore the selected degree of bone atrophy did not allow the placement of longer implants under identical conditions.

Another debatable point of this study is the definition of the “short implant”; many studies have used different definitions. In this clinical study, a short implant was defined as an implant with a maximum length of 9 mm.^{15–17} At the time of placement of the present implants, implants shorter than 10 mm in length were considered to be short, and many authors still use these definitions.^{15–17} However, the definition of short implants has changed over the years. While a 9-mm implant was considered short at the time of placement in this study, nowadays it is considered to be a standard-length implant by several authors. In addition, the same implant company currently produces 6-mm-long implants; however, no long-term results (> 5 years) on this implant length have yet been published.

With regard to the value of short implants, it must be kept in mind that not all degrees of bone atrophy and types of defects can be treated with short implants. While in the lateral region of the arch, the implant-to-crown ratio (with longer crowns resulting from the use of short implants) may not be an esthetic impairment for the patient, it will certainly compromise esthetics in the anterior maxilla. To achieve a functionally and esthetically satisfying result, the bone in this area must be reconstructed, eg, with autologous block grafts. In such cases, the higher morbidity related to bone grafting procedures must be accepted even if it would be possible to place a short implant. Also, in cases of severe atrophy (ie, Cawood and Howell classes V and VI¹⁴), grafting will be required prior to implant placement. Otherwise, a satisfactory implant-retained solution is impossible.

CONCLUSION

This study followed and evaluated short implants (ie, < 10 mm) inserted for various indications over an average period of 10 years. The implant survival and success rates were 100%. The success of prosthetic restorations supported solely by these short implants was also 100%. Thus, the use of short implants can be a reliable, long-term stable treatment option, particularly in areas of insufficient or atrophied residual bone, and can help to reduce morbidity for patients. However, it must always be kept in mind that the use of short implants cannot be regarded to represent a general alternative to all bone grafting procedures. Nevertheless, it can be a good solution for various indications and a certain degree of atrophy.

ACKNOWLEDGMENTS

The study was supported by Astra Tech AB, Mölndal, Sweden. The authors declare that there are no conflicts of interest in this study.

REFERENCES

- Chiapasco M, Consolo U, Bianchi A, Ronchi P. Alveolar distraction osteogenesis for the correction of vertically deficient edentulous ridges: A multicenter prospective study on humans. *Int J Oral Maxillofac Implants* 2004;19:399–407.
- Chiapasco M, Zaniboni M, Boisco M. Augmentation procedures for the rehabilitation of deficient edentulous ridges with oral implants. *Clin Oral Implants Res* 2006;17(suppl 2):136–159.
- Chiapasco M, Zaniboni M, Rimondini L. Autogenous onlay bone grafts vs. alveolar distraction osteogenesis for the correction of vertically deficient edentulous ridges: A 2-4-year prospective study on humans. *Clin Oral Implants Res* 2007;18:432–440.
- Esposito M, Grusovin MG, Felice P, Karatzopoulos G, Worthington HV, Coulthard P. Interventions for replacing missing teeth: Horizontal and vertical bone augmentation techniques for dental implant treatment. *Cochrane Database Syst Rev* 2009;CD003607.
- Winkler S, Morris HF, Ochi S. Implant survival to 36 months as related to length and diameter. *Ann Periodontol* 2000;5:22–31.
- Herrmann I, Lekholm U, Holm S, Kultje C. Evaluation of patient and implant characteristics as potential prognostic factors for oral implant failures. *Int J Oral Maxillofac Implants* 2005;20:220–230.
- Friberg B, Jemt T, Lekholm U. Early failures in 4,641 consecutively placed Bränemark dental implants: A study from stage 1 surgery to the connection of completed prostheses. *Int J Oral Maxillofac Implants* 1991;6:142–146.
- Jemt T. Failures and complications in 391 consecutively inserted fixed prostheses supported by Bränemark implants in edentulous jaws: A study of treatment from the time of prosthesis placement to the first annual checkup. *Int J Oral Maxillofac Implants* 1991;6:270–276.
- Buser D, Mericske-Stern R, Bernard JP, et al. Long-term evaluation of non-submerged ITI implants. Part 1: 8-year life table analysis of a prospective multi-center study with 2359 implants. *Clin Oral Implants Res* 1997;8:161–172.
- Feldman S, Boitel N, Weng D, Kohles SS, Stach RM. Five-year survival distributions of short-length (10 mm or less) machined-surfaced and Osseotite implants. *Clin Implant Dent Relat Res* 2004;6:16–23.
- Testori T, Wiseman L, Woolfe S, Porter SS. A prospective multicenter clinical study of the Osseotite implant: Four-year interim report. *Int J Oral Maxillofac Implants* 2001;16:193–200.
- Fugazzotto PA, Beagle JR, Ganeles J, Jaffin R, Vlassis J, Kumar A. Success and failure rates of 9 mm or shorter implants in the replacement of missing maxillary molars when restored with individual crowns: Preliminary results 0 to 84 months in function. A retrospective study. *J Periodontol* 2004;75:327–332.
- Renouard F, Nisand D. Short implants in the severely resorbed maxilla: A 2-year retrospective clinical study. *Clin Implant Dent Relat Res* 2005;7(suppl 1):S104–110.
- Cawood JI, Howell RA. A classification of the edentulous jaws. *Int J Oral Maxillofac Surg* 1988;17:232–236.
- das Neves FD, Fones D, Bernardes SR, do Prado CJ, Neto AJ. Short implants—An analysis of longitudinal studies. *Int J Oral Maxillofac Implants* 2006;21:86–93.
- Kotsovilis S, Fournousis I, Karoussis IK, Bamia C. A systematic review and meta-analysis on the effect of implant length on the survival of rough-surface dental implants. *J Periodontol* 2009;80:1700–1718.
- Morand M, Irinakis T. The challenge of implant therapy in the posterior maxilla: Providing a rationale for the use of short implants. *J Oral Implantol* 2007;33:257–266.
- Mombelli A, van Oosten MA, Schurch E Jr, Lang NP. The microbiota associated with successful or failing osseointegrated titanium implants. *Oral Microbiol Immunol* 1987;2:145–151.
- Albrektsson T, Zarb G, Worthington P, Eriksson AR. The long-term efficacy of currently used dental implants: A review and proposed criteria of success. *Int J Oral Maxillofac Implants* 1986;1:11–25.
- Karoussis IK, Salvi GE, Heitz-Mayfield LJ, Bragger U, Hammerle CH, Lang NP. Long-term implant prognosis in patients with and without a history of chronic periodontitis: A 10-year prospective cohort study of the ITI Dental Implant System. *Clin Oral Implants Res* 2003;14:329–339.
- Lekholm U, Gunne J, Henry P, et al. Survival of the Bränemark implant in partially edentulous jaws: A 10-year prospective multicenter study. *Int J Oral Maxillofac Implants* 1999;14:639–645.
- Naert I, Koutsikakis G, Duyck J, Quirynen M, Jacobs R, van Steenberghe D. Biologic outcome of implant-supported restorations in the treatment of partial edentulism. Part I: A longitudinal clinical evaluation. *Clin Oral Implants Res* 2002;13:381–389.
- ten Bruggenkate CM, Asikainen P, Foitzik C, Krekeler G, Sutter F. Short (6-mm) nonsubmerged dental implants: Results of a multicenter clinical trial of 1 to 7 years. *Int J Oral Maxillofac Implants* 1998;13:791–798.
- Rangert BR, Sullivan RM, Jemt TM. Load factor control for implants in the posterior partially edentulous segment. *Int J Oral Maxillofac Implants* 1997;12:360–370.
- Bahat O. Bränemark System implants in the posterior maxilla: Clinical study of 660 implants followed for 5 to 12 years. *Int J Oral Maxillofac Implants* 2000;15:646–653.
- Friberg B, Grondahl K, Lekholm U, Bränemark PI. Long-term follow-up of severely atrophic edentulous mandibles reconstructed with short Bränemark implants. *Clin Implant Dent Relat Res* 2000;2:184–189.
- Blanes RJ. To what extent does the crown-implant ratio affect the survival and complications of implant-supported reconstructions? A systematic review. *Clin Oral Implants Res* 2009;20(suppl 4):67–72.
- Blanes RJ, Bernard JP, Blanes ZM, Belser UC. A 10-year prospective study of ITI Dental Implants placed in the posterior region. II: Influence of the crown-to-implant ratio and different prosthetic treatment modalities on crestal bone loss. *Clin Oral Implants Res* 2007;18:707–714.
- Anitua E, Orive G. Short implants in maxillae and mandibles: A retrospective study with 1 to 8 years of follow-up. *J Periodontol* 2010;81:819–826.
- Fugazzotto PA. Shorter implants in clinical practice: Rationale and treatment results. *Int J Oral Maxillofac Implants* 2008;23:487–496.
- Grant BT, Pancko FX, Kraut RA. Outcomes of placing short dental implants in the posterior mandible: A retrospective study of 124 cases. *J Oral Maxillofac Surg* 2009;67:713–717.
- Al-Nawas B, Kammerer PW, Morbach T, Ladwein C, Wegener J, Wagner W. Ten-year retrospective follow-up study of the TiOblast dental implant. *Clin Implant Dent Relat Res* 2012;14:127–134.
- Gotfredsen K. A 10-year prospective study of single tooth implants placed in the anterior maxilla. *Clin Implant Dent Relat Res* 2012;14:80–87.

34. Vroom MG, Sipos P, de Lange GL, et al. Effect of surface topography of screw-shaped titanium implants in humans on clinical and radiographic parameters: A 12-year prospective study. *Clin Oral Implants Res* 2009;20:1231–1239.
35. Meijer HJ, Kuiper JH, Starmans FJ, Bosman F. Stress distribution around dental implants: Influence of superstructure, length of implants, and height of mandible. *J Prosthet Dent* 1992;68:96–102.
36. Himmlova L, Dostalova T, Kacovsky A, Konvickova S. Influence of implant length and diameter on stress distribution: A finite element analysis. *J Prosthet Dent* 2004;91:20–25.
37. Yokoyama S, Wakabayashi N, Shioya M, Ohyama T. The influence of implant location and length on stress distribution for three-unit implant-supported posterior cantilever fixed partial dentures. *J Prosthet Dent* 2004;91:234–240.
38. Pierrisnard L, Renouard F, Renault P, Barquins M. Influence of implant length and bicortical anchorage on implant stress distribution. *Clin Implant Dent Relat Res* 2003;5:254–262.
39. Ivanoff CJ, Grondahl K, Bergstrom C, Lekholm U, Bränemark PI. Influence of bicortical or monocortical anchorage on maxillary implant stability: A 15-year retrospective study of Bränemark System implants. *Int J Oral Maxillofac Implants* 2000;15:103–110.
40. Renouard F, Nisand D. Impact of implant length and diameter on survival rates. *Clin Oral Implants Res* 2006;17(suppl 2):35–51.
41. Bergkvist G, Simonsson K, Rydberg K, Johansson F, Derand T. A finite element analysis of stress distribution in bone tissue surrounding uncoupled or splinted dental implants. *Clin Implant Dent Relat Res* 2008;10:40–46.

Retention Characteristics of Different Attachment Systems of Mandibular Overdentures Retained by Two or Three Implants

Bulent Uludag, DDS, PhD¹/Serdar Polat, DDS, PhD²

Purpose: The purpose of this study was to quantify and compare the retentive forces of five different prosthetic attachment designs on mandibular overdentures retained by two or three implants. **Materials and**

Methods: Two photoelastic acrylic resin models of an edentulous mandible were cast. In one model, three implants were aligned parallel to each other and oriented perpendicular to the occlusal plane. The distal implants were placed in the canine regions, with an interimplant distance of 22 mm. In the other model, two implants were placed using the same approach, with an interimplant distance of 22 mm. Five retention mechanisms were studied on both models: a bar with yellow clips, a milled galvanoformed bar, a bar with two clear distal locator attachments, a bar with two distal Ceka attachments, and a bar with clear locator attachments. Ten dentures were fabricated in clear acrylic resin. The specimens were loaded in tension at a crosshead speed of 50 mm/min in a universal testing machine. Five hundred forty cycles of repeated insertions and removals were performed to simulate 6 months of clinical function. **Results:** Initial retention forces ranged from 23.33 to 54.32 N. Retentive values of the clear locator attachments on the three-implant model were higher than those for other attachments. **Conclusion:** All designs demonstrated a decrease in retention from the initial testing to the final pull-out test. This decrease was significant for all designs. INT J ORAL MAXILLOFAC IMPLANTS 2012;27:1509–1513

Key words: attachment systems, implant-retained mandibular overdentures, retention

Implant-retained mandibular overdentures could be considered as a potential alternative to fixed prostheses in terms of cost-effectiveness and reduced chair-side time.¹ Use of two to four interforaminal implants to support an overdenture has been proven successful in improving the oral function and psychologic well-being of edentulous patients.^{2–4}

Patient satisfaction with mandibular overdentures is related to function and esthetics.⁵ In addition to design, stability, and retention of the definitive denture, the quality of the denture base area, previous experience with removable dentures, and patient personality and expectations play roles in the efficacy of implant-retained mandibular overdentures.⁶ Patient comfort depends on several factors, such as the amount of retention provided by the implants, fit of the prosthetic

components and attachments, and precision of the denture.⁵

Currently, many different attachments are available for use with implant-tissue-supported overdentures. Factors that influence decision making in the selection and use of attachment systems are the available interocclusal space, load distribution to the mucosa and the implants, the amount of retention required, jaw morphology, prosthetic maintenance requirements, and prospective patient compliance.^{7,8} The ideal attachment should provide sufficient retention to ensure stability of the denture.⁹ When the placement of a minimal number of implants is planned, the design of the attachments should rely on the denture-bearing capacity of the soft tissue and the relative movements that may be allowed by differential support.⁵ In such circumstances, the attachments are subjected to increased functional stress and, eventually, wear as a result of greater dependence on soft tissue support. Placement of more than two implants in the interforaminal region may create a staggered rather than a straight-line arrangement of the implants. This configuration increases retention and reduces the number of planes of rotation. Moreover, placement of the third implant provides indirect retention for the prosthesis.^{9,10} The implants can be splinted with bars, or

¹Professor, Department of Prosthodontics, University of Ankara, Ankara, Turkey.

²Assistant Professor, Department of Prosthodontics, University of Ankara, Ankara, Turkey.

Correspondence to: Dr Bulent Uludag, Ankara Universitesi Dis Hekimligi Fakultesi, Protetik Dis Tedavisi Ab. D., 06500 Besevler, Ankara, Turkey. Fax: +90-312-2123954.
Email: bculudag@gmail.com



Fig 1a Internal views of the two-implant overdentures.



Fig 1b Internal views of the three-implant overdentures.



Fig 2 A model in position on the universal testing machine.

unsplinted implants could be used with ball, locator, or magnetic attachments.¹¹ The design of bar attachments and bar units, which are manufactured in resilient and rigid designs, has led to their widespread acceptance.^{5,11-14}

A number of studies^{11,15-25} have already investigated the effect of short- and long-term function on dislodging forces of individual attachments^{15,16,20,21,23} both with^{17-19,22,24} and without simulation of oral function and environment. The purpose of the present study was to quantify and compare the retentive forces of five different prosthetic attachment designs on mandibular overdentures retained by two or three implants.

MATERIAL AND METHODS

Implants and Fabrication of Experimental Models

Two acrylic resin models (PL-2, Vishay Intertechnology) of an edentulous mandible were fabricated. The configuration of the arch was adapted from a mandibular

cast of an edentulous patient. A condensational polymerization silicone mold (Speedex, Coltène/Whaledent) of the mandibular cast was obtained to duplicate the cast in wax (Poliwax; Bilkim Kimya). Implants (3.75 × 13 mm; Tapered Screw-Vent, Zimmer Dental) were embedded in the cortical bone at the bone level and at an interimplant distance of 1 mm in the wax models using a surveyor (Ney Surveyor, Dentsply). In one model, three implants were aligned parallel to each other and perpendicularly oriented to the horizontal plane. The distal implants were placed in approximately the canine areas with an interimplant distance of 22 mm.^{26,27} In the other model, two implants were placed using the same approach with an interimplant distance of 22 mm.

Five retention mechanisms were studied:

1. A bar with yellow-colored clips (Bredent),
2. A milled galvanoformed bar (Gramm Technik GmbH),
3. A bar with two clear distal locator attachments (Attachments Intl Inc),
4. A bar with two distal Ceka attachments (Ceka / Preci-Line, Alphadent NV), and
5. Clear locator attachments (Attachments Intl Inc).

The bar attachments used in the current study were cast from a base metal alloy (Bosil F, DeguDent) and were 2 mm in diameter and round, except for the milled bar. Ten dentures were fabricated in clear acrylic resin (Figs 1a and 1b).

Retention Tests

The attachments were tested to determine peak load-to-dislodgement on a universal testing machine (LRX, Lloyd Instruments Ltd). The occlusal plane of each denture was first set parallel to the horizontal plane and the model was secured to the base of a universal connector. Three chains connected the hooks of the dentures to the load cell of the universal testing machine.²⁸ A three-point vertical pull-out force

Table 1 Mean (\pm Standard Deviations) Retentive Forces of the Attachments at Baseline and After Simulation of 6 Months of Use

Denture type/attachment	Initial retention values	6-mo retention values	P
A1 Two implants, bar-clips	23.33 \pm 2.36	14.44 \pm 0.57	< .001
A2 Two implants, galvano bar	25.56 \pm 0.39	21.16 \pm 0.75	< .001
A3 Two implants, clear locators	42.19 \pm 3.41	30.44 \pm 0.56	< .001
A4 Two implants, bar-Ceka	48.74 \pm 1.45	43.88 \pm 0.99	< .001
A5 Two implants, bar/clear locators	45.71 \pm 1.22	31.63 \pm 0.97	< .001
B1 Three implants, bar-clips	26.58 \pm 0.77	23.38 \pm 1.19	< .001
B2 Three implants, galvano bar	28.71 \pm 1.21	23.26 \pm 0.66	< .001
B3 Three implants, clear locators	54.32 \pm 3.47	38.95 \pm 1.41	< .001
B4 Three implants, bar-Ceka	52.74 \pm 2.28	48.03 \pm 1.33	< .001
B5 Three implants, bar/clear locator	47.47 \pm 2.86	42.02 \pm 1.58	< .001

was applied at a crosshead speed of 50 mm/min to determine the direct retention against a peak axial dislodging force coinciding with the path of insertion until failure^{23,25} (Fig 2). In addition, each denture was subjected to 540 cycles of repeated insertion and removal to simulate 6 months of clinical function (on the assumption of three removals/insertions per day to clean the denture¹⁶).

Statistical Analysis

Repeated-measures analysis of variance was used to analyze the data (SPSS 15.0, SPSS Inc). The Tukey B post hoc test was used for pairwise comparisons ($\alpha = .05$).

RESULTS

Baseline and 6-month peak retentive forces (means and standard deviations) of the attachments are presented in Table 1. Statistical analysis revealed significant differences in the retention of all connectors ($F = 396,036$; $P < .001$): the mean baseline retention forces ranged between 23.33 and 54.32 N. The three-implant models required significantly higher dislodgment forces than the two-implant models. A decrease in the peak dislodgment force was observed between baseline and the 6-month measurements, regardless of attachment design. The bar-Ceka attachments exhibited the lowest percentage of reduction in retentive values (initial versus 6-month retentive values) in comparison to the other attachments. The bar-clip attachment on the two-implant model showed the greatest percentage of reduction in retentive values (Table 2).

Peak dislodging forces of the locator attachments were higher than for other attachments on the three-implant model ($P = .000$). The peak dislodging forces of bar-Ceka attachments were higher than for other at-

Table 2 Mean Percent Reduction in Peak Dislodgment Force After 540 Insertion/Removal Cycles

Attachment type	% reduction in retention
Two implants, bar-clips	38.10
Two implants, galvano bar	17.21
Two implants, clear locator	27.85
Two implants, bar-Ceka	9.9
Two implants, bar/clear locator	30.80
Three implants, bar-clips	12.03
Three implants, galvano bar	18.98
Three implants, clear locators	28.29
Three implants, bar-Ceka	8.9
Three implants, bar/clear locators	11.48

tachments on the two-implant model ($P = .000$), and the retentive force of the bar-clips on the two-implant model was the lowest ($P = .000$).

DISCUSSION

In the present study, the peak retentive forces of the attachments were tested initially and after 540 cycles of pull-out/insertion simulation on a universal testing machine. Testing was performed under limited, specific, and expected mechanical conditions without a simulation of *in vivo* conditions.²⁵ The presence of saliva and constant occlusal load may have an additional influence on the amount of wear in the attachments.¹⁹ In addition, the dislodging forces were applied vertically in the present study, whereas intraoral forces are more complex in nature.²⁴

The resiliency of the soft tissue may increase the load on the attachments and therefore can affect their retentive values; this was also not simulated in the present analysis.¹⁹ The use of four implants to support a bar-retained mandibular overdenture seems a more common clinical approach than the use of three implants. In the present study, the rationale for excluding a four-implant scenario relied on the fact that the four implants would certainly result in remarkably higher dislodging forces than a two-implant situation, and it is not cost-effective.

The initial retention of attachment systems may indicate its clinical predictability and performance and might influence patient satisfaction. The minimal amount of retention that provides patient satisfaction has been reported to be around 8 to 20 N for a removable prosthesis.^{9,23} These values are rather arbitrary, but they nonetheless provide a reference for clinicians in deciding what to select and how to incorporate the retentive elements. The peak retentive forces of attachments (23.33 to 54.32 N) found in this study therefore appear sufficient to ensure patient acceptance and are in line with those reported previously. Setz et al²⁴ reported that the retentive forces of stud attachments ranged from 3 to 85 N.

In the current study, the peak retentive forces of bar-clips on two implants after simulation of 6 months of insertion/removal were below 20 N. The loss of baseline retention values ranged between 8.9% and 38.10%. While the bar-Ceka attachment showed the lowest reduction (8.9%) in the three-implant configuration, the bar-clip design (38.10%) provided the lowest dislodging force in the two-implant configuration. With the exception of two reports,^{16,17} many studies have demonstrated a common trend toward reduction or even total loss of retentive force with the majority of attachment systems.¹¹ In the present study, the bar-clip design exhibited the greatest reduction in the two-implant model and the bar-Ceka attachment with each model exhibited the smallest reduction.

Previous investigations have studied the absolute retentive capacity of overdenture attachments. Stud attachments have been found to provide varying degrees of resiliency in both vertical and horizontal directions.²⁵ Chung et al²⁵ found higher retentive values with stud attachments (ERA gray and Locator LR clear) than with a Hader bar and metal clips. Evtimovska et al¹⁹ demonstrated that locator attachments had higher retentive values than yellow Hader clips and recommended the use of locators when greater retention is needed.

In the present study, the clear locator attachments showed higher retentive values than other attachments in the three-implant model. In addition, the clear locator attachments showed higher retentive

forces than the bar-clip and galvanoformed milled bar attachments in the two-implant model. However, the clear locator attachments showed lower retentive values than a bar with distal Ceka attachments and a bar with clear distal locator attachments in the two-implant model.

CONCLUSION

Within the limitations of this study, the following conclusions were drawn:

1. For all attachment designs tested, the three-implant model required significantly higher dislodging forces than the two-implant model.
2. All designs demonstrated a decrease in retentive force from the initial to final pull-out test.
3. The retentive forces of clear locator attachments on the three-implant model were higher than the retentive forces of other attachments. The bar-Ceka attachments exhibited the smallest reduction in retentive force.
4. The bar-clip attachment on the two-implant model showed the greatest reduction in retentive force.

ACKNOWLEDGMENTS

The authors reported no conflicts of interest related to this study.

REFERENCES

1. Mericske-Stern RD, Taylor TD, Belser U. Management of the edentulous patient. *Clin Oral Implants Res* 2000;11(suppl):108-125.
2. Zarb GA. The edentulous milieu. *J Prosthet Dent* 1983;49:825-831.
3. Van Steenberghe D, Lekholm U, Bolender C, et al. The applicability of osseointegrated oral implants in the rehabilitation of partial edentulism: A prospective multicenter study of 558 fixtures. *Int J Oral Maxillofac Implants* 1990;5:272-281.
4. Mericske-Stern RD. Clinical evaluation of overdenture restorations supported by osseointegrated titanium implants: A retrospective study. *Int J Oral Maxillofac Implants* 1990;5:375-383.
5. Williams BH, Ochiai KT, Hojo S, Nishimura R, Caputo AA. Retention of maxillary implant overdenture bars of different designs. *J Prosthet Dent* 2001;86:603-607.
6. Boerrigter EM, Geertman ME, Van Oort RP, et al. Patient satisfaction with implant-retained mandibular overdentures. A comparison with new complete dentures not retained by implants: A multicentre randomized clinical trial. *Br J Oral Maxillofac Surg* 1995;33:282-288.
7. Zitzmann NU, Marinello CP. A review of clinical and technical considerations for fixed and removable implant prostheses in the edentulous mandible. *Int J Prosthodont* 2002;15:65-72.
8. Sadowsky SD, Caputo AA. Effect of anchorage systems and extension base contact on load transfer with mandibular implant-retained overdentures. *J Prosthet Dent* 2000;84:327-334.
9. Trakas T, Michalakis K, Kang K, Hirayama H. Attachment systems for implant-retained overdentures: A literature review. *Implant Dent* 2006;15:24-34.
10. Ben-Ur Z, Gorfil C, Shifman A. Anterior implant-supported overdentures. *Quintessence Int* 1996;27:603-606.

11. Alsabeeha NHM, Payne AGT, Swain MV. Attachment systems for mandibular two-implant overdentures: A review of in vitro investigations on retention and wear features. *Int J Prosthodont* 2009;22: 429–440.
12. Mericske-Stern RD. Overdentures supported by ITI implants. In: Schroeder A, Sutter F, Buser D, Krekeler G (eds). *Oral Implantology: Basics, ITI Hollow Cylinder System*. New York: Thieme Medical, 1996: 330–367.
13. Bueno-Samper A, Hernandez-Aliaga M, Calvo-Guirado JL. The implant-supported milled bar overdenture: A literature review. *Med Oral Patol Oral Cir Bucal* 2010;15:375–378.
14. Uludag B, Sahin V, Celik G. Fabrication of a maxillary implant-supported overdenture retained by two cemented bars: A clinical report. *J Prosthet Dent* 2007;97:249–251.
15. Besimo CH, Gruber G, Fluhler M. Retention force changes in implant-supported titanium telescope crowns over long-term use in vitro. *J Oral Rehabil* 1996;23:372–378.
16. Besimo CH, Guarneri A. In vitro retention force changes of prefabricated attachments for overdentures. *J Oral Rehabil* 2003;30:671–678.
17. Botega DM, Mesquita MF, Henriques GE, Vaz LG. Retention force and fatigue strength of overdenture attachment systems. *J Oral Rehabil* 2004;31:884–889.
18. Doukas D, Michelinakis G, Smith PW, Barclay CW. The influence of interimplant distance and attachment type on the retention characteristics of mandibular overdentures on 2 implants: 6 month fatigue retention values. *Int J Prosthodont* 2008;21:152–154.
19. Evtimovska E, Masri R, Driscoll CF, Romberg E. The changes in retentive values of locator attachments and Hader clips over time. *J Prosthodont* 2009;18:479–483.
20. Fromentin O, Picard B, Tavernier B. In vitro study of the retention and mechanical fatigue behavior of four implant overdenture stud-type attachments. *Pract Periodontics Aesthet Dent* 1999;11:391–397.
21. Gamborena JI, Hazelton LR, Nabadalung D, Brudvik J. Retention of ERA direct overdenture attachments before and after fatigue loading. *Int J Prosthodont* 1997;10:123–130.
22. Rutkunas V, Mizutani H, Takahashi H. Influence of attachment wear on retention of mandibular overdenture. *J Oral Rehabil* 2007;34: 41–51.
23. Sadig W. A comparative in vitro study on the retention and stability of implant-supported overdentures. *Quintessence Int* 2009;40:313–319.
24. Setz J, Hyung S, Engel E. Retention of prefabricated attachments for implant stabilized overdentures in the edentulous mandible: An in vitro study. *J Prosthet Dent* 1998;80:323–329.
25. Chung KH, Chung CY, Cagna DR, Cronin RJ Jr. Retention characteristics of attachment systems for implant overdenture. *J Prosthodont* 2004;13:221–226.
26. Sinclair PM, Little RM. Maturation of untreated normal occlusions. *Am J Orthod* 1983;83:114–123.
27. Celik G, Uludag B. Photoelastic stress analysis of various retention mechanisms on 3-implant-retained mandibular overdentures. *J Prosthet Dent* 2007;97:229–235.
28. Petropoulos VC, Smith W. Maximum dislodging forces of implant overdenture stud attachments. *Int J Oral Maxillofac Implants* 2002; 17(4):526–535.

Evaluation of Buccal Alveolar Bone Dimension of Maxillary Anterior and Premolar Teeth: A Cone Beam Computed Tomography Investigation

Carolina Vera, DDS¹/Ingeborg J. De Kok, DDS, MD²/Dominik Reinhold, MS³/

Praephun Limpiphipatanakorn, DDS¹/Alan K. W. Yap, BDS, MRACDS⁴/

Donald Tyndall, DDS, PhD⁵/Lyndon F. Cooper, DDS, PhD⁶

Purpose: Clinical guidelines suggest that a minimal buccal alveolar bone thickness of 1 to 2 mm is required to maintain the tissue architecture following tooth extraction and implant placement. The aim of this study was to evaluate the thickness of buccal alveolar bone at the maxillary first premolars and anterior teeth using cone beam computed tomography (CBCT). **Materials and Methods:** CBCT images of the maxillae of 43 implant patients were obtained. Two examiners manually measured the distance from the cementoenamel junction (CEJ) to the buccal alveolar bone crest and the thickness of the buccal alveolar bone at the crest, midroot, and apex of the maxillary first premolars and anterior teeth. The absence of bone and presence of radiographic artifacts were recorded. Average bone thicknesses were calculated and compared. Both parametric and nonparametric statistics were used to analyze the findings. **Results:** The median distance from the CEJ to the buccal alveolar bone crest was 2.79 mm, and measurements were similar among tooth positions. The median buccal alveolar bone thickness 1 mm apical to the alveolar bone was 1.13 mm in the premolar area and 0.83 mm for the anterior maxillary teeth. The median buccal alveolar bone thickness at the midroot was 1.03 mm in the premolar area and 0.70 mm for the other anterior maxillary teeth. Measurements of the buccal plate at 1 mm from the tooth apex were similar in all teeth positions, with a median thickness of 0.88 mm. **Conclusions:** The presence or absence of buccal alveolar bone can be discerned by CBCT evaluation. Few maxillary anterior teeth displayed buccal alveolar bone thickness greater than 1 mm. The implications for implant therapy must be fully discerned regarding tissue biotypes and dental implant outcomes. *INT J ORAL MAXILLOFAC IMPLANTS* 2012;27:1514–1519

Key words: alveolar bone resorption, cone beam computed tomography, dental implant

Dental implants are used to replace teeth that are failing as a result of disease, trauma, or unfavorable

¹Graduate Student, Department of Prosthodontics, University of North Carolina, Chapel Hill, North Carolina, USA.

²Assistant Professor, Department of Prosthodontics, and Bone Biology and Implant Therapy Laboratory, University of North Carolina, Chapel Hill, North Carolina, USA.

³Research Assistant, Department of Statistics and Operations Research, University of North Carolina, Chapel Hill, North Carolina, USA.

⁴Prosthodontist, The University of Sydney, Sydney, Australia.

⁵Professor, Department of Diagnostic Sciences and General Dentistry, University of North Carolina, Chapel Hill, North Carolina, USA.

⁶Professor and Chair, Department of Prosthodontics, and Director, Bone Biology and Implant Therapy Laboratory, University of North Carolina, Chapel Hill, North Carolina, USA.

Correspondence to: Dr Lyndon F. Cooper, Department of Prosthodontics, 330 Brauer Hall CB#7450, University of North Carolina, Chapel Hill, NC 27599, USA. Email: Lyndon_Cooper@dentistry.unc.edu

restorative conditions. Various dental implant procedures have been recommended based on a complex array of clinical and pragmatic factors. For example, implants may be placed into extraction sockets immediately¹ or at some period of time following extraction and wound healing.² Following implant placement, provisionalization or direct occlusal loading may be implemented immediately³ or after the process of osseointegration has been completed. Both submerged (two-stage) and nonsubmerged (single-stage) approaches may be utilized. At present, the clinical data indicate that implant survival is possible following all these routes of treatment.^{4–6} All these methods require tooth extraction, which results in changes in the alveolar architecture.

Unanticipated and excessive tissue changes can result in unacceptable esthetic deficits ranging from soft tissue asymmetry to facial tissue discoloration, marked tissue dehiscence, or abutment or implant exposure.⁷ Loss of osseointegration, pain, and peri-implantitis

may occur.⁸ Alveolar resorption is a consequence of tooth extraction or avulsion, and dental implant therapy must include thorough consideration of this phenomenon. Until recently, few data were available regarding the fate of the buccal alveolar plate after implant placement in extraction sockets in humans.

It has long been known that alveolar resorption occurs following tooth loss. This process for the edentulous patient has been characterized as inevitable and progressive residual ridge resorption. Remarkable changes in the maxillary alveolar ridge following the removal of teeth have been reported.^{9,10} Renewed interest in this phenomenon has surfaced in the context of single missing teeth and the residual alveolar ridge of bound edentulous spaces. In such instances, the maxillary alveolar ridge width decreases by approximately 50% following tooth extraction.¹¹ Alveolar bone resorption occurs following tooth extraction and implant placement in premolar regions, with marked loss of horizontal and vertical buccal architecture.¹² These clinical studies have been paralleled by animal studies that have demonstrated that both buccal and lingual alveolar bone resorbs despite augmentation with different biomaterials and despite implant placement in the fresh extraction socket.^{13,14} Buccal bone resorption is of greater magnitude and may be the result of preferential loss of bundle bone following tooth extraction.

Buccal bone resorption has varied in magnitude among studies, among individuals, and among sites.¹⁵⁻¹⁷ Factors implicated in this variation include the presence and absence of existing infection, flap versus flapless extraction and implant placement, the extent of trauma during extraction, and the thickness of the buccal bone plate prior to tooth extraction. The width of the buccal plate of bone may be an important determinant of bone morphologic changes following extraction.¹⁸ Tomasi et al¹⁹ determined, through refined multivariate analysis of factors affecting architectural bone changes after tooth extraction and implant placement, that the thickness of the buccal plate, the horizontal and vertical position of the implant in the socket, age, and smoking habit were factors influencing buccal bone responses. In a related study, buccal wall thickness was identified as an important anatomic feature affecting the eventual outcome of immediate implant placement in sockets.²⁰ If the thickness of the buccal wall is a preexisting feature of potential tooth extraction sites that affects dental implant outcomes, then it is important to define the buccal wall thickness of human alveolar bone at the anterior maxillary teeth. The aim of this study was to define the buccolingual thickness of the alveolar bone facial to the maxillary anterior teeth and premolars using cone beam computed tomography (CBCT).

Table 1 Demographic Data of Study

	n
Patients	43
Sites analyzed	1,376
Measurable sites	1,036
Nonmeasurable sites	
Missing	108
Implants	36
Very thin bone	111
Scatter/lack of clarity	85

MATERIALS AND METHODS

A retrospective study using CBCT was performed to measure the thickness of the buccal alveolar bone at first premolar and maxillary anterior teeth.

Patient Recruitment

The study population comprised 43 participants in whom a CBCT was acquired prior to single-tooth replacement utilizing dental implants. All subjects included in this investigation were recruited under an institutional review board-approved protocol. A total of 1,376 sites in the anterior maxillary arch, between and including the first premolars (Table 1), were analyzed (eight teeth per person, four measurements per tooth); 1,036 sites were measurable. The sites that could not be measured were divided into four different categories: edentulous sites, sites with an implant, sites with insufficient bone thickness for measurement, and images that presented with too much scatter or lack of clarity (Table 1).

CBCT Evaluation

Participants were scanned using a Galileos Comfort CBCT, and Sidexis software was used to format all images. Galaxis/Galileos Implant Software was used to complete all the measurements.

Two examiners made four distinct measurements of the buccal bone relative to the tooth in question (Fig 1). Measurements were made with an integral tool in the software. The dimension from the radiographic cementoenamel junction (CEJ) to the buccal alveolar bone crest (distance AB) was recorded. The thickness of the buccal bone plate in the buccopalatal direction perpendicular to the long axis of the tooth root was measured in three locations: (1) 1 mm apical to the buccal alveolar bone crest (measurement C), (2) midroot (measurement F), and (3) 1 mm coronal to the root apex (measurement G) (Fig 1). Measurement values were not recorded in areas where bone was not visualized or when there was an artifact in the image.

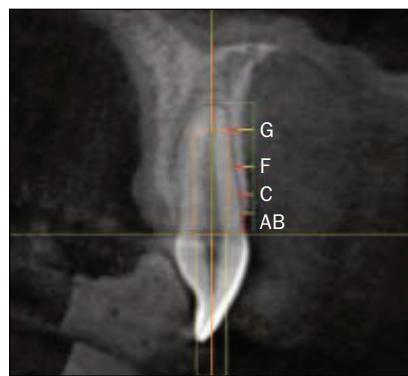


Fig 1 Measurement locations utilized in this investigation. AB = distance from the radiographic representation of the CEJ to the buccal alveolar bone crest; C = buccal alveolar bone thickness at 1 mm apical to the alveolar bone crest; F = midroot alveolar bone thickness; G = apical alveolar bone thickness at 1 mm coronal to the root apex.

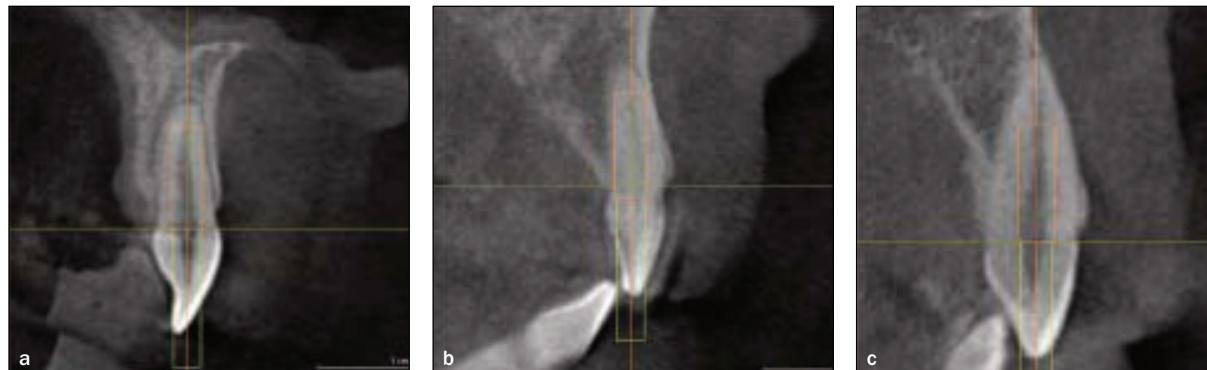
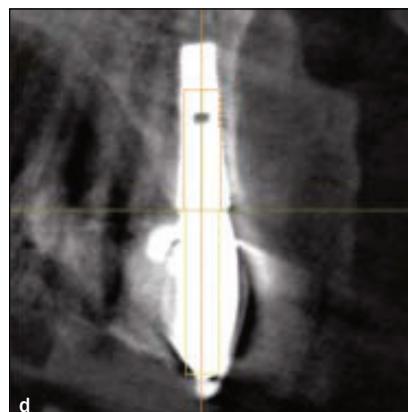


Fig 2a Representative CBCT image of a central incisor with an intact buccal plate.

Fig 2b Representative CBCT image of a central incisor missing the buccal alveolar bone in the midroot region (F).

Fig 2c Representative CBCT image of a canine missing buccal alveolar bone in both the midroot and apical regions (F and G).

Fig 2d Representative CBCT image of an existing implant in the central incisor position. Note that the buccal bone is visible and intact.



RESULTS

Data Collection and Statistical Analysis

The data were obtained by averaging the measurements from two observers for each tooth and site. Excel (Microsoft) was used to obtain descriptive statistics. The remaining analyses and plots were performed with the statistical software package R (R Development Core Team). Dependent-samples sign tests were performed to determine the statistical significance of the differences between teeth. That is, for each patient, the difference in measurements for a pair of teeth was considered, and the test determined whether the median of these differences was significantly different from 0. The sign test is nonparametric and based only on the signs of the differences in measurements; therefore, it was more appropriate for the data than, for example, a *t* test.

Data from all 43 included patients were analyzed. CBCT images were used to identify the presence or absence of alveolar buccal bone around teeth. Figure 2 shows representative CBCT images illustrating this concept.

The dimension AB (the distance from the radiographic CEJ to the buccal alveolar bone crest parallel to the long axis of the tooth) was measured on all maxillary first premolar and anterior teeth present in 43 subjects (Fig 3). The median value for AB was 2.79 mm. The sign test did not show a significant difference (at level $\alpha = 0.1$) between tooth positions. The overall first and third quartiles (Q1 and Q3) were 2.21 and 3.48 mm, respectively, meaning that approximately 50% of the AB measurements were between 2.21 and 3.48 mm.

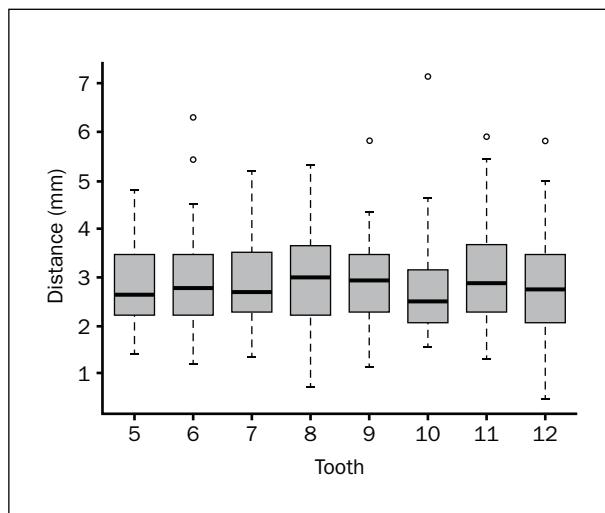


Fig 3 Box plot of the distances from the radiographic representation of the CEJ to the buccal alveolar crest (AB) for the measured teeth (Universal tooth-numbering system). Circles indicate outliers.

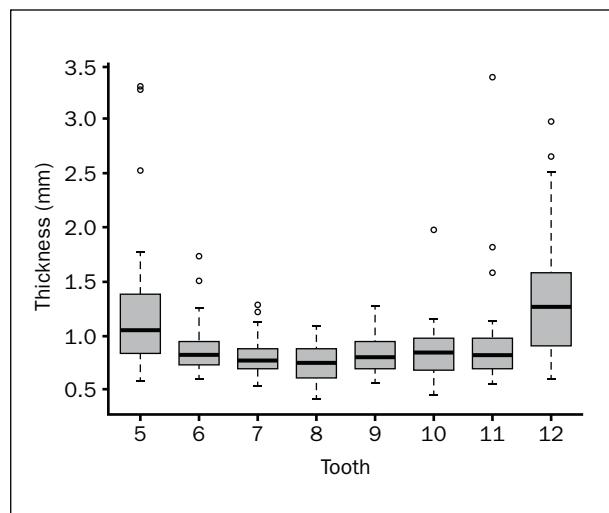


Fig 4 Box plot of the C measurements, ie, the thickness of buccal alveolar bone at 1 mm apical to the alveolar bone crest for the measured teeth (Universal tooth-numbering system). Circles indicate outliers.

Table 2 Distribution of Buccal Alveolar Bone Thickness at Sites F and C for All Measured Teeth

Tooth	Site C		Site F	
	Median	Q1, Q3	Median	Q1, Q3
R first premolar	1.04	0.83, 1.38	0.91	0.79, 1.23
R canine	0.82	0.73, 0.95	0.70	0.63, 0.83
R lateral	0.77	0.68, 0.87	0.64	0.52, 0.73
R central	0.73	0.61, 0.87	0.68	0.58, 0.80
L central	0.81	0.70, 0.93	0.70	0.64, 0.80
L lateral	0.84	0.68, 0.98	0.74	0.62, 0.87
L canine	0.82	0.70, 0.97	0.73	0.64, 0.86
L second pre-molar	1.28	0.90, 1.58	1.13	0.78, 1.65

C = 1 mm apical to the buccal alveolar bone crest; F = midroot of the long axis of the tooth.

The dimension C (the thickness of the buccal plate measured 1 mm from the midfacial alveolar crest) varied between premolar sites and the anterior maxillary teeth (Fig 4). The median dimension at the anterior teeth (canine to canine) was 0.83 mm (Q1 = 0.87 mm, Q3 = 1.46 mm); it was 1.13 mm (Q1 = 0.69 mm, Q3 = 0.94 mm) for premolars (Table 2). The sign tests between measurements of the right first premolar and each of the anterior teeth, and between the left premolar and the anterior teeth, had *P* values smaller than .05. The behavior of the right and left anterior maxillary teeth was similar.

The dimension F (the thickness of the buccal plate measured midroot) varied between premolar sites and the anterior maxillary teeth (Fig 5). The behavior of the right and left anterior maxillary teeth was simi-

lar. The overall medians and quartiles of buccolingual thickness were: median = 1.03 mm, Q1 = 0.79 mm, and Q3 = 1.51 mm for premolars; and median = 0.70 mm, Q1 = 0.60 mm, and Q3 = 0.84 mm for anterior teeth (Table 2). In all anterior teeth, most measurements of the bone thicknesses were below 1 mm.

