

Bone Reformation and Implant Integration following Maxillary Sinus Membrane Elevation: An Experimental Study in Primates

Vinicius C. Palma, DDS;* Osvaldo Magro-Filho, DDS;* José Américo de Oliveira, PhD;†
Stefan Lundgren, DDS, PhD;‡ Luiz A. Salata, DDS, PhD;§ Lars Sennerby, DDS, PhD||

ABSTRACT

Background: Recent clinical studies have described maxillary sinus floor augmentation by simply elevating the maxillary sinus membrane without the use of adjunctive grafting materials.

Purpose: This experimental study aimed at comparing the histologic outcomes of sinus membrane elevation and simultaneous placement of implants with and without adjunctive autogenous bone grafts. The purpose was also to investigate the role played by the implant surface in osseointegration under such circumstances.

Materials and Methods: Four tufted capuchin primates had all upper premolars and the first molar extracted bilaterally. Four months later, the animals underwent maxillary sinus membrane elevation surgery using a replaceable bone window technique. The schneiderian membrane was kept elevated by insertion of two implants (turned and oxidized, Brånemark System®, Nobel Biocare AB, Göteborg, Sweden) in both sinuses. The right sinus was left with no additional treatment, whereas the left sinus was filled with autogenous bone graft. Implant stability was assessed through resonance frequency analysis (Osstell™, Integration Diagnostics AB, Göteborg, Sweden) at installation and at sacrifice. The pattern of bone formation in the experimental sites and related to the different implant surfaces was investigated using fluorochromes. The animals were sacrificed 6 months after the maxillary sinus floor augmentation procedure for histology and histomorphometry (bone-implant contact, bone area in threads, and bone area in rectangle).

Results: The results showed no differences between membrane-elevated and grafted sites regarding implant stability, bone-implant contacts, and bone area within and outside implant threads. The oxidized implants exhibited improved integration compared with turned ones as higher values of bone-implant contact and bone area within threads were observed.

Conclusions: The amount of augmented bone tissue in the maxillary sinus after sinus membrane elevation with or without adjunctive autogenous bone grafts does not differ after 6 months of healing. New bone is frequently deposited in contact with the schneiderian membrane in coagulum-alone sites, indicating the osteoinductive potential of the membrane. Oxidized implants show a stronger bone tissue response than turned implants in sinus floor augmentation procedures.

KEY WORDS: augmentation, bone formation, dental implants, experimental model, maxillary sinus, membrane elevation, osseointegration, surface treatments

*Assistant professor, Department of Oral and Maxillofacial Surgery and Integrated Clinic, University of the State of Sao Paulo, Faculty of Dentistry of Aracatuba, Brazil; †professor, Department of Basic Sciences, University of the State of Sao Paulo, Faculty of Dentistry of Aracatuba, Brazil; ‡professor, Department of Oral and Maxillofacial Surgery, Umeå University, Umeå, Sweden; §associate professor, Department of Oral and Maxillofacial Surgery and Periodontics, University of Sao Paulo, Faculty of Dentistry of Ribeirao Preto, Brazil; ||professor, Department of Biomaterials, Institute for Surgical Science, The Sahlgrenska Academy, Göteborg University, Göteborg, Sweden

Reprint requests: Prof. Lars Sennerby, Department of Biomaterials, Institute for Surgical Science, The Sahlgrenska Academy, Göteborg University, PO Box 412, SE 405 30 Göteborg, Sweden; e-mail: lars.sennerby@biomaterials.gu.se

Endosseous implants can predictably replace missing teeth in edentulous patients with adequate bone height and width. Inadequate alveolar bone volume is a common limitation in the posterior maxilla since advanced resorption following premature tooth loss is frequently combined with the pneumatization of the maxillary sinus.¹ Various maxillary sinus floor augmentation procedures have been used for reconstruction of

the posterior maxilla in conjunction with simultaneous or delayed placement of endosseous dental implants.^{2,3} Different surgical techniques for sinus floor augmentation can be used depending on the residual bone height. The expansive osteotome technique through the alveolar ridge allows bone compaction by gentle pushing and tapping of instruments, so the adjacent bone layer can be compressed and the schneiderian membrane elevated and a bone graft placed.⁴ This technique can be applied with simultaneous placement of implants where more than 6 mm of residual bone is present and an increase of about 3 to 4 mm is expected. In case of more advanced resorption, a bone window in the lateral wall is required to elevate the schneiderian membrane and augment the sinus floor.⁵ The window technique has been reported to deliver a significantly larger increase in bone height than the osteotome technique.⁶

A large variety of grafting materials have been tested for maxillary sinus floor augmentation in both clinical⁷⁻⁹ and experimental studies,⁹⁻¹³ including autogenous,^{8,14-18} allogeneous,^{16,19-22} and a combination of these materials.^{3,7,8} An ideal graft material for sinus floor augmentation should be biocompatible, increase bone volume in the grafted area to promote initial stability at implants sites, and be absorbed with time and replaced by native bone.²³ Autogenous bone grafts are considered to be the gold standard because of the lack of immunologic rejection mechanisms, and they have both osteoinductive and osteoconductive properties.²⁴ But they require additional surgery for harvesting procedure, which means increased morbidity, considerable demands on the patients, more time, higher cost, paresthesia, and residual defects.^{25,26} Generally good results have been reported from sinus floor augmentation with different graft materials. To date, the autogenous bone graft either used alone or mixed with cancellous bovine bone mineral or bioactive glass particles is the most common grafting approach for sinus floor augmentation.^{3,8,20}