The overall median for dimension G (thickness of the buccal plate 1 mm from the tooth apex) was 0.88 mm (Q1 = 0.65 mm, Q3 = 1.31 mm). This was similar for all tooth positions (Fig 5), and differences were generally not statistically significant (based on the sign test at level $\alpha = .05$) among the tooth positions. However, a *P* value smaller than .05 ($P = .04$) was calculated for the comparison between the right central incisor and the left lateral incisor.

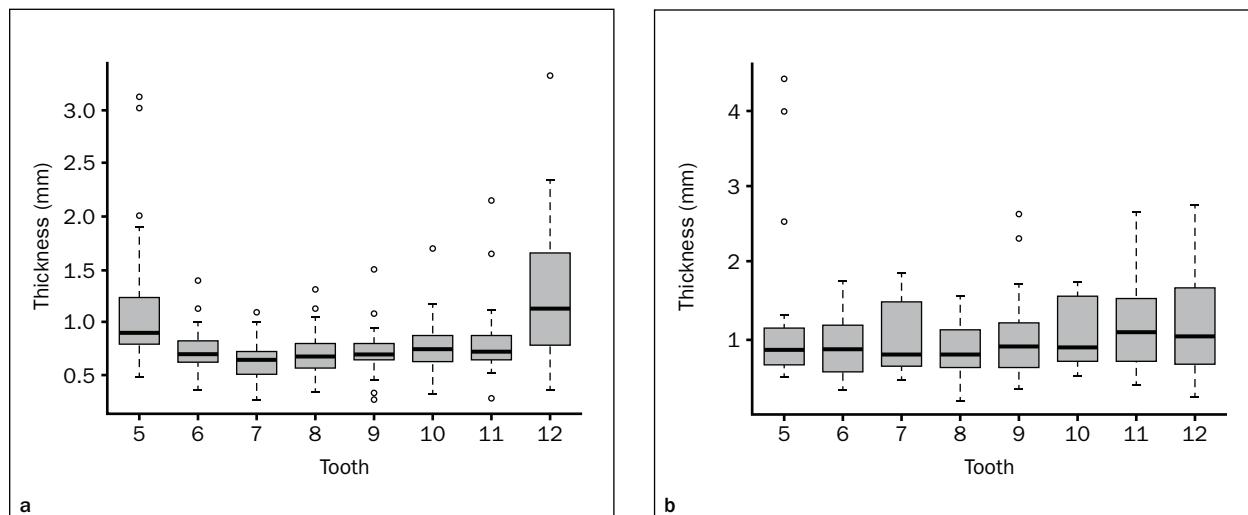


Fig 5 Box plots of the measurements (a) F and (b) G for the measured teeth (Universal tooth-numbering system). Circles indicate outliers.

DISCUSSION

The control of implant esthetics requires a more complete understanding of the architecture of the alveolus and enveloping soft tissues. Included is the influence of the buccal bone around teeth prior to intentional extraction. Both historical observations^{9,10} and current clinical studies^{11,12} indicate that alveolar resorption following tooth extraction must be expected. Contemporary discussions regarding biotype as a prognostic factor implicate a thin buccal alveolar socket wall (< 1 mm) as a risk for greater resorption following implant placement.

The magnitude of alveolar architectural change that occurs following tooth extraction must be better anticipated or predicted. In a recent prospective investigation, the mean horizontal reduction of buccal alveolar bone, measured from the implant surface to the outer aspect of the crest, was 1.0 mm (50% of the existing dimension) for anterior teeth and 1.1 mm (33% of the existing dimension) for posterior teeth.¹⁸ This study further indicated that the dimension of the buccal plate of bone (prior to extraction) was a major factor affecting the degree of resorption following tooth extraction. Additionally, the thickness of the buccal plate was associated with the degree of defect fill following implant placement.¹⁹ In another study, a robust buccal alveolar wall located at a distance from the implant-abutment interface was associated with greater fill of the gap between the implant and buccal wall and less resorption of the buccal alveolus. From a clinical perspective, however, this investigation also demonstrated that a thick buccal wall (> 1 mm) was present frequently at premolar teeth, but not at canine and incisor teeth of the maxilla.²⁰

This CBCT investigation reiterates that anterior maxillary teeth typically possess buccal bone thickness of less than 1 mm (average 0.8 mm; Fig 3). While the accuracy of the CBCT measurements may be scrutinized because of instrumentation error, motion artifact, scatter artifact, and the inherent 0.3-mm voxel size of the system, the present measurements are similar to those obtained by direct measurement.²⁰ It may be concluded that few maxillary anterior tooth alveolar buccal walls are thicker than 1 mm.

When considering the focus on "biotype," which refers to thick gingival biotypes associated with buccal wall thicknesses greater than 1 mm, the present investigation suggests that few anterior maxillary teeth may be associated with such a "thick biotype." If the risk of resorption of the alveolus is greater if the buccal plate is less than 1 mm (a "thin biotype"), then the majority of anterior maxillary tooth sites present an osseous architecture that is a higher risk for resorption. Again, the recent observations that anterior tooth sites experience greater horizontal and vertical bone loss than posterior sites are consistent with such an interpretation.²⁰

When considering premolar sites, the buccal alveolar plate width was larger than for anterior maxillary teeth. This may be important in considering existing data regarding the outcomes of current immediate loading studies. The tissue stability observed following implant placement in premolar extraction sockets²¹ may reflect favorable buccal bone thickness, a result that may not be directly inferred to sockets with thinner buccal walls, such as anterior tooth sites.

Socket classification systems have been proposed to aid in decision making for dental implant therapy.^{22,23}

The present study did not reconstruct each periradicular alveolar structure, but the presentation of midroot buccal bone in the CBCT images suggested that the majority of anterior maxillary teeth have bone present near the cervical portion of the tooth (position C). Few dehiscences were observed prior to extraction. In contrast, far more tooth sites were observed to lack bone in positions F or G or both. The relative impact of a dehiscence on esthetics can be debated, but the absence of bone in this region requires additional intervention and risk assessment.²² The presence of fenestrations, on the other hand, may complicate implant placement and can preclude attainment of sufficient primary stability. The present investigation suggests that pre-extraction evaluation of the anterior maxillary teeth may inform the clinician regarding the presence or absence, abundance, and location of buccal alveolar bone.

CONCLUSIONS

The present evaluation of cone beam computed tomography images to determine the presence and architecture of the buccal alveolar bone residing at maxillary anterior teeth and first premolars indicated that: (1) cone beam computed tomographic assessment of socket morphology is possible and informative, (2) the buccal alveolar bone in anterior tooth positions is typically less than 1.0 mm thick, (3) premolar teeth possess greater buccal alveolar bone thickness than anterior teeth, and (4) the median vertical distance from the cementoenamel junction to the buccal bone crest of 2.79 mm was consistent among all sites measured. Clinicians should keep in mind, prior to extraction, that maxillary anterior teeth typically possess a thin buccal plate.

ACKNOWLEDGMENTS

The authors reported no conflicts of interest related to this study.

REFERENCES

- Lang NP, Tonetti MS, Suvan JE, et al. Immediate implant placement with transmucosal healing in areas of aesthetic priority. A multicentre randomized-controlled clinical trial I. Surgical outcomes. *Clin Oral Implants Res* 2007;18:188–196.
- Esposito M, Grusovin MG, Polyzos IP, Felice P, Worthington HV. Timing of implant placement after tooth extraction: Immediate, immediate-delayed or delayed implants? A Cochrane systematic review. *Eur J Oral Implantol* 2010;3:189–205.
- Donati M, La Scala V, Billi M, Di Dino B, Torrisi P, Berglundh T. Immediate functional loading of implants in single tooth replacement: A prospective clinical multicenter study. *Clin Oral Implants Res* 2008;19:740–748.
- Buser D, Halbritter S, Hart C, et al. Early implant placement with simultaneous guided bone regeneration following single-tooth extraction in the esthetic zone: 12-month results of a prospective study with 20 consecutive patients. *J Periodontol* 2009;80:152–162.
- Cooper LF, Raes F, Reside GJ, et al. Comparison of radiographic and clinical outcomes following immediate provisionalization of single-tooth dental implants placed in healed alveolar ridges and extraction sockets. *Int J Oral Maxillofac Implants* 2010;25:1222–1232.
- Sanz M, Cecchinato D, Ferrus J, Pjetursson EB, Lang NP, Lindhe J. A prospective, randomized-controlled clinical trial to evaluate bone preservation using implants with different geometry placed into extraction sockets in the maxilla. *Clin Oral Implants Res* 2010;21:13–21.
- Chen ST, Buser D. Clinical and esthetic outcomes of implants placed in postextraction sites. *Int J Oral Maxillofac Implants* 2009;24 (suppl):186–217.
- Manor Y, Oubaid S, Mardinger O, Chaushu G, Nissan J. Characteristics of early versus late implant failure: A retrospective study. *J Oral Maxillofac Surg* 2009;67:2649–2652.
- Atwood DA. Some clinical factors related to rate of resorption of residual ridges. *J Prosthet Dent* 2001 Aug;12:441–450.
- Tallgren A. The continuing reduction of the residual alveolar ridges in complete denture wearers: A mixed-longitudinal study covering 25 years. *J Prosthet Dent* 1972;27:120–132.
- Schropp L, Wenzel A, Kostopoulos L, Karring T. Bone healing and soft tissue contour changes following single-tooth extraction: A clinical and radiographic 12-month prospective study. *Int J Periodontics Restorative Dent* 2003;23:313–323.
- Botticelli D, Persson LG, Lindhe J, Berglundh T. Bone tissue formation adjacent to implants placed in fresh extraction sockets: An experimental study in dogs. *Clin Oral Implants Res* 2006;17:351–358.
- Araujo MG, Sukekava F, Wennstrom JL, Lindhe J. Ridge alterations following implant placement in fresh extraction sockets: An experimental study in the dog. *J Clin Periodontol* 2005;32:645–652.
- Cardaropoli G, Araujo M, Hayacibara R, Sukekava F, Lindhe J. Healing of extraction sockets and surgically produced—augmented and non-augmented—defects in the alveolar ridge. An experimental study in the dog. *J Clin Periodontol* 2005;32:435–440.
- Schropp L, Isidor F. Timing of implant placement relative to tooth extraction. *J Oral Rehabil* 2008;35(suppl 1):33–43.
- Evans CD, Chen ST. Esthetic outcomes of immediate implant placements. *Clin Oral Implants Res* 2008;19:73–80.
- Kois JC. Predictable single tooth peri-implant esthetics: Five diagnostic keys. *Compend Contin Educ Dent* 2001;22:199–206.
- Ferrus J, Cecchinato D, Pjetursson EB, Lang NP, Sanz M, Lindhe J. Factors influencing ridge alterations following immediate implant placement into extraction sockets. *Clin Oral Implants Res* 2010;21:22–29.
- Tomasi C, Sanz M, Cecchinato D, et al. Bone dimensional variations at implants placed in fresh extraction sockets: A multilevel multivariate analysis. *Clin Oral Implants Res* 2010;21:30–36.
- Huynh-Ba G, Pjetursson BE, Sanz M, et al. Analysis of the socket bone wall dimensions in the upper maxilla in relation to immediate implant placement. *Clin Oral Implants Res* 2010;21:37–42.
- Oh TJ, Shotwell JL, Billy EJ, Wang HL. Effect of flapless implant surgery on soft tissue profile: A randomized controlled clinical trial. *J Periodontol* 2006;77:874–882.
- Caplanis N, Lozada JL, Kan JY. Extraction defect assessment, classification, and management. *J Calif Dent Assoc* 2005;33:853–863.
- Elian N, Cho SC, Froum S, Smith RB, Tarnow DP. A simplified socket classification and repair technique. *Pract Proced Aesthet Dent* 2007;19:99–104.

Effects of Implant Surgery on Blood Pressure and Heart Rate During Sedation with Propofol and Midazolam

Daisuke Ueno, DDS¹/Junichi Sato, DMD, PhD²/Jun Nejima, MD, PhD³/
Keisuke Maruyama, DMD⁴/Mariko Kobayashi, DMD, PhD⁴/Toshikazu Iketani, DMD⁴/
Rei Sekiguchi, DDS⁵/Hiroshi Kawahara, DDS, PhD⁶

Purpose: Intravenous (IV) sedation is commonly used in dentistry. However, no report has yet been published regarding age, hypertension, and antihypertensive drugs during implant surgery and their relationship with changes in blood pressure (BP) and heart rate in implant surgery under IV sedation with propofol and midazolam.

Materials and Methods: Medical records of 252 patients who underwent implant surgery were retrospectively analyzed. Patients were classified into four groups according to their age (in years) and hypertension status: A = ≤ 64, no hypertension; B = ≥ 65, no hypertension; C = ≤ 64, hypertension; or D = ≥ 65, hypertension. Hypertensive patients were further characterized by their antihypertensive medications: E = calcium channel blockers (CCBs), F = angiotensin II receptor blockers (ARBs), G = CCBs+ARBs, or H = no medication. IV sedation was administered in two stages. After midazolam injection to prevent angialgia, propofol was infused at the rate of 4 mg/kg/h, followed by a dose reduction. Systolic and diastolic BP and heart rate were recorded before, during, and after surgery. **Results:** Systolic BP increased significantly after patients were draped in groups A, C, and D, with group D showing the most pronounced increase. Sedatives decreased BP in all groups. Diastolic BP in group F decreased significantly compared to group H after induction and before infiltration of local anesthetic. After infiltration, systolic BP decreased more significantly in group G than in group H. Intraoperative hypotension was observed in 25% of patients. The incidence of intraoperative hypertension in group D was markedly higher than in group A (23% vs 4%). **Conclusion:** IV sedation using midazolam and propofol reduces hypertensive risks during implant surgery. Nevertheless, care must be taken, especially in older hypertensive patients and in hypertensive patients on ARBs or ARBs+CCBs. *INT J ORAL MAXILLOFAC IMPLANTS* 2012;27:1520–1526

Key words: angiotensin II receptor blockers, dental implant, hemodynamics, midazolam, moderate sedation, oral surgery propofol

¹Assistant Professor, Unit of Oral and Maxillofacial Implantology, Tsurumi University School of Dental Medicine, Yokohama, Japan.

²Associate Professor, Unit of Oral and Maxillofacial Implantology, Tsurumi University School of Dental Medicine, Yokohama, Japan.

³Professor, Department of Internal Medicine, Tsurumi University School of Dental Medicine, Yokohama, Japan.

⁴Clinical Research Associate, Unit of Oral and Maxillofacial Implantology, Tsurumi University School of Dental Medicine, Yokohama, Japan.

⁵Resident, Division of Periodontics, Eastman Institute for Oral Health, University of Rochester, Rochester, New York.

⁶Professor, Department of Dental Anesthesiology, Tsurumi University School of Dental Medicine, Yokohama, Japan.

Correspondence to: Dr Daisuke Ueno, Unit of Oral and Maxillofacial Implantology, Tsurumi University, School of Dental Medicine, 2-1-3 Tsurumi Tsurumi-ku Yokohama, Japan. Fax: +81-45-581-1001, ext 8536. Email: ueno-d@tsurumi-u.ac.jp

Implant surgery is one of the most invasive treatments in dentistry and requires close and constant cardiovascular monitoring.¹ The causes of hypertension include fear reactions, pain responses, and vasoconstrictor-containing local anesthesia.² A remarkable increase in blood pressure (BP) can trigger cerebrovascular disorders and burden the heart. Patients with a history of hypertension experience an increase in systolic BP (SBP) at a faster rate than normotensive patients.³ Increases in heart rate and BP are induced by the patient's anticipation of scheduled treatment and by the actual dental treatment. Dental phobic patients need extra attention and care because they also manifest a profound increase in BP in a dental setting.²

Intravenous (IV) sedation plays an increasingly important role in implant dentistry, as it offers many advantages. IV sedation depresses the central nervous system, minimizes pain and anxiety, and helps to maintain cardiovascular stability. Although they are relaxed, patients can still respond to physical stimulation and

verbal commands.⁴ Compared to general anesthesia, IV sedation is less expensive and requires less recovery time.⁴ Propofol and midazolam, in particular, have been extensively used together because of their synergistic effects. Previous research indicated increases in sedative, amnesic, and anxiolytic effects with IV midazolam (2 mg) used as a premedication immediately before propofol induction.⁵ Propofol and midazolam both lower BP and thus prevent hypertension; however, they could cause intraoperative hypotension.

The combined effect of IV sedation and antihypertensive medications remains incompletely understood. Calcium channel blockers (CCBs) obstruct the voltage-gated calcium channels in cardiac muscle and blood vessels, reducing cardiac contractility and dilating vessels. Angiotensin II receptor blockers (ARBs) are inhibitors of the renin-angiotensin-aldosterone system, which reduce BP by blocking the activation of AT II, the angiotensin II receptor. ARBs blunt the endogenous sympathetic response to hypotension and exogenous effects of catecholamine infusion.^{6,7} Hypotension in patients taking antihypertensive medications is a potentially serious condition, because the combined use of ARBs and CCBs could produce a synergistic impact by limiting the effectiveness of both endogenous and exogenously administered catecholamines.⁸

Although increasing age and preexisting hypertension have been shown to be associated with an increased incidence of perioperative hemodynamic instability,^{9,10} the association in dental patients receiving IV sedation also requires further investigation. In third molar extraction under local anesthesia, older patients experienced a greater increase in BP than younger patients.⁹ Preexisting hypertension, too, makes intraoperative blood pressure control difficult¹¹—especially in patients with severe hypertension (SBP \geq 180 mm Hg, diastolic BP [DBP] \geq 110 mm Hg).¹⁰

Accordingly, it was hypothesized that cardiovascular changes under IV sedation would be affected by age, hypertensive status, and antihypertensive medications. Older patients were predicted to experience more cardiovascular complications than younger counterparts. Compared to normotensive patients, hypertensive patients were expected to exhibit greater instability in hemodynamic response. Hypertensive patients taking ARBs and CCBs were predicted to have a higher risk of developing hypotension, owing to the combined BP-lowering effect of ARBs, CCBs, midazolam, and propofol. To prove these hypotheses, the present study retrospectively assessed cardiovascular changes in implant surgery under IV sedation with propofol and midazolam. With special attention to hypertensive and hypotensive episodes, the data were analyzed according to three variables: age, hypertensive status, and antihypertensive medications.

MATERIAL AND METHODS

Subjects

This retrospective study was approved by the Ethics Committee at Tsurumi University, School of Dental Medicine (no. 812). The authors screened the medical records of 444 Japanese patients who had received IV sedation for implant surgery at Tsurumi University Dental Hospital between 2006 and 2009. Included were patients who: (1) received both midazolam and propofol, (2) received local anesthesia of 2% lidocaine with 1:80,000 epinephrine, and (3) received implant placement with or without vertical sinus elevation (osteotome technique). Exclusion criteria included patients who: (1) had a history of previous implant surgery, (2) had incomplete medical records, (3) underwent bone harvesting before graft and sinus elevation procedures (lateral window technique), or (4) received any local anesthetic other than 2% lidocaine with 1:80,000 epinephrine.

Sedation Protocol

Supplemental oxygen was delivered at 2 to 4 L/min via a nasal cannula. An indwelling cannula was placed in either the dorsum of the hand or the antecubital fossa. IV sedation was performed in two stages⁵ by a dental anesthesiologist certified by the Japanese Board of Dental Anesthesiologists. The first step involved a 2- to 4-mg midazolam injection to prevent angialgia. Propofol was first infused at the rate of 4 mg/kg/h and was followed by a dose reduction (Telfusion Pump, Terumo).

The intended level of sedation was moderate; that is, a minimally depressed level of consciousness retains patients' ability to maintain a regular breathing pattern and respond to verbal commands. After the intended sedation depth was achieved, local anesthesia was administered using 2% lidocaine with 1:80,000 epinephrine. All patients were given dexamethasone via a cannula during suturing. The amount of sedation was adjusted to maintain the sedation level throughout the procedure.

Physiologic Data Collection

All patients were monitored with continuous electrocardiography and pulse oximetry (Hemo Moneo BP-88 S, Colin Japan). BP was measured automatically every 5 minutes. An anesthesiologist recorded SBP, DBP, and heart rate 10 times per patient: t0 = preoperative baseline, t1 = after draping a patient, t2 = after midazolam induction, t3 = before local anesthetic injection, t4 = after local anesthetic injection, t5 = after mucosal incision, t6 = after osteotomy for the implant bed, t7 = after implant placement, t8 = after dexamethasone administration, and t9 = postoperatively (after recovery from anesthesia).

Table 1 Medical History of the Included Subjects

Disease	No. of patients	%
Circulatory	61	24
Digestive	61	24
Respiratory	7	3
Endocrine/metabolic	30	12
Kidney/urologic	23	9
Blood	3	1
Cerebrovascular	7	3
Immune/allergic	47	19
Psychiatric	10	4
Other	20	8

Table 2 Mean Doses of Local Anesthetic, Midazolam, and Propofol, by Group

Group	Local anesthetic (mL)	Midazolam (mg)	Propofol (mg)
A	4.6 ± 2.0	2.4 ± 0.7	144 ± 79
B	4.3 ± 1.6	2.4 ± 0.7	113 ± 55
C	4.0 ± 1.7	2.1 ± 0.8	140 ± 65
D	4.7 ± 1.8	2.1 ± 0.8	114 ± 64
E	4.0 ± 1.7	2.2 ± 0.8	127 ± 85
F	4.6 ± 2.1	2.2 ± 0.8	152 ± 51
G	3.7 ± 1.5	2.5 ± 0.7	134 ± 71
H	4.9 ± 1.6	2.3 ± 0.7	117 ± 62

There were no significant differences between groups.

Data Analysis

Patients were classified into four groups according to their age and hypertension status: group A = ≤ 64 years old, no hypertension; group B = ≥ 65 years old, no hypertension; group C = ≤ 64 years old, hypertension; or group D = ≥ 65 years old, hypertension. Hypertensive patients (groups C and D) were further categorized into four groups according to prescribed antihypertensive medications: E = CCBs; F = ARBs; G = CCBs+ARBs; or H = no medication.

The total dose of midazolam and propofol was compared between groups A, B, C, and D and among the hypertensive groups E, F, G, and H.

Intraoperative hypotension was defined as a ≥ 30% decrease in SBP and/or DBP. Intraoperative hypertension was defined as a ≥ 30% increase in SBP and/or DBP compared to preoperative baseline.¹²

Table 3 Mean Changes in SBP, DBP, and Heart Rate

Parameter/group	Baseline	Measurement point	
		1	2
SBP			
A	118 ± 20	7 ± 14*†	3 ± 15
B	127 ± 18	11 ± 21	2 ± 21
C	129 ± 16	13 ± 18*	3 ± 17
D	130 ± 17	17 ± 14*†	6 ± 23
DBP			
A	75 ± 13	-2 ± 11*	-5 ± 14**
B	76 ± 13	-1 ± 12	-3 ± 12
C	81 ± 12	2 ± 10	-2 ± 11
D	77 ± 10	2 ± 14	-4 ± 10
Heart rate			
A	73 ± 10	-2 ± 9	-3 ± 9
B	75 ± 13	-3 ± 10	-5 ± 9
C	73 ± 13	-2 ± 11	1 ± 11
D	71 ± 13	2 ± 15	0 ± 12

*P < .05 vs baseline; **P < .001 vs baseline; †P < .05 group A vs group D.

Statistical Analysis

All numeric data were expressed as mean values and standard deviations. Statistical analysis was performed with a statistical commercial software program (SPSS 18.0 for Windows, Evaluation Version, IBM). The obtained values from baseline and measurement periods were analyzed using one-way analysis of variance followed by the Tukey test. Between-group comparisons were also performed by analysis of variance followed by the Tukey test. Incidence of intraoperative hypertension and hypotension was analyzed by Pearson's chi-square test. P < .05 was considered as significant.

RESULTS

Patient Demographics

Of the 444 patient records that were screened, 252 (160 men and 92 women) were included and evaluated. The patients were between the ages of 17 and 84 years, with a mean age of 57 ± 12 years. Their weights ranged from 36 to 87 kg, with a mean weight of 57 ± 11 kg. Their medical problems were mostly circulatory and digestive diseases (Table 1). Of the patients with a history of circulatory diseases, 88% had hypertension. The mean duration of implant surgery was 57 ± 24 minutes. The

at Each Measurement Point Versus Preoperative Baseline Values in All Patients

Measurement point							
3	4	5	6	7	8	9	
-5 ± 14	-8 ± 20*	-9 ± 17**	-8 ± 18*	-7 ± 17*	-6 ± 22	-19 ± 4	
-9 ± 21	-10 ± 23	-12 ± 24	-11 ± 22	-10 ± 22	-8 ± 21	-9 ± 20	
-6 ± 16	-6 ± 20	-11 ± 19	-11 ± 16	-10 ± 18	-11 ± 16	-7 ± 19	
-2 ± 20	-7 ± 28	-10 ± 24	-14 ± 23	-8 ± 22	-8 ± 20	-6 ± 21	
<hr/>							
-10 ± 10**	-13 ± 12**	-15 ± 11**	-14 ± 11**	-13 ± 11**	-11 ± 12**	-10 ± 11**	
-9 ± 13*	-10 ± 12**	-13 ± 13**	-15 ± 11**	-13 ± 13**	-11 ± 14**	-9 ± 14*	
-9 ± 9*	-10 ± 12*	-13 ± 9**	-14 ± 9**	-15 ± 10**	-13 ± 11**	-11 ± 11*	
-8 ± 12	-8 ± 12	-12 ± 13*	-13 ± 13**	-12 ± 12*	-11 ± 12*	-10 ± 11	
<hr/>							
-2 ± 11	0 ± 12	1 ± 10	-0 ± 10	-2 ± 9	-3 ± 10	-5 ± 9	
-3 ± 12	-1 ± 10	2 ± 11	2 ± 10	-1 ± 10	-3 ± 10	-5 ± 11	
-2 ± 12	1 ± 13	2 ± 12	1 ± 13	1 ± 12	-1 ± 12	-1 ± 12	
-1 ± 11	-1 ± 10	0 ± 10	0 ± 13	0 ± 11	-2 ± 12	-1 ± 11	

mean number of implants placed was 2.8 ± 1.4 . The total dose of midazolam for initial sedation varied between 0.5 and 4.0 mg, with the mean dose being 2.3 ± 0.7 mg. The total dose of propofol ranged from 18 to 500 mg (mean, 133 ± 74 mg). The mean dose of local anesthetic was 4.5 ± 2.0 mL. No significant difference was observed in the dosage of local anesthetic, midazolam, and propofol among the different groups (Table 2).

Effects of Age and Hypertension Status on Responses to Sedation

Hemodynamic changes were analyzed based on the age and the hypertension status of the patients, as shown in Table 3. Group A included 149 patients, group B had 47 patients, group C had 34 patients, and group D included 22 patients. Compared to the preoperative baseline values, SBP significantly increased at t1 in groups A, C, and D (A: 7 ± 14 mm Hg, C: 13 ± 18 mm Hg, D: 17 ± 14 mm Hg), with group D experiencing the most marked increase. After IV sedation induction, SBP decreased in all groups. SBP in group A significantly decreased between t4 and t7, whereas groups B, C, and D did not show any significant difference. During the measurement periods t5 to t8, DBP significantly decreased in all groups. No significant differences in heart rates were observed.

Effects of Antihypertensive Medication on Responses to Sedation

Of the participating hypertensive patients, 82% were prescribed chronic medications, which included CCBs (25%), ARBs (25%), and CCBs+ARBs together (18%) (Table 4). Hemodynamic changes of the hypertensive patients are shown in Table 5. The number of patients in each group was: E = 14, F = 14, G = 10, and H = 10. SBP in group G significantly decreased compared to group H between t4 and t8. A marked decrease in the mean DBP in group F was observed in comparison to group H at t2 and t3. No significant differences in heart rates were observed.

Effects of Age and Hypertensive Status on Hypertensive and Hypotensive Episodes

Intraoperative hypotension was observed in 64 patients (25%) (Table 6). Patients in groups B, C, and D experienced hypotension more often (30% to 35% of patients) compared to the younger nonhypertensive group A (31 patients, 21%). Intraoperative hypertension was observed in 8% (n = 21) of the subjects; a statistically significant difference was found between group A (8 patients, 4%) and D (5 patients, 23%). Implant surgery was postponed in two cases because of severe preoperative hypertension (SBP > 210 mm Hg).

Table 4 Medication Usage in the Hypertensive Patients

Drug	No. of patients	%
ARB only	14	25
CCB only	14	25
α blocker only	1	2
β blocker only	1	2
Vasodilator only	2	4
Diuretic only	1	2
ACE inhibitor only	1	2
α blocker + ARB	1	2
CCB + ARB	10	18
ARB + vasodilator	1	2
No medication	10	18
Total	56	

ACE = angiotensin-converting enzyme.

Table 5 Mean Changes in SBP, DBP, and Heart Rate at

Parameter/group	Baseline	Measurement point	
		1	2
SBP			
E	128 ± 18	19 ± 23*	8 ± 21
F	134 ± 16	16 ± 19	2 ± 21
G	132 ± 12	14 ± 12	-1 ± 22
H	132 ± 20	15 ± 11	5 ± 14
DBP			
E	79 ± 13	6 ± 10	1 ± 11
F	86 ± 9	-1 ± 9	-10 ± 7§
G	76 ± 9	6 ± 11	-3 ± 12
H	79 ± 12	2 ± 13	1 ± 7§
Heart rate			
E	76 ± 13	1 ± 7	-1 ± 8
F	72 ± 14	-2 ± 9	-1 ± 11
G	67 ± 8	3 ± 14	0 ± 10
H	72 ± 12	0 ± 5	1 ± 8

*P < .05 vs baseline; **P < .001 vs baseline; †P < .05 group H vs groups F and G;

‡P < .05 group H vs group G; ¶P < .05 group E vs group G;

§P < .05 group F vs group H.

Table 6 Adverse Events After Administration of Sedatives

Group	Group A (n = 149)	Group B (n = 47)	Group C (n = 34)	Group D (n = 22)	Total (n = 252)
Hypertension	8 (4%)	6 (13%)	2 (6%)	5 (23%)*	21 (8%)
Hypotension	31 (21%)	14 (30%)	12 (35%)	7 (31%)	64 (25%)

*P < .05, group A vs group D.

DISCUSSION

The findings coincided with the proposed hypotheses: older hypertensive patients faced a higher risk of intraoperative hypertension, whereas hypertensive patients on ARBs or ARBs+CCBs were at a greater risk of developing intraoperative hypotension. Although the current literature lacks such evidence, the finding on hypotension suggests that ARBs and CCBs may potentiate the BP-lowering effect of propofol and midazolam. Throughout the procedure, a substantial reduction in BP was seen in hypertensive patients who were taking chronic antihypertensive medications (ARBs and/or CCBs) compared to hypertensive patients who were taking no medication. Similar results were previously reported on a higher incidence of hypotension during anesthetic induction in patients prescribed CCBs and β blockers.¹³ Some investigators recommend discontinuation of angiotensin-converting enzyme inhibitors (renin-angiotensin-aldosterone system blockers) the day before surgery to minimize

intraoperative hypotension.¹⁴ Prior to implant surgery, health care providers must carefully weigh the risks and benefits of continuing or discontinuing antihypertensive medications. Older hypertensive patients may require additional measures to control pain, anxiety, and hypertension during implant surgery.

The benefits of IV sedation still outweigh the risks of intraoperative BP lability. The pain and anxiety associated with implant surgery most likely affect the release of endogenous catecholamines, which may lead to cardiovascular instability. Prior studies have shown cardiovascular effects of tooth extraction and periodontal surgery.¹⁵⁻¹⁹ The most marked cardiovascular change in tooth extraction was observed immediately before local anesthetic administration and during extraction.² In third molar extraction, a significant increase in heart rate immediately after flap reflection and osteotomy was also reported.¹⁸ Other research demonstrated that heart rates increased by 5 bpm before extraction,¹⁶ while SBP showed an increase of 3 to 15 mm Hg during extraction.^{12,20}

Each Measurement Point Versus Preoperative Baseline Values in All Hypertensive Patients

Measurement point							
3	4	5	6	7	8	9	
-3 ± 19	-9 ± 23	-11 ± 17	-12 ± 18	-11 ± 17	-10 ± 19	-4 ± 23¶	
-5 ± 20	-13 ± 19†	-15 ± 26	-10 ± 22	-6 ± 23	-7 ± 20	-6 ± 17	
-14 ± 15	-21 ± 16*†	-27 ± 12*†	-29 ± 12**†	-26 ± 13*†	-27 ± 8**†	-24 ± 7*¶	
1 ± 14	12 ± 21†	0 ± 20†	-13 ± 15†	-8 ± 18†	-6 ± 14†	-10 ± 20	
-6 ± 10	-9 ± 15	-11 ± 10	-12 ± 10	-11 ± 11	-10 ± 12	-9 ± 12	
-14 ± 8*§	-14 ± 9*§	-17 ± 11**	-18 ± 11**	-18 ± 10**	-13 ± 14*	-14 ± 11*	
-11 ± 11*	-12 ± 10*	-15 ± 9**	-22 ± 10**	-20 ± 7**	-17 ± 11**	-14 ± 8*	
-4 ± 9§	-5 ± 14§	-7 ± 11	-10 ± 11	-11 ± 11	-10 ± 12	-10 ± 11	
-4 ± 8	2 ± 10	0 ± 9	-1 ± 11	2 ± 8	2 ± 9	-1 ± 9	
-3 ± 9	-1 ± 12	0 ± 11	2 ± 14	0 ± 11	-2 ± 12	-2 ± 12	
-2 ± 10	-3 ± 9	-2 ± 8	-2 ± 9	-4 ± 10	-4 ± 7	-4 ± 8	
-4 ± 13	3 ± 11	4 ± 6	2 ± 7	1 ± 10	-3 ± 12	-1 ± 6	

Preoperative hypertension begins when the oral surgery appointment is made. One study revealed increases in SBP (13 mm Hg) and DBP (5 mm Hg) when a dental appointment was made.¹⁹ In the present study, draping caused a pronounced increase in SBP in all patients. Furthermore, implant surgery was postponed in two cases because of severe preoperative hypertension. Neither of the two patients had previously been diagnosed with hypertension. Later medical examination revealed white-coat hypertension as a cause of the preoperative hypertension. Anxiolytics may help to avoid this.

The vasoconstrictors in local anesthetics also contribute to hemodynamic changes. Prior studies reported that the administration of lidocaine with 1:100,000 epinephrine caused an increase in the mean SBP by 3 to 16 mm Hg and heart rate by 1 to 8 bpm.^{2,18,20} Another study reported a heart rate increase of 9.5% after epinephrine infusion at a rate of 50 ng/kg per minute, which is equivalent to 2.5 carpules of local anesthetic (1:80,000 epinephrine).²¹ Sedative medications counteract the effects of epinephrine; while SBP remained stable, DBP significantly decreased after epinephrine infusion with midazolam and propofol.²¹ The type of injection technique employed may also affect BP and heart rate, as infiltration and block techniques differ in systemic absorption. In the present study, local anesthetic was delivered only via infiltration, and an average

of 2.3 carpules of anesthetic was used (1.8 mL per capsule). No significant BP change was observed in any groups after administration of anesthetic.

Although the present results indicate a powerful BP-lowering effect following the combined use of propofol and midazolam, propofol alone may also prevent intraoperative hypertension because it decreases BP and cardiac output in a dose-dependent manner.^{22–24} Ronan et al reported the effects of long-term administration (12 to 24 hours) of propofol or midazolam in an intensive care unit.²⁵ Throughout the procedure, SBP significantly decreased from baseline in the propofol group, whereas no change was observed in the midazolam group. Similarly, no change in heart rate was observed in the midazolam group, while a marked decrease was seen in the propofol group.

One of the limitations of the present retrospective study is the inability to control all variables that may contribute to hemodynamic changes. The study also presents with a possible dose-response issue regarding the effect of propofol and midazolam on vital signs. Preoperative anxiety level, extent of surgery, and the anesthesia techniques employed by different anesthesiologists might all have contributed to the varying amount of sedative that was required to reach the intended level of sedation. Further research is required to establish a more accurate assessment of sedative medications.

CONCLUSION

Implant surgery not only provokes a great deal of anxiety but necessitates the use of epinephrine-containing local anesthetic for pain control and hemostasis, which could lead to cardiovascular complications. Intravenous sedation offers many benefits and plays a critical role in the prevention of hypertension and management of pain and anxiety. Nonetheless, careful monitoring must take place to maintain hemodynamic stability, especially in high-risk patients (ie, older hypertensive patients and hypertensive patients on angiotensin receptor blockers and/or calcium channel blockers). Health care professionals should be prepared and equipped to provide emergency care in case complications arise.

ACKNOWLEDGMENTS

The authors report no conflicts of interest related this study.

REFERENCES

- Nagao H, Munakata M, Tachikawa N, Shiota M, Kasugai S. Clinical study of risk management for dental implant treatment—Changes of blood pressure and pulse rate during implant surgery under local anesthesia [in Japanese]. Kokubyo Gakkai Zasshi 2002;69:27–33.
- Brand HS, Abraham-Inpijn L. Cardiovascular responses induced by dental treatment. Eur J Oral Sci 1996;104:245–252.
- Pérusse R, Goulet JP, Turcotte JY. Contraindications to vasoconstrictors in dentistry: Part II. Hyperthyroidism, diabetes, sulfite sensitivity, cortico-dependent asthma, and pheochromocytoma. Oral Surg Oral Med Oral Pathol 1992;74:687–691.
- Craig DC, Boyle CA, Fleming GJ, Palmer P. A sedation technique for implant and periodontal surgery. J Clin Periodontol 2000;27:955–959.
- Taylor E, Ghouri AF, White PF. Midazolam in combination with propofol for sedation during local anesthesia. J Clin Anesth. 1992;4:213–216.
- Brabant SM, Eyraud D, Bertrand M, Coriat P. Refractory hypotension after induction of anesthesia in a patient chronically treated with angiotensin receptor antagonists. Anesth Analg 1999;89:887–888.
- Licker M, Neidhart P, Lustenberger S, et al. Long-term angiotensin-converting enzyme inhibitor treatment attenuates adrenergic responsiveness without altering hemodynamic control in patients undergoing cardiac surgery. Anesthesiology 1996;84:789–800.
- Smith SW, Ferguson KL, Hoffman RS, Nelson LS, Greller HA. Prolonged severe hypotension following combined amlodipine and valsartan ingestion. Clin Toxicol 2008;46:470–474.
- Alemany-Martínez A, Valmaseda-Castellón E, Berini-Aytés L, Gay-Escoda C. Hemodynamic changes during the surgical removal of lower third molars. J Oral Maxillofac Surg 2008;66:453–461.
- Howell SJ, Sear JW, Foeck P. Hypertension, hypertensive heart disease and perioperative cardiac risk. Br J Anaesth 2004;92:570–583.
- Polk SL, Hill CH, Marotta JJA, Schneider AJL. Anesthesiology. In: Lawrence PF, Bell RM, Dayton MT (eds). Essentials of Surgical Specialties, ed 3. Baltimore, MD: Lippincott Williams & Wilkins, 2006:1–50.
- Meiller TF, Overholser CD, Kutcher MJ, Bennett R. Blood pressure fluctuations in hypertensive patients during oral surgery. J Oral Maxillofac Surg 1983;41:715–718.
- Brabant SM, Bertrand M, Eyraud D, Darmon PL, Coriat P. The hemodynamic effects of anesthetic induction in vascular surgical patients chronically treated with angiotensin II receptor antagonists. Anesth Analg 1999;88:1388–1392.
- Bertrand M, Godet G, Meerschaert K, Brun L, Salcedo E, Coriat P. Should the angiotensin II antagonists be discontinued before surgery? Anesth Analg 2001;92:26–30.
- Paramaesvaran M, Kingon AM. Alterations in blood pressure and pulse rate in exodontia patients. Aust Dent J 1994;39(5):282–286.
- Beck FM, Wewer JM. Blood pressure and heart rate responses to anticipated high-stress dental treatment. J Dent Res 1981;60:26–29.
- Frabetti L, Checchi L, Finelli K. Cardiovascular effects of local anesthesia with epinephrine in periodontal treatment. Quintessence Int 1992;23:19–24.
- Santos CF, Modena KC, Giglio FP, et al. Epinephrine concentration (1:100,000 or 1:200,000) does not affect the clinical efficacy of 4% articaine for lower third molar removal: A double-blind, randomized, crossover study. J Oral Maxillofac Surg 2007;65:2445–2452.
- Cheraskin E, Prasertsuntarasai T. Use of epinephrine with local anesthesia in hypertensive patients. IV. Effect of tooth extraction on blood pressure and pulse rate. J Am Dent Assoc 1959;58:61–68.
- Knoll-Köhler E, Knoller M, Brandt K, Becker J. Cardiohemodynamic and serum catecholamine response to surgical removal of impacted mandibular third molars under local anesthesia: A randomized double-blind parallel group and crossover study. J Oral Maxillofac Surg 1991;49:957–962.
- Niwa H, Tanimoto A, Sugimura M, Morimoto Y, Hanamoto H. Cardiovascular effects of epinephrine under sedation with nitrous oxide, propofol, or midazolam. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2006;102:e1–9.
- Claeys MA, Gepts E, Camu F. Haemodynamic changes during anaesthesia induced and maintained with propofol. Br J Anaesth 1988;60:3–9.
- Tsubokawa T, Yamamoto K, Kobayashi T. Propofol clearance and distribution volume increase in patients with hyperthyroidism. Anesth Analg 1998;87:195–199.
- Sellgren J, Ejnell H, Elam M, Pontén J, Wallin BG. Sympathetic muscle nerve activity, peripheral blood flows, and baroreceptor reflexes in humans during propofol anesthesia and surgery. Anesthesiology 1994;80:534–544.
- Ronan KP, Gallagher TJ, George B, Hamby B. Comparison of propofol and midazolam for sedation in intensive care unit patients. Crit Care Med 1995;23:286–293.

Restoration of Immediately Loaded Implants in a Minimal Number of Appointments: A Retrospective Study of Clinical Effectiveness

Carlo Ercoli, DDS¹/Alessandro Geminiani, DDS²/Heeje Lee, DDS³/
Changyong Feng, PhD⁴/Carlo E. Poggio, DDS, MSD, PhD⁵

Purpose: The purpose of this study was to assess the clinical effectiveness of an experimental technique versus the conventional method for the fabrication of implant-supported fixed complete dentures. **Materials**

and Methods: Between January 2005 and June 2010, edentulous patients who had received rehabilitation by means of nonsegmented fixed implant-supported complete dentures were identified from the pool of individuals treated at Eastman Institute for Oral Health, University of Rochester. Data collection consisted of a chart review and recording of treatment variables in a customized database. Variables of interest included number of implants per patient, time of implant placement, number of appointments required to complete prosthesis fabrication, type of appointments, manufacturing process used for creation of the framework, and fit of the framework. The number of appointments for conventional and experimental protocols was evaluated for statistical significance using two-way analysis of variance. Presence or absence of clinically acceptable prosthesis fit with the two techniques was evaluated using the Fisher exact test and exact logistic regression analysis. **Results:** Forty-two patients (48 arches) were included. When the experimental technique was used, prosthesis fabrication and delivery required an average of 4 appointments, whereas the conventional technique required an average of 7.8 appointments to deliver the definitive prosthesis. The prostheses fabricated with the experimental technique showed clinically passive fit on the implants in 17 of 18 arches. The frameworks fabricated with the conventional technique achieved clinically passive fit in 18 of 30 arches. **Conclusions:** The experimental technique significantly reduced the number of appointments required to fabricate a nonsegmented fixed implant-supported prosthesis. Moreover, this experimental technique provided clinically acceptable fit of the prosthesis in a significantly greater number of cases compared to a conventional implant elastomeric impression technique. INT J ORAL MAXILLOFAC IMPLANTS 2012;27:1527–1533

Key words: dental implants, edentulous mandible, edentulous maxilla, immediate loading, implant-supported prosthesis

¹Associate Professor, Chair, and Program Director, Division of Prosthodontics, Eastman Institute for Oral Health, School of Medicine and Dentistry, University of Rochester, Rochester, New York, USA.

²Postgraduate Student, Division of Periodontics, Eastman Institute for Oral Health, School of Medicine and Dentistry, University of Rochester, Rochester, New York, USA.

³Clinical Assistant Professor, Division of Prosthodontics, Eastman Institute for Oral Health, School of Medicine and Dentistry, University of Rochester, Rochester, New York, USA.

⁴Associate Professor, Department of Biostatistics and Computational Biology, University of Rochester, Rochester, New York, USA.

⁵Adjunct Assistant Professor, Division of Prosthodontics, Eastman Institute for Oral Health, School of Medicine and Dentistry, University of Rochester, Rochester, New York, USA.

Presented at the Academy of Prosthodontics Annual Meeting, Albuquerque, New Mexico, May 2010.

Correspondence to: Dr Carlo Ercoli, Division of Prosthodontics, University of Rochester, Eastman Institute for Oral Health, 625 Elmwood Ave, Rochester, NY 14620, USA. Fax: +585-244-8772. Email: carlo_ercoli@urmc.rochester.edu

The quality of life of edentulous patients has been greatly improved by the adoption of implant-supported prostheses.^{1,2} While the original Brånenmark protocol advocated the placement of dental implants in healed edentulous crests and a period of undisturbed healing without loading,^{3,4} several authors have reported on the predictability of implant placement in fresh extraction sockets^{5–7} or immediate loading of dental implants.^{8–11} Indeed, Schnitman et al¹² in 1990 first reported the 3.5-year results of fixed dental prostheses (FDPs) loaded immediately (at the time of implant placement). Since then, immediate loading of FDPs has been advocated by several authors with a progressively increasing level of scientific evidence.^{8,13,14} Protocols for immediate loading of implant prostheses show implant survival rates (1 to 3 years) of 95.4% to 100%^{8–11} and prosthodontic survival rates that range from 87.5% to 100%.^{8–11} Higher levels of evidence are generally found for immediately

loaded dental implants placed in a healed edentulous crest, while the immediate loading of dental implants placed in fresh extraction sockets is not currently supported by adequate levels of evidence.¹⁵

However, even when immediate loading protocols are adopted to shorten treatment times and provide the patient with an FDP at the time of surgery, several appointments are still required to gather all the information necessary for the fabrication of the definitive prosthesis, such as impression making and assessment of maxillomandibular relationships, occlusal vertical dimension, and tooth positions. Recently, Ercoli et al¹⁶ proposed a new clinical and laboratory protocol for the fabrication of implant-supported prostheses that allows the clinician to considerably shorten treatment time while maintaining a clinically adequate level of prosthesis fit. This technique has been suggested to allow the clinician to immediately load the implants with a provisional fixed complete denture at the time of implant placement, as previously described,^{8,17,18} but, then, rather than using multiple appointments to gather all the information needed for the fabrication of the definitive prosthesis, the clinician can use the information provided by the provisional to record and transfer to the laboratory the relative positions of the implants and soft tissues, the occlusal vertical dimension, maxillomandibular relationships, and tooth positions to allow insertion of the definitive prosthesis at the third appointment. The authors claimed that this technique not only allows a significant reduction in the chair time required for prosthesis fabrication, but it also permits the laboratory technologist to fabricate the definitive prosthesis in a single laboratory phase rather than in multiple steps. Unfortunately, definitive data on the applicability of this technique to different patient scenarios (maxillary and mandibular cases) and for different clinicians with different levels of experience are lacking. Therefore, the purpose of this retrospective study was to determine whether there was a difference in the number of appointments required for the fabrication of a cross-arch, nonsegmented, implant-supported prosthesis in completely edentulous patients with a conventional clinical and laboratory protocol versus a similar prosthesis fabricated following the guidelines recommended by Ercoli et al. In addition, the clinical fit of the prostheses achieved with both protocols was compared to assess whether any difference in framework fit was present. Other outcomes of interest, such as implant success and survival, will be the topic of subsequent analyses. The null hypothesis is that there would be no difference in the number of appointments required to fabricate a nonsegmented fixed implant-supported complete denture with the conventional or the experimental technique. Also, the second null hypothesis is that there would be no difference in the fit of the framework fabricated by the conventional or the experimental technique.

MATERIAL AND METHODS

Between January 2005 and June 2010, edentulous patients requiring oral rehabilitation by means of a nonsegmented fixed implant-supported complete denture were identified from the pool of individuals treated at Eastman Institute for Oral Health, University of Rochester. Implants were placed (Straumann Tissue Level and Straumann Bone Level implants, Straumann) and prostheses fabricated by faculty members or residents. Arches were treated with an FDP supported by four to eight implants and loaded according to an immediate loading protocol (implant-supported prostheses connected within 48 hours after implant placement).¹⁵ After 2 to 3 months of loading with the provisional, the definitive prosthesis was fabricated. Prostheses were completed either with a conventional prosthodontic protocol^{19,20} or according to the technique described by Ercoli et al in 2006.¹⁶

Data collection was performed by one investigator (AG) and reviewed by a second investigator (CE). The data collection consisted of a chart review and recording of all the variables in a customized Excel spreadsheet (Excel 2003, Microsoft). These treatment variables included: number of implants per patient; timing of implant placement (immediate or delayed placement); total number of appointments required to complete the prostheses; type of appointment (impression, jaw relation recording, try-in or adjustment of framework, try-in or adjustment of teeth setup, emergency adjustment to provisionals, delivery); type of manufacturing process utilized for the fabrication of the framework (computer-aided design/computer-assisted manufacture [CAD/CAM] or cast); and clinical fit of the framework (recorded as clinically passive or not passive). The framework fit was clinically verified by the prosthodontist/resident who fabricated the prostheses using the Sheffield test.²¹ Briefly, this test consisted of selectively screwing (one screw only) the framework into position and by evaluating the fit by clinical (direct inspection with 3.5× to 4.5× magnification loupes) and radiographic means (periapical and/or panoramic radiographs). If the fit was not clinically passive, the framework was sectioned, luted with autopolymerizing acrylic resin (Pattern Resin, GC America), and picked up in a positional impression recorded with polyether (Permadyne, 3M ESPE) or vinyl polysiloxane (VPS) impression material (Elite, Zhermack). Other recorded treatment variables included the material chosen for the veneering of the framework (porcelain or acrylic resin) and the time of loading (immediate or conventional loading).¹⁵

The CAM framework patterns were designed on the master cast with titanium implant abutments (temporary restoration abutment 048.650, Straumann) and autopolymerizing acrylic resin (Pattern Resin,

GC America) and then sent to a manufacturing facility (Nobel Biocare Procera) for the machining of the titanium framework. The cast frameworks were fabricated by connecting each implant to an abutment (SynOcta abutment 048.602, Straumann) and a corresponding prosthetic component (gold abutment 048.632, Straumann), which were then connected with autopolymerizing acrylic resin (GC Pattern Resin, GC America). After the pattern was completed, it was invested (Hi-Temp, Whip Mix) and, following a conventional lost-wax technique, cast in high noble metal alloy (Leo, Ivoclar Vivadent). Metal-acrylic resin prostheses were veneered with acrylic resin (Lucitone 199, Dentsply) and denture teeth (Vivodent PE, Ivoclar Vivadent), while metal-ceramic prostheses were veneered with feldspathic porcelain (Ceramco, Dentsply; or Creation, Jensen Dental).

For the purpose of this article, only the number of appointments required to complete the fabrication of the prosthesis and the presence or absence of clinically acceptable fit of the prosthesis were considered as outcomes of interest. The implant impression appointment was considered as the first appointment; delivery of the definitive prostheses was considered the last appointment. Postdelivery adjustments were recorded but were not considered in the calculation of the numbers of appointments required for prosthesis fabrication; any appointment required to adjust or repair the provisional was included.

Two-way analysis of variance (ANOVA) was used to study the effect of technique (experimental versus conventional), operator (experienced prosthodontist versus residents), and their interaction on the number of appointments required to complete the prosthesis. The presence or absence of clinically acceptable prosthetic fit with the two techniques was evaluated using the Fisher exact test and exact logistic regression analysis.²² All analyses were implemented with SAS 9.2 (SAS Institute).

RESULTS

Forty-two edentulous patients participated in the study (for a total of 48 edentulous arches; 22 maxillae, 26 mandibles). The mean age was 47 to 76 years (mean age, 64 years). Implants were placed either by a faculty member in the divisions of periodontics or oral and maxillofacial surgery (14 patients; 8 maxillae, 11 mandibles) or by a resident in one of these divisions (28 patients; 14 maxillae, 15 mandibles). Prostheses were fabricated either by a faculty member (prosthodontist) (14 patients; 8 maxillae, 11 mandibles) or by several residents (28 patients; 14 maxillae, 15 mandibles) in the division of prosthodontics.

Table 1 No. of Appointments Required for Complete Rehabilitation Using Two Different Techniques

Technique/ operator	No. of appointments		
	No. of prostheses	Mean	SD
Experimental			
Experienced prosthodontist	10	2.9	0.9
Residents	7	5.6	1.5
Overall	17	4.0	1.8
Conventional			
Experienced prosthodontist	9	6.3	1.2
Residents	20	8.4	3.1
Overall	29	7.8	2.8

Table includes a total of 46 prostheses, because two patients did not return for delivery of the definitive prosthesis.

SD = standard deviation.

Twenty-three (5 maxillae, 18 mandibles) of the 48 arches were treated with a FDP supported by four to eight implants and loaded immediately (implant-supported prostheses connected within 48 hours after implant placement).¹⁵ After 2 to 3 months of loading with the provisional, fabrication of the definitive prosthesis began. Of the remaining prostheses, six (1 maxilla, 5 mandibles) were completed by a conventional prosthodontic protocol^{19,20} and seventeen (4 maxillae, 13 mandibles) were fabricated according to the technique described by Ercoli et al in 2006.¹⁶ Unfortunately, two patients (two arches; one maxilla, one mandible) who had received a provisional did not return for delivery of the definitive prosthesis; when contacted, they stated that they could not continue the planned treatment for financial reasons. Sixteen (4 maxillae and 12 mandibles) of the 23 arches in the immediate loading group were rehabilitated on immediately placed implants. The remaining 25 arches (17 maxillae, 8 mandibles) were rehabilitated with a FDP supported by four to six implants^{19,20} and loaded according to a conventional protocol.¹⁵

Eleven definitive titanium frameworks were fabricated by a CAM technique and veneered with acrylic resin; 37 definitive frameworks were fabricated in a cast high noble alloy and veneered either with acrylic resin (31 prostheses) or porcelain (6 prostheses). When the experimental technique¹⁶ was used, the prosthesis fabrication and delivery required, on average, 4.0 appointments (Table 1): The experienced prosthodontist was able to deliver the definitive prostheses in an average of 2.9 appointments, while the residents delivered the definitive prostheses in an average of 5.6 appointments.

Table 2 Results of Two-Way ANOVA for No. of Appointments Required for Prosthesis Fabrication

Source of variation	df	Type I sum of squares	Mean square	F	P
Operator	1	26.40	26.40	3.31	.7610
Technique	1	129.55	129.55	16.22	.0002
Operator × technique	1	10.68	10.68	1.34	.2540
Error	42	335.38	7.99		
Total	45	502.01			

Table 3 Influence of Technique Used to Rehabilitate Patients on Fit of Framework

Technique	Framework fit		
	No	Yes	Total
Experimental technique	1	17	18
Conventional technique	12	18	30
Total	13	35	48

Table 4 Effect of Different Variables on Framework Fit

Factors	OR	95% CI	P*
Technique (experimental vs conventional)	14.11	1.46–136.53	.02
Operator (prosthodontist vs resident)	0.62	0.14–2.74	.53
Arch (maxilla vs mandible)	1.23	0.29–5.17	.77

*Fisher exact test.

OR = odds ratio; CI = confidence interval.

When the conventional technique was used to fabricate and deliver the prosthesis, an average of 7.8 appointments was required to deliver the definitive prosthesis. It took an average of 6.3 appointments for the experienced prosthodontist to complete the rehabilitation, while it took an average of 8.4 appointments for the residents. Two-way ANOVA shows that the experimental technique significantly reduced the required number of appointments ($P = .0002$) (Table 2). In addition, the frameworks fabricated with the experimental technique showed clinically acceptable fit in 17 of 18 arches, while the frameworks fabricated with the conventional technique exhibited clinically adequate fit in only 18 of 30 arches (Table 3). The exact logistic regression (Table 4) indicated that the framework fit was highly correlated with the use of the experimental technique ($P = .02$), while the experience of the operator ($P = .53$) or the type of arch ($P = .77$) were not significantly correlated.

DISCUSSION

Two null hypotheses were investigated in this study: (1) there would be no difference in the number of appointments required to fabricate a nonsegmented fixed implant-supported complete denture with the conventional or the experimental technique; (2) there would be no difference in the fit of frameworks fabricated with the conventional or the experimental technique. Both null hypotheses were rejected.

For this study, the charts of all patients with at least one edentulous arch who received an implant-supported prosthesis were reviewed, but only those with a nonsegmented cross-arch prosthesis were included in the study. This was done to decrease the possibility that complete-arch prostheses with different framework construction designs (segmented and nonsegmented) could be compared in the same database. Indeed it is likely clinically easier and more predictable to achieve clinically passive fit when a complete-arch framework can be segmented into several sections; hence the decision to compare only single complete-arch frameworks, although the number of implants varied.

From the data of the study, it was evident that the proposed experimental technique significantly reduced the number of appointments required for the fabrication of the definitive prostheses. The experienced prosthodontist was able to reduce the total chair time by half (from a mean of 6.3 to a mean of 2.9 appointments). A similar reduction in the time needed for completion and delivery of the prostheses was also noticed for the less experienced clinician (resident), with a reduction in the mean number of appointments from 8.4 to 5.6.

The experimental technique gathers diagnostic information from the implant-supported fixed provisional complete denture of the patient, created on the day of surgery, to fabricate a definitive metal-acrylic resin or metal-ceramic fixed complete denture (Figs 1 to 3). This information is transferred to the laboratory by



Fig 1 The immediate removable complete denture is used for fabrication of implant-supported fixed provisional prostheses.



Fig 2 Acrylic resin is injected into the spaces between the implants and the complete denture. Reprinted from Ercoli et al¹⁶ with permission.



Fig 3 Implant-supported fixed provisional complete denture in place. Reprinted from Ercoli et al¹⁶ with permission.



Fig 4 Metal pins are placed in the access holes of the implant-supported provisional complete denture.

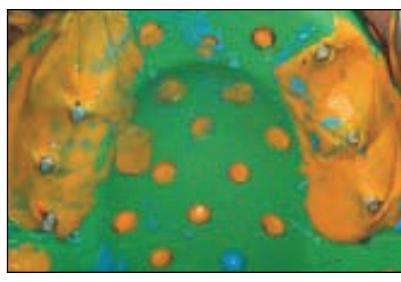


Fig 5 Impression tray with impression material in mouth. Note how the metal pins are emerging through the impression material.

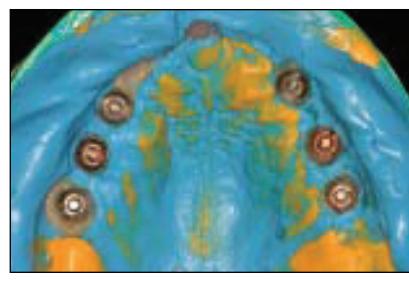


Fig 6 VPS positional impression of the provisional prosthesis. Note how the low-viscosity impression material was injected under the provisional prosthesis to record the relationship between the prosthesis and the soft tissues.

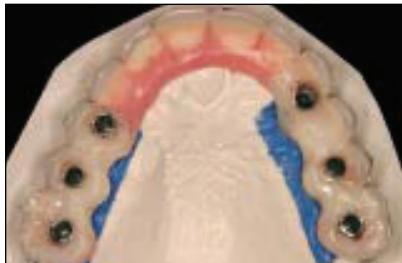


Fig 7 The impression tray is removed from the master cast.



Fig 8 The elastomeric index is used to record the positions of the teeth.



Fig 9 Definitive metal-ceramic prosthesis on the master cast. Reprinted from Ercoli et al¹⁶ with permission.

making an impression with elastomeric material, with the clinician ensuring that the impression material is injected below the provisional prosthesis (Figs 4 to 6). The impression is then poured in type IV dental stone and slurry water to accelerate setting of the stone, and the master cast with the provisional prosthesis is mounted (Fig 7). Then, four notches are made on the buccal surface of the cast for indexing purposes with a VPS buccal index extending to the occlusal surfaces of the denture teeth (Fig 8). This information is then sent to the laboratory technologist, who can fabricate the definitive prosthesis (Fig 9). At the following clinical appointment, the prosthesis is delivered to the patient (Fig 10).

Data analysis revealed some interesting trends. Indeed, when the prostheses were fabricated according to the conventional prosthodontic technique, maxillary prostheses required more appointments (average 8.9, range 5 to 16) to be completed than the mandibular prostheses (average 5.8, range 4 to 10) ($P = .007$). When the nature of these appointments was analyzed, it was seen that the majority of them consisted of prosthesis setup and try-in appointments. As would be expected, the esthetic and phonetic requirements placed on a maxillary prosthesis might require the clinician to spend significantly more time to achieve a satisfactory result. However, the difference in the



Fig 10 Panoramic radiograph of a nonsegmented fixed implant-supported complete denture at the 5-year follow-up appointment. (In the patient shown, only the mandibular prosthesis was included in the current study.) Reprinted from Ercoli et al¹⁶ with permission.

number of appointments between maxillary and mandibular prostheses was not significantly different when the experimental technique was used: all but one of the maxillary prostheses required three appointments, whereas all mandibular prostheses required two appointments for completion. It is conceivable that the provisional prosthesis that patients used for several weeks after the surgery might have allowed them to better evaluate and accommodate esthetic demands and develop proper phonetics.^{23–26} Therefore it is the authors' suggestion that the possibility of easily incorporating and transferring the provisional prosthesis tooth positions into the definitive prosthesis design using the experimental technique is likely the main reason why no difference was seen in the number of appointments required for prosthesis fabrication.

Another variable analyzed in this retrospective study was the fit of the metal framework. This study aimed to assess the influence of the experimental technique on the likelihood of obtaining clinically passive fit, as assessed by a clinician in the patient's mouth and with the method described herein (Sheffield test). Indeed, it was not the aim of the present study to measure and compare the fit of the frameworks in terms of absolute measurements, as was done in previous studies.^{27–29} While absolute measurements of framework accuracy are certainly relevant to prosthodontics, it is nonetheless evident from the existing literature that true absolute passive fit is not achievable with current prosthodontic techniques and likely not even relevant to the long-term clinical prognosis of implant restorations.⁴ However, marginal inaccuracy of frameworks has been related to prosthetic screw loosening,³⁰ and clinical techniques, such as the Sheffield test used here, are routinely used to make sure that clinical fit of the framework is present before the prosthesis is delivered. When the definitive prostheses were fabricated with the experimental technique, frameworks exhibited clinically passive fit in 17 of 18 arches, as compared to only 18 of 30 frameworks fabricated with the conventional

technique. It is worth mentioning that, for the experimental technique group, the only framework that did not show clinically passive fit displayed instability of one of the most distal temporary titanium posts during the impression and master cast fabrication procedures. This instability was itself caused by a fracture of the acrylic provisional prosthesis, which caused the temporary post to be partially mobile within the acrylic material. The statistically significant difference in the fit of the prostheses was not related to the experience of the prosthodontist (experienced versus resident) or to the arch treated (maxilla versus mandible), but only to the technique used (Table 4). It is therefore suggested that, because of the greater chance of achieving clinically adequate fit, not only by experienced prosthodontists, but also by less experienced clinicians, that the experimental technique should be used routinely for the fabrication of nonsegmented implant restorations.

It is important to recognize the limitations of this study. The investigated experimental technique was based on meticulous examination, diagnosis, and treatment planning of the planned tooth positions before implant placement actually occurred. In this case, the clinician must ensure that prosthetically driven implant placement is actually carried out, so that no changes or only minor adjustments to the planned tooth positions actually occur after implant placement. Therefore, it could be argued that the same appointment time required for the conventional technique after implant placement to establish ideal tooth positions is roughly spent for the experimental technique prior to implant placement, therefore negating any reduction in treatment time when the two techniques are considered in their complexity (essentially from the diagnostic phase to delivery of the definitive prosthesis). The authors, however, disagree with this statement, as the number of appointments required for the experimental technique to establish ideal tooth positions in the provisional prosthesis is likely the same as what would be required if the patient was to receive a removable complete denture at the time of surgery.

It is also recognized that this technique is more easily used in situations where the patient is edentulous in the arch that will receive implants or when the remaining hopeless teeth, scheduled for extraction in cases of immediate placement/immediate loading, are already in adequate positions. In other cases, for example, when the remaining teeth are severely extruded or otherwise malpositioned, the clinician must rely on anthropometric measurements and other anatomic landmarks to select ideal tooth positions for the provisional prosthesis.³¹

CONCLUSIONS

Within limitations of the study, it was concluded that:

1. The experimental technique significantly reduced the number of appointments required to fabricate a nonsegmented fixed implant-supported prosthesis.
2. The proposed technique provided clinically adequate fit of the prosthesis in a significantly greater percentage of cases compared to a conventional implant elastomeric impression, regardless of the experience level of the clinician.

ACKNOWLEDGMENTS

The authors reported no conflicts of interest related to this study.

REFERENCES

1. Allen PF, McMillan AS. A longitudinal study of quality of life outcomes in older adults requesting implant prostheses and complete removable dentures. *Clin Oral Implants Res* 2003;14:173–179.
2. Heydecke G, Klemetti E, Awad MA, Lund JP, Feine JS. Relationship between prosthodontic evaluation and patient ratings of mandibular conventional and implant prostheses. *Int J Prosthodont* 2003;16:307–312.
3. Bränemark PI, Hansson BO, Adell R, et al. Osseointegrated implants in the treatment of the edentulous jaw. Experience from a 10-year period. *Scand J Plast Reconstr Surg Suppl* 1997;16:1–132.
4. Adell R, Lekholm U, Rockler B, Bränemark PI. A 15-year study of osseointegrated implants in the treatment of the edentulous jaw. *Int J Oral Surg* 1981;10:387–416.
5. Lazzara RJ. Immediate implant placement into extraction sites: Surgical and restorative advantages. *Int J Periodontics Restorative Dent* 1989;9:332–343.
6. Covani U, Crespi R, Cornelini R, Barone A. Immediate implants supporting single crown restorations: A 4-year prospective study. *J Periodontol* 2004;75:982–988.
7. Cornelini R, Cangini F, Covani U, Wilson TG Jr. Immediate restoration of implants placed into fresh extraction sockets for single-tooth replacement: A prospective clinical study. *Int J Periodontics Restorative Dent* 2005;25:439–447.
8. Gallucci GO, Bernard JP, Bertosa M, Belser UC. Immediate loading with fixed screw-retained provisional restorations in edentulous jaws: The pickup technique. *Int J Oral Maxillofac Implants* 2004;19:524–533.
9. Maló P, Rangert B, Nobre M. All-on-4 immediate-function concept with Bränemark System implants for completely edentulous maxillae: A 1-year retrospective clinical study. *Clin Implant Dent Relat Res* 2005;7(suppl 1):88–94.
10. Degidi M, Perrotti V, Piattelli A. Immediately loaded titanium implants with a porous anodized surface with at least 36 months of follow-up. *Clin Implant Dent Relat Res* 2006;8:169–177.
11. De Bruyn H, Van de Velde T, Collaert B. Immediate functional loading of TiOblast dental implants in full-arch edentulous mandibles: A 3-year prospective study. *Clin Oral Implants Res* 2008;19:717–723.
12. Schnitman PA, Wohrle PS, Rubenstein JE. Immediate fixed interim prostheses supported by two-stage threaded implants: Methodology and results. *J Oral Implantol* 1990;16:96–105.
13. Tarnow DP, Emtiaz S, Classen A. Immediate loading of threaded implants at stage 1 surgery in edentulous arches: Ten consecutive case reports with 1- to 5-year data. *Int J Oral Maxillofac Implants* 1997;12:319–324.
14. Esposito M, Grusovin MG, Achille H, Coulthard P, Worthington HV. Interventions for replacing missing teeth: Different times for loading dental implants. *Cochrane Database Syst Rev* 2009;21:CD003878.
15. Gallucci GO, Morton D, Weber HP. Loading protocols for dental implants in edentulous patients. *Int J Oral Maxillofac Implants* 2009; 24(suppl):132–146.
16. Ercoli C, Romano PR, Al Mardini M, Cordaro L. Restoration of immediately placed implants in 3 appointments: From surgical placement to definitive prostheses. *J Prosthet Dent* 2006;96:212–218.
17. Cooper L, Rahman A, Moriarty J, Chaffee N, Sacco D. Immediate mandibular rehabilitation with endosseous implants: Simultaneous extraction, implant placement and loading. *Int J Oral Maxillofac Implants* 2002;17:517–525.
18. Chiapasco M. Early and immediate restoration and loading of implants in completely edentulous patients. *Int J Oral Maxillofac Implants* 2004;19(suppl):76–91.
19. Moberg LE, Kondell PA, Sagulin GB, Bolin A, Heimdahl A, Gynther GW. Bränemark System and ITI Dental Implant System for treatment of mandibular edentulism. A comparative randomized study: 3-year follow-up. *Clin Oral Implants Res* 2001;12:450–461.
20. Rasmusson L, Roos J, Bystedt H. A 10-year follow-up study of titanium dioxide-blasted implants. *Clin Implant Dent Relat Res* 2005;7:36–42.
21. Kan JY, Rungcharassaeng K, Bohsali K, Goodacre CJ, Lang BR. Clinical methods for evaluating implant framework fit. *J Prosthet Dent* 1999;81:7–13.
22. Cox DR. Special logistic analyses. In: Cox DR, Snell EJ (eds). *Analysis of Binary Data*, ed 2. London: Chapman and Hall, 1989:26–102.
23. Worthington P, Bolender CL, Taylor TD. The Swedish system of osseointegrated implants: Problems and complications encountered during a 4-year trial period. *Int J Oral Maxillofac Implants* 1987;2:77–84.
24. Sones AD. Complications with osseointegrated implants. *J Prosthet Dent* 1989;62:581–585.
25. Zarb GA, Schmitt A. The longitudinal clinical effectiveness of osseointegrated dental implants: The Toronto study. Part III: Problems and complications encountered. *J Prosthet Dent* 1990;64:185–194.
26. Lundqvist S, Lohmander-Agerskov A, Haraldson T. Speech before and after treatment with bridges on osseointegrated implants in the edentulous upper jaw. *Clin Oral Implants Res* 1992;3:57–62.
27. De la Cruz JE, Funkenbusch PD, Ercoli C, Moss ME, Graser GN, Tallents RH. Verification jig for implant-supported prostheses: A comparison of standard impressions with verification jigs made of different materials. *J Prosthet Dent* 2002;88:329–336.
28. Vigolo P, Fonzi F, Majzoub Z, Cordioli G. An evaluation of impression techniques for multiple internal connection implant prostheses. *J Prosthet Dent* 2004;92:470–476.
29. Kim S, Nicholls JI, Han C, Lee K. Displacement of implant components from impressions to definitive casts. *Int J Oral Maxillofac Implants* 2006;21:747–755.
30. Kallus T, Bessing C. Loose gold screws frequently occur in full-arch fixed prostheses supported by osseointegrated implants after 5 years. *Int J Oral Maxillofac Implants* 1994;9:169–178.
31. Graser GN, Myers ML, Iranpour B. Resolving esthetic and phonetic problems associated with maxillary implant-supported prostheses. A clinical report. *J Prosthet Dent* 1989;62:376–378.

Immediate Loading of Tooth-Implant-Supported Telescopic Mandibular Prostheses

George E. Romanos, DDS, PhD, Prof Dr med dent¹/Stephan May, DMD²/Dittmar May, DMD, MD, PhD²

Purpose: Extractions in partially edentulous patients often lead to insufficient stability of an existing partial prosthesis and a need for additional anchorage. Implants may therefore be placed as supplementary abutments to increase patient comfort and satisfaction. The aim of this study was to evaluate the long-term clinical outcome of implants combined with teeth to support telescopic abutment-retained removable full-arch prostheses under an immediate functional loading protocol. **Materials and Methods:** The present retrospective study included implants placed and connected via removable prostheses with periodontally healthy teeth immediately postplacement using prefabricated abutments. Secondary copings, precisely fit to the abutments, were placed and the partial dentures were relined chairside. The prosthetic restorations were not removed for 10 days. Clinical and radiographic evaluations of implants loaded for at least 2 years were performed. **Results:** One hundred ten implants with a progressive thread design (Ankylos, Dentsply) were placed in 55 patients (mean age, 63.51 ± 9.95 years). Twenty-five implants were placed in fresh extraction sockets (22.73%) and 85 implants were placed in healed ridges. All implants were placed 2 to 3 mm subcrestally (measured from the midfacial bone level). After a mean follow-up of 61.58 ± 28.47 months (range, 24 to 125 months), there were only three failures (2.73%); another six implants (5.45%) displayed crestal bone loss greater than 2 mm but remained stable. Therefore, the failure rate was 8.18% for the entire observation period of 5.13 years. The success rate was 91.82% and the cumulative survival rate was 97.27%. All patients were satisfied with the stability of their prostheses, and no prosthetic, peri-implant, or abutment tooth problems were observed. **Conclusions:** Telescopic tooth-implant-supported mandibular restorations with immediate loading present an alternative prosthetic solution for partially edentulous patients, providing a long-term predictable clinical outcome. *INT J ORAL MAXILLOFAC IMPLANTS* 2012;27:1534–1540

Key words: dental implants, partial edentulism, prosthesis, telescopic attachments

Partially edentulous patients with residual periodontally healthy teeth and removable partial prostheses often need dental implants as abutments to improve anchorage of their prostheses. In partially edentulous patients with few residual teeth, prosthetic problems may occur with keeping the remaining dentition and combining those teeth with implants for support. Although tooth-implant-supported fixed restorations are generally successful,¹ a number of implants may be needed as supplementary abutments for a full-arch prosthetic rehabilitation. In addition, combined therapies, such as the use of locator and/or

ball attachments, may combine tissue-supported with tooth-supported restorations. There are no long-term studies evaluating such treatment concepts; nevertheless, for unsplinted implants, the most commonly used attachment is the ball attachment, while magnets are used only rarely.^{2–4}

In a previous clinical study, May and Romanos⁵ reported on the use of telescopic abutments for implant restorations in the mandible in conjunction with immediate functional loading to increase the stability of full-arch dentures. Four implants were placed and connected with 4-degree prefabricated telescopic abutments immediately after insertion.^{5,6} The prosthesis was relined using metal prefabricated copings for the telescopic abutments. With this treatment concept in the mandible, researchers have documented a dental implant success rate of 94.06% after at least 2 years of loading, with a maximum of 129 months.⁷ The aim of the present study was to evaluate the long-term survival rate of implants placed in the mandible as supplemental abutments and loaded in combination with residual teeth using the immediate loading concept and a full-arch removable mandibular prosthesis.

¹Professor, University of Frankfurt, Department of Oral Surgery and Implant Dentistry, Frankfurt, Germany; Professor, Stony Brook University, Department of Dental Medicine, Stony Brook, New York, USA.

²Private practice, Clinic for Oral and Maxillofacial Surgery, Lünen, Germany.

Correspondence to: Dr George E. Romanos, School of Dental Medicine, Stony Brook University, 184C Sullivan Hall, Stony Brook, NY 11794-8705, USA. Email: georgios.romanos@stonybrook.edu



Fig 1 Clinical situation immediately after tooth extraction.



Fig 2 Clinical situation after implant placement, abutment connection, and flap closure.

MATERIALS AND METHODS

The present retrospective clinical study documents the clinical and radiologic follow-up of implants placed in the mandible and loaded for a period of at least 2 years. The implants were placed and connected to removable full-arch prostheses supported by periodontally healthy teeth immediately after implant placement using prefabricated abutments.

Specifically, all patients had residual teeth in the mandible without periodontal disease; the remaining teeth had reduced attachment loss and reduced periodontal support but no signs of periodontal disease or mobility. The mandibular prosthesis was a tooth-supported removable partial denture or a telescopic restoration. Some residual teeth had to be extracted because of deep caries lesions, insufficient periodontal support with progressive mobility, or endodontic failures. Implants were planned to be placed as supplementary abutments to increase the retention of the existing denture. The patients were classified as Kennedy Class 1 cases with bilateral edentulous posterior areas and additional edentulous spaces in the anterior zone, especially after loss of some of the residual teeth.

Implant Placement and Prosthetic Protocol

All implants had a progressive thread design and a sandblasted, acid-etched surface (Ankylos, Dentsply). The 2-mm crestal collar of the implants had an etched surface. The implants had a Morse taper (conical) implant-abutment connection and platform shifting. All implants were placed 2 to 3 mm subcrestally (measured from the midfacial crest of bone) and loaded immediately after surgery. According to the manufacturer's guidelines, all implants were connected with their conical (straight or angulated) prefabricated abutments (with an angle of 4, 5 or 6 degrees) using a final torque of 15 Ncm, and the conical implant-abutment connection allowed 360 different position

options. The abutments (SynCone, Dentsply) were set parallel to the residual teeth using special alignment guides (SynCone System, Dentsply). To ensure parallel positioning of the alignment guides, acrylic resin jigs for the residual teeth were prepared in the lab using a paralleloometer and study casts. A guide pin gave the correct direction for osteotomy preparation and implant placement. Finally, the flap was closed with silk or nylon 4–0 sutures (Figs 1 and 2).

Secondary prefabricated copings were placed over the abutments, and the removable prostheses were relined chairside with cold-curing acrylic resin. In cases of multiple tooth extractions, the dentures were relined, with special care taken to avoid deep impaction of the acrylic resin into the extraction sockets. Undercuts in the sulcular areas were blocked using rubber dam or plastic rings placed around the abutments. During relining, the patients were advised to close the mouth without pressure. The patients remained seated during the relining process.

Postoperative Care and Instructions

Antibiotics, such as wide-spectrum penicillin or clindamycin, were prescribed postoperatively for 1 week, and chlorhexidine digluconate mouth rinse was used three times per day. A soft/liquid diet was advised for the first stages of the healing process (6 to 8 weeks postoperatively). Patients who had received implants immediately postextraction had to adhere to a soft/liquid diet for 3 to 4 months after surgery. The prosthetic restorations remained in place for 10 days post-surgery to immobilize the implants. The prostheses were then taken out using a crown remover (Fig 3) and the sutures were removed. All patients had maxillary partial or full-arch dentures.

Follow-up

The protocol for this concept was described previously by May and Romanos.⁵ The implants were evaluated



Fig 3 Clinical situation 10 days postoperatively, immediately before suture removal.

Table 1 Age Distribution of the Patients Included in the Study

Patients	n	Mean age (y)	Age range (y)
Total	55	63.51 ± 9.95	40–84
Women	35	62.03 ± 8.67	40–84
Men	20	66.1 ± 10.44	51–80

Table 2 Sizes of the Implants Included in the Study

Diameter × length (mm)	Men	Women	Total	Immediate
3.5 × 9.5	1	2	3	
3.5 × 11	6	6	12	1
3.5 × 14	12	36	48	3
3.5 × 17	0	3	3	
4.5 × 11	0	3	3	2
4.5 × 14	13	14	27	12
4.5 × 17	5	3	8	4
5.5 × 11	2	1	3	
5.5 × 17	0	2	2	2
6.5 × 14	1	0	1	1

for stability using the Periotest device approximately 3 months after placement. Implants were also assessed for peri-implant soft tissue health, prosthetic stability, prosthetic complications, and radiographic crestal bone loss. Mean survival time, success rate using the Albrektsson et al⁸ criteria, and any other observed complications were also recorded. The comfort of the patient with the retention of the prosthesis was the main criterion for success. Complications, such as fractures of the denture, mobility of the primary or secondary copings, insufficient retention of the restoration, increased mobility of residual teeth, or pain, were evaluated.

After 1 year, the implants were evaluated every year for mobility, suppuration, and other periodontal conditions (eg, gingival overgrowth). Implants were also evaluated radiographically to determine the crestal bone levels. The radiographs were evaluated at 10× magnification to visualize the crestal bone loss around the implants at surgery and at the follow-up visit. Additional visits were initiated by the patients if they noticed problems or discomfort. The patients followed a strict 6-month follow-up program for tooth cleaning and potential relining of both prostheses.

RESULTS

A total of 110 implants were placed in 55 patients (mean age, 63.51 ± 9.95 years) and evaluated clinically and radiographically for a period of at least 2 years. Twenty men and 35 women were included in this study (Table 1). Twenty-five implants (22.73%; 7 in men, 18 in women) were placed in fresh immediate extraction sockets (immediate implants) in areas of extracted canines and first and second premolars (Tables 2 and 3). The remaining 85 implants were inserted into healed mandibular ridges after midcrestal incisions and elevation of a mucoperiosteal flap. The lengths and diameters of the implants placed are presented in Table 2.

The implants were evaluated clinically after a mean of 61.58 months (range, 24 to 125 months). The prostheses in the maxilla and mandible were still in use, and the natural teeth acted as supplemental abutments for the mandibular prosthesis. Twenty-two patients had two natural teeth, 2 patients had three natural abutments, and 25 patients had one natural tooth supporting the prosthesis. Only three implants (2.73%) failed clinically. Six implants (5.45%) had crestal bone loss greater than 2 mm but remained stable and were therefore characterized as radiographic failures (Table 3). The clinically failed implants were mobile within the first 2 months after placement/loading. Two were 14 mm long (one 3.5 mm and the other 4.5 mm in diameter) and one was 17 mm long and 4.5 mm in diameter. All the failed implants had been placed in healed ridges and not in fresh extraction sockets. One implant was in the canine region and two were in first premolar sites. None of these failures were implants placed in the most distal positions.

The implant protocol as a method of rehabilitation in the mandible achieved a success rate of 91.82% over the observation period (survival rate: 97.27%). Patients generally expressed satisfaction (no discomfort) with the stability of the original prostheses, and there were no complaints, such as fracture or insufficient stability.

Table 3 Distribution of Failure Rates and Observation Time in Different Patient Groups

Group/time	Men	Women	Total
Total	40	70	110
Immediate implants	7 (17.5%)	18 (25.71%)	25 (22.73%)
Failures			
Clinical	1 (2.5%)	2 (2.86%)	3 (2.73%)
Radiographic	2 (5%)	4 (5.71%)	6 (5.45%)
Total	3 (7.5%)	6 (8.57%)	9 (8.18%)
Observation time (mo)			
Mean	68.1 ± 28.37	57.86 ± 28.18	61.58 ± 28.47
Min	27	24	24
Max	125	119	125

Fig 4 Clinical condition 5.5 years after immediate loading. Excellent health of the peri-implant soft tissues and the periodontal tissues around the remaining teeth is apparent.

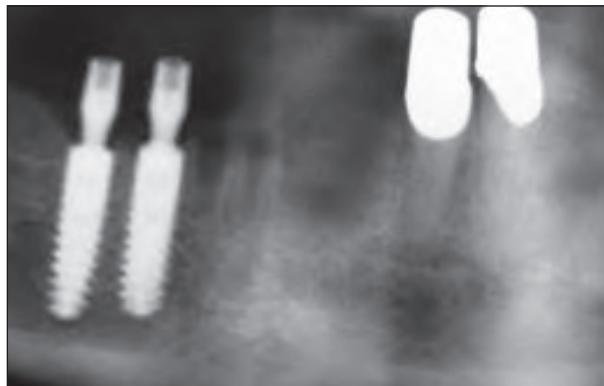


Fig 5 Postoperative radiograph (immediately after surgery) shows the implants with the telescopic abutments attached and ready for immediate loading.

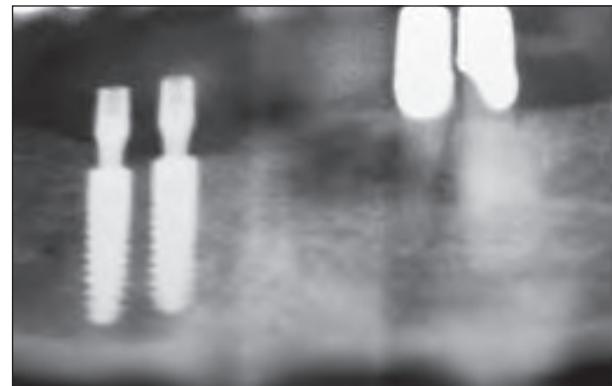


Fig 6 Radiographic examination 5.5 years after loading shows crestal bone stability as well as bone growth over the top of the implant platform (etched surface) in conjunction with platform switching. The abutments were never removed.

of the prostheses. The peri-implant soft tissues were in excellent condition and the crestal bone demonstrated long-term stability (Figs 4 to 8). No residual teeth showed increased mobility at the last evaluation.

Because of the strict 6-month maintenance recall program, periodontal stability (pocket depth less than 3 mm) was observed. The minimum periodontal support of the residual teeth was a 1:1 (crown:root) ratio. None of the abutment teeth at the initial follow-up evaluation had

ill-fitting telescopic retained crowns, root decay, endodontic complications, fractures, or signs of periodontal disease. In addition, clinical signs of tooth intrusion leading to misfit of the prosthesis were not observed. However, nine natural teeth were later extracted over the duration of the follow-up period because of periodontal problems and/or deep decay. Seven of them were replaced with new implants; another two were lost and not replaced, but the prostheses were relined.



Fig 7 Partial denture before implant placement.



Fig 8 Partial denture after implant placement, relining, and polishing.

DISCUSSION

The present retrospective analysis of implants placed in the mandible and restored with telescopic abutments and then combined with periodontally healthy teeth for the support of existing removable prostheses demonstrates an interesting alternative solution for mandibular prosthetic rehabilitation. The combined use of teeth and implants in partially edentulous patients with removable prostheses is rarely discussed in the literature.^{9–11} Dental implants in strategically favorable positions can provide better anchorage for a mandibular prosthesis. In this way, a failing partial denture can be saved with just one or two additional implants as supplemental abutments. This has benefits for the patient and is much less expensive than a new prosthetic rehabilitation.

Within the limitations of the study, which was not a prospective randomized clinical trial but a series of patients who underwent the same treatment, the authors demonstrated the viability of both surgical and prosthetic protocols using immediate functional loading. The biomechanical aspects of the telescopic (prefabricated) abutments were introduced in a 2-year follow-up study, and the long-term (10-year) data were evaluated earlier in another group of subjects.^{5,7} In the present study, the combination of telescopic-retained abutments and residual teeth increased the retention of the partial dentures in the mandible. There was a 97% survival rate after a long-term evaluation period (minimum of 2 years of follow-up). Comfort scores for the patients were not available, since this was a retro-

spective study. In addition, the patients did not wear provisional prostheses, since the teeth were extracted and implants were placed and immediately loaded at the same visit.

The double-crown technique represents an ideal type of anchorage.^{12–14} The possibility of pairing residual teeth with implants allows the transfer of the loading forces to the periodontal and peri-implant tissues in a manner that more closely resembles an implant-supported prosthesis rather than a tissue-retained prosthesis. The fact that periodontally compromised teeth in this patient group did not show intrusion is important compared to what has been observed in previous studies.^{11,15}

In general, there are many studies supporting the hypothesis of the long-term clinical outcome of tooth-implant-supported fixed restorations.^{1,16,17} Only one paper has been published regarding success rates of tooth-implant-supported partial dentures that used the same implant system with progressive thread design as used in the present study.¹⁸ Considering the age of the patients included in this study, the present protocol may have advantages for patients with complex medical histories (especially older patients), who are not able to be treated with a large number of implants and who may require hospitalization or treatment by the specialist. The long-term data (mean loading period: 5 years) reported no complications in terms of insufficient stability of the prosthesis with the use of a prefabricated telescopic anchorage system. Other studies showed maintenance problems for patients with ball attachments or resilient telescopic crowns as

attachments for implant-supported overdentures.¹⁹ In the present concept of mandibular rehabilitation, there is simplicity in the maintenance of the abutment teeth and implants for patients as well as dental hygienists. The results of the present study show that periodontally compromised teeth with attachment loss and reduced periodontal support, but without signs of periodontal disease, may be used with high success rates for removable anchorage, together with dental implants, without negatively influencing the clinical outcome, as has been previously reported.^{20,21}

Further studies with a larger number of patients and multicenter evaluations are needed to confirm that this treatment concept could be the standard of care for patients with remaining natural dentition. In contrast to other prosthetic concepts presented in the literature, which used implants and ball attachments, magnets, or resilient telescopic crowns,^{18,22–24} the present treatment protocol shows long-term success. Tissue-retained overdentures are associated with peri-implant soft tissue complications (ie, gingival overgrowths) or loosening of the abutments.²⁵ This has been observed particularly with bar-retained restorations, which limit plaque control and have been associated with general maintenance problems.²⁶

There is no doubt that this protocol can be used in a delayed loading protocol as well. Because no differences have been observed in the success or survival rates of implants loaded delayed or immediately in the mandible^{27,28} and with this same implant design,^{7,29,30} the immediate loading protocol as a treatment of choice is recommended. This will reduce the length of the treatment period and the number of patient visits. Strict patient selection criteria to minimize complications may be performed. However, removable prostheses in the mandible with early loading showed higher success rates (100%). The present protocol describes an immediate treatment solution that does not use provisional dentures, thereby improving patient comfort and reducing the cost of treatment.³¹

Because of the limitations of this retrospective study, which was performed in a private practice for oral and maxillofacial surgery, the authors did not have standardized periapical radiographs to determine possible crestal bone loss. However, magnification of panoramic radiographs taken under the same conditions in the clinical setting has been performed. Certainly, a future prospective clinical study focused on precise measurement of crestal bone levels would be of great importance. The soft tissue characteristics and plaque control around implants with platform switching (shifting), compared to that of residual teeth, is also of significant clinical interest. This topic is presently under investigation (data not shown).

CONCLUSION

Within the limitations of this retrospective clinical evaluation, the combination of immediately loaded implants and residual teeth with telescopic attachments to support restorations in the mandible seems to be a viable prosthetic option that may be used for the treatment of partially edentulous patients. It provides economic, technical, and clinical advantages.

ACKNOWLEDGMENT

The authors would like to thank Michael Yunker, DDS, for his support in the preparation of the manuscript. The authors reported no conflicts of interest related to this study.