Efforts have been directed at developing different types of implant surface textures to achieve better osseointegration. Previous reports have demonstrated that a higher extent and faster bone formation occurred directly on oxidized than on turned implant surfaces.²⁷⁻²⁹ It is expected that in challenging bone-forming situations such as sinus floor augmentation, the osseointegration is highly dependent on the surface characteristics of the implant. Using sinus grafting with platelet-rich plasma and hydroxyapatite, Fürst and colleagues found

inferior bone-implant contact with turned implants than others who had used the same experimental surgical procedure but roughened implant surfaces.^{10,19,21,30,31} Ellegaard and colleagues reported on surface-treated implants placed in the maxillary sinus without any grafting procedure.³² Thirty-five of 38 implants were successfully integrated with a follow-up period of 27 months. Haas and colleagues, using sinus floor augmentation in sheep, observed that the control group was related to better bone-implant contact at titanium plasma-sprayed (TPS) implants than in sinuses implanted with human or sheep decalcified freeze-dried bone.¹⁶ Recently, a clinical study reported a simplified technique to increase bone at the sinus floor.³³ Ten patients received 19 oxidized implants in conjunction with lifting of the maxillary sinus membrane using a lateral replaceable bone window. Twelve months after functional loading, all implants had remained stable, as measured by resonance frequency analysis (RFA), and new bone had formed in the void left by sinus membrane elevation, as assessed by radiographic examination. The authors concluded that the creation of a secluded space between the bone surfaces and the sinus membrane results in spontaneous bone formation in the maxillary sinus.³³

The mechanisms behind bone formation underneath the elevated membrane are not yet fully understood. Considering that the autogenous bone graft has been ranked as gold standard material for bone formation, experimental investigations are needed to support the clinical findings using this novel technique. This experimental study aimed at comparing the histologic outcomes of sinus membrane elevation and simultaneous placement of implants with and without adjunctive autogenous bone grafts. The purpose was also to investigate the role played by the implant surface in osseointegration under such circumstances.

MATERIALS AND METHODS

This animal study was carried out in accordance with the rules of the Brazilian Institute for Protection of the Environment and was approved by the Animal Ethics Committee at the Faculty of Dentistry of the University of the State of Sao Paulo – UNESP, Aracatuba, Brazil.

Four young adult male tufted capuchin primates (*Cebus apella*),³⁴ 8 to 12 years old and weighing between 2 and 3 kg, were included in this study. Before surgery, the animals were maintained in individual cages at the Primate Procreation Nucleus Faculty of Dentistry,

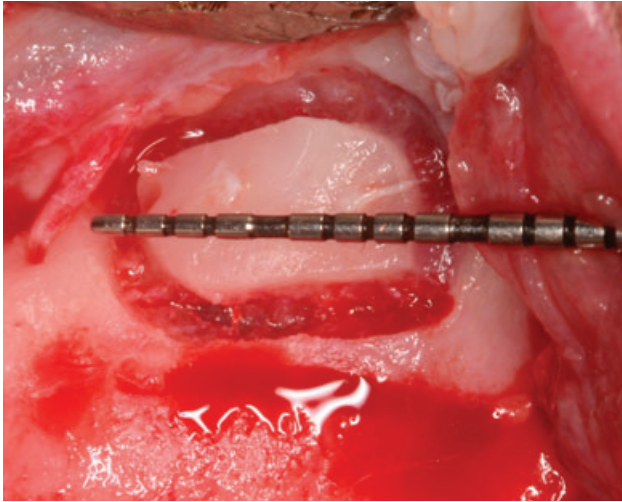


Figure 1 Clinical photograph showing the standardized outline of the bone window before removal.

UNESP, Aracatuba, Brazil, with water and food *ad libitum*. For all procedures involved in the study, the animals were first sedated with ketamine hydrochloride (Ketamin™, Cristalia Produtos Químicos Farmacêuticos Ltd, Campinas, Brazil), 10 mg/kg body weight, administered intramuscularly. Prior to surgery or any animal manipulation, general anesthesia was obtained with pentobarbital sodium (Abbott Laboratories North Chicago, Chicago, IL, USA), at a dosage of 30 mg/kg. The anesthesia was supplemented by local administration of 2% mepivacaine HCl with 1:100,000 epinephrine (DFL Ltd, Rio de Janeiro, Brazil). Prior to surgery, the animals received dental prophylaxis and all of the surgical sites were washed with 0.12% chlorhexidine gluconate solution (Periogard™, Colgate-Palmolive Ltd, Sao Paulo, Brazil). The surgeries were performed under sterile conditions.