REFERENCES

1. Gunne J, Astrand P, Lindh T, Borg K, Olsson M. Tooth-implant and implant supported fixed partial dentures: A 10-year report. *Int J Prosthodont* 1999;12:216–221.
2. Davis DM, Packer ME. Mandibular overdentures stabilized by AstraTech implants with either ball attachments or magnets: 5-year results. *Int J Prosthodontics* 1999;12:222–229.
3. Cune M, van Kampen F, van der Bilt A, Bosman F. Patient satisfaction and preference with magnet, bar-clip, and ball-socket retained mandibular implant overdentures: A cross-over clinical trial. *Int J Prosthodont* 2005;18:99–105.
4. McEntee MI, Walton JN, Glick N. A clinical trial of patient satisfaction and prosthodontic needs with ball and bar attachments for implant-retained complete overdentures: Three-year results. *J Prosthet Dent* 2005;93:28–37.
5. May D, Romanos GE. Immediate implant-supported mandibular overdentures retained by conical crowns: A new treatment concept. *Quintessence Int* 2002;33:5–12.
6. Romanos GE, May D. Immediate loading in the anterior mandible using overdentures. In: Romanos GE. Advanced Immediate Loading. Chicago: Quintessence, 2012:55–62.
7. Romanos GE, May S, May D. Treatment concept of the edentulous mandible with prefabricated telescopic abutments and immediate functional loading. *Int J Oral Maxillofac Implants* 2011;26:593–597.
8. Albrektsson T, Zarb G, Worthington P, Eriksson AR. The long term efficacy of currently used dental implants: A review and proposed criteria of success. *Int J Oral Maxillofac Implants* 1986;1:11–25.
9. Mitrani R, Brudvik JS, Phillips KM. Posterior implants for distal extension removable prostheses: A retrospective study. *Int J Periodontics Restorative Dent* 2003;23:353–359.
10. Hug S, Mantokoudis D, Mericske-Stern R. Clinical evaluation of 3 overdenture concepts with tooth roots and implants: 2-year results. *Int J Prosthodont* 2006;19:239–243.
11. Krennmair G, Krainhofdner M, Waldenberger O, Piehslinger E. Dental implants as strategic supplementary abutments for implant-tooth-supported telescopic crown-retained maxillary dentures: A retrospective follow-up study for up to 9 years. *Int J Prosthodont* 2007;20:617–622.
12. Wenz HJ, Hertrampf K, Lehmann KM. Clinical longevity of removable partial dentures retained by telescopic crowns: Outcome of the double crown with clearance fit. *Int J Prosthodont* 2001;14:207–213.
13. Widbom T, Lofquist L, Widbom C, Soderfeldt B, Kronstrom M. Tooth-supported telescopic crown-retained dentures: An up to 9-year retrospective clinical follow-up study. *Int J Prosthodont* 2004;18:29–34.
14. Krennmair G, Weinlaender M, Krainhofdner M, Piehslinger E. Implant-supported mandibular overdentures retained with ball or telescopic crown attachments: A 3-year prospective study. *Int J Prosthodont* 2006;19:164–170.

15. Cordaro L, Ercoli C, Rossini C, Torsello F, Feng C. Retrospective evaluation of complete-arch fixed partial dentures connecting teeth and implant abutments in patients with normal and reduced periodontal support. *J Prosthet Dent* 2005;94:313–320.
16. Olsson M, Gunne J, Astrand P, Borg K. Bridges supported by free-standing implants versus bridges supported by tooth and implant. A five-year prospective study. *Clin Oral Implants Res* 1995;6:114–121.
17. Greenstein G, Cavallaro J, Smith R, Tarnow D. Connecting teeth to implants: A critical review of the literature and presentation of practical guidelines. *Compend Contin Educ Dent* 2009;30:440–453.
18. Klaus R, Romanos GE, Egerer C, Nentwig GH. Die Versorgung von Freiendsituationen mit zahnimplantatgetragenen und rein implantatgetragenen Rekonstruktionen auf der Basis des Ankylos-Systems. Ergebnisse nach 4 Jahren [in German]. *Z Zahnräztl Implantol* 1997;13:183–186.
19. Krennmaier G, Seemann R, Weinlaender M, Piehslinger E. Comparison of ball and telescopic attachments in implant-retained mandibular overdentures: A 5-year prospective study. *Int J Oral Maxillofac Implants* 2011;26:598–606.
20. Braegger U, Buergin WB, Haemmerle CH, Lang NP. Association between clinical parameters assessed around implants and teeth. *Clin Oral Implants Res* 1997;8:412–421.
21. Ellegaard NB, Baelum V, Karring T. Implant therapy in periodontally compromised patients. *Clin Oral Implants Res* 1997;8:180–188.
22. Heckmann SM, Schrott A, Graef F, Wichmann M, Weber HP. Mandibular two implant telescopic overdentures. *Clin Oral Implants Res* 2004;15:560–569.
23. Eitner S, Schlegel A, Emeka N, Holst S, Will J, Hamel J. Comparing bar and double-crown attachments in implant retained prosthetic reconstruction: A follow-up investigation. *Clin Oral Implants Res* 2008;19:530–537.
24. Chen JR, Tomotake Y, Watanabe M, Ishida Y, Nagao K, Ichikawa T. Telescopic magnetic attachment for implant-supported denture: Evaluation of splint effect. *Int J Oral Maxillofac Implants* 2011;26:657–664.
25. Einsele F, Merkel U, Romanos GE, Strub JR, Weingart D. Implantatretinierte Hybridprothesen auf Bränemark- sowie Bonefit (ITI)-Implantaten mit Kugelkopfattachments im Unterkiefer. Eine Longitudinalstudie über vier Jahre [in German]. *Implantologie* 1994;1:23–37.
26. den Dunnen AC, Slagter AP, de Baat C, Kalk W. Professional hygiene care, adjustments and complications of mandibular implant-retained overdentures: A three-year retrospective study. *J Prosthet Dent* 1997;78:387–390.
27. Del Fabbro M, Testori T, Franscetti L, Taschieri S, Weinstein R. Systematic review of survival rates for immediately loaded dental implants. *Int J Periodontics Restorative Dent* 2006;26:249–263.
28. Romanos GE, Froum S, Hery C, Cho SC, Tarnow D. Survival rate of immediately vs. delayed loaded implants: Analysis of the literature. *J Oral Implantol* 2010;36:315–324.
29. Romanos GE, Nentwig GH. Immediate versus delayed functional loading of implants in the posterior mandible: A 2-year prospective clinical study of 12 consecutive cases. *Int J Periodontics Restorative Dent* 2006;26:459–469.
30. Romanos GE, Nentwig GH. Immediate loading using cross-arch fixed restorations in heavy smokers: Nine consecutive case reports for edentulous arches. *Int J Oral Maxillofac Implants* 2008;23:513–519.
31. Turkyilmaz I, Tozum TF, Fuhrmann DM, Tumer C. Seven-year follow up results of TiUnite implant supporting mandibular overdentures: Early versus delayed loading. *Clin Implant Dent Relat Res* 2012 May;14(suppl 1):e83–90. Epub ahead of print 2011 Jul 11.

The Influence of Substitute Materials on Bone Density After Maxillary Sinus Augmentation: A Microcomputed Tomography Study

Sebastian Kühl, Dr Med Dent¹/Hermann Götz, Dipl-Phys²/Christoph Brochhausen, Dr Med³/Norbert Jakse, Prof Dr Med, Dr Med Dent⁴/Andreas Filippi, Prof Dr Med Dent⁵/Bernd d'Hoedt, Prof Dr Med Dent⁶/Matthias Kreisler, Prof Dr Med Dent⁷

Purpose: To evaluate whether adding bone substitute materials to autogenous particulated bone (PAB) might have an effect on the density of the grafted bone after maxillary sinus augmentation. **Materials and Methods:** Thirty healthy patients undergoing lateral antrostomy were included. Sinuses were augmented at random with PAB ($n = 10$) (control group); a mixture of PAB and beta-tricalcium phosphate (β -TCP) ($n = 10$) (experimental group); or a mixture of PAB, β -TCP, and hydroxyapatite (HA) ($n = 10$) (experimental group). A sample of each graft material was obtained at time of maxillary sinus augmentation, and microcomputed tomography (μ -CT) analyses were performed. Five months later, samples of the augmented areas ($n = 23$) were harvested by means of a trephine bur, and μ -CT analyses of these samples were performed. Density values for the bone were compared to the data obtained 5 months before from the original material. **Results:** All groups showed increasing density values after a healing time of 5 months. Because of a high dropout rate, the sample size was too small to compare the groups statistically. **Conclusions:** Bone density increased after maxillary sinus augmentation for both PAB alone or in combination with substitute materials based on HA and/or β -TCP particles. A larger sample size and a split-mouth design would help to reliably reveal significant differences between the single materials. INT J ORAL MAXILLOFAC IMPLANTS 2012;27:1541–1546

Key words: bone mineral density, bone replacement materials, maxillary sinus floor augmentation, microcomputed tomography

¹Lecturer, School of Dental Medicine, Department of Oral Surgery, Oral Radiology and Oral Medicine, University of Basel, Switzerland.

²Researcher, Institute for Applied Structural and Microanalysis, University Medical Center, Johannes-Gutenberg-University, Mainz, Germany.

³Lecturer, REPAIR-lab, Institute of Pathology, University Medical Center, Johannes-Gutenberg-University, Mainz, Germany.

⁴Professor, Department of Oral Surgery and Radiology, School of Dentistry, Medical University of Graz, Austria.

⁵Professor, Lecturer, School of Dental Medicine, Department of Oral Surgery, Oral Radiology and Oral Medicine, University of Basel, Switzerland.

⁶Professor, Lecturer, School of Dental Medicine; Department of Oral Surgery, University Medical Center, Johannes-Gutenberg-University, Mainz, Germany.

⁷Professor, School of Dental Medicine; Department of Oral Surgery, University Medical Center, Johannes-Gutenberg-University, Mainz, Germany.

Correspondence to: Dr Sebastian Kühl, School of Dental Medicine, Department of Oral Surgery, Oral Radiology and Oral Medicine, University of Basel, Hebelstrasse 3, 4056 Basel, Switzerland. Email: sebastian.kuehl@unibas.ch

Maxillary sinus augmentation using a lateral antrostomy as described by Boyne and James or Tatum is a highly predictable way to successfully graft the severely atrophic posterior maxilla prior to implant placement.^{1–10} Autogenous bone, bone substitute materials (BSM), or combinations of these can be used for this purpose.^{11–17} Autogenous bone has osteoinductive properties, provided by proteins, that directly induce the differentiation of mesenchymal stem cells into osteoblasts for bone formation.¹⁸ On the other hand, harvesting of autogenous bone is associated with donor site morbidity, limited availability, and unpredictable resorption. Alternatively, natural or synthetic BSM have been used successfully for maxillary sinus augmentation.^{11–17} However, BSM have only osteoconductive properties and do not directly affect mesenchymal stem cell differentiation. Although many studies have evaluated the suitability of materials of different origins, it still remains unknown which is the most favorable for maxillary sinus augmentation.^{18–21} Histologic analyses of ex vivo samples retrieved several months after lateral antrostomy demonstrated that allogenic and xenogenic substitute materials based on hydroxyapatite (HA) or tricalcium phosphate (TCP)

have osteoconductive properties, which seem to sufficiently compensate for the missing osteoinductive properties with regard to the amount of new bone that is formed.^{3,4,12,22–25} The use of BSM is always associated with an inflammatory reaction, which activates osteoclastic cells and macrophages.^{26,27} These cells induce resorption and biodegradation of the BSM particles over time. During biodegradation, ions such as sodium, phosphate, and calcium are dissolved from the BSM particles. At the same time, because of the release of many different cytokines with osteogenic effects, new osteoblasts in this environment initiate mineralization of the collagen matrix. The dissolved substances might be directly involved in the mineralization process. This could increase the density of the autogenous bone graft, helping provide primary stability for the implant. This is the most limiting factor for single-stage surgery in maxillary sinus augmentation. With regard to stage-two surgery, the timing of implant placement is dependent on the quantity and quality of the grafted bone. This, however, is related to bone density.

To date, it is unknown whether BSM might influence the density of autogenous grafted bone when used for maxillary sinus augmentation. To determine this, it is necessary to compare the density of the grafted bone at time of maxillary sinus augmentation (baseline) with its density several months after the grafting procedure. No study has yet compared the densities of bone and BSM at these two different time points.

It is also difficult to compare the density of particulated material with that of block material. An ideal methodology for evaluation of bone density changes should be nondestructive and allow for evaluation of both particulated and dense material. Microcomputed tomography (μ -CT) is a technique to nondestructively image and quantify the internal structure of an object in three dimensions (3D).²⁸ It has been used successfully to perform histomorphometric evaluations of the 3D structure of different substitute materials and of samples retrieved from the grafted maxillary sinus in human ex vivo samples.^{29,30} It provides hierarchical biologic imaging capabilities with an isotropic resolution ranging from tens of micrometers (μ -CT) down to 100 nm (synchrotron radiation nano-CT).³¹ It can be used successfully to evaluate bone density.³² Since μ -CT allows for analysis of both particulated and block materials, it would seem to be suitable to compare bone density at the time of maxillary sinus augmentation with that of samples retrieved several months after grafting. The aim of the present study, therefore, was to use μ -CT to evaluate whether the addition of BSM to particulated autogenous bone (PAB) would influence the density of the grafted bone after maxillary sinus augmentation. The hypothesis was that BSM would have a positive impact on the bone density.

MATERIALS AND METHODS

The study protocol was approved by the ethical committee of the Johannes-Gutenberg-University of Mainz (no. 837.158.08 [6155]).

Thirty systemically healthy patients were included in this study and were consecutively scheduled for maxillary sinus augmentation. Exclusion criteria were advanced systemic diseases, osteoporosis, pregnancy, infectious diseases, radiation, current medication with corticosteroids or bisphosphonates, chemotherapy, and smoking. Perforation of the sinus membrane and insufficient size of the retrieved sample (less than 5 mm length) were also considered criteria for exclusion. Informed consent was obtained from all patients prior to participation in this study.

Before surgical treatment, patients were randomly enrolled in one of three treatment groups:

- Group A: Mixture of blood, PAB, and β -TCP (Cerasorb, 1,000 to 2,000 μ m, Curasan) (n = 10)
- Group B: Mixture of blood, PAB, and β -TCP/HA (Straumann BoneCeramic, 500 to 1,000 μ m, Institut Straumann) (n = 10)
- Group C: Mixture of blood and PAB (n = 10)

Surgical Procedure

A mucoperiosteal flap was elevated to conduct the lateral antrostomy. An oval hollow was drilled into the facial sinus wall with a thick diamond bur. The bone at the center of this created window was gently infracted, and the intact sinus membrane was carefully elevated. After the sinus membrane was completely mobilized, the infracted bone was folded inward and upward, imitating a trap-door effect. Autogenous bone was harvested as a block, either from the chin or the external oblique ridge of the mandible, and was particulated with a surgical bone mill (Quentin Bone Mill, Quentin Dental). The material was mixed with autogenous blood in group C, which served as a control group. BSM was added to the particulated bone in a ratio of approximately 1:1 in groups A and B; β -TCP was used in group A and a β -TCP/HA mixture was used in group B.

Prior to sinus elevation surgery, a sample of each particulated graft was obtained and plugged into a standard polypropylene snap-lock tube (Eppendorf Safe Lock Tubes, 0.5 mL, Eppendorf) (Fig 1). The two experienced (more than 10 years' experience) oral surgeons (SK and MK) who performed the maxillary sinus augmentations attempted to apply identical forces when plugging the graft material into the tubes. Paraformaldehyde fixative solution (pH 7.0, Roti Histofix 4.5%, Carl Roth) was added to the tubes (Fig 1) and μ -CT was performed.



Fig 1 A snap-lock tube was filled with a sample of the grafting material at time of maxillary sinus augmentation for μ -CT evaluation.

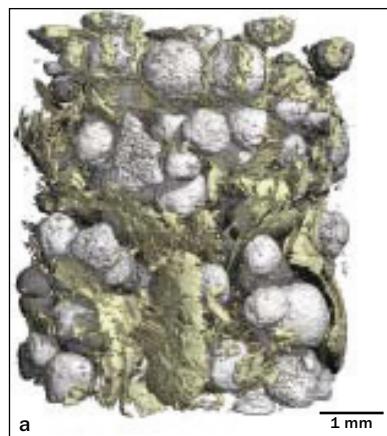
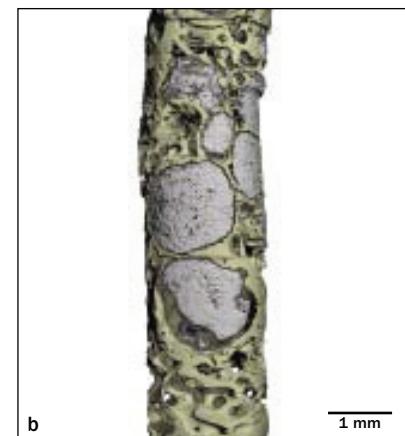


Fig 2a and 2b Three-dimensional reconstruction of group A sample (PAB + β -TCP) after segmentation of the μ -CT data with autogenous bone (green) and BSM (gray). (a) Sample of the graft at t0; (b) sample retrieved at t1 from the same patient. Bone trabeculae surround the BSM particles.



Five months after sinus elevation, bony cylinders were harvested from the grafted areas (the premolar or molar regions) by means of a trephine bur with an internal diameter of 3.2 mm. The cylinders were immediately immersed in 4.5% buffered paraformaldehyde fixative (pH 7.0, Roti Histofix 4.5%, Carl Roth GmbH) for at least 7 days. Then they were dehydrated in an ascending series of ethanols (concentration) and embedded in paraffin according to standard protocols (Hypercenter XP, Shandon) and μ -CT was performed.

μ -CT Examinations

All analyses were carried out using a high-resolution μ -CT with a nominal isotropic resolution of $6 \times 6 \times 6\text{-}\mu\text{m}^3$ voxel size (SCANCO μ -CT 40, SCANCO Medical) at identical settings (70 kV, 113 μ A, 0.18-degree angular increment, 300-ms integration time). Gray scale images were obtained. Based on a gray scale histogram, the μ -CTs were segmented and the PAB and BSM were separated as described in a previous study.³⁰ The mean densities of the bone samples were evaluated by measuring the absorption of the x-ray beam. The level of absorption was plotted in relation to the absorption of a standard reference block of the SCANCO System, which allowed determination of density equivalents in mg HA/cm³. Mean density values for the bone were determined for every sample of the graft taken at the time of maxillary sinus augmentation (t0) and the corresponding trephine samples that were retrieved 5 months after augmentation (t1). Based on the segmentation, 3D reconstructions of the data were performed.

Statistical Analyses

Mean density and mean standard error (MSE) values were obtained. Analysis of variance with $P < .05$ was performed to determine significant differences in the densities of the bone specimens at baseline and 5 months later. Additionally, one-way analysis of variance was performed to find significant differences between the three groups after 5 months of healing. Bar charts and the statistical evaluations were generated using SPSS (SPSS Statistics 2010 version 18, IBM). The statistical power was determined using nQuery (nQuery advisor 6.0, Statistical Solutions).

RESULTS

Of the original 30 participants, 23 were included in the study (10 men, 13 women; mean age 53 years, range 36 to 79 years). Seven patients were consecutively excluded from the study: one from group A, two from group B, and two from group C because of insufficient sample retrieval at stage-two surgery, and another two patients from group C because they received steroids after maxillary sinus augmentation. Therefore, 46 samples were available for evaluation (23 samples retrieved at t0 and 23 samples retrieved at t1).

The 3D reconstructions after segmentation clearly showed the PAB and BSM (Figs 2 to 4). In contrast to the t0 samples (Figs 2a, 3a, and 4a), the t1 samples showed an organized bone structure with trabeculae (Figs 2b, 3b, and 4b). These were in direct contact with the

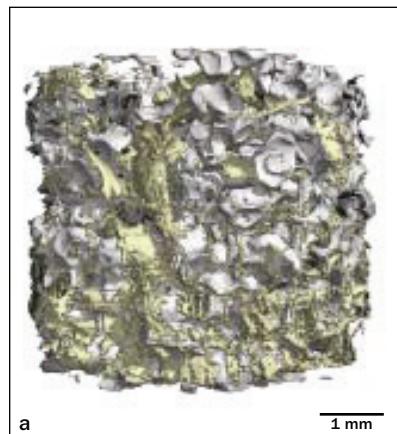


Fig 3a and 3b Three-dimensional reconstruction of group B sample (PAB + β -TCP + HA) after segmentation of the μ -CT data with bone (green) and BSM (gray). (a) Sample of the graft at t0; (b) sample retrieved at t1 from the same patient. In contrast to (a) the graft material at t0, (b) after 5 months of healing, the bone has built connecting trabeculae.

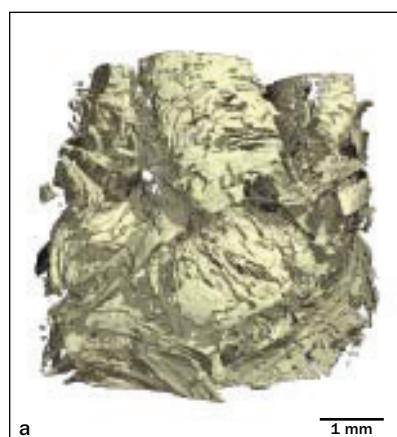


Fig 4a and 4b Three-dimensional reconstruction of a group C sample (PAB only) after segmentation of the μ -CT data. (a) Sample of the graft at t0; (b) sample retrieved at t1 from the same patient. Following 5 months of healing the bone has built connecting trabeculae.

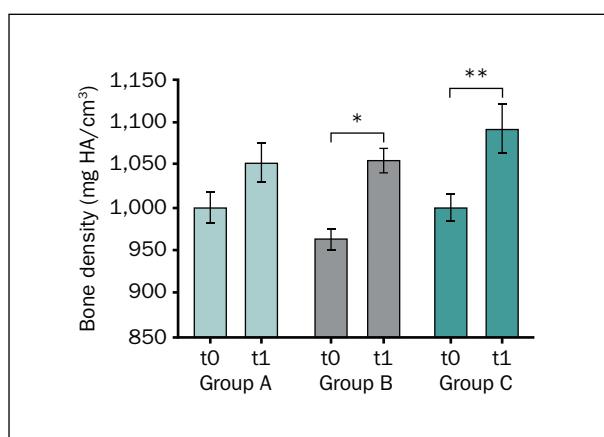


Fig 5 Mean density values of the BSM particles in all groups at t0 (sinus elevation) and t1 (5 months after grafting). *Significant differences ($P = .00031$) between t0 and t1; **significant differences ($P = .05$) between t0 and t1. Bars indicate MSE.

substitute material particles in groups A and B (Figs 2b and 3b). The bone trabeculae of group C seemed to be thicker than those in groups A and B. The marrow space appeared scarce in all samples (Figs 2b, 3b, 4b).

The mean bone density value in group A at t0 was 1,000 mg HA/cm³ (MSE = 18) (Fig 5). At t1, this had increased to a mean of 1,053 mg HA/cm³ (MSE = 23)

(Fig 5). The bone density changes between t0 and t1 were not significant ($P = .08$) at a statistical power of 42%.

The mean bone density value in group B at t0 was 963 mg HA/cm³ (MSE = 13.3) (Fig 5). At t1, the mean was 1,056 mg HA/cm³ (MSE = 14.2). The mean bone density increased significantly between t0 and t1 ($P = .00031$), with a statistical power of 99%.

The mean bone density values in group C were 1,000 mg HA/cm³ at t0 (MSE = 16) (Fig 5) and 1,076 mg HA/cm³ (MSE = 29) at t1. The increase in density between t0 and t1 was significant ($P = .05$), with a statistical power of 98%.

No significant differences ($P = .341$) in bone density were found between the three groups at t1.

DISCUSSION

The current investigation is the first to compare the density of bone at the time of sinus augmentation with density values obtained 5 months after grafting. This comparison makes it possible to determine the increase in bone density and thereby evaluate the influence of different BSM on the bone density when added to autogenous bone for sinus augmentation.

The study showed a high dropout rate. This resulted in an inhomogenous distribution of samples per group and seems too few to reveal significant differences between groups. For this reason, a power analysis was performed retrospectively based on the obtained data. Generally, a power of 80% is regarded as adequate.³³ This level was reached in groups B and C, but not in group A. The reason for this is because of the smaller differences between the t0 and t1 bone density values and additionally by the relatively high common standard error of the measured data. A total of 22 samples would have been needed in group A to achieve a statistical power of 80%. Thus, the number of samples retrieved in group A is too small to determine differences in results but may be interpreted in terms of a reliable tendency. In contrast, the data obtained from group B and C show high statistical power of 99% and 98%, respectively.

Despite the weak statistical power in group A, the current investigation using μ -CT revealed an increase in bone density in all samples retrieved 5 months after maxillary sinus augmentation. Significant increases in bone density were also observed in groups B and C. However, highly significant differences after 5 months were observed only in group B. One reason for the bone density increase in group B may be related to the presence of HA particles. These resorb much more slowly than β -TCP particles.^{34,35} The slower resorption allows for early and quick bone apposition around the individual particles, which could result in an accelerated increase of bone density. In contrast to this, the bone formation around β -TCP particles may be slowed by dissolution of the particles. This might result in less bone apposition and more porous bone and could explain the differences between the two experimental groups.

The increase in bone density in the control group, in which only PAB was used, is surprising because

autogenous bone was previously described to quickly resorb when used for grafting procedures.³⁶ This was not confirmed in the present study. Nevertheless, it should be emphasized that the P values indicated only a slight significance. Taking into account that the sample size is rather small ($n = 6$), it can be suggested that additional samples might have changed the significance for this group. As such, these results should not be overestimated.

The healing time of 5 months was chosen based on other studies.³⁷ It is well known that the amount of newly formed bone after maxillary sinus augmentation is time-dependent. An extended healing time would have resulted in higher density values of the bone in all samples.

To imitate *in vivo* conditions as closely as possible, the particulated grafts were placed into the snap-lock tubes with the same pressure used for sinus augmentation. All snap-lock tubes were filled by the same surgeon who had performed the maxillary sinus augmentation. Despite this, the distribution of bone and BSM may have differed between the *in vitro* and *in vivo* situations. The trephine had a smaller diameter than the snap-lock tubes in which the graft was plugged for μ -CT acquisition. Differences in volume have a potential impact on density values. The absorption of material generally increases with growing volume. Since this inaccuracy was equivalent for all sample pairs, however, it represents a systematic mistake and should not negatively influence the conclusion of the study. With regard to the differences in volume, the changes in bone density would probably have been even greater if samples of identical diameters had been compared.

The results of this study are strongly dependent on the settings for image acquisition and on the thresholds used for bone and BSM segmentation. Every sample was evaluated at identical settings for μ -CT, and the conditions for evaluation were identical for all samples.

The current study has presented a new and innovative design to evaluate the influence of different grafting materials when mixed with PAB for maxillary sinus augmentation. Unfortunately, the sample size is inadequate to determine the significance of differences in the results or to make clinical recommendations. Nevertheless, the results of this study indicate that the bone density increases after maxillary sinus augmentation with both PAB alone or in combination with BSM based on HA and/or β -TCP particles. To reach a more definitive conclusion, larger samples and a split-mouth design are proposed to reliably discover significant differences between the materials. Further studies are needed to verify the observed changes in bone density and to focus on the biochemical reactions that follow maxillary sinus grafting.

ACKNOWLEDGMENTS

The study was funded in part by a study grant from the University of Mainz (MAIFOR). The authors kindly thank Prof Dr Heinz Duschner for the facilities in terms of µCT acquisition and Irene Mischak for the statistical analysis. The authors reported no conflicts of interest related to this study.

REFERENCES

- Boyne PJ, James RA. Grafting of the maxillary sinus floor with autogenous marrow and bone. *Int J Oral Maxillofac Surg* 1980;38:613–619.
- Tatum OH. Maxillary and sinus implant reconstruction. *Dent Clin North Am* 1986;30:207–229.
- Hürzeler MB, Kirsch A, Ackermann KL, Quinones CR. Reconstruction of the severely resorbed maxilla with dental implants in the augmented maxillary sinus: A 5-year clinical investigation. *Int J Oral Maxillofac Implants* 1996;11:466–475.
- Hürzeler MB, Quinones CR, Kirsch A, et al. Maxillary sinus augmentation using different grafting materials and dental implants in monkeys. Part I. Evaluation of anorganic bovine-derived bone matrix. *Clin Oral Implants Res* 1997;8:476–486.
- Quinones CR, Hürzeler MB, Schuepbach P, et al. Maxillary sinus augmentation using different grafting materials and osseointegrated dental implants in monkeys. Part II. Evaluation of porous hydroxyapatite as a grafting material. *Clin Oral Implants Res* 1997;8:87–96.
- Wallace SS, Froum ST. Effect of maxillary sinus augmentation on the survival of endosseous dental implants. A systematic review. *Ann Periodontol* 2003;8:328–343.
- Szabo G, Huys L, Coulthard P, et al. A prospective multicenter randomized clinical trial of autogenous bone versus beta-tricalcium phosphate graft alone for bilateral sinus elevation: Histologic and histomorphometric evaluation. *Int J Oral Maxillofac Implants* 2005;20:371–381.
- Peleg M, Garg AK, Mazor Z. Predictability of simultaneous implant placement in the severely atrophic posterior maxilla: A 9-year longitudinal experience study of 2132 implants placed into 731 human sinus grafts. *Int J Oral Maxillofac Implants* 2006;21:94–102.
- Kreisler M, Moritz O, Weihe CH, d’Hoedt B. Die externe Sinus-bodenlevation vor dem Hintergrund der Evidenzbasierten Medizin, Teil I [in German]. *J Dent Implant* 2006;22:299–323.
- Kreisler M, Moritz O, Weihe CH, d’Hoedt B. Die externe Sinus-bodenlevation vor dem Hintergrund der Evidenzbasierten Medizin, Teil II [in German]. *J Dent Implant* 2007;23:68–86.
- Froum SJ, Tarnow DP, Wallace SS, Rohrer MD, Cho SC. Sinus floor elevation using bovine bone mineral (OsteoGraf/N) with and without autogenous bone: A clinical, histologic, radiographic and histomorphometric analysis—Part 2 of an ongoing prospective study. *Int J Periodontics Restorative Dent* 1998;18:528–543.
- Hallman M, Sennersby L, Lundgren S. A clinical and histologic evaluation of implant integration in the posterior maxilla after sinus floor augmentation with autogenous bone, bovine hydroxyapatite, or a 20:80 mixture. *Int J Oral Maxillofac Implants* 2002;17:635–643.
- Schlegel KA, Fichtner G, Schultze-Mosgau S, Wilfang J. Histologic findings in sinus augmentation with autogenous bone chips versus a bovine substitute material. *Int J Oral Maxillofac Implants* 2003;18:53–58.
- Hatano N, Shimizu Y, Ooya K. A clinical long-term radiographic evaluation of graft height changes after maxillary sinus floor augmentation with a 2:1 autogenous/xenograft mixture and simultaneous placement of dental implants. *Clin Oral Implants Res* 2004;15:339–345.
- Guarnieri R, Grassi R, Ripari M, Pecora G. Maxillary sinus augmentation using granular calcium sulfate (surgiplaster sinus): Radiographic and histologic study at 2 years. *Int J Periodontics Restorative Dent* 2006;26:79–85.
- Wanschitz F, Figl M, Wagner A, Ewers R. Measurement of volume changes after sinus floor augmentation with phycogenic hydroxyapatite. *Int J Oral Maxillofac Implants* 2006;21:422–438.
- Johansson LA, Isaksson S, Lindh C, Becktor JP, Sennerby L. Maxillary sinus floor augmentation and simultaneous implant placement using locally harvested autogenous bone chips and bone debris: A prospective clinical study. *Int J Oral Maxillofac Implants* 2010;25:837–844.
- Caubet J, Petzold C, Sáez-Torres C, et al. Sinus graft with safescraper—5-year results. *Int J Oral Maxillofac Surg* 2011;40:482–490.
- Yildirim M, Spiekermann H, Biesterfeld S, Edelhoff D. Maxillary sinus augmentation using xenogenic bone substitute material Bio-Oss in combination with venous blood. A histologic and histomorphometric study in humans. *Clin Oral Implants Res* 2000;11:217–229.
- Maiorana C, Sigurta D, Mirandola A, Garlini G, Santoro F. Sinus elevation with alloplast or xenogenic materials and implants: An up-to-4-year clinical and radiologic follow-up. *Int J Oral Maxillofac Implants* 2006;21:426–432.
- Esposito M, Grusovin MG, Rees J, et al. Interventions for replacing missing teeth: Augmentation procedures of the maxillary sinus. *Cochrane Database Syst Rev* 2010;3:CD008397.
- Artzi Z, Kozlovsky A, Nemcovsky CE, Weinreb M. The amount of newly formed bone in sinus grafting procedures depends on tissue depth as well as the type and residual amount of the grafted material. *J Clin Periodontol* 2005;32:193–199.
- Artzi Z, Weinreb M, Carmeli G, Lev-Dor R, Dard M, Nemcovsky CE. Histomorphometric assessment of bone formation in sinus augmentation utilizing a combination of autogenous and hydroxyapatite/biphase tricalcium phosphate graft materials: At 6 and 9 months in humans. *Clin Oral Implants Res* 2008;19:686–692.
- Scarano A, Degidi M, Iezzi G, et al. Maxillary sinus augmentation with different biomaterials: A comparative histologic and histomorphometric study in man. *Implant Dent* 2006;15:197–207.
- Hürzeler MB, Quinones CR, Kirsch A, et al. Maxillary sinus augmentation using different grafting materials and dental implants in monkeys. Part III. Evaluation of autogenous bone combined with porous hydroxyapatite. *Clin Oral Implants Res* 1997;8:401–411.
- Glowacki J, Altobelli D, Mulliken JB. Fate of mineralized and demineralized osseous implants in cranial defects. *Calcif Tissue Int* 1981;33:71–76.
- Mulliken JB, Glowacki J, Kaban LB, Folkman J, Murray JE. Use of demineralized allogenic bone implants for the correction of maxillolacrimal deformities 2. *Ann Surg* 1981;194:366–372.
- Feldkamp LA, Goldstein SA, Parfitt AM, Jesion G, Kleerekoper M. The direct examination of three-dimensional bone architecture in vitro by computed tomography. *J Bone Miner Res* 1989;4:3–11.
- Trisi P, Rebaudi A, Calvari F, Lazzara RJ. Sinus graft with Biogran, autogenous bone, and PRP: A report of three cases with histology and micro-CT. *Int J Periodontics Restorative Dent* 2006;26:113–125.
- Kühl S, Götz H, Hansen T, et al. Three dimensional analysis of bone formation after maxillary sinus augmentation by means of micro computerized tomography (µ-CT): A pilot study. *Int J Oral Maxillofac Implants* 2010;25:930–938.
- Van Lenthe HG, Hagenmüller H, Bohner M, Hollister JS, Meinel L, Müller R. Nondestructive micro-computed tomography for biological imaging and quantification of scaffold-bone interaction in vivo. *Biomaterials* 2007;28:2479–2490.
- Rebaudi A, Trisi P, Celli R, Cecchini G. Preoperative evaluation of bone quality and bone density using a novel CT/micro CT-based hard-normal-soft classification system. *Int J Oral Maxillofac Implants* 2010;25:75–85.
- Park HM. Hypothesis Testing and Statistical Power of a Test. Working Paper. The University Information Technology Services (UITS) Center for Statistical and Mathematical Computing, Indiana University, 2010:13. <http://www.indiana.edu/~statmath/stat/all/power/index.html>. Accessed 5 September 2012.
- Detsch R, Mayr H, Ziegler G. Formation of osteoclast-like cells on HA and TCP ceramics. *Acta Biomater* 2008;4:139–148.
- Walsh RW, Vizesi F, Michael D, et al. Beta-TCP bone graft substitutes in a bilateral rabbit tibial defect model. *Biomaterials* 2008;29:266–271.
- Burchardt H. The biology of bone graft repair. *Clin Orthop Relat Res* 1983;174:28–42.
- Nkenke E, Stelzle F. Clinical outcomes of sinus floor augmentation for implant placement using autogenous bone or bone substitutes: A systematic review. *Clin Oral Implants Res* 2009;20:124–133.

Modified Surgical Protocol for Placing Implants in the Pterygomaxillary Region: Clinical and Radiologic Study of 454 Implants

Xavier Rodríguez, MD, PhD¹/Victor Méndez, DDS²/Xavier Vela, MD, DDS³/Maribel Segalà, MD, DDS³

Purpose: To review a series of 454 pterygoid implants placed more vertically than the previous standard angle (45 degrees) over a functional loading period ranging from 2 months to 14 years with a mean follow-up period of 6 years. **Materials and Methods:** A retrospective study was made. The sample was composed of patients rehabilitated with pterygoid implants between January 1997 and December 2010. Patient selection criteria included: edentulism on the posterior area of an atrophic maxilla, with less than 8 mm remaining from the sinus floor to the alveolar crest, and the presence of an anterior implant or tooth to ensure mesial support for a partial denture. After a healing period between 2 and 7 months, panoramic x-rays were taken at the time of loading. The implant length, implant diameter, implant success, and the angulation of the pterygoid implants were measured. **Results:** Three hundred ninety-two patients (206 women and 186 men) ranging in age from 34 to 75 years were fitted with 454 pterygoid implants and followed up. The 18-mm implant length was the most favored implant to fit in the pterygoid area. Implant diameter was 3.75 mm in 448 cases (98.6%). The mean mesiodistal angulation of the pterygoid implants was 70.4 degrees \pm 7.2. After a mean follow-up period of 6 years, 96.5% of the implants placed were successfully osseointegrated.

Conclusions: The findings indicate that a mesiodistal inclination of the pterygoid implant at 70 degrees relative to the Frankfort plane following the bony column of the pterygoid region decreases the non-axial loads of the rehabilitations and exhibits good long-term survival; however, further studies are needed to assess the long-term survival of implants in the pterygomaxillary region. INT J ORAL MAXILLOFAC IMPLANTS 2012;27:1547–1553

Key words: atrophic maxilla, follow-up period, pterygoid buttress, pterygoid implant

The posterior area of the maxilla presents many limitations to implant placement. These anatomical factors include bone quality, quantity, location of the antrum, and physical accessibility to operate.¹ Pterygoid implant technique is a treatment option for the atrophic edentulous posterior maxilla, as first described by Tulasne.² The pterygoid implant passes through the maxillary tuberosity, pyramidal process of palatine bone, and then engages the pterygoid process of the sphenoid bone.^{3,4} Anchored in the pterygomaxillary area, such implants avoid the need for bone grafting and/or prosthetic cantilevering (Fig 1).

To simplify this technique, several authors advise the clinician to place the implant(s) with an inclination of 45 degrees relative to the Frankfort plane.^{5–9}

However, there is no publication showing any pterygoid implant inclination series. It has been shown that the angle of the maxillary-pterygoideal column in the edentulous maxilla is 67.3 degrees \pm 5.0 in an antero-posterior direction relative to the Frankfort plane, and also has been shown that the buccopalatal angle is 14.1 degrees \pm 2.1.¹⁰ This bony corridor differs slightly from the 45 degrees described by several authors.^{5–7} Despite having a high rate of success, most studies about pterygoid implants present a mean follow-up period of less than 3 years.^{3,5,11–13} There is insufficient data about pterygoid implant failures beyond 3 years of loading, which makes it difficult to draw any conclusion about their long-term survival.

The purpose of this study was to assess the effect of placing pterygoid implants more vertically than has heretofore been the standard (45 degrees), following previous anatomical series and presenting a follow-up period over 14 years.

¹Private practice, Barcelona-Madrid, Spain.

²Private practice, Madrid-Lleida, Spain.

³Private practice, Barcelona, Spain.

Correspondence to: Dr Xavier Rodríguez, C/ Ganduxer 122, 08022 Barcelona, BCN Spain. Email: headquarters@borgroup.net

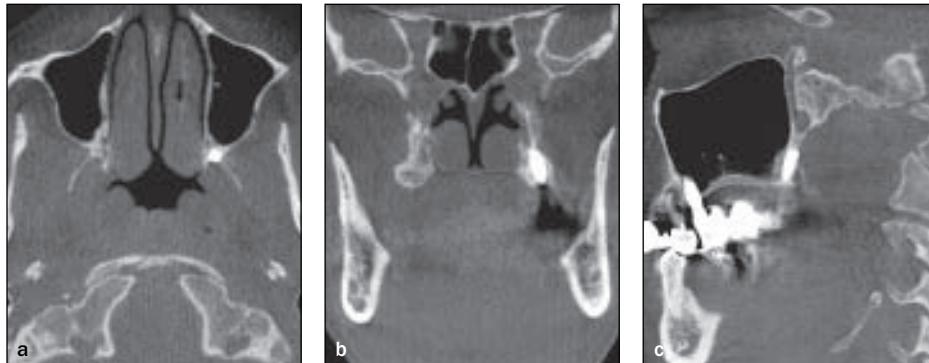
Fig 1 CT scan Image of pterygoid implant after 4 years of loading.

Fig 1a Axial view: the pterygoid implant is located between the posterior wall of the maxillary sinus, the palatine bone, and the pterygoid process of sphenoid.

Fig 1b Coronal view: the implant body runs parallel to the palatine bone.

Fig 1c Sagittal view: the implant body and apex is located between the posterior wall of the maxillary sinus and the pterygoid process of sphenoid.

Fig 2a Panoramic radiographs after 6 years of loading.**Fig 2b** Teleradiography after 6 years of loading.**Fig 2c** Radiographs after 3 months of surgery, before stage-two surgery.

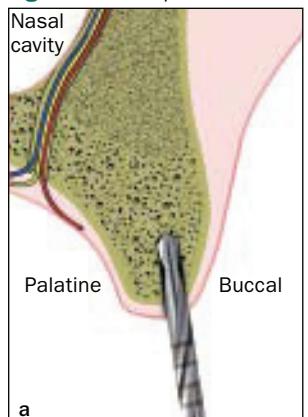
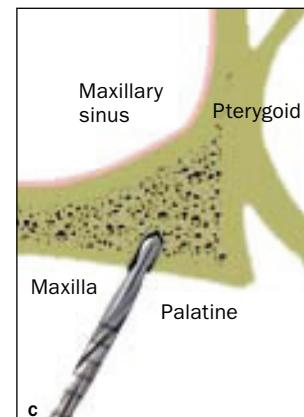
MATERIALS AND METHODS

This study included all patients who had implants placed in the pterygoid-maxillary region between January 1997 and December 2010 (range, 2 to 168 months). Patient selection criteria included edentulism on the posterior sector of an atrophic maxilla, with less than 8 mm remaining from the sinus floor to the alveolar crest, as measured by orthopantomography, and the presence of an anterior implant or tooth to ensure the mesial support for a partial denture (see Fig 2). Exclusion criteria included metabolic bone disease, an unstable systemic condition, such as uncontrolled diabetes or untreated hypothyroidism, or the discovery of a malignancy.

All patients received a preoperative orthopantomography (Planmeca Proline, Planmeca OY). In the panoramic radiograph, the patient should be positioned through the guides lights along three major axes (anterior-posterior, vertically (Frankfort plane), and midsagittal alignment) to standardized the radiologic measures.

To prevent infection and reduce inflammation, preoperative medication was prescribed for every patient to be taken 24 hours before the operation. This medication included amoxicillin (750 mg) or clindamycin (600 mg), one tablet every 8 hours; ibuprofen (600 mg), one tablet every 8 hours; and metamizol (75 mg), one tablet every 8 hours after surgery. A single doctor placed all the implants in the pterygomaxillary region between January 1997 and December 2010 (range 2 to 168 months).

Local anesthetic (articaine with epinephrine 40:0.005 mg/mL) was infiltrated into the maxillary nerve and the palatine nerve, plus anesthetic booster that was infiltrated into the tuberosity. A posterior incision was made in the alveolar crest of the maxillary tuberosity to expose it, and a straight contra-angle handpiece was used on the drill, with a bur guide and long burs 2 and 3 mm in diameter and 13 to 20 mm long at 500 to 1,500 rpm, and external irrigation with saline solution. Antero-posterior drilling angles were adapted to the patient's anatomy, entering 10 to 15 degrees medially.

Fig 3 The handpiece moves in a posterior, medial direction.**Fig 3a** Coronal view.**Fig 3b** Surgical view.**Fig 3c** Mesiodistal view.**Fig 4** CT scan: implants anchored in the palatine bone and the pterygoid process.

The mesiodistal angle of the implant was adjusted continuously to fit each patient's anatomy (Fig 3). In this technique, it is extremely important to feel one's way along while perforating and gradually going from soft cancellous bone to hard cortical bone, without a break that might indicate the bur was penetrating the maxillary sinus or nasal cavity. In some cases, it is advisable to perform the extraction of the wisdom teeth to avoid direct contact between the molar and the pterygoid abutment position.⁶ Following Tulasne's recommendation to ensure anchorage in the pterygo-maxillary region, all implants used in this series were at least 13 mm long.^{2,3} All the implants were seated with bicortical anchorage (Fig 4). The cover screw or the abutment was positioned, and the flap was sutured. In cases where the width of the gingiva reached more than 4 mm, the soft tissues were removed in order to fit an abutment of 4 to 6 mm in length.

Panoramic radiographs were taken before stage-two surgery or while the prostheses were fabricated. For this reason, a panoramic radiographic view was used to measure the pterygoid implant inclination. An accurate patient positioning was achieved while the radiographs were taken: the vertebral column had to be straight, the patient had to bite a plastic bite-block, and an accurate position of the midsagittal plane perpendicular to the floor had to fit by means of the guide to avoid errors due to insufficient or incorrect shape and size that would result in distorted images. Lack of a peri-implant radiolucency on radiographs and implant mobility and/or pain were the principal factors for assessing osseointegration success.

The implant length, diameter, success, and the angulation of the pterygoid implants were measured. Descriptive statistics was done using SPSS version 12.0 (IBM). The angulation of the pterygoid implants was

measured relative to the Frankfort plane at the time of stage-two surgery or when the prostheses were made if the abutments had been previously inserted at the first surgery. All radiographs were taken using Dimaxis version 2.4.3, (Planmeca OY). Figure 5 shows in a clinical case how the measurements were done. The mean time between implant placement and stage-two surgery, along with any complications were also reported. Patients were scheduled for annual follow-up.

RESULTS

Four hundred fifty-four pterygoid implants were placed in 392 patients (206 women and 186 men, ranging in age from 34 to 75 years). All implants had a rough surface. Four hundred fifty-three implants showed a dual acid-etched surface (Osseotite, 3i/Implant Innovations) and one implant showed a sandblasted and acid-etched surface (Mis, Israel DV Dent). With one exception, all surgeries were performed under local anesthesia.

Three hundred one patients (66.3%) were smokers. For all implants, the functional loading period ranged between 2 months and 14 years (168 months) with a mean follow-up period of nearly 6 years (71.1 ± 44.2 months). It must be noted that 227 implants (50%) were followed for longer than 5.7 years.

The 18 mm-length implant was the most chosen implant to fit in the pterygoid area. In 349 cases (76.9%), the implant length was 18 mm. In 51 cases (11.2%), the implant length was 20 mm. In 45 cases (9.9%), the implant length was 15 mm. In 9 cases (1.9%), the implant length was 13 mm. Implant diameter was 3.75 mm in 448 cases (98.6%). In 5 cases, a 4-mm-diameter implant was used, and in one case, a 4.2-mm-diameter implant was chosen.



Fig 5a Buccal and occlusal views before prosthesis placement.

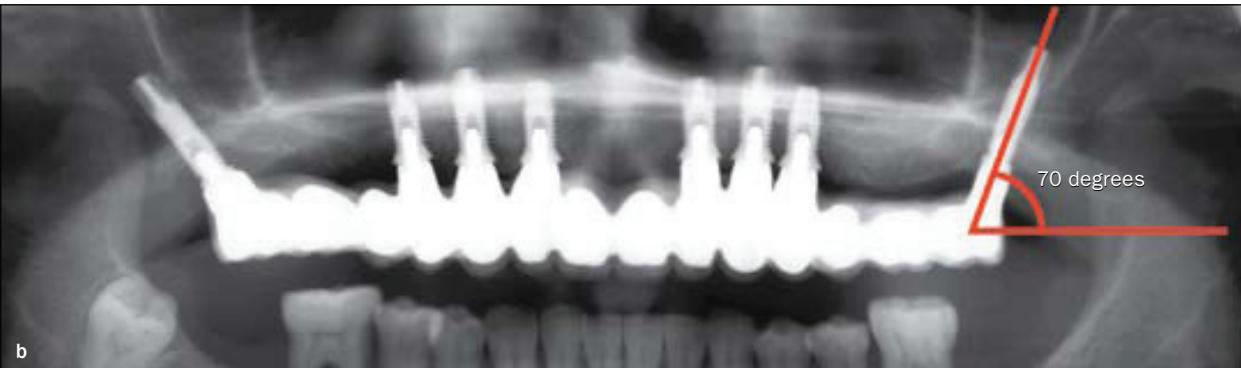


Fig 5b Orthopantomographic image of the restoration and angulation of the pterygoid implant on the left side.



Fig 5c Buccal and occlusal views of a fixed prosthesis.

The following complications were encountered in the present study:

- Intraoperative: Four cases of hemorrhage that stopped when the implants were seated, and three cases of pain while inserting the implant, relieved with booster anesthesia via the palatine and intra-alveolar route (the surgical bed).
- Postoperative: One case of transient hypoesthesia of the palatine nerve lasting 4 weeks, and one case of pterygomaxillary pain that needed the implant removed.

- Prosthetic: One patient that exhibited bruxism fractured two bilateral pterygoid implants after 5 years of loading. It must be noted that this patient also fractured the implants placed in the premolar region. Three bruxism patients also fractured the hybrid prosthesis.

Of the 454 pterygoid implants, 438 (96.5%) osseointegrated successfully and 16 (3.5%) failed. Thirteen of these 16 implants did not osseointegrate at the stage-two surgery. The mean time between implant placement and stage-two surgery was $4.2 \text{ months} \pm 1.2 \text{ months}$ with a

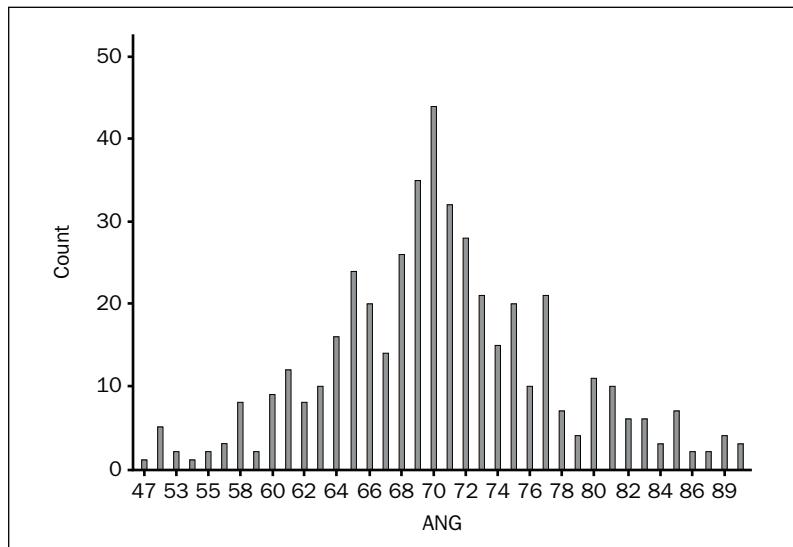


Fig 6 Graphic of the implant mesiodistal angulation (ANG) relative to the Frankfort plane.

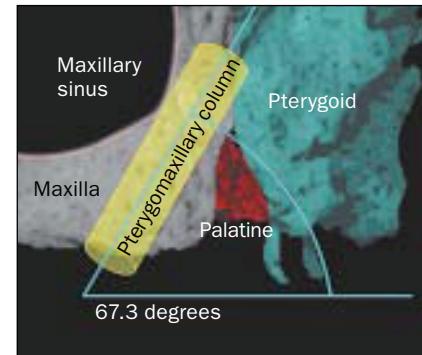


Fig 7 Anthropometric representation of the pterygomaxillary column angulation. Sagittal view.

range of 2 to 7 months. The time until functional loading depended on the stability of the mesial implants and their osseointegration status. In five cases, a sinus bone graft was made in order to achieve good stability for the mesial implant; these patients had to wait 7 months before the implant loading.

The implant mesiodistal angulation relative to the Frankfort plane ranged between 47 degrees and 90 degrees. The mean mesiodistal angulation of the pterygoid implants was $70.4 \text{ degrees} \pm 7.2 \text{ degrees}$. Two hundred seventy-nine implants (61.4%) showed an implant mesiodistal angulation between 65 and 75 degrees. Four hundred forty-four implants (94.7%) showed an implant mesiodistal angulation between 60 and 90 degrees (Fig 6).

Tissue-integrated prosthesis forms included: 313 metal-ceramic multifixture partial-arch fixed prostheses, 38 metal-ceramic multifixture complete-arch fixed prostheses, 17 hybrid multifixture complete-arch fixed prostheses, 13 complete removable overdentures, and 11 partial fixed prostheses connected to the teeth.

Regarding the 16 failed implants, 7 took place in men and 8 took place in women. Ten of these implants failed due to a lack of osseointegration in smokers (60%) and 4 implants in nonsmokers (40%). All 14 implants failed before loading at stage two. Two osseointegrated implants fractured after 5 years of loading in a bruxism patient. No significant differences in success index were found when considering smoking versus nonsmoking patients ($P > .05$). Again, no significant difference was found when considering sex, age, or time of implant loading and failed implants ($P > .05$).

DISCUSSION

According to Tulasne, 80% of atrophic maxillae retain a bone corridor that is sufficient to enable seating of an implant 13 to 20 mm long.^{2,3}

This bony pillar consists of: (1) the maxillary tuberosity, (2) the pyramidal process of the palatine bone, and (3) the pterygoid process. The position of this bony pillar has been measured anthropometrically. Yamakura et al observed that the angle of the tuberosity-pyramid-pterygoid pillar in the edentulous maxilla is $67.3 \text{ degrees} \pm 5 \text{ degrees}$ in an anteroposterior direction relative to the Frankfort plane, and the buccopalatal angle is $14.1 \text{ degrees} \pm 2.1 \text{ degrees}$ ¹⁰ (Fig 7).

This bony corridor inclination differs from the pterygoid implant inclination (45 degrees) described by several authors.⁵⁻⁷ In the present study, the mean mesiodistal angulation of the pterygoid implants relative to the Frankfort plane was $70.4 \text{ degrees} \pm 7.2 \text{ degrees}$. Furthermore, 61.4% of cases showed an implant angulation between 65 and 75 degrees and 94.7% showed an angulation between 60 and 90 degrees relative to the Frankfort plane (Figs 5c and 6).

The results of the present study differ from the 45 degree pterygoid implant inclination described by several authors but is consistent with the results of the anatomical study by Yamakura et al.¹⁰ Placing the implant more vertically than 45 degrees improves the loading conditions because the non-axial forces are diminished and the angle approximates that of natural molar teeth.^{6,14} Bahat recommends a mesial angle of 10 to 20 degrees (70 to 80 degrees relative to the

Frankfort plane) for posterior implants as a way to imitate the emergence of second molars.¹⁵

One of the drawbacks of the traditional pterygoid implant placement technique is the presence of nonaxial forces and the possibility that they might compromise the long-term restoration. A 45 degree angle in an implant reduces its axial load capacity by half⁶ when comparing the same implant at 90 degrees. The axial load on a 20-mm implant angled at 45 degrees would thus be equivalent to that of a 10-mm implant. In contrast, if the angle is 75 degrees, the axial load capacity of a 20-mm implant is 72.2% (comparable with that on a 14.4-mm implant). By placing two implants in the premolar region and a pterygoid implant in the posterior region, a plane in a tripod shape is created that protects the entire framework from transverse force and load, making it suitable for restoring the posterior sector.

Tulasne advised implants of 13 mm length, at least in the pterygoid region.³ In the present study, the 18-mm implant length was the most chosen length to fit in the pterygoid area. The use of 13- to 20-mm-length implants helps the clinician achieve good primary stability and avoid damaging fine structures as the base of the skull or the maxillary artery.¹⁶

Maxillary implant-supported restorations are less successful than those in the mandible. Olsson et al found an osseointegration rate of 86% in the maxilla versus 99% in the mandible.¹⁷ Widmark et al presented a 74% success rate at 5 years in atrophic maxillae.¹⁸ The success rate for pterygoid implants is one of the highest in the maxilla. Tulasne obtained 97% success, Raspall and Rodríguez 98%, Graves 89%, Balshi et al 88%, Venturelli 97%, Fernández and Fernández 93%, and Pi 97.2%.^{3,5,6,11–13,19} The success rate of the present study agrees with the previous studies (96.5%).

For most studies, the lower end of the range of follow-up period is less than 3 years, signifying that the 3-year survival of several implants is unknown. Fernández and Fernández analyzed 152 implants with a range of follow-up between 0.1 and 169 months.¹² The implant survival rate reported by Fernández and Fernández's study was a 93%.¹² Pi reported a 97.2% survival rate in 177 implants in a follow-up ranging between 1 and 10 years.¹³ Ridell et al reported 22 pterygoid implants with a range between 1 and 12 years, and presented a 100% success rate.²⁰ Balshi et al reported 356 pterygoid implants with a range between 0.06 and 9.2 years with a 88.2% rate of survival.¹⁹ Peñarrocha et al reported 68 pterygoid implants followed for 1 year with a 97% survival rate.²¹ In the pterygomaxillary region, most failures occurred before implant loading.⁷ The present study showed a success rate of 96.5%, according to those long-term studies.

Taking into account those studies, it can be said that pterygoid implant rehabilitations present good long-term survival. Rough-surfaced implants can reduce the waiting time before functional loading.²² Balshi et al achieved a success rate of 96.3% for osseointegration with rough-surfaced pterygoid implants.²³ These results were statistically significant when compared to his previous series using machined pterygoid implants.²³

In the present study, all implants had a rough surface and the implant survival rate (96.5%) was similar to that obtained by Balshi et al.²³ Pterygoid implants have provided abutment support for a variety of prosthetic rehabilitation forms that include partial or complete-arch fixed prostheses, complete removable overdenture, and terminal abutment for partial fixed prostheses connected to the natural dentition.^{7,19,23–25}

Some complications related to the surgical procedure have been reported: venous bleeding, trismus, misplacement of implant, and a unique case of a continuous episode of pain and discomfort.^{6,7,11,26} Reyhler and Olszewski reported a unique intracerebral penetration of a zygomatic implant inserted in the pterygoid region.²⁶ In the present study, minor hemorrhagic and neurologic complications have been shown. The authors consider that the use of drills and implants as much of 20 mm in length make this a safe technique.

In the present study, although smokers had a higher number of failures, no significant difference in success index was found when considering smoking versus nonsmoking patients ($P > .05$). Several authors note the low morbidity associated with the pterygoid implant^{3,5–7,11,21} and, therefore, the use of pterygoid implants can be a prudent option in patients who are smokers, diabetic, osteoporotic, or who have Crohn's disease or severe parafunctional habits.²⁷ The main drawback with this method is that it requires detailed knowledge of the pterygomaxillary region and surgical skill to achieve adequate anchorage.

CONCLUSION

In conclusion, the findings of the present study about pterygoid implants indicate that mesiodistal inclination of the pterygoid implant at 70 degrees to the Frankfort plane following the bony column of the pterygoid region decreases the non-axial loads of the rehabilitations and exhibits good long-term survival; however, further studies are needed to assess the long-term survival of implants in the pterygomaxillary region.

ACKNOWLEDGMENTS

The authors reported no conflicts of interest related to this study.

REFERENCES

1. Balshi TJ, Lee HY, Hernandez RE. The use of pterygomaxillary implants in the partially edentulous patient: A preliminary report. *Int J Maxillofac Implants* 1995;10:89–98.
2. Tulasne JF. Implant treatment of missing posterior dentition. In: Albrektson T, Zarb G (eds). *The Bränemark Osseointegrated Implant*. Chicago: Quintessence, 1989:103–115.
3. Tulasne JF. Osseointegrated fixtures in the pterygoid region. In: Worthington P, Bränemark PI (eds). *Advanced Osseointegration Surgery, Applications in the Maxillofacial Region*. Chicago: Quintessence, 1992:182–188.
4. Laney WR (ed). *Glossary of Oral and Maxillofacial Implants*. Chicago: Quintessence, 2007: 133.
5. Graves SL. The pterygoid plate implant: A solution for restoring the posterior maxilla. *Int J Periodontics Restorative Dent* 1994;14:513–523.
6. Venturelli A. A modified surgical protocol for placing implants in the maxillary tuberosity: Clinical results at 36 months after loading with fixed partial denture. *Int J Oral Maxillofac Implants* 1996;11:743–749.
7. Bidra AS, Huynh-Ba G. Implants in the pterygoid region: A systematic review of the literature. *Int J Oral Maxillofac Surg* 2011;40:773–781.
8. Haskel Y, Moreira PE, Villar WA. Implants in the pterygomaxillary region: An option for maxillary sinus floor elevation [in Spanish]. *Actas Odontológicas* 2008;5;5–13.
9. Mateos L, García-Calderón M, González-Martín M, Gallego D, Cabezas J. Inserción de implantes dentales en la apófisis pterigoides: Una alternativa en el Tratamiento Rehabilitador del Maxilar Posterior Atrófico [in Spanish]. *Avan Periodoncia Implantol* 2002;14:37–45.
10. Yamakura T, Abe S, Tamatsu Y, Rhee S, Hashimoto M, Ide Y. Anatomical study of the maxillary tuberosity in Japanese men. *Bull Tokyo Dent Coll* 1998;39:287–292.
11. Raspall-Martin G, Rodríguez X. Implantes pterigoideos [in Spanish]. *Revista Colegio Odontológico Estomatológico* 1998;3:461–467.
12. Fernández Valerón J, Fernández Velázquez J. Placement of screw-type implants in the pterygomaxillary-pyramidal region: Surgical procedure and preliminary results. *Int J Oral Maxillofac Implants* 1997;12:814–819.
13. Pi-Urgell J. Implantes en la región pterigomaxilar: Estudio retrospectivo con seguimiento de 1 a 10 años [in Spanish]. *Revista Consejo Odontológico Estomatológico* 1998;3:339–348.
14. Rodríguez X, Vela X, Méndez V, Segalà M. Alternatives to maxillary sinus lift: Posterior area of the atrophic maxilla rehabilitation by means pterygoideal implants. *Revista Española Cirugía Oral Maxilofacial* 2008;30:412–419.
15. Bahat O. Osseointegrated implants in the maxillary tuberosity: Report on 45 consecutive patients. *Int J Oral Maxillofac Implants* 1992;7:459–467.
16. Turvey I, Fonseca R. The anatomy of the internal maxillary artery in the pterygopalatine fossa: Its relationship in maxillary surgery. *J Oral Surg* 1980;38:92–95.
17. Olsson M, Friberg B, Nilson H, Kultje C. Mk II—A modified self-tapping Bränemark implant: 3-year results of a controlled prospective pilot study. *Int J Oral Maxillofac Implants* 1995;10:15–21.
18. Widmark G, Andersson B, Carlsson GE, Lindvall AM, Ivanoff CJ. Rehabilitation of patients with severely resorbed maxillae by means of implants with or without bone grafts: A 3- to 5-year follow-up clinical report. *Int J Oral Maxillofac Implants* 2001;16:73–79.
19. Balshi TJ, Wolfinger GJ, Balshi SF. Analysis of 356 pterygomaxillary implants in edentulous arches for fixed prosthesis anchorage. *Int J Oral Maxillofac Implants* 1999;14:398–406.
20. Ridell A, Gröndahl K, Sennerby L. Placement of Branemark implants in the maxillary tuber region: Anatomical considerations, surgical technique and long term results. *Clin Oral Implants Res* 2009;20:94–98.
21. Peñarrocha M, Carrillo C, Boronat A, Peñarrocha M. Retrospective study of 68 implants placed in the pterygomaxillary region using drills and osteotomes. *Int J Oral Maxillofac Implants* 2009;24:720–726.
22. Alsaadi G, Quirynen M, Steenberghe D. The importance of implant surface characteristics in the replacement of failed implants. *Int J Oral Maxillofac Implants* 2006;21:270–274.
23. Balshi SF, Wolfinger GJ, Balshi TJ. Analysis of 164 titanium oxide-surface implants in completely edentulous arches for fixed prosthesis anchorage using the pterygomaxillary region. *Int J Oral Maxillofac Implants* 2005;20:946–952.
24. Balshi TJ. Single, tuberosity-osseointegrated implant support for a tissue-integrated prosthesis. *Int J Periodontics Restorative Dent* 1992;12:345–357.
25. Balshi TJ, Wolfinger GJ. Teeth in a day for the maxilla and mandible: Case report. *Clin Implant Dent Relat Res* 2003;5:11–16.
26. Reyehler H, Olszewski R. Intracerebral penetration of a zygomatic dental implant and consequent therapeutic dilemmas: Case report. *Int J Oral Maxillofac Implants* 2010;25:416–418.
27. Balshi TJ, Wolfinger GJ. Management of the posterior maxilla in the compromised patient: Historical, current and future perspectives. *Periodontology 2000* 2003;33:67–81.

Two-Year Follow-up of Early- and Conventionally-Placed Two-Stage Implants Supporting Fixed Prostheses

Burak Bekcioglu, DDS, PhD¹/Elcin Sagirkaya, DDS, PhD²/
Durdur Karasoy, MSc, PhD³/Murat Cehreli, DDS, PhD⁴

Purpose: The objective of this study was to compare the biologic and prosthetic outcomes of early- and conventionally-placed implants supporting fixed prostheses. **Materials and Methods:** Using inclusion/exclusion criteria, early- and conventionally-placed implant patient groups, rehabilitated with Brånenmark System implants supporting fixed prostheses for 2 years, were selected from the patient archives. Kaplan-Meier survival estimates, time-dependent marginal bone loss, Plaque Index, peri-implant infection, Bleeding Index scores, and prosthetic complications data of the groups were compared. **Results:** A total of 212 implants were placed in early-placed ($n = 42$, 101 implants) and conventionally-placed ($n = 45$, 111 implants) patient groups and 5 implants failed during the 2-year follow-up. The 1- and 2-year Kaplan-Meier survival probabilities of early-placed (0.98) and conventionally-placed (0.973) groups were comparable ($P = .735$). The 6-month to 2-year marginal bone loss in the conventionally-placed group was higher than in the early-placed group ($P < .05$). There were differences between groups on soft tissue scores between the 2 years of function ($P < .05$). The frequency of prosthetic complications was very low and comparable in both groups ($P = .476$). **Conclusions:** Early- and conventionally-placed implants supporting fixed prostheses showed comparable clinical outcomes during the 2-year follow-up, although the marginal bone loss was higher in the latter group. *INT J ORAL MAXILLOFAC IMPLANTS* 2012;27:1554–1559

Key words: conventional implant placement, early implant placement, marginal bone loss, peri-implant soft tissue, prosthetic complication

The optimum timing of implant placement with regard to healing of extraction sockets has long been a topic of research interest. According to the proposed original protocol,¹ a healing period of several months was mandatory prior to placement of implants, followed by a 3- to 6-month unloaded phase for uneventful interface healing. As a considerably long treatment time was its main drawback, this protocol was challenged by reducing the time between tooth extraction and implant placement. Although a variety of classifications with a lack of uniformity is present,² an implant placed into a fresh extraction socket is denoted as an

"immediate implant"³ and an implant placed into an extraction socket within 4 to 8 weeks is called "early" or "immediate-delayed implant."^{2,4} In the later option, complete soft tissue coverage is obtained before implant surgery, increased soft tissue area and volume facilitates soft tissue flap management, and resolution of local pathology can be provided.^{2,5} In comparison to immediate placement, however, the technique is burdened by some disadvantages including increased treatment time, need for adjunctive surgical procedures, and the possibility of bone resorption in socket walls.^{5–7}

The long-term survival and marginal bone loss, as well as prosthetic complications, of conventionally-placed implants supporting fixed prostheses have been well-documented.^{8–14} Regarding early-placed implants, however, there is still a small pool of up to 5-year clinical studies on different implant systems. These studies reveal a failure rate of 3.6%, ranging from 0.0% to 6.4%, mixed data on marginal bone loss that could not be considered useful to estimate the treatment outcome, and a lack of data on prosthetic complications.^{2,15–19} Accordingly, the purpose of this survey was to report the biologic and prosthetic outcomes of early- and conventionally-placed implants supporting fixed prostheses.

¹Assistant Professor, Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Ordu University, Ordu, Turkey.

²Assistant Professor, Department of Prosthodontics, Faculty of Dentistry, Ordu University, Ordu, Turkey.

³Associate Professor, Department of Statistics, Faculty of Science, Hacettepe University, Ankara, Turkey.

⁴Professor, Department of Prosthodontics, Faculty of Dentistry, Ordu University, Ordu, Turkey.

Correspondence to: Dr Murat Cehreli, Department of Prosthodontics, Faculty of Dentistry, Ordu University, 52100 Ordu, Turkey. Fax: 90-452-2121289. Email: mcehreli@hotmail.com

MATERIALS AND METHODS

Subjects

Data of patients with early- and conventionally-placed implants were selected from the archives based on the following inclusion criteria: (1) ASA I or ASA II according to the American Society of Anesthesiologists; (2) mandibular and/or maxillary partial or complete edentulism rehabilitated by implant-supported fixed prostheses; (3) no history of previous implant surgery, (4) no history of previous periodontal flap surgery due to periodontitis; (5) absence of local inflammation and oral mucosal diseases; (6) adequate residual bone volume to receive at least Ø 4 mm × 10 mm implants in the edentulous region; (7) absence of systemic problems hindering surgery.

The following criteria were used for excluding patients from this study: (1) a history of drug abuse and/or life-threatening diseases (ASA Classification); (2) a history of radiotherapy in the head and neck region; (3) a history of preprosthetic surgery; (4) a history of implant surgery with grafting; (5) severe intermaxillary skeletal discrepancy; (6) excessive parafunctional activity leading to wear of natural teeth; (7) pregnancy or lactation; (8) physical disability to perform adequate oral hygiene.

Treatment planning for each patient was based on the individual anatomic-morphologic situation, patients' expectations, as well as esthetic and cosmetic aspects.

Study Procedures

All patients were rehabilitated with Bränemark System implants (predominantly MK III or IV TiUnite, Nobel Biocare). In the early-placed ($n = 42$) and conventionally-placed ($n = 45$) groups, 101 and 111 implants were placed, respectively. Prior to treatment, the optimum location of the implants was determined using periapical and panoramic radiographs, and in some cases computed tomography scans. Bone quantity and quality were assessed at surgery according to Lekholm and Zarb.²⁰ Most jaws had a resorption degree corresponding to score B and a bone quality score of 2. A two-stage surgical protocol was undertaken under local anesthesia and following the guidelines determined by the manufacturer. In the early group, the implants were placed between 4 to 5 weeks postextraction, which corresponds to type 2 or the early-placement protocol, as suggested by Hammerle and colleagues.⁵ The surgical procedures started with an intraoral crestal incision followed by subperiosteal dissection of mucoperiosteum, and slight flattening of the alveolar crest was performed with a bur under copious sterile saline irrigation, when indicated. At insertion, the implants were placed at a depth according to the guidelines given by the manufacturer. Standard postoperative treatment was composed of analgesics and chlorhexidine 0.2%

mouthrinses, and antibiotics and nonsteroidal analgesics postoperatively for 3 consecutive days. Sutures were removed 1 week after surgery. The patients who received immediate tooth/tissue-supported interim removable prostheses (13 patients in the early-placed group and 6 patients in the conventionally-placed group) resumed a soft diet for 2 weeks postsurgery and did not use the site of surgery for chewing during soft tissue healing. The patients were also recalled every 3 weeks to renew the soft tissue liner of the denture (ViscoGel, Denstply). Standard oral hygiene instructions were given to the patients, including brushing of the healing abutments upon stage-two surgery at 3 months. Metal-ceramic restorations were fabricated and delivered to the patients 3 weeks after stage-two surgery. The occlusion was checked for each prosthesis and occlusal concepts derived from tooth-supported fixed partial prostheses were carried out.²¹

Clinical Evaluation

The index according to Mombelli et al²² was used for detecting plaque around implants (score 0: no detection of plaque; score 1: plaque can be detected by running a probe across the smooth marginal surface of the implant; score 2: plaque can be seen by the naked eye; score 3: abundance of plaque). In addition, the Bleeding Index according to Mombelli et al²² was used to detect bleeding (score 0: no bleeding when using a periodontal probe; score 1: isolated bleeding spots visible; score 2: a confluent red line of blood along the mucosal margin; score 3: heavy or profuse bleeding). The degree of peri-implant inflammation was evaluated by the modified Löe and Silness²³ (score 0: normal peri-implant mucosa; score 1: mild inflammation, slight change in colour, slight edema; score 2: moderate inflammation, redness, edema and glazing; score 3: severe inflammation, marked redness and edema, ulceration). In addition, apart from the patients' referral for any prosthetic complaint, each prosthesis was evaluated to explore loosening associated with cement wash-out for cement-retained prostheses, loosening or fracture of the abutment screws, and fracture of prosthetic connectors or veneering porcelain indicating renewal of the prosthesis.

Radiographic Evaluation

Standard periapical and panoramic radiographs were obtained at recalls. The panoramic radiographs were used to evaluate both jaws. Periapical radiographs were obtained using a paralleling device (Dentsply Rinn, Rinn Cooperation) and were used to measure marginal bone loss. The periapical radiographs were approved for evaluation when threads on both sides were clearly observed.²⁴ The radiographs were digitized at 2,400 dpi using a scanner (Epson Perfection

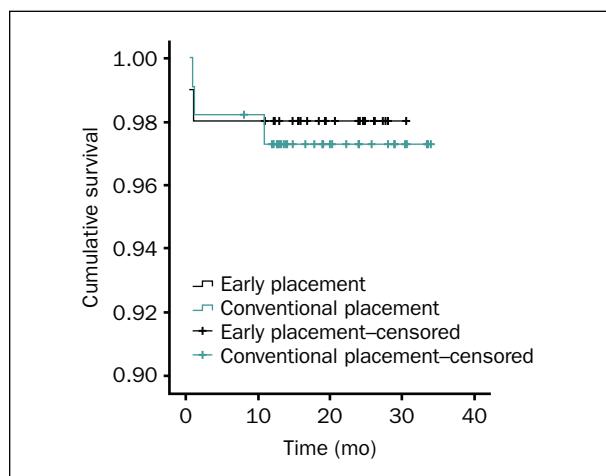


Fig 1 Kaplan-Meier survival estimates of early- and conventionally-placed implants.

2400 Photo, Seiko Epson). The marginal bone, as well as the entire bone-implant interface, was examined for changes indicating loss of bone or osseointegration. Radiographs were evaluated and linear distance measurements from first bone-to-implant contact to implant neck at mesial and distal sides of implants were made referring the actual distance between two consecutive threads in an image analysis software (ImageJ 1.32j, NIH) at $\times 400$ magnification.

Statistical Analyses

For the comparison of implant survival between groups, the first incidence of any complication indicating removal was taken into account and the timing was referred to as failure period. An implant was considered "failed" when any of the following was detected: peri-implantitis, excessive marginal bone loss, implant fracture, or a combination of these problems. Replacement of the implant was undertaken upon detection of any of these complications. An implant was considered as "survived" when any of the above-mentioned problems were not detected. During statistical assessment, the absence of the complication was referred to as "censored." The survival of the implants was evaluated by Kaplan-Meier estimator and comparative evaluation between groups on survival probabilities (maximum time in function without experiencing any complications) was undertaken by log-rank test at a 95% confidence level. Comparative assessment of plaque index, peri-implant infection, and bleeding index scores were performed by Fischer exact tests and chi-square tests at a 95% confidence level. Marginal bone loss levels of the groups were compared by independent *t* test at a 95% confidence level. Prosthetic outcomes of both groups were compared by Fischer exact tests at a 95% confidence level.

RESULTS

Patient Demographics

The survey of the archives revealed 42 patients with early-placed implants (31 women and 11 men; mean [\pm SD] age: 53.32 ± 12.42 years) and 45 patients with conventionally-placed implants (30 women and 15 men; mean [\pm SD] age: 50.47 ± 13.73 years). The number of patients who had dental cleaning in the early- and conventionally-placed groups was 15 and 27, respectively, and 5 patients in each group had flap surgery before implant treatment for crown lengthening in the posterior region. The number of patients with signs of nocturnal bruxism in the early- and conventionally-placed groups was 13 and 14, respectively, and of the patients in the later group, one patient was rehabilitated with a muscle relaxation splint. Because the bruxers did not have excessive parafunctional activity and wear of the natural teeth, they were not excluded from the study. The number of smokers in the early- and conventionally-placed groups was 7 and 15, respectively. The mean implant lengths in the early- and conventionally-placed groups were 13.89 mm (anterior [$n = 20$]; mean = 15.32 mm and posterior [$n = 20$]; mean 13.18 mm) and 12.54 mm (anterior [$n = 16$]; mean = 14.12 mm and posterior [$n = 95$]; mean = 12.27 mm), respectively. Among the 101 implants in the early-placed group, 52 implants were placed in the mandible and 49 implants were placed in the maxilla. Among the 111 implants in the conventionally-placed group, 67 implants were placed in the mandible and 44 implants were placed in the maxilla. The patients were predominantly rehabilitated with partial-arch restorations and the number of full-arch restorations in early- and conventionally-placed groups was 5 and 2, respectively. In the patient records, there was a lack of information on baseline bone levels and on the presence or absence of keratinized mucosa at baseline in both groups.

Survival Analysis

Overall, a total of five implants failed during the 2-year follow-up. Of these, four implants (1.9%) in four patients, equally distributed in the groups, failed prior to the prosthetic stage. Three implants failed due to peri-implantitis (two implants in the mandible and one implant in the maxilla) and one mandibular implant in the early group failed due to apical downgrowth of the epithelium. Of the 212 implants, the number of late implant failures was one in the conventionally-placed group and all implants survived in the early-placed group. The late failure in the conventional group was typically characterized by excessive breakdown of bone. The 1- and 2-year Kaplan-Meier survival estimate of 212 implants was 0.976 with a mean survival time of 33.33 ± 0.33 (Fig 1). The mean survival time

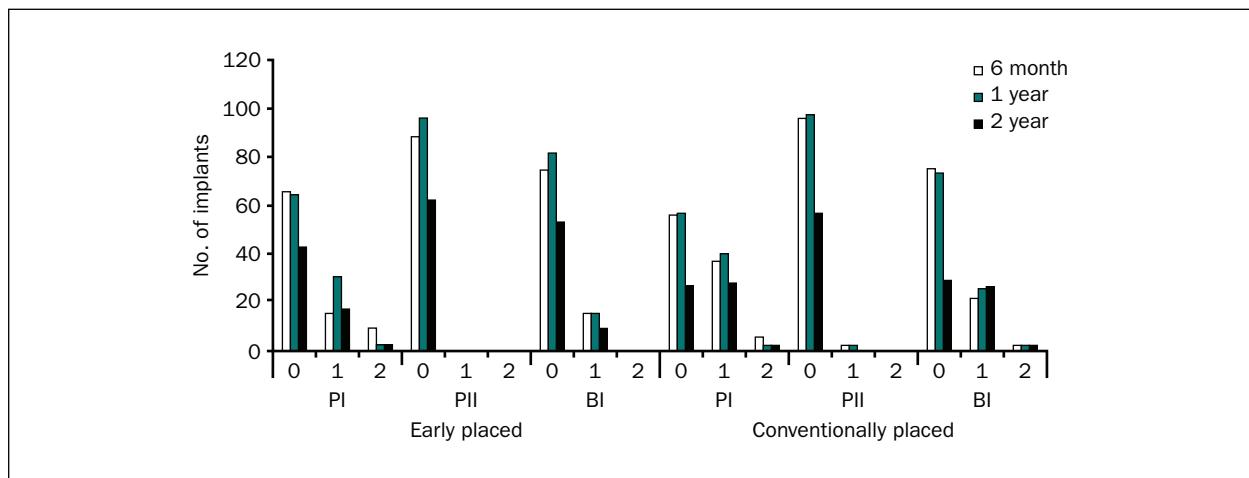


Fig 2 Plaque Index, peri-implant infection, and Bleeding Index scores of early- and conventionally-placed groups, including failed late implants.

Table 1 Marginal Bone Loss (mm) of Implants in Early- and Conventionally-Placed Groups

	Early placed						Conventionally placed						<i>P</i>
	n	Mean	SD	SEM	Min	Max	n	Mean	SD	SEM	Min	Max	
6-month	87	0.53	0.59	0.06	0.00	2.20	95	0.83	0.70	0.07	0.00	3.50	.002
1-year	96	0.78	0.58	0.05	0.00	2.40	98	1.07	0.71	0.07	0.05	3.50	.002
2-year	62	0.83	0.63	0.08	0.1	3.05	57	1.32	0.79	0.1	0.05	3.50	.001

SD = standard deviation; SEM = standard error for mean; Min = minimum; Max = maximum.

of the early- and conventionally-placed groups were 30.11 ± 0.42 and 33.27 ± 0.46 , respectively. The 1- and 2-year Kaplan-Meier survival probabilities of early- and conventionally-placed groups were 0.98 and 0.973, respectively, and the difference between the groups was insignificant ($P = .735$).

Marginal Bone loss, Soft Tissue, and Prosthetic Outcome

The time-dependent marginal bone loss and peri-implant soft tissue scores are presented in Table 1 and Fig 2, respectively. The 6-month to 2-year marginal bone loss in the conventionally-placed group was higher than the early-placed group ($P < .05$) (Table 1). The plaque index scores of the early-placed group were better than the conventionally-placed group at the 6-month and 2-year recalls ($P = .005$ and $P = .015$, respectively) and comparable to the conventionally-placed group at the 1-year recall ($P = .164$). The peri-implant infection scores of the early-placed group was comparable to the conventionally-placed group at the 6-month and 1-year recalls ($P = .49$). The bleeding index scores of the early-placed group was comparable to the conventionally-placed group at the 6-month and 1-year recalls ($P = .262$ and $P = .052$, respectively) and better than the conventionally-placed group at

the 2-year recall ($P = .00$). The frequency of prosthetic complications was very low and comparable in both groups ($P = .476$). Re-cementation of prosthesis ($n = 1$) was needed in the early-placed group.

DISCUSSION

In the present survey of patient archives, a comparative assessment of biologic and prosthetic outcomes of early- and conventionally-placed implants followed for 2 years was undertaken. Implant failures due to peri-implantitis were observed in three implants and these mandibular and maxillary implants were associated with excessive pain a few days after placement and swelling after 1 to 3 weeks. In comparison with the present study, the number of early-placed implants in previous studies^{15–19} is relatively low and in some studies different implant systems have been used. Therefore, a comparison in the strict sense cannot be carried out. The number of early implant failures in the early- and conventionally-placed groups ($n = 4$; 1.9%) was very low in the present study and this is in agreement with the 0% to 9% failure rate² of previous studies. In the study by Grunder and colleagues,¹⁶ 2 out of 34 delayed Nobel Biocare implants placed 4 to 5 weeks

postextraction failed prior to the prosthetic stage. Similarly, Polizzi et al¹⁷ observed 3 early failures out of 34 delayed Nobel Biocare implants placed 3 to 5 weeks postextraction. Considering late failures, the results of this study suggest comparable 1- to 2-year survival of early- and conventionally-placed implants with a very limited number of implant loss. This outcome is also in agreement with previous reports.

Measurement of the marginal bone loss over time is regarded as a sensitive tool for assessment of the clinical/biologic functioning of implants, as progressive loss of peri-implant bone will eventually lead to failure of the implant. Although general criteria for success have been proposed, the time required for individual implants as well as implant systems to reach a steady marginal bone level might differ.^{25,26} Besides, the impact of placement protocol on bone and soft tissue changes has not been comprehensively reported for early-placed implants.² The bone loss levels were around 1 mm, but this could not be compared to previous data on Nobel Biocare implants^{16,17} due to mixed data. Perry and Lenchewski¹⁵ and Schropp et al¹⁸ did not report mean marginal bone loss levels of early-placed implants and Gotfredsen¹⁹ measured less than 1 mm bone loss for Astra Tech implants for an observation period of 5 years. Regarding assessment of peri-implant soft tissue health, the present study showed that regardless of the placement protocol, most implants had 0 or 1 plaque, peri-implant infection, and bleeding index scores. While previous work on Frialit-2,¹⁵ Nobel Biocare,^{16,17} and Osteotite¹⁸ implants did not report such data with regard to placement protocol, Gotfredsen¹⁹ did not observe any difference on soft tissue outcome between early- and conventionally-placed implants. According to the pooled data, plaque was visible for 16%, 24%, and 21% of the implants at baseline, 3 years, and 5 years of function. Similar to the present data, Gotfredsen¹⁹ reported that 70% of all surfaces had no sign of mucositis (a bleeding score of 0) at the baseline registration.

CONCLUSIONS

Prosthetic materials and implant components used for implant-supported fixed prostheses should allow clinicians to pursue durable, cost-effective, and simple interventions with the lowest maintenance requirements to meet the functional demands of patients. Currently, the longevity of implant-supported fixed prostheses is imperiled not only by biologic complications, but also by prosthetic maintenance requirements. By far, documentation of the prosthetic maintenance requirements (and presentation of the frequency of problems) has been on an ad hoc basis rather than

by strict prior categorization. Regarding early-placed implants, Gotfredsen¹⁹ observed retightening of abutment screw, one re-cementation, one crown renewal, and one minor porcelain fracture in the experimental "early placement" study group. However, these implants were restored with standard abutments, while preparable abutments were used for the conventional implants and the author believed that the technical complications were probably more related to this difference. In the present study, the type and incidence of prosthetic complications were extremely low and the differences between groups were insignificant.

There are a number of limitations of the present survey. First, the study was not designed intentionally at the outset, but the data were extracted from patient records to compare the biologic/prosthetic outcome of early- and conventionally-placed implants. There were missing data on spontaneous exposure of cover screws and radiographic data between stage-one and stage-two surgeries, which may have better explained the bone remodeling during the first year. The files of the patients did not routinely include soft tissue height measurements, and therefore, any possible correlations between the peri-implant soft tissue height on early bone remodeling could not be undertaken. Indeed, animal studies suggest that a certain height of peri-implant mucosa is required to allow proper epithelial-connective tissue attachment and at lower soft tissue dimensions, bone resorption will occur to ensure the establishment of biological width.^{27,28}

ACKNOWLEDGMENTS

The authors reported no conflicts of interest related to this study.

REFERENCES

- Bränemark PI. Introduction to osseointegration. In: Bränemark PI, Zarb G, Albrektsson T (eds). *Tissue-Integrated Prostheses: Osseointegration in Clinical Dentistry*. Chicago: Quintessence; 1985:11–76.
- Quirynen M, Van Assche N, Botticelli D, Berglundh T. How does timing of implant placement affect treatment outcome? *Int J Oral Maxillofac Implants* 2007;22:203–223.
- Schulte W, Kleineikenscheidt H, Lindner K, Schareyka R. The Tübingen immediate implant in clinical studies [in German]. *Dtsch Zahnärztl Z* 1978;33:348–359.
- Esposito MA, Koukoulopoulou A, Coulthard P, Worthington HV. Interventions for replacing missing teeth: Dental implants in fresh extraction sockets (immediate, immediate-delayed and delayed implants). *Cochrane Database Syst Rev* 2006;CD005968.
- Hammerle CH, Chen ST, Wilson TG Jr. Consensus statements and recommended clinical procedures regarding the placement of implants in extraction sockets. *Int J Oral Maxillofac Implants* 2004;19(suppl): 26–28.
- Schropp L, Wenzel A, Kostopoulos L, Karring T. Bone healing and soft tissue contour changes following single tooth extraction: A clinical and radiographic 12-month prospective study. *Int J Periodontics Restorative Dent* 2003;23:313–323.

7. Camargo PM, Lekovic V, Weinlaender M, et al. Influence of bioactive glass on changes in alveolar bone dimensions. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2000;90:581–586.
8. Berglundh T, Persson L, Klinge B. A systematic review of the incidence of biological and technical complications in implant dentistry reported in prospective longitudinal studies of at least 5 years. *J Clin Periodontol* 2002;29:197–212.
9. Pjetursson B, Tan K, Lang N, Brägger U, Egger M, Zwahlen M. A systematic review of the survival and complication rates of fixed partial dentures (FPDs) after an observation period of at least 5 years. I. Implant supported FPDs. *Clin Oral Implants Res* 2004;15:625–642.
10. Lekholm U, Gröndahl K, Jemt T. Outcome of oral implant treatment in partially edentulous jaws followed 20 years in clinical function. *Clin Implant Dent Relat Res* 2006;8:178–186.
11. Jemt T, Johansson J. Implant treatment in the edentulous maxillae: A 15-year follow-up of 76 consecutive patients provided with fixed prostheses. *Clin Implant Dent Relat Res* 2006;8:61–69.
12. Lindquist LW, Carlsson GE, Jemt T. A prospective 15-year follow-up study of mandibular fixed prostheses supported by osseointegrated implants. Clinical results and marginal bone loss. *Clin Oral Implants Res* 1996;7:329–336.
13. Roos-Janåker AM, Lindahl C, Renvert H, Renvert S. Nine to fourteen-year follow-up of implant treatment. Part II: Presence of peri-implant lesions. *J Clin Periodontol* 2006;33:290–295.
14. Astrand P, Ahlvist J, Gunne J, Nilson H. Implant treatment of patients with edentulous jaws: A 20-year follow-up. *Clin Implant Dent Relat Res* 2008;10:207–217.
15. Perry J, Lenchewski E. Clinical performance and 5-year retrospective evaluation of Frialit 2 implants. *Int J Oral Maxillofac Implants* 2004;19:887–891.
16. Grunder U, Polizzi G, Goené R, et al. A 3-year prospective multicenter follow-up report on immediate and delayed placement of implants. *Int J Oral Maxillofac Implants* 1999;14:210–216.
17. Polizzi G, Grunder U, Goené R, et al. Immediate and delayed implant placement into extraction sockets. A five-year report. *Clin Implant Dent Relat Res* 2000;2:93–99.
18. Schropp L, Kostopoulos L, Wenzel A. Bone healing following immediate versus delayed placement of titanium implants into extraction sockets: A prospective clinical study. *Int J Oral Maxillofac Implants* 2003;18:189–199.
19. Gotfredsen K. A 5-year prospective study of single tooth replacements supported by Astra Tech implant: A pilot study. *Clin Implant Dent Relat Res* 2004;6:1–8.
20. Lekholm U, Zarb GA. Patient selection and preparation. In: Bränemark PI, Zarb GA, Albrektsson T, eds. *Tissue Integrated Prostheses: Osseointegration in Clinical Dentistry*. Chicago: Quintessence, 1985:199–209.
21. Shillingburg HT, Hobo S, Whitsett LD, Jacobi R, Brackett SE (eds). *Fundamentals of Fixed Prosthodontics*. Chicago: Quintessence, 1997:11–23.
22. Mombelli A, Van Oosten MAC, Schurch E, Lang N. The microbiota associated with successful or failing osseointegrated titanium implants. *J Oral Microbiol Immun* 1987;2:145–151.
23. Löe H, Silness J. Periodontal disease in pregnancy. II: Correlation between oral hygiene and periodontal condition. *Acta Odontol Scand* 1963;21:533–551.
24. Sewerin IP. Errors in radiographic assessment of marginal bone height around osseointegrated implants. *Scand J Dent Res* 1990;98:428–433.
25. Albrektsson T, Zarb G. Current interpretations of the osseointegrated response: Clinical significance. *Int J Prosthodont* 1993;6:95–105.
26. Schwartz-Arad D, Herzberg R, Levin L. Evaluation of long-term implant success. *J Periodontol* 2005;76:1623–1628.
27. Abrahamsson I, Berglundh T, Wennstrom J, Lindhe J. The peri-implant hard and soft tissues at different implant systems. A comparative study in the dog. *Clin Oral Implants Res* 1996;7:212–219.
28. Berglundh T, Lindhe J. Dimension of the periimplant mucosa. Biological width revisited. *J Clin Periodontol* 1996;23:971–973.