Surgeries

All animals underwent two surgical procedures. The first was designed for the extraction of the first, second, and third upper premolars and the first molar bilaterally. The teeth were extracted with special care, avoiding osteotomy. The sinus floor augmentation procedure took place after 4 months of dental socket healing. Just before the second surgery, the animals were subjected to axial and coronal computed tomographic scans (Toshiba Xvision™, Tokyo, Japan) of the edentulous alveolar bone and sinus to determine the anatomic structure, sinus volume, and evidence of maxillary sinusitis.

After a midcrestal incision and vertical releasing incisions, mucoperiosteal flaps were raised and reflected

at the edentulous posterior maxilla on both sides to access the alveolar bone. The lateral aspect of the maxillary sinus was fully exposed using a number 3 diamond round bur to create a $1.0 \times 0.6 \pm 0.2$ cm rectangular window under continuous saline irrigation (Figure 1). An osseous window was freed by fracturing along the osteotomy lines, removed, and stocked in saline solution. The schneiderian membrane was then carefully elevated with specially designed elevators (Friatec™, Friedrichsfeld, Germany). All four animals received two implants sized 3.75 mm wide and 8.5 mm long, one with a turned and one with an oxidized surface (Mk III and Mk III TiUnite™, respectively, Brånemark System®, Nobel Biocare AB, Göteborg, Sweden) on each side. The oxidized implant was always inserted mesially in relation to the turned implant (Figure 2). The right sinus was always used as a control side (membrane elevation alone), whereas the left sinus was filled with autogenous bone (bone graft group) (Figures 3 and 4). The autogenous bone graft was obtained from the midshaft of the right tibia in each animal using bone scrapers (3i™ Inc, USA). The average volume of harvested bone was 1.2 cm^3 ; the bone was immediately stored in a glass well at room temperature. The elapsed time between bone harvesting and grafting procedures ranged from 15 to 20 minutes. Once the presence of coagulum beneath the elevated schneiderian membrane on the right side was confirmed and the bone graft was filling up this space like a tent on the left side, the bone windows were repositioned (Figure 5). The mucoperiosteal flap was sutured with Vicryl 5-0® (Ethicon, Johnson & Johnson, Sao Jose

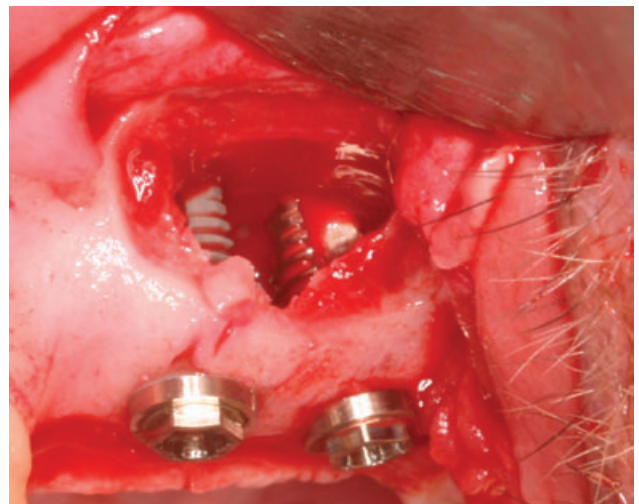


Figure 2 Clinical photograph showing one turned and one oxidized implant after installation.

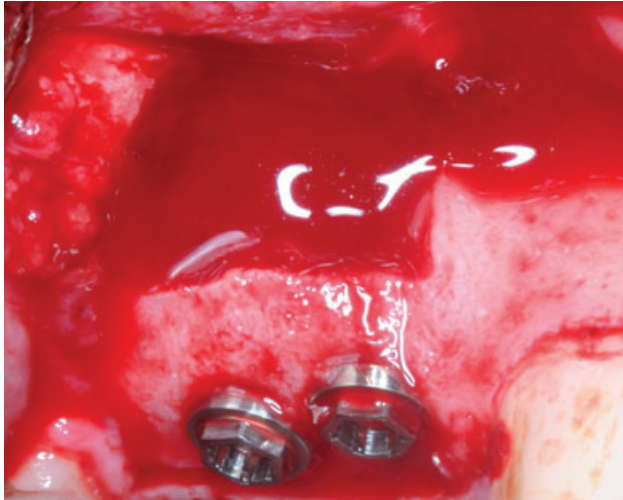


Figure 3 Clinical photograph after sinus elevation showing blood fill of the space between the implants and the elevated sinus membrane.

dos Campos, Brazil). The wound was finally rinsed with 0.12% chlorhexidine gluconate solution.