Patient Preference and Satisfaction with Implant-Supported Mandibular Overdentures Retained with Ball or Locator Attachments: A Crossover Clinical Trial

Gerald Krennmaier, MD, DMD, PhD¹/Rudolf Seemann, MD, DMD²/Andres Fazekas, MD, DMD, PhD³/
Rolf Ewers, MD, DMFD, PhD⁴/Eva Piehslinger, MD, DMD, PhD⁵

Purpose: To determine patient satisfaction and preference for implant-supported mandibular overdentures (IOD) retained with ball or Locator attachments. In addition, peri-implant conditions and prosthodontic maintenance efforts for the final attachments were evaluated after 1 year of function. **Material and Methods:** In this crossover clinical trial, 20 edentulous patients were recruited to receive two mandibular implants in the canine region and were provided with implant-retained mandibular overdentures and new complete maxillary dentures. Implant-retained mandibular overdentures were stabilized with either ball attachments or Locator attachments, in random order. After 3 months of function, the attachments in the existing denture were changed. Questionnaires on satisfaction/complaints with the prostheses were administered at baseline (with the old dentures) and after 3 months of function with each attachment, thus providing for an intraindividual comparison. The decision for the final attachment chosen was based on the patient's preference. For the definitive attachment, peri-implant conditions (peri-implant marginal bone resorption, pocket depth, and Plaque Index, Gingival Index, and Bleeding Index) as well as prosthodontic maintenance efforts and satisfaction score were evaluated after an insertion period of 1 year. **Results:** Nineteen (95%) patients completed the study (1 dropout). Patient satisfaction improved significantly ($P < .05$) from baseline (old dentures) to the new prostheses retained with each of the two attachment types for all domains of satisfaction. However, there were no differences between ball or Locator attachment for any items of satisfaction evaluated and neither attachment had a significant patient preference. No differences for peri-implant parameters or for patient satisfaction were noted between the definitive attachments (ball, $n = 10$; Locator, $n = 9$) after 1 year. Although the overall incidence rate of prosthodontic maintenance did not significantly differ between both retention modalities, the Locator attachment required more postinsertion aftercare (activation of retention) than the ball anchors. INT J ORAL MAXILLOFAC IMPLANTS 2012;27:1560–1568

Key words: ball-locator attachment, crossover trial, mandibular overdenture

Implant prosthodontic rehabilitation of edentulous mandibles using implant-supported overdentures (IOD) represents an effective and established treatment modality.^{1–5} There is a wide variety of different implant-

supported prosthodontic rehabilitation designs for implant prosthodontic treatment of the edentulous mandible depending on the number of implants used and the attachments selected.^{6–12} Prosthetic concepts may vary, basically distinguishing between primarily implant-supported, combined implant-retained and mucosa-supported, and purely implant-supported prostheses.^{1,7–11}

However, considering cost and treatment effectiveness, use of the two-interforaminal-implant modality has been recommended for basic standard treatment with IODs.^{1,5,13} The abutment types commonly used for the two-implant-supported mandibular overdentures include bars of different designs, balls, and magnet attachments.^{7,9,14–16} Compared with conventional complete dentures, all anchoring mechanisms used for retaining IODs have been described to be superior to complete dentures without any significant patient

¹Professor, Clinical Lecturer, Department of Prosthodontics, Medical University of Vienna, Vienna, Austria.

²Fellow, Department of Prosthodontics, Medical University of Vienna, Vienna, Austria.

³Professor, Dental School, Department of Prosthodontics, Szeged, Hungary.

⁴Professor, Head Department of Oral & Maxillofacial Surgery, Medical University of Vienna, Vienna, Austria.

⁵Professor, Head Department of Prosthodontics, Medical University of Vienna, Vienna, Austria.

Correspondence to: Univ-Prof DDr med Gerald Krennmaier, Austria 4600 Wels, Trauneggsiedlung 8. Fax: +7243/518136. Email: krennmaier@aon.at



Figs 1a and 1b Patrice and matrix (replaceable nylon insert with different degrees of retention forces) of Locator attachment.

preference.^{1,2,14–16} However, differences have been described for the different anchoring mechanisms used with regard to the extent of prosthetic postinsertion maintenance during the follow-up period for patients and clinicians.^{17–20} In separate studies, Cune et al¹⁵ and MacEntee et al¹⁷ found more postinsertion maintenance for ball anchors (versus bars), while other investigators could not confirm these findings.²¹ In detailed studies of Naert and colleagues¹² using three attachments (bar, ball, and magnets), the bar attachment was reported to be the technically most demanding one compared with both types of unlinked attachments.

Moreover, the rates of patient preference and satisfaction with different attachment systems were compared between ball anchor, bar, and magnetics by van Kampen et al¹⁴ and Cune et al^{15,22} in separate clinical crossover studies. Although bar clips were found by patients to be the most favorable attachment systems for two-implant retained overdentures within the group of unlinked implants,^{12,23} ball attachments still represent the most common attachment, while magnets are only used in rare instances.^{14–16,24}

However, for the use of single attachment systems anchoring IODs, a new prefabricated anchoring system, the Locator system, has recently been presented and is available as a prefabricated device.^{25–27} The Locator system, which has become widely applied and is being marketed by several implant companies, has been introduced and advocated as an alternative single attachment to the established ball anchor. The Locator consists of a patrice (Fig 1a), as the overdenture abutment on the implant, and of a matrix, which is a replaceable nylon insert (with different degrees of retention forces) on the underside (Fig 1b) of the overdenture. Although the Locator system has been in clinical use for several years, there is still a lack of detailed information on its effectiveness.^{25–27} Recently, patient satisfaction and postinsertion prosthodontic maintenance efforts have been described and compared between Locator and ball anchors in separate clinical studies.^{25–27} In these studies, borderline ben-

efits have been reported for the Locator versus ball anchors in regard to patient satisfaction²⁵; however, significantly higher prosthodontic maintenance efforts were described for the Locator system compared with ball anchors.²⁷

Because both single attachment systems consist of similar devices, such as matrix and patrice, similarities in patient satisfaction, preference, and postinsertion care may be anticipated. Therefore, the primary aim of this crossover clinical study was to evaluate which retainer design (ball attachment or Locator) provides for patient preference and for the highest satisfaction rates 3 months after placement. The secondary aim was to determine the postinsertion prosthodontic efforts required and the peri-implant/attachment parameters for the retainer selected after at least 1 year of loading. The null hypothesis was that there would be no differences between both retention modalities regarding patient preference and satisfaction rates, as well as for postinsertion prosthodontic maintenance and peri-implant parameters.

MATERIALS AND METHODS

Patient Population and Treatment

Twenty edentulous patients participated in this randomized crossover trial. All patients were referred because of functional complaints with their complete mandibular dentures. The group consisted of 11 women and 9 men (age, 62.4 ± 9.1 years). All patients included received two endosteal implants (Camlog, Screw-line, Alitatec) located in the canine region. Following implant placement and a healing period of 3 months, the implants were uncovered and healing abutments were inserted. Each patient was given a detailed description of the procedures and signed an informed consent prior to participation. The study was sponsored by the Camlog Foundation and the study protocol was approved by the Ethics Committee for Upper Austria, Linz.



Figs 2a and 2b Two implant-supported ball attachments and underside of mandibular overdentures with matrix devices.



Figs 3a and 3b Two implant-supported Locator attachments and underside of mandibular overdentures with matrix devices

Prosthodontic Procedure

Prosthodontic treatment was started 2 weeks after stage-two surgery in which new maxillary dentures and implant-retained mandibular overdentures were made according to a standard prosthetic protocol of the Department of Prosthodontics, Medical University Vienna, Vienna, Austria. A canine guidance articulation using anatomically-shaped acrylic resin teeth (Ivoclar, Vivadent), maximal extension of denture base, and compensation/generation of the vertical dimension were made. Depending on the respective alveolar ridge dimension, one or two molars were used in each quadrant.

For implant prosthodontic rehabilitation, patients were randomly selected to initially receive either ball attachments (ball group, Figs 2a and 2b) or Locator attachments (Locator group, Figs 3a and 3b) for retaining the implant-supported metal-reinforced overdenture. Abutments were initially selected in a random procedure. Subsequently, the patients were supplied with either Locator or ball attachments in alternating sequence. Patients were randomly assigned to start treatment with one of the attachment systems used and the attachments were changed after 3 months of function. Because the same denture base was used, similar occlusion, articulation, height, and denture base ex-

tension were maintained during the course of the trial for the study and the control group attachments.

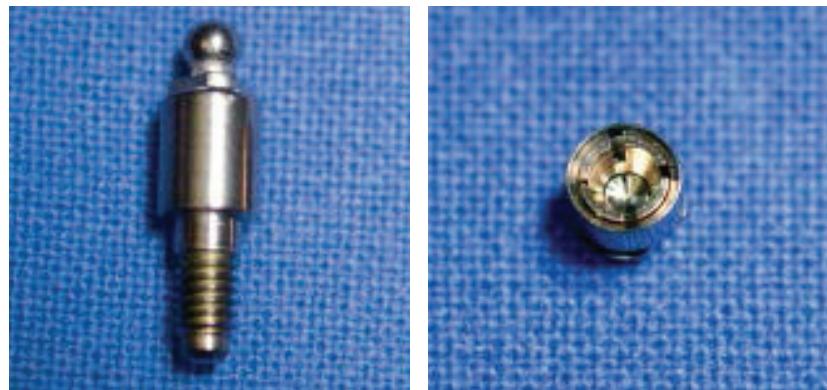
Locator Attachment

The Locator implant attachment system comprises a self-aligning double retention cylinder with retention surfaces on the inner and outer areas (Figs 1a and 3a). A metal body is incorporated in the base of the denture and, in this body, nylon elements in the negative form of the abutment connect the prostheses with the implant.^{25,26} The nylon male elements (Fig 1b) are available in different color-coded designs with different retention forces (blue 6.7 N [light], pink 13.4 N [medium], clear 22.3 N [strong]). In the present study, all patients were initially provided with pink inserts (13.4 N; medium force, Fig 3b), providing possibilities for strengthening or loosening the retention force.

Ball Attachment

The control group consisted of traditional ball attachments (Fig 4a) to connect implants with the bottom part of the overdenture. The matrix consisted of a metal body and an inner element with four circular arranged metal lamellae (Fig 4b). The retention force was variable depending on the activation of the lamellae.

Figs 4a and 4b Patrix and matrix (metal body and an inner element with four circular arranged metal lamellae) of ball attachment.



Clinical Evaluation and Postinsertion Maintenance

Patient satisfaction was evaluated using the McGill patient satisfaction questionnaires.²⁸ Recording of the different aspects of patient satisfaction was modified by using a discrete analog scale ranging from 0 to 10, with 0 = fully dissatisfied and 10 = completely satisfied. Questionnaires were provided for general satisfaction, cleaning, comfort, esthetics, speech, chewing ability, denture stabilization, function, and oral condition as previously described.^{2,28} Cleaning instructions were provided by clinicians and dental hygienists at denture incorporation as well as at recall visits.

Patient satisfaction was evaluated at baseline (old dentures without retention elements, old dentures had been fabricated by previous dentists/technicians) and after wearing the IODs with both attachments for 3 months. The satisfaction scores obtained were compared for baseline versus both attachments used for implant-retained overdentures, as well as for one attachment system versus the other. Additionally, patient preference for attachment type was evaluated and the preferred attachment was finally incorporated in the dentures.

After termination of the 3-month crossover trial, the study was extended to include a 1-year longitudinal follow-up extension study under the provision that two different comparable patient populations would be available. For this extension study, subjective satisfaction with the ultimately selected retention elements, as well as peri-implant parameters and prosthodontic maintenance efforts with both attachments, were evaluated. One-year data for both attachment systems were assessed and compared.

Examination of peri-implant conditions included evaluation of peri-implant marginal bone loss (mm) and probing pocket depth (mm), as well as Plaque Index, Bleeding Index, Gingival Index, and presence of calculus. Modified Plaque Index (score: 0 to 3, 0 = no visible plaque; 1 = local plaque accumulation;

2 = general plaque accumulation > 25%; 3 = abundance of plaque) was assessed according to Mombelli et al²⁹ and Salvi et al.³⁰ Bleeding Index (BI) and Gingival Index (GI) were assessed using criteria defined in previous studies^{30,31} (BI: score 0 to 3; 0 = no bleeding; 1 = isolated bleeding spots; 2 = blood forms a confluent red line on mucosal margin; 3 = heavy bleeding; GI: 0 to 3: 0 = normal mucosa; 1 = minimal inflammation with color change and minor edema; 2 = moderate inflammation with redness, edema, and glazing; 3 = severe inflammation with redness, edema, ulceration, and spontaneous bleeding. The presence of calculus (score 1) or the absence of calculus (score 0) was scored.³¹

Peri-implant marginal bone loss (mm) was assessed radiographically using a digital imaging system (Orthophos XG Plus, Sirona). The radiographic evaluation included an orthopantomogram and single periapical radiographs based on the paralleling technique where the reduction of the bone height level was determined in relation to the implant shoulder. For this purpose, the initial postoperative radiograph (baseline) was compared with the most recent one to calculate implant crestal bone level and the effective marginal bone loss as the result of the difference.⁸⁻¹¹ Probing (pocket) depth was defined as a mean value of measurements at four sites (mesial, distal, lingual, buccal) using the calibrated periodontal probe (Hu-Friedy), as described previously.^{30,31} Implant mobility was measured with the Periotest (Siemens) at the abutment closest to the implant edge.³²

Prosthodontic complications and repairs during the 12-month follow-up were registered and calculated according to the following events: attachment loosening (ball/Locator loosening), attachment worn/fracture (ball/Locator worn/fracture), matrix activation/replaced (ball-matrix activation/renewed, acrylic Locator insert renewed), overdenture teeth fracture/renewed, overdenture fracture/remade, overdenture relined/rebased, and opposing prosthesis rebased/remade.^{11,16-19}

Table 1a Satisfaction Scores for Three Data Gathering Points

	Baseline				3 mo after Locator attachment				3 mo after ball attachment			
	Mean	SD	Median	IQR	Mean	SD	Median	IQR	Mean	SD	Median	IQR
General satisfaction	0.9	0.4	1.0	0.5	9.6	0.5	9.5	1.0	9.6	0.4	9.5	0.8
Cleaning	8.7	0.9	8.5	1.2	9.0	0.6	9.0	1.0	9.0	0.6	9.0	1.0
Speech	7.1	1.1	7.5	1.8	9.2	0.6	9.2	1.0	9.2	0.6	9.0	0.8
Comfort	2.2	0.8	2.5	1.0	9.3	0.5	9.5	0.6	9.2	0.7	9.5	0.8
Appearance	4.7	0.9	4.5	1.2	9.4	0.6	9.5	1.0	9.4	0.4	0.4	9.5
Stability	0.5	1.1	0.5	0.5	9.3	0.5	9.2	0.6	9.4	0.5	9.3	0.5
Ability to chew	0.5	0.4	0.5	0.4	9.6	0.4	9.5	0.6	9.8	0.3	10.0	0.5
Function	1.5	1.4	1.0	1.8	8.9	0.7	9.0	1.0	9.1	0.7	8.5	1.0

SD = standard deviation; IQR = interquartile range.

Table 1b Differences in Satisfaction Between Baseline and Two Attachment Designs, and Between the Two Attachment Designs as Determined by Nonparametric Two-Related Samples Test (Wilcoxon's signed rank)

	Baseline (ball)			Baseline (Locator)			Ball-Locator		
	Median of difference	P	IQR	Median of difference	P	IQR	Median of difference	P	IQR
General satisfaction	8.5	.5	8.57E-08	8.5	0.5	9.10 E-08	0	0	0.662
Cleaning	0.5	2.0	0.252	0.5	1.75	0.218	0	0	0.892
Speech	2.0	1.15	1.65E-06	2.0	1.5	1.61E-06	0	.25	1.0
Comfort	7.0	1.0	1.26E-07	7.0	1.25	1.20E-07	0	.75	0.451
Appearance	4.5	1.25	1.12E-07	4.5	1.5	1.25E-07	0	0	0.704
Stability	9.0	1.0	8.33E-08	9.0	1.0	9.38E-08	0	.5	0.56
Ability to chew	9.5	.7	7.14E-08	9.0	0.5	1.08E-07	0	.5	0.0658
Function	7.7	1.6	1.24E-07	7.7	1.5	1.29E-07	0	.5	0.798

Data Analysis

The primary outcome variables were patient preference and satisfaction ratings on the VAS. The satisfaction scores for each of the domains of the satisfaction questionnaires were entered into a spreadsheet and analyzed using SPSS for Windows (IBM). Mean values, standard deviation, median values, and interquartile ranges were calculated for each attachment type and at baseline for each of the domains. Comparison between baseline scores and each of the two retaining designs and between both retainer designs was done using nonparametric tests for two related samples (Wilcoxon signed rank test). The secondary objective was determination of peri-implant conditions and the postinsertion maintenance efforts for the retainer selected for the follow-up period. These parameters were recorded in a descriptive statistical manner, tabulated, and evaluated. Categorical variables for nonparametric data were compared using the chi-square test; continuous variables were tested with the Mann-Whitney *U* test. *P* < .05 was taken as the statistical significance level.

RESULTS

Nineteen patients (38 implants) could be followed throughout the clinical crossover study and could also be included in the 1-year follow-up program. Only one patient discontinued the study at an early stage as a result of a cerebral stroke. Thus, attachment preference and subjective satisfaction after wearing both attachment systems for 3 months could be evaluated for 19 patients in a crossover trial.

The subjective satisfaction scores with mandibular edentulism treated with implant-retained mandibular overdentures using ball attachments or Locator systems as obtained in this crossover trial are presented in Table 1a. Significant improvement (*P* < .05) was seen for all items between complete dentures (baseline = old dentures without implants) and implant retained ball/Locator anchored overdentures (Tables 1a and 1b). However, after comparing both attachment types for the 19 patients, no significant differences for general satisfaction, comfort, speech, esthetics, chewing ability, or denture stability could be identified (Table 1b).

Table 2 Satisfaction Scores for Definitive Attachments After 1 Year of Clinical Function

	Ball attachment (n = 10)				Locator attachment (n = 9)			
	Mean	SD	Median	IQR	Mean	SD	Median	IQR
General satisfaction	9.5	0.43	9.5	0.87	9.6	0.43	10.0	0.5
Cleaning	8.7	0.48	8.7	0.5	8.7	0.56	9.0	0.5
Speech	9.05	0.68	9.0	1.0	9.9	0.63	9.0	1.0
Comfort	9.05	0.72	9.0	0.87	9.2	0.66	9.5	0.5
Appearance	9.2	0.35	9.0	0.37	9.05	0.72	9.0	1.0
Stability	9.3	0.35	9.25	0.5	9.38	0.54	9.5	1.0
Ability to chew	9.7	0.42	10.0	0.5	9.55	0.46	9.5	1.0
Function	8.9	0.17	9.5	1.0	9.27	0.71	9.5	1.0

SD = standard deviation; IQR = interquartile range.

Table 3 Peri-implant Parameters for Ball and Locator Attachment After 1 Year of Function

	Ball attachments*			Locator attachments†		
	Mean	SD	Median	Mean	SD	Median
Bone loss (mm)	1.6	0.4	1.7	1.5	0.8	1.6
Probing depth (mm)	3.6	0.8	4.0	3.3	0.8	3.0
Periotest values	-3.4	1.1	-3.0	-3.5	1.1	-3.0
Plaque Index (0–3)	0.4	0.6	0.0	0.4	0.6	0.0
Gingival Index (0–3)	0.3	0.4	0.0	0.3	0.5	0.0
Bleeding Index (0–3)	0.4	0.5	0.0	0.5	0.5	0.0
Calculus Index (0–1)	0.2	0.4	0.0	0.3	0.4	0.0

* = 10 patients, 20 implants. † = 9 patients, 18 implants. SD = standard deviation.

At the end of the comparative crossover experiment, 10 patients voted for the ball attachments and 9 for the Locator attachments, thereby indicating them as their preferred attachments. No preference for one attachment type versus the other was seen and no attachment had to be changed so that the last attachment inserted was also the definitive attachment.

As a result of the number of patients, and of the finally selected attachments, two similar-sized study populations were generated (10 patients with ball attachments and 9 patients with Locator attachments) who fulfilled the criteria for a cohort sample to be compared. Table 2 shows the final evaluation of patient satisfaction with ball or Locator attachment systems after 1 year of clinical function. There were no differences for patient satisfaction scores when 3-month and 1-year data were compared (Tables 1a, 1b, and 2).

With no implant losses seen for the 19 patients evaluated, the cumulative survival rate was 100%. In addition, all implants fulfilled the success criteria as previously defined, thus providing a 100% success rate.

The peri-implant/attachment parameters after 1 year of clinical use of the implant-retained overdentures using both ball anchor and Locator attachments are presented in Table 3. There were no differences for marginal

bone resorption, pocket depth, Plaque Index, Bleeding Index, Gingival Index, and Calculus Index between ball anchor and Locator attachments for all patients evaluated.

Table 4 illustrates the incidence of postinsertion prosthodontic maintenance efforts for patients (19 two-implant retained mandibular overdentures with a total of 38 attachments) with ball anchors (n = 20) and Locator attachments (n = 18) during the 1-year follow-up period. The majority of visits for complications/repairs were not directly related to the respective attachment system used. The overall incidence of postinsertion maintenance efforts did not differ between the two types of retention modalities used (maintenance/year/patients: 1.2 [ball] versus 1.4 [Locator]; Table 4). However, 2 of 20 attachments (10%) required activation of the ball anchors and 4 of 18 attachments needed renewing (increasing) of the acrylic retention of Locator attachments (22.2%) ($P < .05$). Ten patients (5 in ball group, 5 in Locator group) described soft tissue discomfort, which was resolved by rebasing or relining (denture margin adaptation) of the prostheses. Opposite denture maintenance efforts (n = 4; 2 rebasing, 1 denture fracture, and 1 tooth fracture) showed no significant difference between the two retention systems.

Table 4 Prosthodontic Maintenance and Complications for Implant-Supported Mandibular Overdentures Retained by Ball or Locator Attachment After 1 Year of Function

Implant prosthesis (IP)	Ball attachment*	Locator attachment†	Total
Implant component maintenance			
Attachment (ball/Locator) loosening	1	1	2
Attachment (ball/Locator) worn/fracture	1	0	1
Implant prosthodontic maintenance			
Matrix activation/renewed	2	4	6
Prosthesis teeth fracture/renewed	0	1	1
Overdenture (prosthesis) fracture	1	0	1
Denture margin adaption (red/relined)	5	4	9
Overdenture rebased	0	1	1
Opposite prosthodontic maintenance (OpD)			
Denture teeth fracture (renewed)	0	1	1
Denture rebased	1	1	2
Denture renewed	1	0	1
Total (OpD)	12	13	25
Mainetance/y/patient	1.2	1.4	1.3

* = 10 patients; † = 9 patients.

DISCUSSION

The present results confirm the established evidence showing a significantly improved satisfaction among edentulous patients with their prostheses when implants were used for retaining mandibular overdentures.^{1–5} Regardless of the attachment system used, IODs and the anchoring mechanisms have been described as superior to complete dentures.^{2–5} Several studies have reported successful use of balls, magnets, and double crowns for IOD retention.^{14–16,33} Nevertheless, the ball attachment continues to be the most common attachment type used for unlinked implants, while magnets or double crowns are used only in rare instances.^{12,14–16,23,33}

However, differences in the extent of prosthetic postinsertion maintenance efforts and in subjective patient preference for attachments have been described for different anchoring mechanisms.^{9,17–20,26} In separate clinical crossover studies, van Kampen et al¹⁴ and Cune et al^{15,22} compared ball anchors and magnets and reported a significantly higher patient satisfaction score for the ball anchors. Data for postinsertion maintenance efforts comparing single attachments, such as ball anchors, and other devices such as bars, magnets, and double crowns are controversial.^{12,16,33–35} In separate studies, Walton et al,²⁰ Cune et al,^{12,22} and Krennmaier et al³³ found more postinsertion maintenance for ball anchors (versus bar or double crowns), while other investigators could not confirm these findings.²⁴

As a result of the intensive postinsertion prosthodontic aftercare required,^{17–20} several manufacturers have

developed a new self-aligning single attachment system called Locator.^{25–27} The Locator system was introduced in clinical practice to compete with the ball anchor for clinicians and patients.²⁷ The Locator system features inserts with different retention modalities which can be easily renewed and changed by clinicians to improve potential loosening. As yet, only a few comparative studies have reported on the Locator system in the anchoring of two-implant supported overdentures.²⁷

While the present study initially had a crossover design, it was extended to comprise a 1-year longitudinal follow-up extension study on account of the homogenous distribution of the patient population after 3 months. In the initial crossover trial, patients had the opportunity to experience all treatment modalities and could personally compare and finally choose the attachment they considered as best.^{2,14,15} The basic scores for the old prostheses and, thereafter, for the implant-supported mandibular overdentures retained with either ball or Locator attachment are consistent with those obtained in other investigations using the same questionnaires and scale setup.^{15,28} However, the patient satisfaction observed with Locator and conventional ball anchors showed no significant differences between the two single attachment systems. Interestingly, all patients were similarly satisfied with Locator and ball anchors and when questioned regarding their preference, the patients showed no differentiation and no marked preference for either system.²⁷ In this respect, the results obtained differ from the results for comparisons between ball anchors and magnets, invariably showing significant differences and a preference in favor of

ball anchors.^{14,15,22} As comparisons of ball anchors and double crowns showed similar subjective evaluations with regard to satisfaction, the properties of matrix and patrix as being used with ball anchors, double crowns, and Locator attachments are to be considered as being the primary reasons for subjective patient satisfaction.^{14,33–35}

Different single attachments for anchoring implant-retained overdentures show different incidence rates with regard to prosthodontic postinsertion care.^{17–20,25,36} In a recently published study of ball anchors and Locator in overdenture anchoring, the authors reported an increased need of aftercare with the Locator compared with the ball anchor.²⁷ The 12-month longitudinal study in the present study allowed confirmation of the finding of increased postinsertion maintenance with the Locator attachment. Such general comparisons of different types of matrixes with ball anchors have already been reported by other authors.^{14,15,35} As compared to the different matrixes of ball attachments, it could be shown that matrixes with rubber O-rings required more postinsertion maintenance efforts than those with metal lamellae.^{12,23,36,37} Rubber O-rings are susceptible to stress and environmental forces such as friction, heat, and commercially available denture cleaning agents. Thus, the large amount of maintenance for ball attachments as observed by Burns et al^{36,37} and Naert et al^{12,23} must be attributed to the use of rubber O-ring attachments. As the Locator attachments also dispose of a plastic matrix, similar to that of the rubber O-ring attachments of ball anchors, similarity and, consequently, similar reasons for the increased aftercare can be assumed.^{25,35,36} It is a known fact that the two-implant retained overdenture forms a rotational axis³⁸ and, consequently, abrasion and increased wear of the acrylic parts of the Locator attachment are possible.^{12,39,40} The results of the present study confirm recently reported data describing increased postinsertion maintenance needs for retention with Locators and allow for discussion of the increased abrasion of the vicrylic insert on the Locator compared with that of the metallic lamellae of conventional anchors as a possible reason for this increased maintenance.^{25,39,40}

In regard to peri-implant conditions, both anchoring elements showed no marked differences throughout the follow-up period and thus confirmed the data for other successfully used single attachments.^{12,14–17,23,42} Especially, the soft tissue parameters such as Plaque Index and Bleeding Index showed no differences between ball anchors and Locator attachments, confirming that both types of attachment allow for adequate cleaning care by the patient population and thus acceptable hygiene findings.^{12,23,42}

These 1-year data for peri-implant parameters can only be considered as preliminary results. However, it was the authors' intention to include these patients

in the present study, having decided for either Locator attachments or ball anchors in an extended prospective 3-year study, and to especially evaluate and compare the postinsertion maintenance needs with the two types of attachment. As a secondary objective of this proposed study, potential differences in purchasing and maintenance costs between the two types of retention elements shall be assessed.²⁵

Overall, the results obtained for the present study show that the null hypothesis could be confirmed. No differences between the two retention types in regard to patient satisfaction or preference for one of the attachment systems could be identified. While no differences with regard to peri-implant parameters and prosthetic maintenance efforts could be discerned, the Locator attachment showed a slightly (nonsignificant) increased maintenance need with more frequent matrix activation.^{27,43}

CONCLUSION

Based on this clinical review, the following was observed:

1. Both Locator and ball attachments used on isolated implants in the atrophic mandible are viable treatment options retaining two-implant supported mandibular overdentures.
2. Excellent general satisfaction from a patient perspective was noted without subjective differences or any preference for one of the retention systems used.
3. Prosthodontic maintenance efforts did not differ between ball and Locator attachment systems but showed a slightly (nonsignificant) increased maintenance need for the Locator with more frequent matrix activation.

ACKNOWLEDGMENTS

The Camlog Foundation of Switzerland supported this study. The authors reported no conflicts of interest related to this study.

REFERENCES

1. Attard NJ, Zarb GA. Long-term treatment outcomes in edentulous patients with implant overdentures: The Toronto study. *Int J Prosthodont* 2004;17:425–433.
2. Awad MA, Lund JP, Dufresne E, Feine JS. Comparing the efficacy of mandibular implant-retained overdentures and conventional dentures among middle-aged edentulous patients: Satisfaction and functional assessment. *Int J Prosthodont* 2003;16:117–122.
3. Jemt T, Chai J, Harnett J, et al. A 5-year prospective multicenter follow-up report on overdentures supported by osseointegrated implants. *Int J Oral Maxillofac Implants* 1996;11:291–298.

4. Batenburg RH, Meijer HJ, Raghoobar GM, van Oort RP, Boering G. Mandibular overdentures supported by two Bränemark, IMZ, or ITI implants. A prospective comparative preliminary study: One year results. *Clin Oral Implants Res* 1998;9:374–383.
5. Feine JS, Carlsson GE, Awad MA, et al. The McGill consensus statement on overdenture. Mandibular two-implant overdentures as first choice standard of care for edentulous patients. *Int J Oral Maxillofac Implants* 2002;17:601–602.
6. Batenburg RH, Raghoobar GM, van Oort RP, Heijdenrijk K, Boering G. Mandibular overdentures supported by two or four endosteal implants: A prospective, comparative study. *Int J Oral Maxillofac Surg* 1998;27:435–439.
7. Meijer HJ, Batenburg RH, Raghoobar GM, Vissink A. Mandibular overdentures supported by two Bränemark, IMZ or ITI implants: A 5-year prospective study. *J Clin Periodontol* 2004;31:522–526.
8. Krennmaier G, Krainhöfner M, Piehslinger E. The influence of bar design (round versus milled bar) on prosthodontic maintenance of mandibular overdentures supported by 4 implants: A 5-year prospective study. *Int J Prosthodont* 2008;21:514–520.
9. Weinländer M, Piehslinger E, Krennmaier G. Removable implant-prosthetic rehabilitation of the edentulous mandible: 5-year results of different prosthetic anchorage concepts. *Int J Oral Maxillofac Implants* 2010;25:589–597.
10. Visser A, Raghoobar GM, Meijer HJ, Batenburg RH, Vissink A. Mandibular overdentures supported by two or four endosseous implants. A 5-year prospective study. *Clin Oral Implants Res* 2005;16:19–25.
11. Krennmaier G, Krainhöfner M, Piehslinger E. Implant-supported mandibular overdentures retained with a milled bar: A retrospective study. *Int J Oral Maxillofac Implants* 2007;22:987–994.
12. Naert I, Gizani S, Vuylsteke M, van Steenberghe D. A 5-year prospective randomized clinical trial on the influence of splinted and unsplinted oral implants retaining a mandibular overdenture: Prosthetic aspects and patient satisfaction. *J Oral Rehabil* 1999;26:195–202.
13. Zitzman NU, Sendi P, Marinello CP. An economic evaluation of implant treatment in edentulous patients: Preliminary results. *Int J Prosthodont* 2005;18:20–27.
14. Kampen van F, Cune M, van der Bilt A, Bosman F. Retention and postinsertion maintenance of bar-clip, ball and magnet attachments in mandibular implant overdenture treatment: An in vivo comparison after 3 months of function. *Clin Oral Implants Res* 2003;14:720–726.
15. Cune M, van Kampen F, van der Bilt A, Bosman F. Patient satisfaction and preference with magnet, bar-clip, and ball-socket retained mandibular implant overdentures: A cross-over clinical trial. *Int J Prosthodont* 2005;18:99–105.
16. Ellis JS, Burawi G, Walls A, Thomason JM. Patient satisfaction with two designs of implant supported removable overdentures; ball attachment and magnets. *Clin Oral Implants Res* 2009;20:1293–1298.
17. MacEntee MI, Walton JN, Glick N. A clinical trial of patients satisfaction and prosthodontic needs with ball and bar attachments for implant-retained complete overdentures: Three-year results. *J Prosthet Dent* 2005;93:28–37.
18. Payne AG, Solomons YF. Mandibular implant-supported overdentures: A prospective evaluation of the burden prosthodontic maintenance with 3 different attachment systems. *Int J Prosthodont* 2000;13:246–253.
19. Payne AG, Solomons YF. The prosthodontic maintenance requirements of mandibular mucosa- and implant-supported overdentures: A review of the literature. *Int J Prosthodont* 2000;13:238–243.
20. Walton JN, MacEntee MI. A prospective study on the maintenance of implant prostheses in private practice. *Int J Prosthodont* 1997;10:453–458.
21. Cooper LF, Moriarty JD, Guckles AD, et al. Five-year prospective evaluation of mandibular overdentures retained by two microthreaded, TiOblast nonsplinted implants and retentive ball anchors. *Int J Oral Maxillofac Implants* 2008;23:696–704.
22. Cune M, Burgers M, van Kampen F, de Putter C, van der Bilt A. Mandibular overdentures retained by two implants: 10-year results from a crossover clinical trial comparing ball-socket and bar-clip attachments. *Int J Prosthodont* 2010;23:310–317.
23. Naert I, Alsaadi G, van Steenberghe D, Quirynen M. A 10-year randomized clinical trial on the influence of splinted and unsplinted oral implants retaining mandibular overdentures: Peri-implant outcome. *Int J Oral Maxillofac Implants* 2004;19:695–702.
24. Gotfredsen K, Holm B. Implant-supported mandibular overdentures retained with ball or bar attachments: A randomized prospective 5-year study. *Int J Prosthodont* 2000;13:125–130.
25. Kleis WK, Kämmerer PW, Hartmann S, Al-Nawas B, Wagner W. A comparison of three different attachment systems for mandibular-two-implant overdentures: One year report. *Clin Implant Dent Relat Res* 2010;12:209–218.
26. Bilhan H, Geckili O, Mumcu E, Bilmenoglu C. Maintenance requirements associated with mandibular implant overdentures: Clinical results after first year of service. *J Oral Implantol* 2011;37:697–704.
27. Bilhan H, Geckili O, Sulun T, Bilgin T. A quality-of-life comparison between self-aligning and ball attachment system for 2-implant-retained mandibular overdentures. *J Oral Rehabil* 2011;37:167–173.
28. De Grandmont P, Feine J, Tache R, et al. Within-subject comparisons of implant-supported mandibular prostheses: Psychometric evaluation. *J Dent Res* 1994;73:1096–1104.
29. Mombelli A, van Oosten MA, Schürch E Jr, Lang NP. The microbiota associated with successful or failing osseointegrated titanium implants. *Oral Microbiol Immunol* 1987;2:145–151.
30. Salvi GE, Lang NP. Diagnostic parameters for monitoring peri-implant conditions. *Int J Oral Maxillofac Implants* 2004;19(suppl):116–127.
31. Apse P, Zarb GA, Schmitt A, Lewis DW. The longitudinal effectiveness of osseointegrated dental implants. The Toronto study: Peri-implant mucosal response. *Int J Periodontics Restorative Dent* 1991;11:95–111.
32. Aparicio C. The use of the Periotest value as the initial success criteria of an implant: 8-year report. *Int J Periodontics Restorative Dent* 1997;17:151–161.
33. Krennmaier G, Weinländer M, Krainhöfner M, Piehslinger E. Implant-supported mandibular overdentures retained with ball or telescopic crown attachments: A 3-year prospective study. *Int J Prosthodont* 2006;19:164–170.
34. Heckmann SM, Schrott A, Graef F, Wichmann MG, Weber HP. Mandibular-two-implant telescopic overdentures. *Clin Oral Implants Res* 2004;15:560–569.
35. Krennmaier G, Seemann R, Weinländer M, Piehslinger E. Comparison of ball and telescopic crown attachments in implant-retained mandibular overdentures. A 5-year prospective study. *Int J Oral Maxillofac Implants* 2011;26:598–606.
36. Burns DR, Unger JW, Elswick RK Jr, Beck DA. Prospective clinical evaluation of mandibular implant overdentures: Part I. Retention, stability and tissue response. *J Prosthet Dent* 1995;73:354–363.
37. Burns DR, Unger JW, Elswick RK Jr, Giglio JA. Prospective clinical evaluation of mandibular implant overdentures: Part II. Patient satisfaction and preference. *J Prosthet Dent* 1995;73:364–369.
38. Kimoto S, Pan S, Drolet N, Feine JS. Rotational movements of mandibular two-implant overdentures. *Clin Oral Implants Res* 2009;20:838–843.
39. Wolf K, Ludwig K, Hartfil H, Kern M. Analysis of retention and wear of ball attachments. *Quintessence Int* 2009;40:405–412.
40. Holst S, Blatz MB, Eitner S, Wichmann M. In vitro wear of different material combinations of intracoronal precision attachments. *Int J Prosthodont* 2006;19:330–332.
41. Cehreli MC, Uysal S, Akca K. Marginal bone level changes and prosthetic maintenance of mandibular overdentures supported by 2 implants: A 5-year randomized clinical trial. *Clin Implants Dent Relat Res* 2010;12:114–121.
42. Ambard AJ, Fanchiang JC, Mueninghoff L, Dasanayake AP. Cleansability of and patients' satisfaction with implant-retained overdentures: A retrospective comparison of two attachment methods. *J Am Dent Assoc* 2002;133:1237–1242.
43. Bayer S, Steinheuser D, Grüner M, et al. Comparative study of four retentive anchor systems for implant supported overdentures—retention force changes. *Gerodontology* 2009;26:268–272.

Immediate Restoration of Delayed Placement of Dental Implants in Patients with Treated Periodontal Disease: 1-Year Results

Jacob Horwitz, DMD¹/Liran Levin, DMD²/Eran Gabay, DMD, PhD³/
Otman Zuabi, DMD³/Eli E. Machtei, DMD⁴

Purpose: To evaluate implant and patient characteristics in a prospective clinical study involving immediate fixed restoration of delayed placement of dental implants. **Materials and Methods:** Patients diagnosed with generalized chronic periodontitis and previously treated were accepted into the study when they expressed a wish to receive immediate restoration of dental implants. Treatment planning and implant placement were computer assisted, using computerized tomography, planning software, and a surgical template. Patients received abutments and cemented provisional prostheses no later than 72 hours following implant surgery. Patients were followed at 2 and 4 weeks, and 3, 6, and 12 months. **Results:** Eighteen patients were accepted and completed the study, ages ranged from 34 to 69 years (mean 54.5 ± 8.5 years). Five patients (27.8%) were smokers (2.5 to 60 pack years). Fifty implants were placed, ranging between 1 to 8 implants per patient. Median implant length was 13 mm (range, 10 to 13 mm) and median implant diameter was 3.75 mm (range, 3.75 to 5 mm). Mean insertion torque was $43 \text{ Ncm} \pm 6.2 \text{ SD}$ (range 30 to 50 Ncm). Mean implant stability quotient was 71 ± 11 (range 37 to 85). One implant in a patient who smoked and three implants in another patient who smoked failed for a total of four failed implants. At 12 months, the overall survival rate was 92% (100% and 73% among nonsmokers and smokers, respectively). **Conclusions:** The survival of immediately restored dental implants in periodontally treated patients is greater than 90%. Smokers with a past history of chronic periodontitis seem to have a lower implant survival rate. INT J ORAL MAXILLOFAC IMPLANTS 2012;27:1569–1575

Key words: bone loss, implant failure, implant success, implant survival, periodontitis

Implant therapy has become a predictable and successful treatment option for the replacement of missing teeth. Currently, this therapeutic approach is an option for the treatment of a large spectrum of patients, including fully edentulous cases,¹ trauma cases,² partial edentulism,^{3,4} as well as single-tooth replacement.⁵ Today, placement protocols include

immediate, delayed, and late implant placement. In a structured review and meta-analysis, Esposito et al suggested that immediate and immediate-delayed implants might be at a higher risk of implant failure and complications compared with delayed implants.⁶ Restoration/loading of implants can also be categorized into immediate, delayed, or late. On a patient, (rather than a per-implant) basis, a structured meta-analysis reported no statistically significant differences between any of these approaches, but suggested that immediately loaded implants failed more often than those conventionally loaded, but less commonly than those loaded early. It was suggested that immediately loading (within 1 week) is preferable over waiting for 1 or 2 months before implant loading. A high degree of primary implant stability (high insertion torque) seemed to be one of the prerequisites for a successful immediate/early loading procedure.⁷ Immediate implant restoration has been gaining popularity, mainly due to a shortened treatment time and the elimination of the need for removable interim restorations.

Patients with a history of periodontal disease, or periodontally compromised patients, are a subgroup of special interest because a moderate level of evidence

¹ Assistant Professor, Acting Director, Department of Periodontology, Rambam School of Graduate Dentistry, Rambam Health Care Campus and Technion Ruth & Bruce Rappaport Faculty of Medicine, Haifa, Israel.

² Assistant Professor, Department of Periodontology, Rambam School of Graduate Dentistry, Rambam Health Care Campus and Technion Ruth & Bruce Rappaport Faculty of Medicine, Haifa, Israel.

³ Private practice, Haifa, Israel.

⁴ Professor, Chair- Department of Periodontology, Rambam School of Graduate Dentistry, Rambam Health Care Campus and Technion Ruth & Bruce Rappaport Faculty of Medicine, Haifa, Israel.

Correspondence to: Dr Jacob Horwitz, Department of Periodontology, School of Graduate Dentistry, Rambam Health Care Campus, PO Box 9602, 31096 Haifa, Israel.
Email: j_horwitz@rambam.health.gov.il

indicates that periodontitis subjects might be at significantly higher risk for implant failure and greater marginal bone loss compared with periodontally healthy subjects.⁸ In a recent review of implant loading protocols for the partially edentulous esthetic zone, Grütter et al found that the survival of immediately loaded implants was 97.3% after 1 year. However, for immediately placed implants with immediate restoration and occlusal loading, the survival rate dropped by approximately 10%.⁹ Also, in the authors' previous study of immediate and delayed restoration of dental implants in periodontally susceptible patients, survival rates of 65% were reported in extraction sites versus 94% in healed sites.¹⁰ Therefore, stricter inclusion criteria were deemed necessary in order to improve the survival rate of immediately restored dental implants.

The aims of the present study were to prospectively evaluate the survival of immediately restored dental implants and examine various implant and patient characteristics in a prospective clinical study involving immediate restoration in delayed (nonextraction) implant sites in partially edentulous patients with treated periodontal disease.

MATERIALS AND METHODS

Patients previously diagnosed with and treated for generalized chronic periodontitis¹¹ at the Rambam Health Care Campus (RHCC) Department of Periodontology, Haifa, Israel, were invited to participate in the study after expressing a wish to receive dental implants with immediate restoration. The study was conducted according to Helsinki declaration guidelines and was initially approved by the RHCC institutional review board (approval #2301). Patients were given detailed explanations on the nature of alternative treatment options and the proposed treatment plan. Upon acceptance, patients signed a consent form. Patients were accepted into the study if they met the following criteria: (1) age between 18 and 75 years; (2) good general health, no complicating systemic conditions that contraindicated surgical periodontal and implant treatment and/or radiographic evaluation (eg, pregnancy, uncontrolled diabetes, cancer/radiation therapy, bisphosphonate therapy), no allergy to antibiotics; (3) active periodontal therapy completed; (4) Plaque Index (PI) ≤ 1 according to a modification of the Silness and Loe Plaque Index,¹² whereby recording only the highest score for each tooth/dental unit and dividing the sum by the number of teeth/dental units; (5) bleeding on probing (BoP)¹³ ≤ 10% (six recordings per tooth); (6) extractions were performed at least 8 weeks prior to proposed implant therapy date; (7) available bone height in periapical radiographs ≥ 10 mm, measured

from the radiographic crestal bone; (8) no bone augmentation indicated in conjunction with proposed implant therapy. Smoking was not an exclusion criterion. Baseline periodontal parameters were recorded, including PI, probing pocket depth (PPD), and BoP. In addition, demographic and environmental data were recorded for each patient.