Postoperative Care

The animals were fed with a soft diet (Sustagen™, Nestle, Brazil) during the first 15 days and with fruits and cooked vegetables afterward. Three times daily, the animals were given an oral dose of amoxicillin (20 mg/kg, Stiefel, Guarulhos, Brazil) mixed with fruit shakes for 7 days and Tylenol™ (30 mg/kg, Janssen-Cilag, Sao Jose dos Campos, Brazil) mixed with fruit shakes for 2 days and water ad libitum. The animals were inspected after the first, third, and fifth postoperative

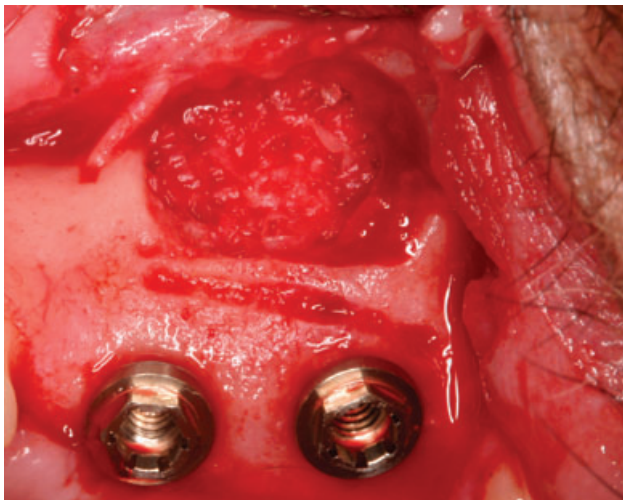


Figure 4 Clinical photograph showing sinus elevation and subsequent fill with autogenous bone graft.



Figure 5 Clinical photograph after replacement of the bone window showing implant stability measurement using an Osstell™ instrument.

months for signs of wound and general health complications. During this period, systematic periodontal care was carried out, as well as local application of 0.12% chlorhexidine gluconate solution.

Resonance Frequency Analysis

The stability of the implants was measured with RFA (Osstell™, Integration Diagnostics AB, Göteborg, Sweden) in implant stability quotient units at implant insertion (see Figure 5) and after 6 months.

Bone Labeling

Calcein (Sigma-Aldrich Chemie GmbH, Steinheim, Germany), 20 mg/kg, and alizarin red S (Sigma-Aldrich Chemie GmbH), 30 mg/kg, were injected subcutaneously at 50 and 100 days, respectively.

Sacrifice and Specimens Postprocessing

Six months after surgery, the animals were anesthetized with pentobarbital sodium associated with analgesics to undertake vascular perfusion with paraformaldehyde. The maxilla was retrieved en bloc, and the surrounding soft tissues were detached (Figure 6). The specimens were trimmed and immersed in 4% paraformaldehyde in 0.1 M in sodium phosphate buffer (pH 7.4).

Histologic Preparation and Assessments

The specimens were dehydrated in a series of ethanol embedded in hard-grade acrylic resin (LR White™, London Resin Company Ltd, Berkshire, England) and

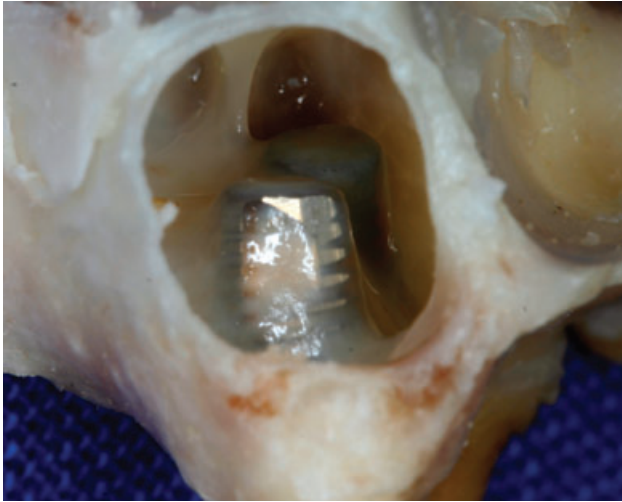


Figure 6 Clinical photograph after harvesting of block sections of the maxilla. The tuber area was opened to expose the sinus cavity. The turned and oxidized implants were seen to be covered by both schneiderian membrane and bone.

polymerized in a dry heat oven at 60°C. The plastic blocks were mounted on slides, sawn to about 40 μm thickness (Microslice 2TM, Ultratec Inc, Santa Ana, USA), and ground manually to about 15 μm thickness and finally stained with toluidine blue/pyronin Y. Three buccal-palatine sections were taken from each implant, two destined for histology and the other for fluorescence analysis.

Histometric Analysis

All ground sections were examined in a Leica DMLBTM microscope equipped with a Leica Digital Camera DFC 300FX (Leica Microsystems Wetzlar GmbH, Germany). The histometric analyses were carried out using Leica QwinTM version 3 software (Leica Microsystems Wetzlar GmbH) and comprised bone-implant contact (BIC) and bone area in implant threads (BA) measurements. Two standardized rectangular areas measuring 2,900 \times 1,060 μm were drawn in contact with both the buccal and the palatal emergent points of the threads at the midthird of all implants outward (Figure 7). The mean of the bone area in rectangle (BAR) at each side of the implant was taken as the percentage of the total area for comparison between different treatments. In addition, the thickness of the marginal corical bone was measured.

Statistics

No statistical tests were applied owing to the low number of animals. Descriptive data were presented in plot charts with group means.

RESULTS

Clinical Examination

The postoperative period was uneventful, and the animals were healthy throughout the follow-up time. One implant (turned in a membrane-elevated site, animal 4) that did not reach sufficient primary stability at placement was removed after 4 weeks. A second turned implant placed in a membrane-elevated site (animal 1) with good primary stability became loose and was removed after 4 weeks. Seven implants became exposed 4 weeks after installation and the surrounding tissues appeared to be clinically normal.

Histologic Examination

A typical section comprised the implant, the buccal and palatal tissues, and the augmented sinus floor, including the schneiderian membrane. The floor of the sinus provided approximately 2.2 mm ($\text{SD} \pm 1.1$) of cortical bone for primary stability, whereas the rest of the implant projected into the sinus cavity. At microscope examination, the schneiderian membrane appeared to be morphologically intact in most cases. In two sinuses (animals 2 and 4) treated with membrane elevation and autogenous bone, the membrane was partially perforated at the apical segment of turned implants, which may have affected the BIC, BA, and BAR figures for this group. Nevertheless, no signs of acute or even moderate inflammation could be seen in these or any case analyzed in this study. As a rule, the intact schneiderian membranes were in contact with the apical surface of the implant except when an intervening bone tissue was

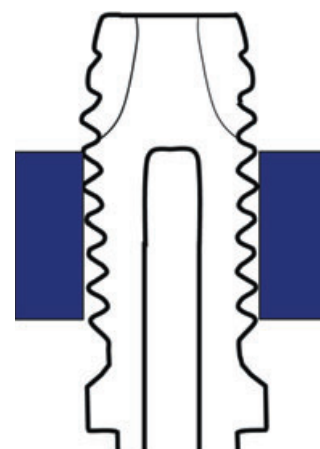


Figure 7 Diagram showing the approximate position (blue rectangles) for bone area in rectangle measurements in all sites.

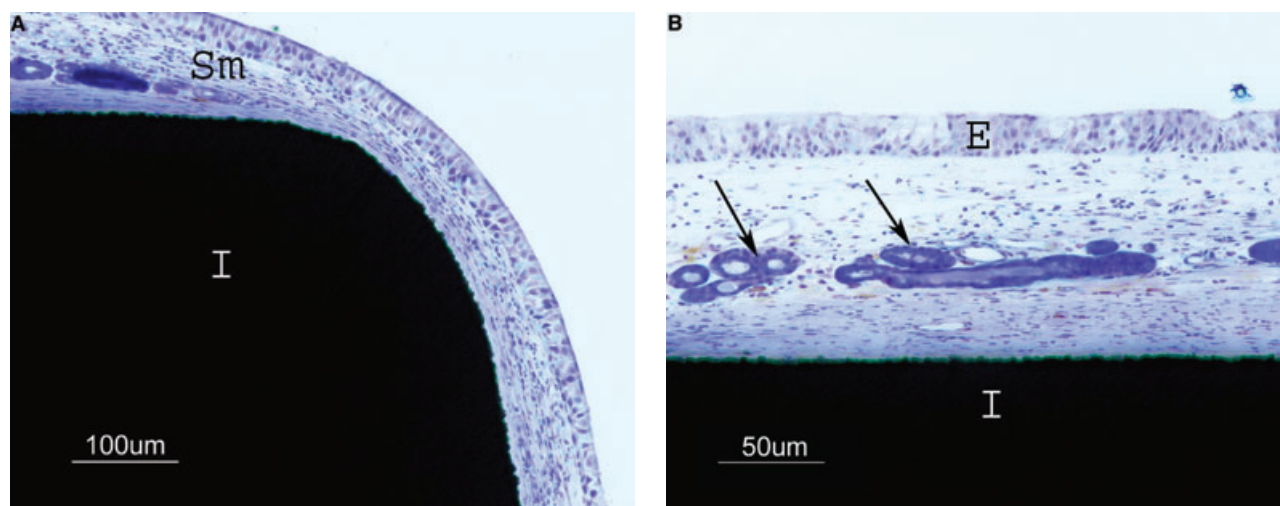


Figure 8 A, Light micrograph featuring a typical interaction between the uppermost apical part of the implant (I) and schneiderian membrane (Sm). B, The membrane is lying at the implant surface without signs of morphologic alteration. Between the implant (I) and the membrane epithelium (E), many vessel sprouts could be captured. (Toluidine blue staining)

present (Figure 8). From this point, the membrane collapsed into the space underneath (Figure 9), irrespective of the treatment group.

The bone windows appeared to be healed. The bone tissue occurring parallel to the implant axis showed different patterns depending on the treatment. Sites treated with membrane elevation alone tended to exhibit larger marrow areas close to implants compared with autogenous bone-treated sites (Figures 10 and 11). Conversely, membrane-elevated sites were related to more bone at the periphery in contact with the schneiderian membrane and sometimes extending downward to the center of the augmented area (Figures 12 and 13). Bone tissue was seldom seen lining the membrane at the uppermost part of the implant in grafted sites. When this did happen, the bone resembled a sequestered island trapped between the implant and the schneiderian membrane during graft insertion. In these cases, the bone was encapsulated by fibrous tissue or showed some degree of resorption (Figure 14).