Plaster models and a radiographic template were prepared and the patients were sent for cone beam computed tomography (CBCT) with the radiographic template. The CBCT was utilized for surgical treatment planning and also to verify the presence of adequate bone volume and absence of pathologies that might prohibit/interfere with implant installation. Implant placement planning was performed using dedicated software (Med3D). After receiving patient consent for the final treatment plan, the dental laboratory fabricated a surgical template. Implant surgery was performed under local anesthesia. A crestal incision was performed, flaps were elevated, and the edentulous ridge exposed. Osteotomies were performed with the aid of the surgical template, using 2-mm and 2.8-mm drills. The final single use drill, provided with the implants, was used without the template in place. Implants (SEVEN, MIS Implants Technologies) were inserted using a torque controlled physio-dispenser with a gradual increase of torque power (in 5 Ncm increments) until proper seating of the implant, and the final torque was recorded. When all implants were in place, transfers were connected to the implants, the area was isolated with a rubber dam, and impressions were obtained using Polyvinylsiloxane putty and wash (GC Exaflex, GC Europe). Healing abutments were connected to the implants, suturing of the flaps was performed, and patients were given postoperative instructions and prescribed a chlorhexidine gluconate 0.2% mouthwash (TaroDent, Taro Pharmaceutical Industries) two times/day and amoxicillin 875 mg with clavulanic acid 125 mg (Augmentin, Glaxosmith Kline) two tabs/day for 7 days, as well as OTC analgesics as necessary. Impressions were sent to the laboratory for selection and adjustment of abutments and fabrication of a provisional metal reinforced acrylic restoration. Three days after implant surgery, healing abutments were replaced with implant abutments, torqued at 20 to 25 Ncm, and the provisional restoration was placed, adjusted, and cemented. Care was taken to adjust the restoration so as to avoid tight contacts with adjacent teeth and to eliminate contact with the opposing dentition at centric occlusion and in excursions. Patients were seen for suture removal 10 to 14 days after surgery and then at 4 weeks and 3, 6, and 12 months for maintenance appointments consisting of data collection, plaque control and motivation, tooth and implant cleaning, and scaling and root planing as necessary. Following

the 6-month visit and verification of implant stability, patients were referred to their dentists for fabrication and delivery of the final fixed prostheses. Patients were discharged from the study following completion of the 12-month examination.

Data were recorded at baseline, 6, and 12 months. The following parameters were recorded for each implant: implant site, length, and diameter; insertion torque and implant stability quotient (ISQ) implant surgery, bone type¹⁴ at implant surgery; digital periapical radiographs were taken with a parallelism appliance, attempting to align the radiographic plate parallel to the implants. Radiographic bone level (mesial and distal) was measured from implant shoulder to the alveolar crest.

Data Management and Analysis

Data analysis was performed using SPSS statistical software (IBM). Descriptive statistics were initially used. Data were further analyzed by implant and by patient in order to account for dependence between them. The speed of change in bone level (rate) was computed as the difference in bone level between measurements in two timepoints divided by the actual time in months, and multiplied by 12, expressed in mm/year. Positive values indicate bone loss and negative values indicate bone gain. A Wilcoxon nonparametric test was used to compare rate between 0–6 months and 6–12 months (rate 0–6 and rate 6–12). Analysis of variance (ANOVA) with Bonferroni adjustment post hoc multiple comparison test was used to evaluate the relationship between rate and baseline bone level. Significance was set at 5%.

RESULTS

Eighteen patients with a total of 50 implants were accepted and treated in this study (Table 1); 1-year radiographic data was missing for one patient who received two implants. Age ranged between 34 and 69 years (mean 54 ± 8.5 years). Implant surgery was completed with only minor postoperative side effects; these included transient gingival redness in one patient and a slight transient facial hematoma in another patient. Five patients were smokers, with an exposure ranging from 2.5 to 60 pack years. Fifty implants were placed, ranging from 1 to 8 implants per patient (See Table 2). Implant length ranged from 10 to 13 mm (median 13 mm) and implant diameter range was 3.75 to 5 mm (median, 3.75 mm). Mean insertion torque was 43 Ncm ± 6.2 SD (range 30 to 50 Ncm). Mean ISQ at implant placement was 71 ± 11 SD (range 37 to 85) (Table 3).

The four implants that failed were all in smokers: one was a single-unit implant in a smoker and three implants in another smoker (of which one was a single

Table 1 Patient and Implant Data

Patient no.	Implant site	Type of restoration	Length (mm)	Diameter (mm)
1	16	M	10	3.75
1	15	M	11.5	3.75
1	14	M	13	3.75
1	22	S	13	3.75
1	24	M	13	3.75
1	25	M	13	3.75
1	26	M	13	4.2
1	27	M	13	4.2
2	14	M	13	4.2
2	15	M	13	4.2
2	16	M	11.5	4.2
3	45	M	13	4.2
3	46	M	10	4.2
3	47	M	10	5
4	36*	S	13	4.2
5	44	M	13	4.2
5	45	M	10	4.2
5	46	M	10	4.2
6	24*	S	13	4.2
6	14*	M	13	3.75
6	15*	M	10	4.2
6	44	S	13	4.2
7	14	M	13	4.2
7	15	M	11.5	4.2
8	32	M	13	3.75
8	42	M	13	3.75
9	35	M	13	4.2
9	36	M	13	4.2
10	24	M	13	3.75
10	26	M	13	4.2
11	24	M	13	4.2
11	25	M	10	4.2
12	22	S	13	3.75
13	24	M	11.5	3.75
13	25	M	11.5	4.2
14	32	M	13	3.75
14	42	M	13	3.75
15	42	M	13	3.75
15	44	M	13	3.75
15	45	M	13	3.75
16	14	M	13	3.75
16	15	M	13	3.75
16	16	M	13	3.75
16	24	M	13	3.75
16	25	M	13	4.2
17	24	M	11.5	3.75
17	25	M	13	3.75
17	26	M	11.5	3.75
18	32	M	13	3.75
18	42	M	13	3.75

*Failed implants.

S = single unit restoration; M = unit in multiple restoration.

Table 2 Distribution of Implants Between Patients

No. of implants per patient	No. of patients	Single restoration	Multiple unit restoration	Total
1	2	2	0	2
2	8	0	16	16
3	5	0	15	15
4	1	2	2	4
5	1	0	5	5
8	1	1	7	8
Total	18	5	45	50

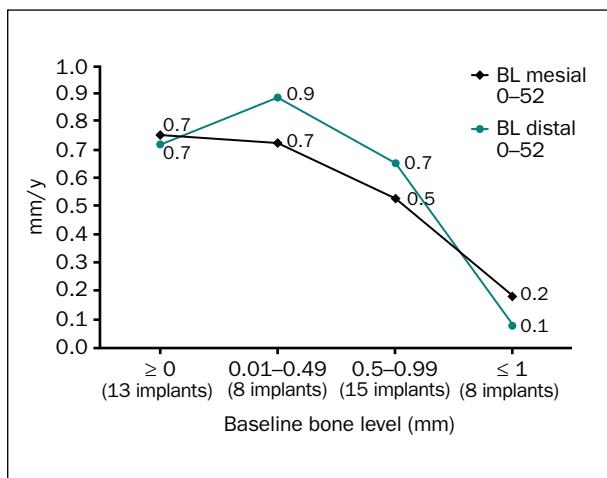


Fig 1 Relation between mean 1-year bone level changes (BL) and baseline bone level. Implants were stratified according to the distance between implant shoulder and the alveolar bone crest at baseline. Four categories of baseline bone levels were used: ≤ 0 mm, 0.01 to 0.49 mm, 0.5 to 0.99 mm, and ≥ 1 mm. Statistically significant differences between group ≥ 1 and ≤ 0 ($P = .03$) and between group ≥ 1 and 0.01 to 0.49 ($P = .01$). Rates as marked in the figure were rounded to the nearest first decimal point.

unit, and the other two were splinted in a two-unit restoration). All these implants were removed and successfully replaced by new implants that were placed 2 to 3 months after removal, without immediate restoration (replacement implants not included in the analysis).

The 12-month overall survival rate was 92% (46 of 50). Implant survival rate among nonsmokers was 100% (35 of 35) while among smokers survival rate was 73% (11 of 15). Survival rate excluding single implant restorations was 96% (43 of 45).

Implant based statistical analysis showed that rate mesial 0–12 was 0.7 ± 0.5 SD mm/year (range –0.3 to 2.1) and rate distal 0–12 was 0.6 ± 0.5 SD mm/year (range –0.5 to 1.8). Rate mesial 0–6 was 0.7 ± 1.0 SD mm/year

Table 3 General Implant Data

	Mean \pm SD	Median	Range
Implant length (mm)	12.37 ± 1.10	13.00	10–13
Implant diameter (mm)	$3.98 \pm .268$	3.75	3.75–5.00
Insertion torque (Ncm)	43.78 ± 6.25	45	30–50
ISQ	71.80 ± 11.10	75.00	37–85

ISQ = implant stability quotient.

(range –2.3 to 3.0) and rate mesial 6–12 was 0.7 ± 1.1 SD mm/year (range –1.3 to 4.3). Rate distal 0–6 was 1.0 ± 0.9 SD mm/year (range –0.6 to 4.0) and rate distal 6–12 was 0.2 ± 0.9 SD mm/year (range –1.4 to 2.7). The difference between rate distal 0–6 and 6–12 and the difference between rate distal 0–6 and 0–12 were statistically significant ($P = .001$ for both) (Table 4b). Patient based statistical analysis showed similar results (data on file), the difference between rate distal 0–6 and rate distal 6–12 and the difference between rate distal 0–6 and rate distal 0–12 being statistically significant ($P = .039$ and $P = .026$, respectively). Bone changes are presented both as absolute changes (Table 4a) as well as the rate of bone change (Table 4b) which accounts for the range of times that patients were actually examined around their scheduled appointments.

The relationship between baseline bone level and rate is presented in Fig 1. Implants were stratified according to baseline bone level to four categories: (1) ≤ 0 mm, (2) 0.01–0.49 mm, (3) 0.5–0.99 mm, and (4) ≥ 1 mm. An inverse ratio can be observed whereby the further away the implant is placed from the alveolar crest, the smaller the BL (the difference being statistically significant between groups (4) and (1) ($P = .03$) and between groups (4) and (2) ($P = .01$)).

DISCUSSION

The overall 1-year survival rate of immediately restored dental implants in patients with a history of chronic periodontitis was 92%. Immediate restoration provides the benefit of shorter treatment time and elimination of the need for provisional removable prostheses. Recent reports of survival rates of immediate restoration of dental implants range between 85%¹⁵ and 100%.¹⁶ For comparison, in a recent publication of a prospective evaluation which reported on implant restoration 8 weeks postsurgery,¹⁷ 2 out of 43 implants in 16 patients failed at 8 weeks (survival rate of 95%).

Table 4a Mesial and Distal Radiographic Absolute Bone Change (mm)

	Mean \pm SD	Median	Range
BC mesial 0–6	0.4 \pm 0.6	0.4	-1.4 to 1.6
BC mesial 6–12	0.4 \pm 0.6	0.3	-0.6 to 2.3
BC mesial 0–12	0.8 \pm 0.6	0.8	-0.3 to 2.6
BC distal 0–6	0.6 \pm 0.5	0.5	-0.4 to 2.0
BC distal 6–12	0.1 \pm 0.5	0.1	-1.1 to 1.3
BC distal 0–12	0.7 \pm 0.6	0.7	-0.7 to 2.1

BC = radiographic absolute bone change. BC is presented for 12 months (0–12), for the first 6 months (0–6) and for the time from 6 to 12 months (6–12).

Survival rate in nonsmokers was 100%. A possible explanation for the high survival rate is the use of stricter patient selection criteria, the inclusion of only patients with a clinically stable periodontal state, an inclusion criterion which was demonstrated by low PI and BoP, and having partially edentulous healed sites only.

The difference in implant survival between smokers (73%) and nonsmokers (100%) is large in magnitude but in line with previous reports. Smoking is considered a dose-dependent risk factor for survival of dental implants with a significant association for heavy smokers > 20 cigarettes/day.¹⁸ Failures in the present study occurred in smokers only; one smoker with 2.8 pack years and one smoker with 30 pack years. Smoking has been long associated with biological failures of oral implants.¹⁹ Immediate restoration in periodontally susceptible patients is also prone to decreased survival rates, eg, in a study conducted by Machtei et al, a 90% survival rate after 1 year was observed.²⁰ But the combination of both smoking and periodontitis may be an even more powerful risk factor. Still, according to the present study, when selecting indications for immediate loading, smoking and periodontitis should be considered risk factors and not causative failure agents, since not all implants in smoking patients failed.

A cluster phenomenon was observed,²¹ whereby three of the four failed implants were in one patient. The small sample size precludes generalization; however, a similar observation was made in other studies^{22,23} and in a previous study by the authors.¹⁰

Failed implants are of special interest because they may shed light on parameters that may influence success or failure, especially in cases of immediate loading. Initial low primary stability, as measured by low insertion torque (and possibly also low ISQ levels), and low bone density may contribute to implant failure.²⁴ It is not yet possible to draw concrete conclusions concerning threshold values for implant stability and bone quality/quantity needed for immediate restoration²⁵; yet two of the three failed implants in one pa-

Table 4b Bone Level Change Rate (mm/y)

	Mean \pm SD	Median	Range
Rate mesial 0–6	0.7 \pm 1.0	0.6	-2.3 to 3.0
Rate mesial 6–12	0.7 \pm 1.1	0.5	-1.3 to 4.3
Rate mesial 0–12	0.7 \pm 0.5	0.6	-0.3 to 2.1
Rate distal 0–6*	1.0 \pm 0.9	0.9	-0.6 to 4.0
Rate distal 6–12*	0.2 \pm 0.9	0.2	-1.4 to 2.7
Rate distal 0–12*	0.6 \pm 0.5	0.6	-0.5 to 1.8

Rate is presented for 12 months (0–12), for the first 6 months (0–6) and for the time from 6 to 12 months (6–12).

*Significant difference between rate distal 0–6 and 6–12 and between rate distal 0–6 and 0–12 ($P = .001$ for both).

tient were inserted in type 3 bone, with relatively low insertion torque (30 to 35 Ncm) and ISQ (57 to 59). It was projected that splinting those two implants would enhance their stability; however, the end result was still implant failure. Degidi et al have splinted implants with low (≤ 20 Ncm) to those with high (≥ 25 and ≤ 50 Ncm) insertion torque which improved the success rate of implants with low primary stability using immediate loading protocols for full-arch prostheses.²⁶ Therefore, a method of predicting implant primary stability would be valuable when exploring the option for immediate restoration. Hounsfield bone density (HU), as measured on preoperative computed tomography, has been proposed as such a method; correlation coefficients between insertion torque and HU values were strong and ranged from 0.768²⁷ to 0.859.²⁸ It was suggested that implants should be loaded in sites where radiographic bone density is over 528 HU.²⁷

The study of the impact of occlusion on implants' success was beyond the scope of this study; however, it was noted that the provisional restoration of the lost single unit 13-mm implant, which was inserted with a torque of 50 Ncm and 85 ISQ, was rebonded 10 days after implant placement. Possible explanations for this incident are inadequate cementation at provisional delivery, or heavy occlusal masticatory forces that acted to dislodge the restoration. Three weeks later the implant was removed because of sensitivity and mobility.

In the present study, both absolute bone change and rate of change were reported in order to account for the issue of participants in the study presenting for their examinations at a range of times around their scheduled appointments. Mean 12-month bone loss in the present study was relatively low (0.6 to 0.7 mm/year). Recently Zembić et al reported 1-year results for immediately restored one-piece 3-mm diameter single-tooth implants.²⁹ Mean 1-year bone loss was higher, at 1.6 ± 1.2 mm (range -0.8 to 4.6). While rate distal 6–12 was significantly lower than rate distal 0–6, there was no difference between rate mesial 6–12 and

rate mesial 0–6. This may indicate that different forces act on the mesial and distal surfaces of implants, it may be incidental or influenced by several unknown factors, eg, operator skills, patient factors, or others, which were not investigated in the present study.

The inverse relationship between baseline bone level and subsequent bone loss is in line with previous publications in animal studies³⁰ and in humans,³¹ indicating that subcrestal implant placement leads to higher bone loss, while supracrestal placement limits bone loss. This may indicate the influence that the implant/abutment microgap has on marginal bone levels. These results, however, do not fit the suggestion that supracrestal implant positions may result in higher stress to the marginal bone.³² To the contrary, no negative effect of such stress on alveolar bone levels was observed.

A major drawback to this study is the lack of a conventional loading control group. However, many such publications are available. Recently, Rismanchian et al³³ reported 1-year clinical and radiographic assessment of immediate loading of Astra implants in the posterior maxilla and mandible of 10 patients with an unknown periodontal status whose smoking status was up to 10 cigarettes/day, and received two implants each. They reported a 100% success rate, baseline ISQ of 76.6 ± 6.57 (range 60 to 86) which was slightly higher than the present study and 1-year bone loss of 0.48 ± 0.21 SD mm (range 0.35 to 1.15 mm), which was slightly lower than the present study. In the authors' previous study,^{10,34} baseline insertion torque and ISQ were lower (39.33 ± 1.27 SE Ncm and 64.07 ± 1.90 SE, respectively), whereas first year bone loss was higher (1.19 ± 0.19 SE mm). This may reflect a combination of a better periodontal status and the inclusion of only healed sites (delayed/late implant placement). As mentioned above, this difference may be incidental or influenced by several unknown factors which were not investigated in the present study. In the effort to get the highest success rate and lowest complication and failure rate, patient inclusion criteria may become too stringent, therefore, the right balance has to be found that would be clinically effective. Thresholds have yet to be determined as to what should constitute the proper criteria for immediate restoration of dental implants.

CONCLUSIONS

One year survival of immediately restored dental implants in periodontally treated patients exceeds 90% and falls within the literature range. Smokers with a past history of chronic periodontitis seem to have a lesser survival rate. Finally, thresholds have yet to be determined as to what should constitute the proper criteria for immediate restoration of dental implants.

ACKNOWLEDGMENTS

The authors are deeply grateful to Ms Tanya Mashiaf from the Rambam Health Care Campus Statistical Unit for the statistical analysis, to "Model" laboratories for supplying the radiographic and surgical templates and the provisional restorations. This project was supported by an educational grant from MIS Implants Technologies Ltd. The authors reported no conflicts of interest related to this study.

REFERENCES

- Bränemark PI, Hansson BO, Adell R, et al. Osseointegrated implants in the treatment of the edentulous jaw. Experience from a 10-year period. *Scand J Plast Reconstr Surg* 1977;16(suppl):1–132.
- Diaz-Arnold AM, Jons RA, LaVelle WE. Prosthodontic rehabilitation of the partially edentulous trauma patient by using osseointegrated implants. *J Prosthet Dent* 1988;60:354–357.
- Zarb GA, Zarb FL, Schmitt A. Osseointegrated implants for partially edentulous patients. Interim considerations. *Dent Clin North Am* 1987;31:457–472.
- Schnitman PA, Rubenstein JE, Woehrle PS, DaSilva JD, Koch GG. Implants for partial edentulism. *Int J Oral Implantol* 1988;5:33–35.
- Van Beek GJ, Versteegh PA, van der Veld RG, et al. The single, hollow titanium cylinder implant (ITI). [in Dutch] *Ned Tijdschr Tandheelkd* 1989;96:95–99.
- Esposito M, Grusovin MG, Polyzos IP, Felice P, Worthington HV. Timing of implant placement after tooth extraction: Immediate, immediate-delayed or delayed implants? A Cochrane systematic review. *Eur J Oral Implantol* 2010;3:189–205.
- Esposito M, Grusovin MG, Achille H, Coulthard P, Worthington HV. Interventions for replacing missing teeth: Different times for loading dental implants. *Cochrane Database Syst Rev* 2009 Jan 21;CD003878.
- Safii SH, Palmer RM, Wilson RF. Risk of implant failure and marginal bone loss in subjects with a history of periodontitis: A systematic review and meta-analysis. *Clin Implant Dent Relat Res* 2010;12:165–174.
- Grütter L, Belser UC. Implant loading protocols for the partially edentulous esthetic zone. *Int J Oral Maxillofac Implants* 2009;24(suppl): 169–179.
- Horwitz J, Zuabi O, Peled M, Machtei EE. Immediate and delayed restoration of dental implants in periodontally susceptible patients: 1-year results. *Int J Oral Maxillofac Implants* 2007;22:423–429.
- Flemmig TF. Periodontitis. *Ann Periodontol* 1999;4:32–37.
- Löe H, Silness J. Periodontal disease in pregnancy. I. Prevalence and severity. *Acta Odontol Scand* 1963;21:533–551.
- Salvi GE, Lindhe J, Lang NP. Examination of patients with periodontal diseases. In: Lindhe J, Lang NP, Karring T (eds). *Clinical Periodontology and Implant Dentistry*. Oxford: Blackwell, 2008:576–577.
- Lekholm U, Zarb GA, Albrektsson T. Patient selection and preparation. In: Branemark P (ed.) *Tissue Integrated Prostheses*. Chicago: Quintessence, 1985:199–209.
- Zembić A, Glauer R, Khraisat A, Hämmmerle CH. Immediate vs early loading of dental implants: 3-year results of a randomized controlled clinical trial. *Clin Oral Implants Res* 2010;21:481–489.
- Grandi T, Garuti G, Guazzi P, Tarabini L, Forabosco A. Survival and success rates of immediately and early loaded implants: 12-month results from a multicentric randomized clinical study. *J Oral Implantol* 2011;38:239–249.
- Chang M, Wennström JL. Peri-implant soft tissue and bone crest alterations at fixed dental prostheses: A 3-year prospective study. *Clin Oral Implants Res* 2010;21:527–534.
- Sánchez-Pérez A, Moya-Villaescusa MJ, Caffesse RG. Tobacco as a risk factor for survival of dental implants. *J Periodontol* 2007;78:351–359.
- Esposito M, Hirsch JM, Lekholm U, Thomsen P. Biological factors contributing to failures of osseointegrated oral implants. (II). Etiopathogenesis. *Eur J Oral Sci* 1998;106:721–764.

20. Machtei EE, Frankenthal S, Blumenfeld I, Guttmacher Z, Horwitz J. Dental implants for immediate fixed restoration of partially edentulous patients: A 1-year prospective pilot clinical trial in periodontally susceptible patients. *J Periodontol* 2007;78:1188–1194.
21. Chuang SK, Cai T, Douglass CW, Wei LJ, Dodson TB. Frailty approach for the analysis of clustered failure time observations in dental research. *J Dent Res* 2005;84:54–58.
22. Roos-Jansåker AM, Lindahl C, Renvert H, Renvert S. Nine- to fourteen-year follow-up of implant treatment. Part I: Implant loss and associations to various factors. *J Clin Periodontol* 2006;33:283–289.
23. Jemt T, Häger P. Early complete failures of fixed implant-supported prostheses in the edentulous maxilla: A 3-year analysis of 17 consecutive cluster failure patients. *Clin Implant Dent Relat Res* 2006;8:77–86.
24. Trisi P, De Benedictis S, Perfetti G, Berardi D. Primary stability, insertion torque and bone density of cylindric implant ad modum Branemark: Is there a relationship? An in vitro study. *Clin Oral Implants Res* 2011;22:567–570.
25. Rocuzzo M, Aglietta M, Cordaro L. Implant loading protocols for partially edentulous maxillary posterior sites. *Int J Oral Maxillofac Implants* 2009;24(suppl):147–157.
26. Degidi M, Daprile G, Piattelli A. Implants inserted with low insertion torque values for intraoral welded full-arch prosthesis: 1-year follow-up. *Clin Implant Dent Relat Res* 2012;14(suppl 1):e39–45.
27. Turkyilmaz I, McGlumphy EA. Is there a lower threshold value of bone density for early loading protocols of dental implants? *J Oral Rehabil* 2008;35:775–781.
28. Farré-Pagés N, Augé-Castro ML, Alaejos-Algarra F, Mareque-Bueno J, Ferrés-Padró E, Hernández-Alfaro F. Relation between bone density and primary implant stability. *Med Oral Patol Oral Cir Bucal* 2011;16:62–67.
29. Zembic A, Johannessen LH, Schou S, et al. Immediately restored one-piece single-tooth implants with reduced diameter: one-year results of a multi-center study. *Clin Oral Implants Res* 2012;23:49–54.
30. Weng D, Nagata MJ, Leite CM, de Melo LG, Bosco AF. Influence of microgap location and configuration on radiographic bone loss in nonsubmerged implants: An experimental study in dogs. *Int J Prosthodont* 2011;24:445–452.
31. Davarpanah M, Martinez H, Tecucianu JF. Apical-coronal implant position: Recent surgical proposals. Technical note. *Int J Oral Maxillofac Implants* 2000;15:865–872.
32. Huang CC, Lan TH, Lee HE, Wang CH. The biomechanical analysis of relative position between implant and alveolar bone: Finite element method. *J Periodontol* 2011;82:489–496.
33. Rismanchian M, Fazel A, Rakhshan V, Eblaghian G. One-year clinical and radiographic assessment of fluoride-enhanced implants on immediate non-functional loading in posterior maxilla and mandible: A pilot prospective clinical series study. *Clin Oral Implants Res* 2011; 22:1440–1445.
34. Horwitz J, Zuabi O, Machtei E. Radiographic changes around immediately restored dental implants in periodontally susceptible patients: 1-year results. *Int J Oral Maxillofac Implants* 2008;23:531–538.

Marginal Bone Loss Around Tilted Implants in Comparison to Straight Implants: A Meta-Analysis

Alberto Monje, DDS¹/Hsun-Liang Chan, DDS, MS²/Fernando Suarez, DDS¹/Pablo Galindo-Moreno, DDS, PhD³/Hom-Lay Wang, DDS, MS, PhD⁴

Purpose: The primary aim of this systematic review was to compare the amount of marginal bone loss around tilted and straight implants. As the secondary aim, the incidence of biomechanical complications was compared. **Materials and Methods:** An electronic literature search from five databases, for the years 2000 to 2011, and a hand search in implant-related journals were conducted. Clinical human studies in the English language that had reported marginal bone loss in tilted and straight implants at 12-months follow-up or longer were included. Mean marginal bone loss and the number of implants that were available for analysis were extracted from original articles for meta-analyses. **Results:** Eight (six prospective and two retrospective) studies were included. One-year data were available in seven articles, which included 1,015 (451 tilted) implants. Three articles provided 3- to 5-year data from 302 (164 tilted) implants. No significant difference in weighted mean marginal bone loss was found between the tilted and straight implants in the short and medium terms. Three articles reported the incidence of biomechanical complications. There was not enough information to make a comparison. **Conclusions:** This meta-analysis failed to support the hypothesis that tilted implants that were splinted for the support of fixed prostheses had more marginal bone loss. Additionally, there was not enough evidence to claim a higher incidence of biomechanical complications in tilted implants. However, due to the nature of the study design of the included articles, caution should be exercised when interpreting the results of this review. *INT J ORAL MAXILLOFAC IMPLANTS* 2012;27:1576–1583

Key words: edentulous, immediate dental implant loading, marginal bone loss, nonaxial loading, splinting, tilted implant

Dental implants, compared to teeth, are less tolerable to traumatic occlusal forces due to the lack of periodontal ligaments. They are more vulnerable to nonaxial forces because of the higher moment, torsional, and shear forces exerted to the surrounding bone that damage the bone-to-implant contact surface.¹ As a result, implants should be placed in line to the direction of the loading. However, the proximity of anatomical structures, such as the maxillary sinus and

the inferior alveolar nerve, often preclude standard implants from being placed axially. Solutions to inadequate ridge height include the use of short implants,² vertical ridge augmentation procedures,³ or cantilever prostheses.⁴ Although having a comparable short-term survival rate, the long-term performance of short implants is less understood, especially in the posterior maxilla with lower bone density.^{5,6} Vertical augmentation procedures increase patient morbidity and the outcome is unpredictable, especially when performed in the posterior mandible.⁷ Cantilever prostheses might incur higher rates of prosthetic complications, such as abutment loosening and denture fracture.^{8–10} Due to the unpredictable long-term prognosis associated with the above-mentioned procedures, the use of tilted implants was proposed.^{11,12}

The use of tilted implants could provide several clinical advantages: (1) to allow for the placement of longer implants, which increases the bone-to-implant contact area as well as implant stability; (2) to create a wider distance between anterior and posterior implants, which results in better load distribution; (3) to reduce or eliminate the use of cantilevers; and (4) to avoid bone augmentation procedures.¹³ One example of using tilted implants is the "All-on-Four" technique in

¹Visiting Scholar, Graduate Periodontics, Department of Periodontics and Oral Medicine, University of Michigan, School of Dentistry, Ann Arbor, Michigan, USA.

²Adjunct Clinical Assistant Professor, Graduate Periodontics, Department of Periodontics and Oral Medicine, University of Michigan, School of Dentistry, Ann Arbor, Michigan, USA.

³Associate Professor, Department of Oral Surgery, University of Granada, Granada, Spain.

⁴Program Director, Professor, Graduate Periodontics, Department of Periodontics and Oral Medicine, University of Michigan, School of Dentistry, Ann Arbor, Michigan, USA.

Correspondence to: Hsun-Liang Chan, Adjunct Clinical Assistant Professor and Research Fellow, University of Michigan, 1011 North University Avenue, Ann Arbor, Michigan 48109-1078, USA. Fax: (734) 936-0374. Email: hlchan@umich.edu

which the fixed prosthesis is supported by two straight and two tilted implants in a fully edentulous mandible.¹⁴ Four implants were splinted together and immediately restored with an acrylic provisional denture, which is replaced with a permanent porcelain prosthesis after 4 to 6 months. The same concept was adopted for the reconstruction of a fully edentulous maxilla and the implant survival rate at 1 year was similar to implants placed in the mandible (98.36% and 99.73%, respectively).¹⁵ Although biomechanical complications are commonly reported, ranging from 15.6%¹⁵ to 27%,¹⁴ patient satisfaction remained high because any complications can be repaired at chairside.

Therefore, combining tilted and straight implants for supporting fixed prostheses can be considered a viable treatment modality because of the high survival rate.¹⁶ However, the stability of peri-implant tissue and, especially, the marginal bone level for these tilted implants has not been extensively studied. Unfavorable loading direction could cause more marginal bone loss around these implants. In vitro studies have suggested accentuated stresses around implant necks that were nonaxially placed.^{17,18} In addition, it is not known if angled implants are associated with a higher incidence of biomechanical complications. For that reason, it is the primary aim of this systematic review to compare marginal bone loss between nonaxially and axially placed implants. The second aim is to assess whether tilted implants are related to a higher incidence of prosthetic complications.

MATERIALS AND METHODS

A search of five electronic databases, including PubMed, Ovid (MEDLINE), EMBASE, Web of Science, and Cochrane Central for relevant studies published in English from January 2000 until July 2011 was performed by one examiner (AM). The search terms used, where mh represented the MeSH term and tiab represented the title or abstract, were: "Mouth, Edentulous"[mh] OR "Jaw"[mh] AND "Dental implants"[mh] OR ("Dental"[tiab] AND "Implants"[tiab]) OR "Dental Implants"[tiab] OR ("Dental"[tiab] AND "Implant"[tiab]) OR "Dental Implant"[tiab] OR "Dental implantation"[mh]) OR "Immediate dental implant loading"[mh] AND "Tilted"[tiab] OR "Angled"[tiab] OR "Angulated"[tiab] OR "Offset"[tiab] OR "Non-axial"[tiab] OR "Axial"[tiab] OR "Axially" OR "Upright"[tiab] OR "Straight"[tiab] OR "All-on-4"[tiab] OR "All-on-four"[tiab]. Additionally, a hand search was carried out in dental and implant-related journals from January 2000 until July 2011, including *Clinical Implant Dentistry and Related Research*, *Journal of Oral and Maxillofacial Implants*, *Clinical Oral Implants Research*, *Implant Dentistry*, *European Journal of Oral Implantology*, *Journal*

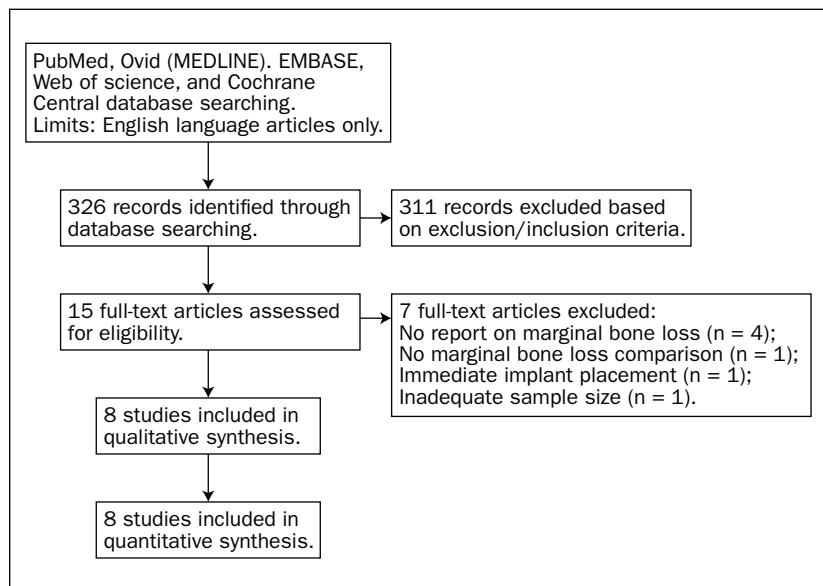
of Oral Implantology, *International Journal of Oral and Maxillofacial Surgery*, *Journal of Oral and Maxillofacial Surgery*, *Journal of Dental Research*, *International Journal of Prosthodontics*, *Journal of Prosthetic Dentistry*, *Journal of Clinical Periodontology*, *Journal of Periodontology* and *The International Journal of Periodontics and Restorative Dentistry*. Furthermore, a search in the references of included papers was conducted for publications that were not electronically identified.

Studies were selected if they fulfilled the following inclusion criteria: human clinical studies, either prospective or retrospective, with data on comparison of marginal bone loss between tilted and straight implants; a minimum sample size of 10 patients and 10 implants in each group that had been in function for at least 1 year; and implants that were placed in a pristine residual ridge with no additional grafting. Animal studies and human trials with insufficient information were excluded. Potential articles were reviewed in full text and confirmed for their eligibility by another examiner (HC).

Data extracted from the selected studies and transported to a commercially available software (CMA, Biostat) for meta-analysis included: number of implants available for analysis and mean value and standard deviation of marginal bone loss. The contributions of each article to the primary outcome were weighed based on sample size and the random effect model was chosen. Publication bias was examined by the funnel plot in which standard deviations of the difference in mean marginal bone loss were plotted against the difference in mean from the included articles. As a second aim, the incidence of biomechanical complications, if reported in the included articles, was recorded separately for straight and tilted implants and compared. The reporting of this meta-analysis adhered to the PRISMA (Preferred Reporting Items for Systematic Review and Meta-Analyses) statement.¹⁹

RESULTS

The screening process was presented in Fig 1. Initial screening of the databases using a combination of the above-mentioned key words, in addition to hand searching, yielded a total of 326 articles. After an evaluation of their titles and abstracts, 15 potentially relevant articles were selected for full-text evaluation. Seven articles were excluded because of several reasons: marginal bone loss was not reported,^{11,12,20,21} no comparison of marginal bone loss between straight and tilted implants,¹⁵ inclusion of immediate implant placement,²² and inadequate sample size²³ (Table 1). Eight articles (numbered 1 to 8, as shown in Tables 2 and 3) fulfilled the inclusion criteria and were included in the meta-analysis.

**Fig 1** Flow chart of the screening process.**Table 1 Excluded Articles and Their Reasons for Exclusion**

Excluded article (y)	Reason for exclusion
Agliardi et al (2010) ¹⁵	No comparison in marginal bone loss
Bedrossian et al (2008) ²³	Insufficient sample size
Francetti et al (2010) ²²	Inclusion of immediate implant placement
Krekmanov et al (2000) ¹¹	No report on marginal bone loss
Maló et al (2005) ¹²	No report on marginal bone loss
Maló et al (2006) ²⁰	No report on marginal bone loss
Maló et al (2007) ²¹	No report on marginal bone loss

Table 2 Characteristics of the Included Studies with Report on Marginal Bone Loss at 1-year Follow-up

#	Authors (y)	Study type	No. of implants (T/S)	No. of patients	Implant location	Degree of angulation of tilted implants	Type of restoration	No. of implants for FF	Loading time (mo)
1	Agliardi et al (2010) ³⁰	P	42/42	24	Mandible	30–40	FF	4	Immediate
2	Aparicio et al (2001) ³⁹	R	40/53	25	Maxilla	35	FP	NA	6–8
3	Calandriello and Tomatis (2005) ⁴⁰	P	22/32	18	Maxilla	45–75	FF or FP	Mean: 5; range: 3–6	Immediate
4	Capelli et al (2007) ¹³	P	74/116	65	Mandible; maxilla	25–35	FF	Maxilla: 6; mandible: 4	Immediate
5	Degidi et al (2010) ⁴¹	P	120/89	30	Maxilla	30–40	FF	7	Immediate
6	Hinze et al (2010) ⁴²	P	73/71	37	Mandible Maxilla	30	FF	4	Immediate
7	Testori et al (2008) ⁴³	P	80/161	41	Maxilla	30–35	FF	6	Immediate

T = tilted implant; S = straight implant; P = prospective; R = retrospective; FF = fixed full-arch prosthesis; FP = fixed partial prosthesis; NA = not applicable.
Significance level set at $P < .05$.

Table 3 Characteristics of the Included Studies with Data on Marginal Bone Loss for More Than 1 Year

#	Authors (y)	Study type	Follow up period (yr)	No. of implants (T/S)	No. of patients	Implant location	Degree of angulation of tilted implants	Type of restoration	Loading time (mo)
2	Aparicio et al (2001) ³⁹	R	5	11/12	NA	Maxilla	35	FP	6–8
5	Degidi et al (2010) ⁴¹	P	3	120/89	30	Maxilla	30–40	FF	Immediate
8	Koutouzis and Wennström (2007) ⁴⁴	R	5	33/36	38	Mandible (33%); Maxilla (67%)	30	FP	3–6

T = tilted implant; S = straight implant; P = prospective; R = retrospective; FF = fixed full-arch prosthesis; FP = fixed partial prosthesis; NA = not applicable.
Significance level set at $P < .05$.

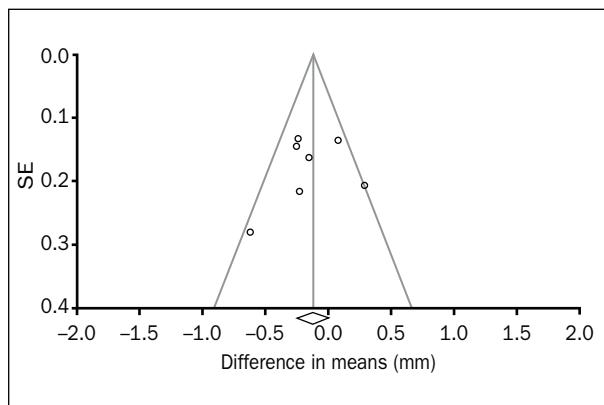


Fig 2 Assessment of publication bias for short-term studies showed symmetrical distributions.

Implant survival rate (%) (T/S)	Marginal bone loss (mm) (T/S)	P
100/100	0.80 ± 0.50/0.90 ± 0.40	> .05
100/96.5	0.57 ± 0.50/0.43 ± 0.45	> .05
96.3/97	0.34 ± 0.76/0.82 ± 0.86	< .05 (favored tilted implants)
98.6/98.2	0.82 ± 0.57/0.95 ± 0.50	> .05
100/100	0.63 ± 0.38/0.60 ± 0.33	> .05
94.6/96	0.76 ± 0.49/0.82 ± 0.31	> .05
98.8/98.8	0.80 ± 0.50/0.90 ± 0.40	> .05

Implant survival rate (%) (T/S)	Marginal bone loss (mm) (T/S)	P
95.2/96.3	1.21 ± 0.68/0.92 ± 0.55	> .05
100/100	1.03 ± 0.69/0.92 ± 0.75	> .05
NA	0.50 ± 0.95/0.40 ± 0.97	> .05

Characteristics of the Included Articles

Study Design and Length of Follow-up. Of the eight articles included in the present study, six were prospective controlled studies (no. 1, 3, 4, 5, 6, and 7) and two were retrospective controlled studies (no. 2 and 8). In addition, three studies (no. 2, 5, and 8) provided data after a study period of 3 to 5 years. To further investigate the effect of time on marginal bone loss of tilted implants, two meta-analyses were performed for short-term (1-year) and medium-term (3 to 5 years) results.

Sample Size. The number of subjects that was available for data analysis ranged from 18 (no. 3) to 65 (no. 4). For short-term results, 1,015 implants were analyzed, in which 451 (44.43%) and 564 (55.57%) were tilted and straight implants, respectively. For comparison at 3- to 5-years follow-up, 164 (54.30%) tilted and 138 (45.70%) straight implants were analyzed, for a total of 302 implants.

Prosthesis Type, Loading Protocol, and Inclination of Implants

All implants were designed to support fixed prostheses. In other words, the tilted implants were splinted with straight implants. Five articles (no. 1, 4, 5, 6, and 7) studied full-arch prostheses only, another two (no. 2 and 8) included partial-arch prostheses only, and the last study (no. 5) had both types of prostheses. For full-arch reconstruction, four implants (two straight and two tilted) were used in the mandibles (no. 1, 4 and 6); in the maxilla, the number of implants ranged from four (no. 6), five (no. 3), six (no. 4 and 7) and seven (no. 5). Regarding the loading protocol, in six studies (no. 1, 3, 4, 5, 6, and 7) implants were loaded immediately; in the other two studies (no. 2 and 8), a conventional loading protocol was adopted. All tilted implants presented a similar angulation, ranging from 25 to 40 degrees, except in one study (no. 3), where the implants had a higher inclination of 45 to 75 degrees.

Results of Meta-analyses

The short-term results (Table 4) showed that the weighted mean difference in marginal bone loss between the tilted and straight implants was -0.054 mm (95% CI = -0.138 to 0.030 mm), favoring the tilted implant group; however, the difference did not reach statistical significance ($P = .207$). The funnel plot (Fig 2) showed overall symmetrical distribution, suggestive of no publication bias. For the medium-term results (Table 5), the weighted mean difference was 0.129 mm (95% CI = -0.041 to 0.298 mm), favoring the straight implant group, but was also not statistically significant ($P = .137$).

Biomechanic Complications

Only three articles (no. 2, 6, and 7) reported biomechanic complications (Table 6). Abutment screw loosening was the most commonly encountered

Table 4 Forest Plot for the Comparison of Marginal Bone Loss between Tilted and Straight Implants at 1-Year Follow-up

Author (y)*	Sample size		Statistics for each study			
	Tilted implants	Straight implants	Difference in means (mm)	SE	Lower limit	Upper limit
Agliardi et al (2010) ³⁰	42	42	-0.100	0.100	-0.296	0.096
Aparicio et al (2001) ³⁹	40	53	0.140	0.100	-0.056	0.336
Calandriello and Tomatis (2005) ⁴⁰	22	32	-0.480	0.220	-0.911	-0.049
Capelli et al (2007) ¹³	74	116	-0.130	0.080	-0.287	0.027
Degidi et al (2010) ⁴¹	120	89	0.030	0.050	-0.068	0.128
Hinze et al (2010) ⁴²	73	71	-0.060	0.070	-0.197	0.077
Testori et al (2008) ⁴³	80	161	-0.100	0.060	-0.218	0.018
Total	451	564	-0.054	0.043	-0.138	0.030

*Seven articles were included for meta-analysis and the mean difference was -0.054 mm ($P = .207$). SE = standard error.

Table 5 Forest Plot for the Comparison of Marginal Bone Loss between Tilted and Straight Implants at Longer than 1-Year Follow-up

Author (y)	Sample size		Statistics for each study			
	Tilted implants	Straight implants	Difference in means (mm)	SE	Lower limit	Upper limit
Aparicio et al (2001) ³⁹	11	12	0.290	0.260	-0.220	0.800
Koutouzis and Wennström (2007) ⁴⁴	33	36	0.100	0.230	-0.351	0.551
Degidi et al (2010) ⁴¹	120	90	0.110	0.100	-0.086	0.306
Total	164	138	0.129	0.086	-0.041	0.298

*Three articles were included for meta-analysis and the mean difference was 0.129 mm ($P = .137$). SE = standard error.

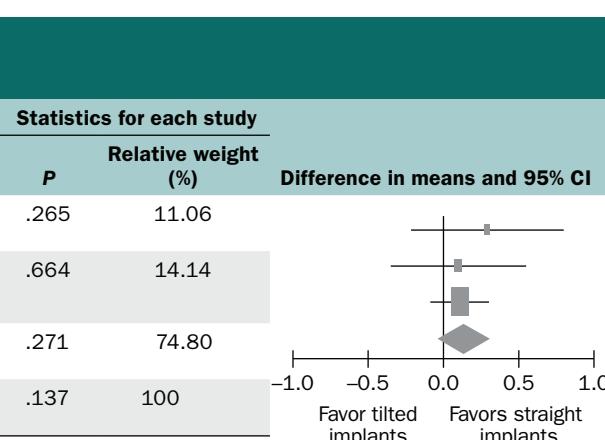
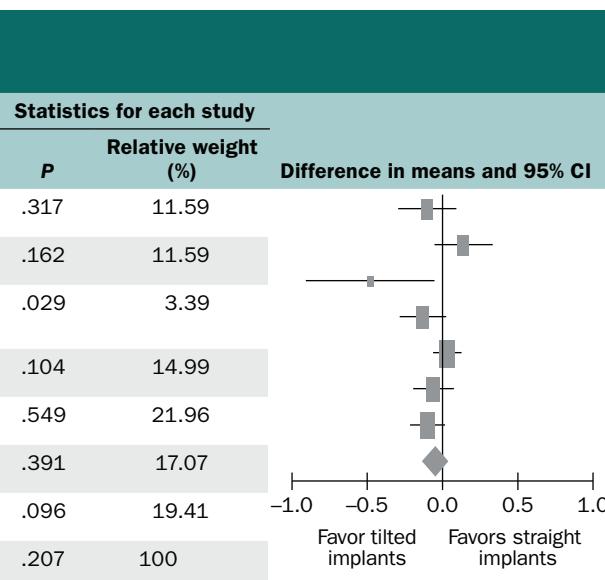
Table 6 Incidence of Biomechanic Complications on Tilted and Straight Implants

#	Type of prosthesis	Prosthetic complication (%)	Comparison between tilted and straight implants
2	FP	Gold screw loosening (17.2); abutment screw loosening (48.3); abutment screw fracture (6.8); occlusal material fracture (6.8)	No difference in % of screw loosening; no report on other type of complications
6	FF	Acrylic provisional veneer fracture (10.8); definitive prosthesis fracture (3.7); Loosening of the screw access hole restoration (9.5) Screw loosening (6)	No report
7	FF	Provisional screw loosening (17.5)	3 tilted/4 axial implants

#1, 3, 4, 5, 8: no report on the incidence of prosthetic complications.
FP = fixed partial prosthesis; FF = fixed full-arch prosthesis.

complication, occurring in 48.3% of the total number of prostheses (no. 2). Other prosthetic complications included screw fracture (6.8%) (no. 2), either provisional (10.8%) or permanent prosthesis fracture (3.7%)

(no. 2 and 6), and loosening of the screw access hole restoration (9.5%) (no. 6). Regardless, no evidence from these three articles suggested that tilted implants incur a higher biomechanic complication rate.