Different patterns of implant integration could be distinguished for oxidized and turned implants. Although the bone contact with the turned surface seemed to be a consequence of bone growth from the periphery onto the implants (Figure 15), the oxidized surface showed direct bone formation without evident trabeculae projection from the surroundings (Figure 16). The dynamics in this process could be easily recognized through bone labeling (Figure 17), as observed

with fluoroscopy. The calcein stain given after 50 days was mainly seen at the implant interface for oxidized implants and at a distance from the surface for turned implants. The pattern of alizarin red given after 100 days was the opposite.

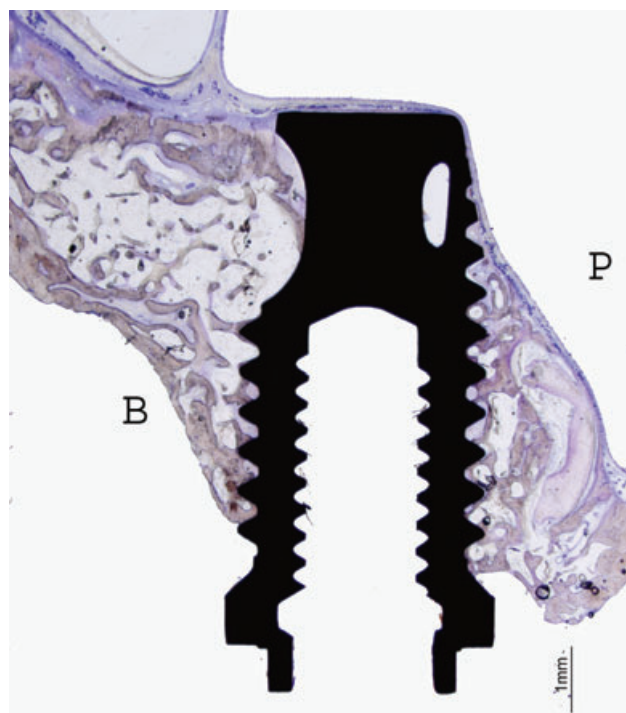


Figure 9 Light micrograph. A tent-like figure is drawn by the sinus membrane from the buccal (B) side of the implant, where the bone window was created, to the palatal (P) side. (Toluidine blue staining)

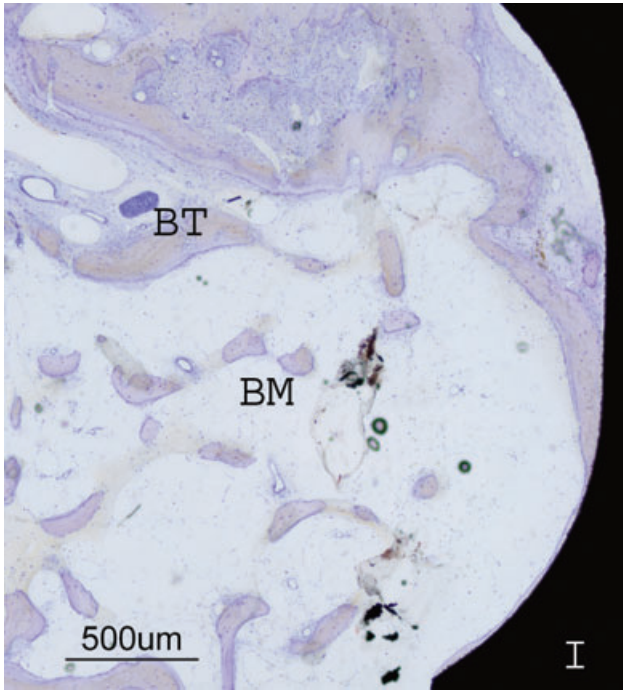


Figure 10 Light micrograph of a site subjected to sinus elevation alone. Despite some sparse bone trabeculae (BT), the most central part of the augmented area was occupied by bone marrow (BM). (Toluidine blue staining)

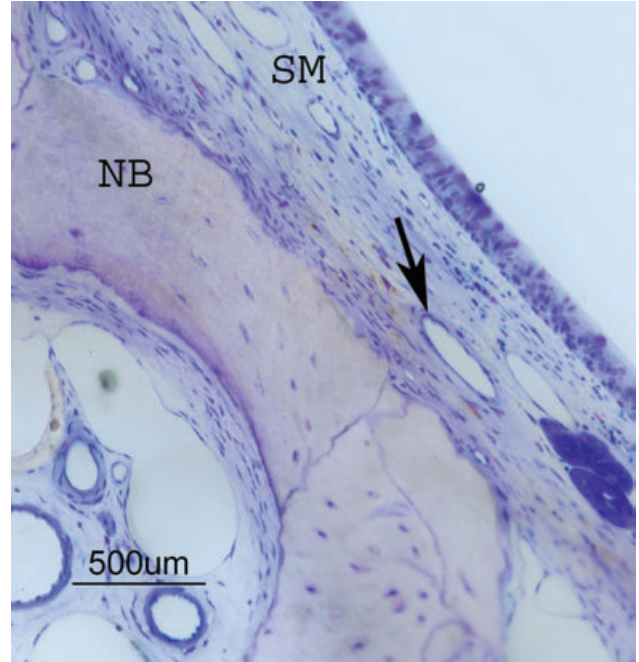


Figure 12 Light micrograph of a membrane-elevated site. New bone (NB) formed in contact with the schneiderian membrane (SM). Many vessels (arrow) occupy the central part of the membrane. (Toluidine blue staining)

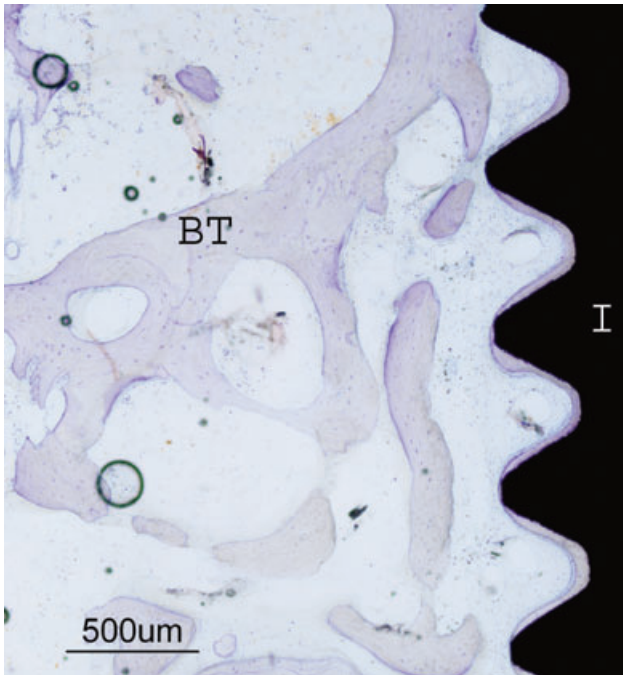


Figure 11 Light micrograph of a site subjected to sinus elevation and autogenous bone grafting. The bone trabeculae (BT) are densely concentrated at the central part of the augmented area. (Toluidine blue staining)

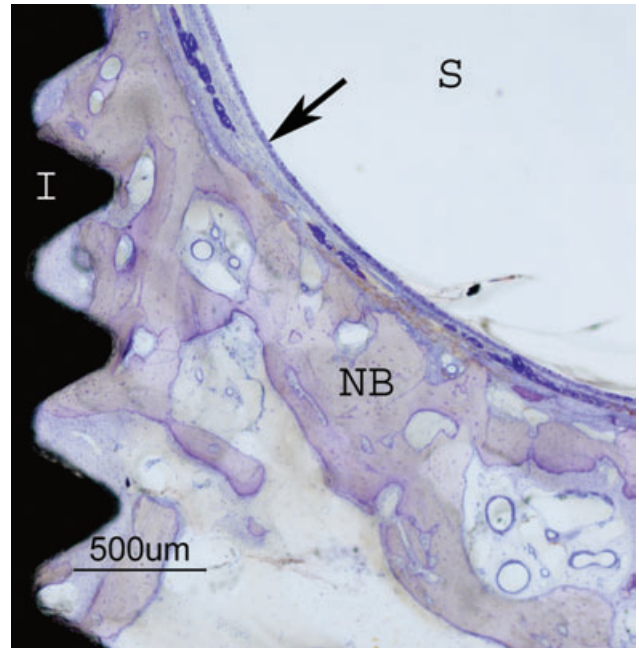


Figure 13 Light micrograph of a membrane-elevated site. New bone (NB) was deposited in contact with the membrane (arrow) that is lining the sinus cavity (S). The process of new bone formation extended toward the center of the augmented area and in contact with the implant (I). (Toluidine blue staining)

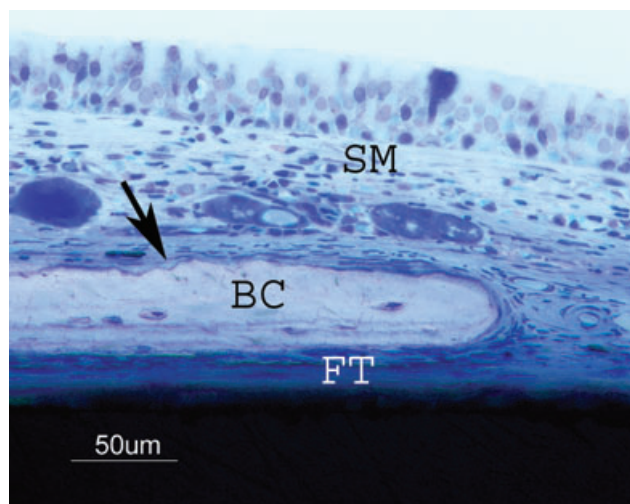


Figure 14 Light micrograph of a bone-grafted site. A bone chip (BC) is trapped in fibrous tissue (FT) between the schneiderian membrane (Sm) and the implant (I). The *arrow* points at resorption pits. (Toluidine blue staining)

Histometric Analysis

The means for BIC, BA, and BAR regarding the two treatments and the means for BIC and BA for implant surfaces are presented in Table 1. The data available showed that the BIC values for oxidized implants were superior to turned implants irrespective of whether they