DISCUSSION

In this systematic review, marginal bone loss was not statistically higher for tilted implants compared to straight implants in the short and medium terms. However, tilted implants lost more marginal bone in the medium term, contrary to the finding observed from the short-term data. Interestingly, one short-term study (no. 3) showed significantly less bone loss in tilted implants (0.34 ± 0.76 versus 0.82 ± 0.86 , $P = .03$). These results suggested that tilted implants may have had continuous bone loss. A 10-year follow-up study²⁴ was recently published for evaluation of the "All-on-Four" concept; however, no data on marginal bone loss was available. Further studies are needed to look into the long-term performance of tilted implants.

Theoretically, tilted implants could receive higher stresses resulting in more marginal bone loss. From computer-simulation studies,^{17,18} higher stresses were

found around the neck of tilted implants. Under vertical loading, the compressive stresses were five times higher around the angled implant.¹⁷ In addition, tensile stresses were concentrated on the opposite side of the inclination.²⁵ As such, angled implants displayed oblique, nonhomogenous stress patterns to the polymeric model.²⁶ Animal studies^{27,28} have shown that non-axial loading elicits a more dynamic remodeling of surrounding cortical bone and, in particular, trabecular bone.

However, the hypothesis that there was more marginal loss around tilted implants was not supported by this meta-analysis, perhaps for the following reasons: (1) the length of the implants used was long and (2) the splinting effect. To engage more bone to maximize implant stability, most included studies utilized implants with a length of at least 10 and up to 20 mm (no. 2). With increasing implant length, more effective stress distributions for cancellous bone were found.²⁹ Another finite element study³⁰ suggested that longer implants distributed stress better, resulting in reduced gap distances between bone and implant. A prospective study³¹ did report that long implants (14 to 16 mm) had significantly less marginal bone loss than average length (12 mm) implants at 1-year postloading. The comparable marginal bone loss for tilted implants could have been partially due to their long length.

A more probable method to reduce stress around the neck of a tilted implant is splinting and reduction of the cantilever length rather than increasing the implant length.³²⁻³⁴ In all cases included in the present review, tilted implants were splinted into a fixed prosthesis, either for a partial or full arch. The reduction of the cantilever span by tilted implants and the rigidity of the prostheses could have helped to reduce stress. Some recent three-dimensional finite element studies³³⁻³⁶ suggested that tilted implants could benefit stress distribution by reducing cantilever length and, therefore, may be a viable option. These computer-simulation studies could have partially explained the favorable marginal bone level around tilted implants.

Prosthetic complications increase costs, treatment time, and frustration to patients as well as clinicians and should be avoided whenever possible. Due to the possibility of unfavorable loading conditions for tilted implants, it was hypothesized that tilted implants incurred higher biomechanical complications. Nevertheless, the present review did not have enough evidence to claim this statement because only three included articles reported prosthetic complication rates. Interestingly, one study (no. 2) reported an overall higher abutment loosening rate (48.3%) compared with the other two studies (no. 6 and 7), although no differences were found between tilted and straight implants. The type of restoration could be

one explanation, ie, in that specific study, fixed partial prostheses were used, which do not provide the same cross-arch stability as fixed full prostheses.

Implant marginal bone loss is primarily assessed by radiographs and the quality of radiographic methods could potentially influence the accuracy of the results. From the eight included articles, four (no. 4, 5, 7, and 8) performed standardized periapical radiographs exclusively. One article (no. 1) used standardized periapical radiographs whenever possible and panoramic films as an alternative. Another article (no. 6) only used panoramic radiographs and the remaining two articles did not mention if the periapical radiographs were standardized. Standardized periapical radiographs are generally desired because their accuracy can be within a range of 0.2 mm from the true measurement.³⁷ Panoramic radiographs are generally less preferred due to low resolution and an average distortion rate of 25%.³⁸ However, it is understandable that taking periapical radiographs could be difficult for edentulous patients with a shallow vestibule. Nevertheless, when interpreting the results, the radiographic methods used could pose an experimental limitation and should be taken into consideration.

CONCLUSIONS

Marginal bone loss around tilted implants that were splinted to support fixed prostheses was not significantly different from straight implants for the short- and medium-term reviews. However, tilted implants had slightly more marginal bone loss at the medium-term review. Long-term results are required to verify this finding. No evidence suggested that tilted implants are associated with a higher incidence of biomechanic complications. There is a potentially high risk of bias for this systematic review because none of the included articles was a randomized clinical trial. Therefore, precautions should be exercised when interpreting the results of this review.

ACKNOWLEDGMENTS

The authors would like to acknowledge Mr Kerby A. Shedd, Associate Professor, Department of Statistics, University of Michigan, for his guidance in conducting meta-analyses, and Mr Mark MacEachern, a liaison services librarian in the Taubman Health Sciences Library, University of Michigan, for providing consultations on the literature search. The authors reported no conflicts of interest related to this study. This paper was partially supported by the University of Michigan Periodontal Graduate Student Research Fund.

REFERENCES

- Kim Y, Oh TJ, Misch CE, Wang HL. Occlusal considerations in implant therapy: Clinical guidelines with biomechanical rationale. *Clin Oral Implants Res* 2005;16:26–35.
- Fugazzotto PA. Shorter implants in clinical practice: Rationale and treatment results. *Int J Oral Maxillofac Implants* 2008;23:487–496.
- Simion M, Jovanovic SA, Trisi P, Scarano A, Piattelli A. Vertical ridge augmentation around dental implants using a membrane technique and autogenous bone or allografts in humans. *Int J Periodontics Restorative Dent* 1998;18:8–23.
- Wennstrom J, Zurdo J, Karlsson S, Ekestubbe A, Grondahl K, Lindhe J. Bone level change at implant-supported fixed partial dentures with and without cantilever extension after 5 years in function. *J Clin Periodontol* 2004;31:1077–1083.
- Renouard F, Nisand D. Impact of implant length and diameter on survival rates. *Clin Oral Implants Res* 2006;17(suppl 2):35–51.
- Telleman G, Raghoobar GM, Vissink A, den Hartog L, Huddleston Slater JJ, Meijer HJ. A systematic review of the prognosis of short (<10 mm) dental implants placed in the partially edentulous patient. *J Clin Periodontol* 2011;38:667–676.
- Felice P, Pellegrino G, Checchi L, Pistilli R, Esposito M. Vertical augmentation with interpositional blocks of anorganic bovine bone vs 7-mm-long implants in posterior mandibles: 1-year results of a randomized clinical trial. *Clin Oral Implants Res* 2010;21:1394–1403.
- Balshi TJ. Preventing and resolving complications with osseointegrated implants. *Dent Clin North Am* 1989;33:821–868.
- Shackleton JL, Carr L, Slabbert JC, Becker PJ. Survival of fixed implant-supported prostheses related to cantilever lengths. *J Prosthet Dent* 1994;71:23–26.
- Salvi GE, Bragger U. Mechanical and technical risks in implant therapy. *Int J Oral Maxillofac Implants* 2009;24(suppl):69–85.
- Krekmanov L, Kahn M, Rangert B, Lindstrom H. Tilting of posterior mandibular and maxillary implants for improved prosthesis support. *Int J Oral Maxillofac Implants* 2000;15:405–414.
- Malo P, Rangert B, Nobre M. All-on-4 immediate-function concept with Brånenmark system implants for completely edentulous maxillae: A 1-year retrospective clinical study. *Clin Implant Dent Relat Res* 2005;7(suppl 1):S88–S94.
- Capelli M, Zuffetti F, Del Fabbro M, Testori T. Immediate rehabilitation of the completely edentulous jaw with fixed prostheses supported by either upright or tilted implants: A multicenter clinical study. *Int J Oral Maxillofac Implants* 2007;22:639–644.
- Malo P, Rangert B, Nobre M. “All-on-Four” immediate-function concept with Branemark system implants for completely edentulous mandibles: A retrospective clinical study. *Clin Implant Dent Relat Res* 2003;5(suppl 1):2–9.
- Agliardi E, Panigatti S, Clerico M, Villa C, Malo P. Immediate rehabilitation of the edentulous jaws with full fixed prostheses supported by four implants: Interim results of a single cohort prospective study. *Clin Oral Implants Res* 2010;21:459–465.
- Del Fabbro M, Bellini CM, Romeo D, Francetti L. Tilted implants for the rehabilitation of edentulous jaws: A systematic review. *Clin Implant Dent Relat Res* 2010 May 13 [epub ahead of print].
- Canay S, Hersek N, Akpinar I, Asik Z. Comparison of stress distribution around vertical and angled implants with finite-element analysis. *Quintessence Int* 1996;27:591–598.
- Lan TH, Pan CY, Lee HE, Huang HL, Wang CH. Bone stress analysis of various angulations of mesiodistal implants with splinted crowns in the posterior mandible: A three-dimensional finite element study. *Int J Oral Maxillofac Implants* 2010;25:763–770.
- Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: Explanation and elaboration. *Ann Intern Med* 2009;151:e65–94.
- Malo P, Nobre Mde A, Petersson U, Wigren S. A pilot study of complete edentulous rehabilitation with immediate function using a new implant design: Case series. *Clin Implant Dent Relat Res* 2006;8:223–232.

21. Malo P, de Araujo Nobre M, Lopes A. The use of computer-guided flapless implant surgery and four implants placed in immediate function to support a fixed denture: Preliminary results after a mean follow-up period of thirteen months. *J Prosthet Dent* 2007;97(suppl 6):S26–S34.
22. Francetti L, Romeo D, Corbella S, Taschieri S, Del Fabbro M. Bone level changes around axial and tilted implants in full-arch fixed immediate restorations. Interim results of a prospective study. *Clin Implant Dent Relat Res* 2012 Oct;14:646–654.
23. Bedrossian E, Sullivan RM, Fortin Y, Malo P, Indresano T. Fixed-prosthetic implant restoration of the edentulous maxilla: A systematic pretreatment evaluation method. *J Oral Maxillofac Surg* 2008;66:112–122.
24. Malo P, de Araujo Nobre M, Lopes A, Moss SM, Molina GJ. A longitudinal study of the survival of All-on-4 implants in the mandible with up to 10 years of follow-up. *J Am Dent Assoc* 2011;142:310–320.
25. Watanabe F, Hata Y, Komatsu S, Ramos TC, Fukuda H. Finite element analysis of the influence of implant inclination, loading position, and load direction on stress distribution. *Odontology* 2003;91:31–36.
26. Markarian RA, Ueda C, Sendyk CL, Lagana DC, Souza RM. Stress distribution after installation of fixed frameworks with marginal gaps over angled and parallel implants: A photoelastic analysis. *J Prosthodont* 2007;16:117–122.
27. Barbier L, Schepers E. Adaptive bone remodeling around oral implants under axial and nonaxial loading conditions in the dog mandible. *Int J Oral Maxillofac Implants* 1997;12:215–223.
28. Barbier L, Vander Sloten J, Krzesinski G, Schepers E, Van der Perre G. Finite element analysis of non-axial versus axial loading of oral implants in the mandible of the dog. *J Oral Rehabil* 1998;25:847–858.
29. Baggi L, Cappelloni I, Di Girolamo M, Maceri F, Vairo G. The influence of implant diameter and length on stress distribution of osseointegrated implants related to crestal bone geometry: A three-dimensional finite element analysis. *J Prosthet Dent* 2008;100:422–431.
30. Agliardi E, Clerico M, Ciancio P, Massironi D. Immediate loading of full-arch fixed prostheses supported by axial and tilted implants for the treatment of edentulous atrophic mandibles. *Quintessence Int* 2010;41:285–293.
31. Cochran DL, Bosshardt DD, Grize L, et al. Bone response to loaded implants with non-matching implant-abutment diameters in the canine mandible. *J Periodontol* 2009;80:609–617.
32. Zampelis A, Rangert B, Heijl L. Tilting of splinted implants for improved prosthodontic support: A two-dimensional finite element analysis. *J Prosthet Dent* 2007;97:S35–S43.
33. Bevilacqua M, Tealdo T, Pera F, et al. Three-dimensional finite element analysis of load transmission using different implant inclinations and cantilever lengths. *Int J Prosthodont* 2008;21:539–542.
34. Fazi G, Tellini S, Vangi D, Branchi R. Three-dimensional finite element analysis of different implant configurations for a mandibular fixed prosthesis. *Int J Oral Maxillofac Implants* 2011;26:752–759.
35. Bellini CM, Romeo D, Galbusera F, et al. A finite element analysis of tilted versus nontilted implant configurations in the edentulous maxilla. *Int J Prosthodont* 2009;22:155–157.
36. Silva GC, Mendonca JA, Lopes LR, Landre J Jr. Stress patterns on implants in prostheses supported by four or six implants: A three-dimensional finite element analysis. *Int J Oral Maxillofac Implants* 2010;25:239–246.
37. De Smet E, Jacobs R, Gijbels F, Naert I. The accuracy and reliability of radiographic methods for the assessment of marginal bone level around oral implants. *Dentomaxillofac Radiol* 2002;31:176–181.
38. Chan HL, Misch K, Wang HL. Dental imaging in implant treatment planning. *Implant Dent* 2010;19:288–298.
39. Aparicio C, Perales P, Rangert B. Tilted implants as an alternative to maxillary sinus grafting: a clinical, radiologic, and periotest study. *Clin Implant Dent Relat Res* 2001;3:39–49.
40. Calandriello R, Tomatis M. Simplified treatment of the atrophic posterior maxilla via immediate/early function and tilted implants: A prospective 1-year clinical study. *Clin Implant Dent Relat Res* 2005;7(suppl 1):S1–S12.
41. Degidi M, Nardi D, Piattelli A. Immediate loading of the edentulous maxilla with a definitive restoration supported by an intraorally welded titanium bar and tilted implants. *Int J Oral Maxillofac Implants* 2010;25:1175–1182.
42. Hinze M, Thalmair T, Bolz W, Wachtel H. Immediate loading of fixed provisional prostheses using four implants for the rehabilitation of the edentulous arch: A prospective clinical study. *Int J Oral Maxillofac Implants* 2010;25:1011–1018.
43. Testori T, Del Fabbro M, Capelli M, Zuffetti F, Francetti L, Weinstein RL. Immediate occlusal loading and tilted implants for the rehabilitation of the atrophic edentulous maxilla: 1-year interim results of a multicenter prospective study. *Clin Oral Implants Res* 2008;19:227–232.
44. Koutouzis T, Wennstrom JL. Bone level changes at axial- and non-axial-positioned implants supporting fixed partial dentures. A 5-year retrospective longitudinal study. *Clin Oral Implants Res* 2007;18:585–590.

All-on-Three Delayed Implant Loading Concept for the Completely Edentulous Maxilla and Mandible: A Retrospective 5-Year Follow-up Study

Josep Oliva, MSc¹/Xavi Oliva, MSc²/Josep D. Oliva, MD²

Purpose: Full-arch implant rehabilitation with four implants has become an accepted modality of treatment for fixed restorations in totally edentulous mandibles or maxillas; however, there is little scientific evidence on the outcome for the same treatment with three implants. The purpose of this study was to evaluate a protocol for three implants (all-on-three) supporting a delayed loaded fixed prosthesis in the completely edentulous maxilla, mandible, or both. **Materials and Methods:** This retrospective clinical study included 17 patients with 72 implants to restore 24 fully edentulous arches. The implants were loaded 4 months after surgery with fixed zirconia prostheses. A 5-year follow-up was performed. **Results:** No implants were lost, giving a 100% success rate. The marginal bone loss was, on average, 0.53 mm (SD, 0.32 mm) for the internal connection implants and 0.84 mm (SD, 0.62 mm) for the external connection implants. **Conclusions:** Within the limits of this small group clinical study, the high survival rate of the all-on-three protocol with delayed loading may be a viable concept. INT J ORAL MAXILLOFAC IMPLANTS 2012;27:1584–1592

Key words: all-ceramic prosthesis, full arch, three implants, zirconia prosthesis

The use of three implants to restore the edentulous mandible was first described by Professor P. I. Bränemark et al¹ with the Novum protocol, and they reported a 98% success rate over 3 years. The same group later reported a 93.3% success rate over a 5-year period.² The Novum protocol included a set of prefabricated surgical and prosthetic components, and the implants were immediately loaded with the final titanium-resin restoration. A drawback of this protocol was the fact that patients were required to have a certain amount of bone in order to create the 7-mm bone platform needed to accommodate the implants and prefabricated prosthesis.

This protocol was only available for the Bränemark system and is no longer commercially available. The outcome of this protocol was sensitive to the angulations of the implants and the prosthetic outcome could be compromised. Moreover, the survival rate appears to be somewhat lower compared with the use of conventional implants for immediate loading in the mandible.^{3,4}

Inspired by the Novum protocol, Hatano et al^{5,6} reported on a technique where three conventional and prefabricated prosthetic components were used for immediate loading of a fixed prosthesis in the edentulous mandible. They studied 396 Bränemark implants over an 11-year period and reported a 96.7% survival rate. Machined implants had a higher failure rate compared with oxidized implants (7% versus 1.2%, respectively). The prostheses were made with a titanium bar framework covered with resin and prefabricated teeth.

Good clinical outcomes from studies^{1–9} using protocols in which three or four implants were placed to support a full-arch prosthesis indicate that the placement of larger numbers of implants may not be necessary for successful implant treatment of edentulous arches.

To the authors' knowledge, no study has previously described the use of three implants in the maxilla for full-arch restoration. The purpose of this study was to retrospectively evaluate a protocol for fixed complete-arch prosthesis supported by three implants (all-on-three) in the maxilla and mandible with a delayed loading protocol.

MATERIALS AND METHODS

The study was performed in a private clinic (Clínica Oliva in Granollers, Barcelona, Spain) from July 2003 to December 2005.

The inclusion criteria were:

¹Professor, Postgraduate Master Degree in Periodontics Program, University of Barcelona, Barcelona, Spain. Private Practice, Barcelona, Spain.

²Private Practice, Barcelona, Spain.

Correspondence to: Dr Josep Oliva, Master of Periodontics, University of Barcelona, Josep umbert, 126, Granollers 08402, Spain. Fax: +34938792373. Email: pepeoliva@clinicaoliva.com.

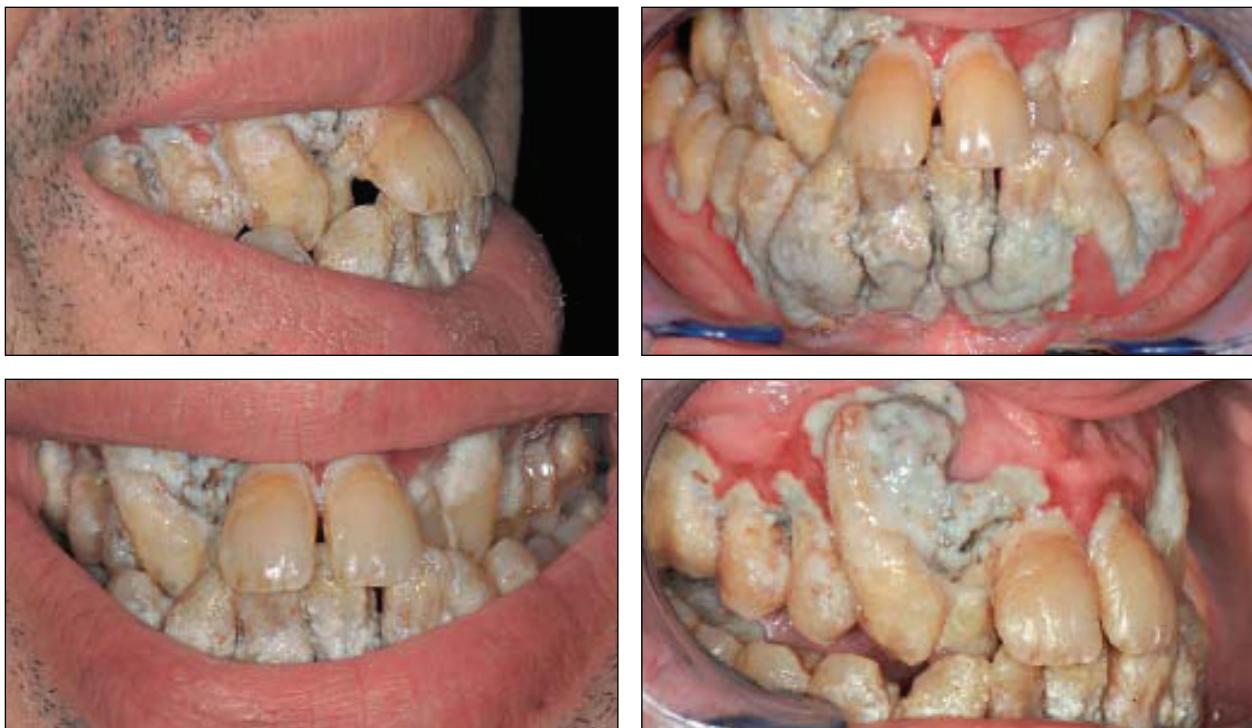


Fig 1 Patient no. 1, case no. 1. Diagnosis: advanced periodontitis, multiple caries, malocclusion Class III dental and skeletal. Treatment plan: full mouth oral rehabilitation with three implants in the maxilla and four implants in the mandible.

- The need for complete rehabilitation of the edentulous maxilla, mandible, or both (see example in Fig 1)
- The possibility of placing a minimum of three implants (at least 10 mm long and 4.1 mm diameter) into the completely edentulous arch
- Patient understands the treatment plan and signs the informed consent to receive treatment
- At least 5 years of follow-up data reported

Implant Survival Criteria

An implant was classified as surviving if it fulfilled its functioning purpose and was stable when tested individually, if no pain or signs of infection were detected during clinical examination, and if no sign of peri-implant pathology was seen at radiographic follow-up.

Follow-up and Marginal Bone Level

Follow-up examinations were performed 6 months and every year after implant placement. Intraoral or panoramic radiograph examinations were performed at the 1-year and 5-year follow-ups (see Fig 5). The restorations were removed for hygiene and cleaning every year.

The implant-prosthetic interface was taken as a reference point for bone level measurements. Measurements were made with a Williams periodontal probe (Hu-Friedy) under local anesthesia. Two points per implant (one mesial and one distal) were recorded at surgery, at 1-year follow-up, and at the 5-year follow-up.

RESULTS

A total of 72 implants (36 maxilla, 36 mandible) were placed to restore 24 full dental arches in 17 patients (11 males and 6 females; mean age 52.88 years). The opposing dentitions were implant-supported prostheses (19 patients), natural teeth (3 patients), or a combination of both (2 patients).

Implant Components

Two different implant systems were used in this study: Straumann (Institut Straumann) (internal morse taper connection) and Osstem (Osstem Implant) (internal morse taper connection or external hexagon connection) implants.

The length of the implants ranged from 10 to 14 mm and the diameter ranged from 4.1 to 4.8 mm. The implants with internal connection received an octagon abutment and the external hexagon implants received the prosthesis without any intermediate abutments.

Each treated arch received three implants. In one case (patient no. 1) the implants were loaded early (15 days postsurgery) because the patient did not accept any temporary removable denture. In all other cases, the implants were allowed to heal for 3 months before final impressions were made and final prostheses were delivered 4 months postsurgery.

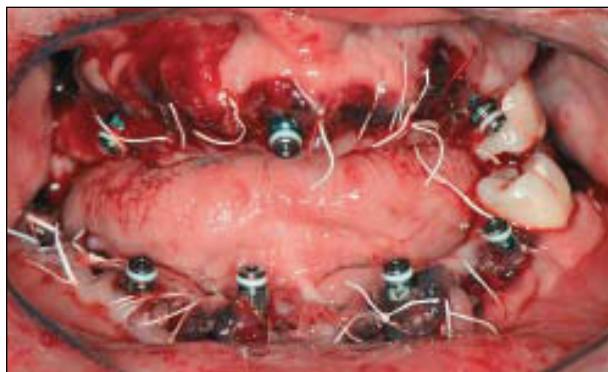


Fig 2 Patient no. 1, case no. 1. Extractions of all teeth except mandibular right lateral incisor and mandibular left first molar to maintain vertical dimension. Flapless surgery and immediate implants placed.

Surgical Protocol

The surgical procedures were performed under local anesthesia with mepivacaine chlorhydrate with epinephrine 1:100,000 (scandinibsa 2%, Inibsa Laboratory). Antibiotics (amoxicillin 500 mg) were given 1 day before surgery and daily for 5 days thereafter. Anti-inflammatory medication (ibuprofen 600 mg) was administered for 2 days postoperatively.

Teeth were extracted (Fig 2), where needed, at the time of surgery before implant placement. Implants in the extraction sockets were placed without raising any flaps. For the implants placed in edentulous areas, a mucoperiosteal flap was raised at the ridge crest with relieving incisions at the buccal aspect.

The insertion of the implants followed standard procedures. The implant neck was positioned at bone level for the external hexagon implants, while for morse tapered implants, the bone level was situated at the polished-acid etched limit.

The distal implants were placed whenever possible in the second premolar or first molar regions. In cases with less available bone, the implants were positioned in a more mesial aspect (see Table 1, patients no. 3 and 5).

The anterior implant was positioned in every case in the area of the central incisor.

Table 1 Distribution of Implants

Patient/ case no.	Gender	Age	Smoker	Maxilla
1/1	M	46	Yes	1 1 1
2/2	F	44	Yes	
3/3	F	61	No	
4/4	M	48	Yes	1 1 1
4/5	M	48	Yes	
5/6	F	47	No	1 1 1
5/7	F	47	No	
6/8	M	79	No	1 1 1
6/9	M	79	No	
7/10	M	58	Yes	1 1 1
7/11	M	58	Yes	
8/12	M	49	Yes	1 1 1
9/13	F	50	Yes	1 1 1
9/14	F	50	Yes	
10/15	F	64	No	1 1 1
11/16	M	55	No	1 1 1
11/17	M	55	No	
12/18	M	51	No	1 1 1
13/19	M	53	Yes	
14/20	M	55	Yes	

Mandible	Brand	L	Ø	Immediate implants	PU CUL CUR	Restoration type	Antagonist
1 1 1	Osstem SSII	13	4.1	1	12	CAD/CAM zirconia	All-on-four zirconia
		13	4.1	1	1		
		13	4.1	1	1		
1 1 1	Osstem USII	13	4.1	0	12	CAD/CAM zirconia	All-on-five zirconia
		13	4.1	0	0		
		13	4.1	1	0		
1 1 1	Straumann	12	4.1	0	12	CAD/CAM zirconia	All-on-six zirconia
		12	4.1	0	3		
		12	4.1	0	3		
1 1 1	Osstem SSII	13	4.1	0	12	CAD/CAM zirconia	All-on-three zirconia
		13	4.1	0	1		
		13	4.1	0	1		
1 1 1	Osstem SSII	13	4.1	0	12	CAD/CAM zirconia	All-on-three zirconia
		13	4.1	1	1		
		13	4.1	0	0		
1 1 1	Straumann	12	4.1	1	12	CAD/CAM zirconia	All-on-three zirconia
		12	4.1	0	1		
		12	4.1	0	1		
1 1 1	Straumann	12	4.1	0	12	CAD/CAM zirconia	All-on-three zirconia
		12	4.1	1	2		
		12	4.1	0	3		
1 1 1	Straumann	12	4.1	0	12	CAD/CAM zirconia	All-on-three zirconia
		12	4.8	1	1		
		12	4.1	1	0		
1 1 1	Straumann	12	4.1	0	12	CAD/CAM zirconia	All-on-three zirconia
		12	4.8	1	0		
		12	4.1	1	0		
1 1 1	Straumann	12	4.1	0	12	CAD/CAM zirconia	All-on-three zirconia
		12	4.8	1	0		
		12	4.1	0	0		
1 1 1	Straumann	12	4.1	1	12	CAD/CAM zirconia	All-on-three zirconia
		12	4.8	1	0		
		12	4.1	0	0		
1 1 1	Straumann	12	4.1	0	12	CAD/CAM zirconia	Natural dentition
		12	4.8	1	0		
		12	4.1	0	0		
1 1 1	Osstem SSII	13	4.1	1	12	CAD/CAM zirconia	All-on-three zirconia
		13	4.1	1	1		
		13	4.1	1	0		
1 1 1	Osstem SSII	11.5	4.1	0	12	CAD/CAM zirconia	All-on-three zirconia
		13	4.1	1	0		
		13	4.1	1	0		
1 1 1	Straumann	12	4.1	1	12	CAD/CAM zirconia	Natural dentition and implants
		12	4.8	0	1		
		12	4.1	1	0		
1 1 1	Straumann	14	4.1	0	12	CAD/CAM zirconia	All-on-three zirconia
		12	4.1	0	1		
		14	4.1	0	0		
1 1 1	Straumann	12	4.1	0	12	CAD/CAM zirconia	All-on-three zirconia
		12	4.1	1	0		
		12	4.1	0	0		
1 1 1	Straumann	12	4.1	1	12	Resin cast-titanium	Natural dentition
		12	4.1	1	0		
		12	4.1	1	0		
1 1 1	Straumann	12	4.1	1	12	Resin cast-titanium	All-on-four resin titanium
		12	4.1	1	1		
		12	4.1	1	1		
1 1 1	Straumann	10	4.1	1	14	CAD/CAM zirconia	All-on-six zirconia
		12	4.1	1	0		
		10	4.1	1	1		



Fig 3 Patient no. 1, case no. 1. Fifteen days after surgery. Delivery of resin provisional restoration, reinforced with fibers and composite. New Class I occlusion is given, with canine and anterior guidance.

Table 1 Distribution of Implants (cont.)

Patient/ case no.	Gender	Age	Smoker	Maxilla
15/21	M	39	No	1 1 1
15/22	M	39	No	
16/23	M	47	No	
17/24	F	43	No	1 1 1
Total	M: 64.70%, F: 35.29%	Mean age 52.88	8 (47.05%)	36 (50%)
			5-year success rate	100%

M = male; F = female; PU = prosthesis dental units;
CUL = cantilever units left; CUR = cantilever units right;
CAD/CAM = computer-aided design/computer-assisted manufacture.

For the implant distribution and location, the aim was to arrange implants with a large interimplant distance and a short cantilever length. Finally, the flap was sutured with 4–0 nonresorbable Gore-Tex sutures (W.L. Gore & Associates).

Provisional Restorations

One patient (no. 1) received an early loaded provisional restoration because he did not accept a complete provisional denture (see Fig 3). All other patients received an immediate complete denture during healing and osseointegration of implants.

Final Prosthetic Protocol

Final impressions were taken 3 months after surgery with Impregum (3M-ESPE). Full-zirconia frameworks (CeraCrown system, Oral Iceberg) were produced with the full dental anatomy. Special attention was made to give enough thickness to the zirconia framework in the area of the fixation screw holes. A minimal portion of porcelain was added to the buccal aspect of the restoration for esthetic reasons (see Fig 4).

The final prosthesis was delivered 4 to 4.5 months postsurgery and all patients received an occlusal night guard to protect the restoration in case of bruxism.

In two cases (see Table 1, patients no. 12 and 13) the patients received a provisional prosthesis made of resin and cast-titanium (Orotig) 4 months postsurgery. These patients were strong bruxers, and it was decided to provisionalize their cases before the final zirconia restorations were made. However, the patients were so comfortable with their provisional prostheses that, at the end of treatment, they did not want to change to the final zirconia restoration, avoiding the extra cost.

Mandible	Brand	L	Ø	Immediate implants	PU CUL CUR	Restoration type	Antagonist
1	Osstem	13	4.1	1	12	CAD/CAM zirconia	All-on-three zirconia
	SSII	13	4.1	1	0		
		13	4.1	1	1		
1	Osstem	11.5	4.1	0	12	CAD/CAM zirconia	All-on-three zirconia
1	SSII	13	4.1	1	0		
1		13	4.1	1	0		
1	Osstem	11.5	4.1	0	12	CAD/CAM zirconia	Natural dentition
1	SSII	13	4.1	1	0		
1		11.5	4.1	1	0		
1	Straumann	12	4.1	1	12	CAD/CAM zirconia	Natural dentition and implant
		12	4.1	1	1		
		12	4.1	1	2		
36 (50%)		42 (58.33%)					
100%							



Fig 4 Patient no. 1, case no. 1. All-on-three zirconia maxillary rehabilitation. All-on-four zirconia mandibular rehabilitation.

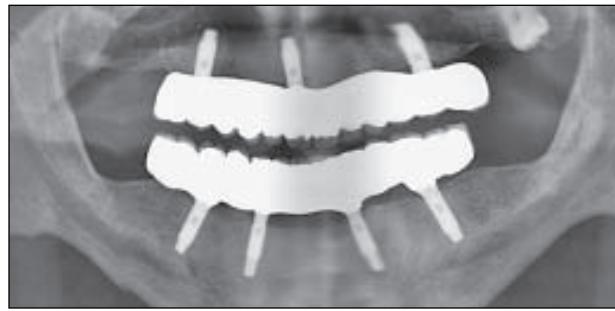


Fig 5 Patient no. 1, case no. 1. One-year and 5-year follow-ups. Panoramic radiograph confirms the bone stability around implants and the fit of the restorations; note the healthy aspect of soft tissues.



Success Rate

No implants were lost in any case, giving a 100% success rate. Figures 6 and 7 show the 5-year follow-up panoramic radiographs.

Marginal Bone Level

The mean marginal bone loss after 5 years of function was 0.53 mm (SD, 0.32 mm) for the internal connection implants and 0.84 mm (SD, 0.62 mm) for the external connection implants.

Clinical Findings

At the 5-year examination, absence of marginal plaque and absence of bleeding on probing was reported for 82.5% and 79.2% of the sites, respectively.

Mechanical Complications

No fractures of zirconia restorations were reported. In one case, the fixation screw of the restoration was loose after the first 3 months of loading. In this case, the screw was fastened again at 20 N and the problem was solved. Porcelain chipping occurred in one case after 1 year of implant loading.

DISCUSSION

In the present study with all-on-three implant protocol and delayed loading, no implants were lost giving a 100% success rate. The results compare favorably with other reported protocols for the same situation.

Hatano et al^{5,6} reported a 97.6% and 96.7% success rate over a 3-year and 11-year period, respectively, for

three implants and immediate loading in the mandible. These values appear better than those originally reported by Bränemark with the Novum protocol that reported a 93% success rate over a 5-year period. All studies were done with an immediate loading protocol. In the present study, all cases except one were loaded after osseointegration had occurred. Most of the patients already had a previous removable denture before treatment and there was no need for a provisional fixed denture. Because there is no previous experience with the all-on-three concept, immediate loading should be tested in a follow-up to this study and compared with actual results.

Biomechanical analysis indicates that the most anterior and posterior implants supporting a reconstruction take the major load share at cantilever loading, irrespective of the number of intermediate implants that support the restoration.^{7,8} This information is supported by *in vivo* measurements.⁹ In this study, in order to avoid cantilever loading and whenever bone was available, the posterior implants were placed distal to the mental foramen in the area of the first or second molar.

One of the advantages of placing three implants for a full arch is that the implants are placed in areas where more bone is available, reducing the need for bone regeneration. Another advantage is the good stability of the restoration on the implants due to the tripod effect. Another important advantage of placing fewer implants is reduced postsurgery trauma with less inflammation and pain. Last but not least, reducing the number of implants may be important for some patients with financial restrictions.

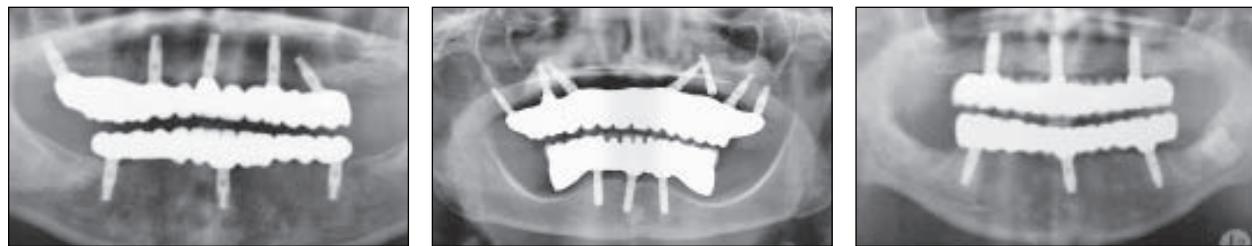


Fig 6 Patients no. 2 to 9. Five-year follow-up with panoramic radiographs.

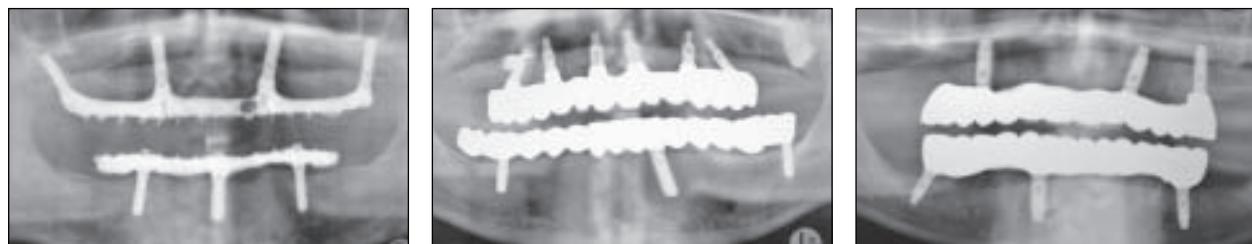
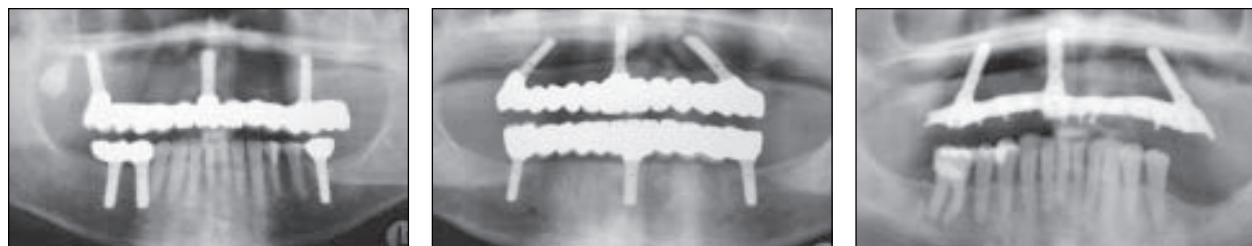
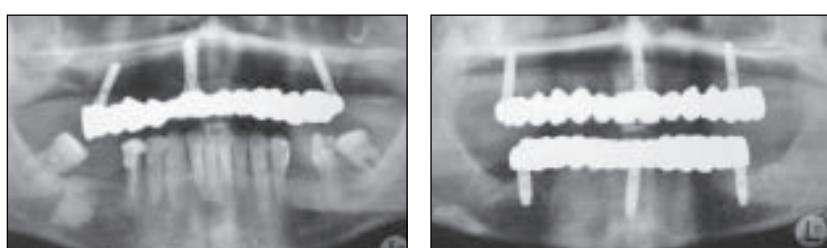
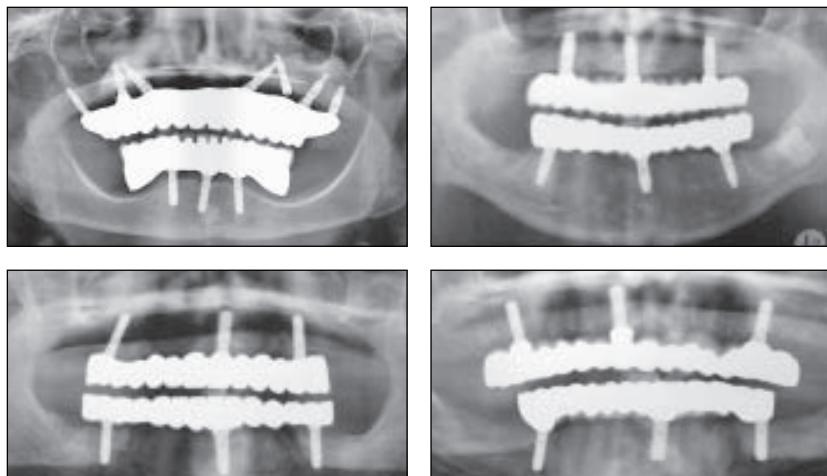
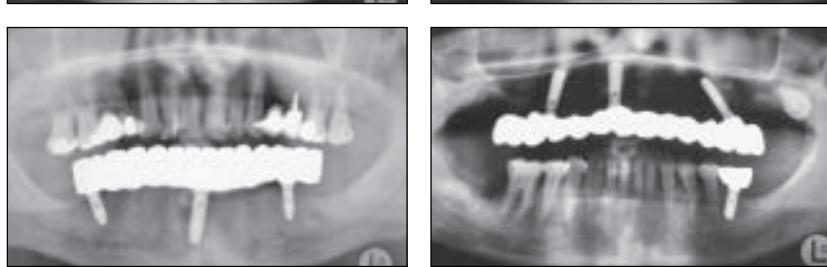


Fig 7 Patients no. 10 to 17. Five-year follow-up with panoramic radiographs.



A disadvantage of placing only three implants to restore a full maxilla or mandible is the risk of prosthetic fracture if the material used is not rigid enough. In this

sense, it is very important for the dental technician to be well-trained and have ample experience in zirconia full-arch restorations.

In the present study, some patients received treatment with the all-on-three concept in one arch and a different approach using more implants in the opposing dentition. There were two main reasons for this: (1) some patients received treatment in the maxilla and mandible during different time frames before the all-on-three concept was an alternative option; (2) if a patient lacked the bone availability to place three implants with a perfect foundation, then more implants were placed to restore the patient in a more conventional fashion.

In the present study, only one case of porcelain chipping was reported. This contradicts the scientific literature that show results with much higher incidences of porcelain chipping. This may be due to the fact that the zirconia frameworks were manufactured to full contour, giving a minimal layer of porcelain veneer in the esthetic area. The zirconia frameworks were reinforced in the palatal and lingual aspects to increase the strength of the prosthesis. Moreover, all patients wore a nightguard that may be very beneficial in avoiding chipping problems in bruxers.

CONCLUSIONS

Within the limitations of the study, the following conclusions were drawn:

- Using three implants as support for a full-arch prosthesis demonstrated a 100% success rate after 5 years.
- Long-span zirconia frameworks with up to 14 units have been delivered with no failures or fractures after 5 years.
- Studies with a larger number of patients are needed to obtain significant results and comparisons with an immediate loading approach.

ACKNOWLEDGMENTS

The authors reported no conflicts of interest related to this study.

REFERENCES

1. Bränemark PI, Engstrand P, Öhrnell LO, et al. Bränemark Novum—A new treatment concept for rehabilitation of the edentulous mandible. Preliminary results from a prospective clinical follow-up study. *Clin Implant Dent Relat Res* 1999;1:2–14.
2. Engstrand P, Grondahl K, Ohrnell LO, Nilsson P, Nannmark U, Bränemark PI. Prospective follow-up study of 95 patients with edentulous mandibles treated according to the Bränemark Novum concept. *Clin Implant Dent Relat Res* 2003;5:3–10.
3. Östman PO. Immediate/early loading of dental implants. Clinical documentation and presentation of a treatment concept. *Periodontology 2000* 2008;47:90–112.
4. Esposito M, Grusovin MG, Achille H, Coulthard P, Worthington HV. Interventions for replacing missing teeth: Different times for loading dental implants. *Cochrane Database Syst Rev* 2009 Jan 21: CD003878.
5. Hatano N, Yamaguchi M, Suwa T, Watanabe K. A modified method of immediate loading using Bränemark implants in edentulous mandibles. *Odontol* 2003;91: 37–42.
6. Hatano N, Yamaguchi M, Yaita T, Ishibashi T, Sennerby L. New approach for immediate prosthetic rehabilitation of the edentulous mandible with three implants: A retrospective study. *Clin Oral Implants Res* 2011;22:1265–1269.
7. Krekmanov L, Kahn M, Rangert B, Lindstrom H. Tilting of posterior mandibular and maxillary implants for improved prosthesis support. *Int J Oral Maxillofac Implants* 2000;15:405–414.
8. Rangert B, Jemt T. Forces and moments on Bränemark implants. *Int J Oral Maxillofac Implants* 1989;4:241–247.
9. Duyck J, Van Oosterwyck H, Vander Sloten J, De Cooman M, Puers R, Naert I. Magnitude and distribution of occlusal forces on oral implants supporting fixed prostheses: An in vivo study. *Clin Oral Implants Res* 2000;11:465–475.