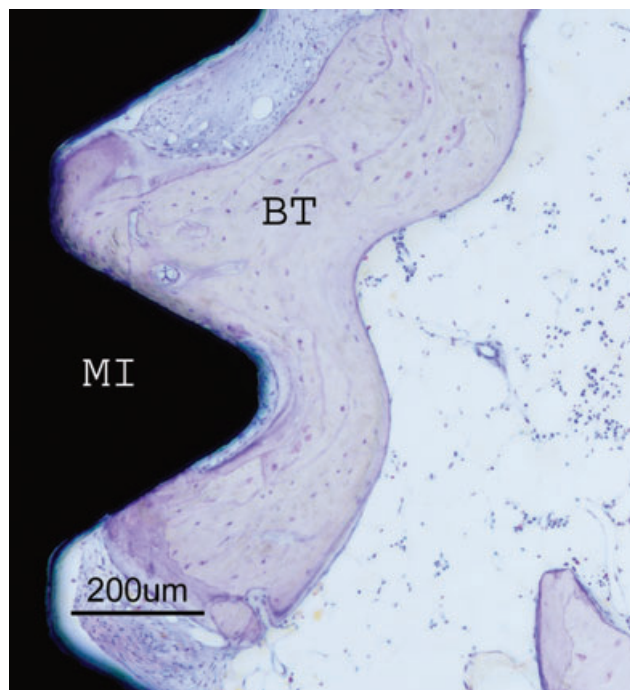


Figure 15 Light micrograph featuring a turned implant (MI). The bone-implant contact is established through bone trabeculae (BT) extending from the surroundings. (Toluidine blue staining)

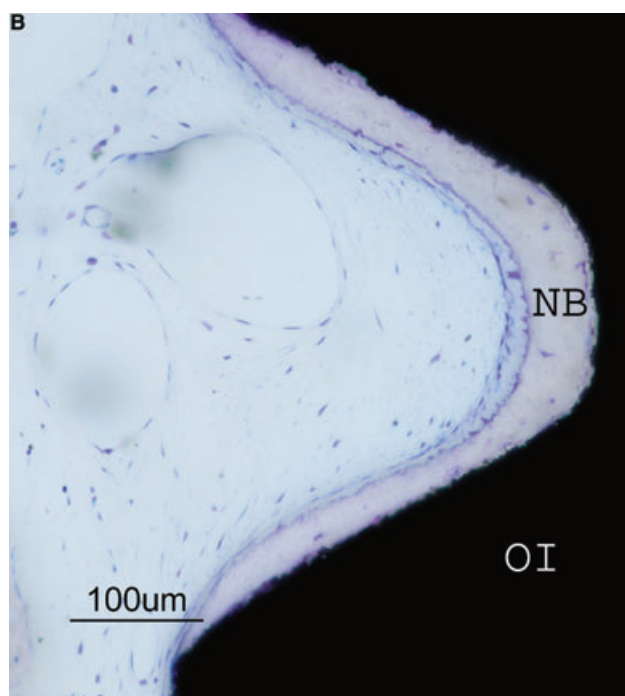
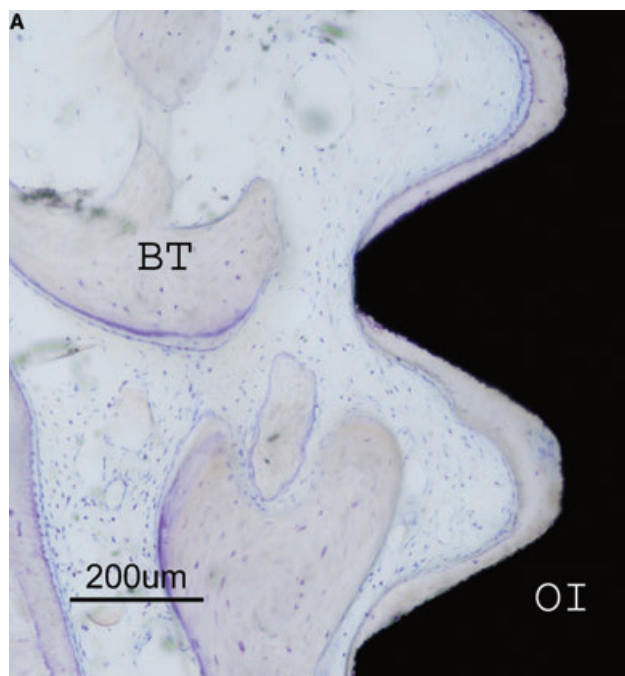


Figure 16 Light micrograph featuring an oxidized implant (OI). *A*, The bone trabeculae (BT) do not show connections with the new bone (NB) in contact with the implant surface. *B*, The newly formed bone (NB) is seen in intimate contact with the implant surface. (Toluidine blue staining)

were placed in membrane-elevated or bone-grafted sites (Figure 18). In general, the BIC for individual implant surfaces does not seem to vary from one implantation site to another. The BA data in Figure 19 revealed the same trends as seen in Figure 18. No obvious differences

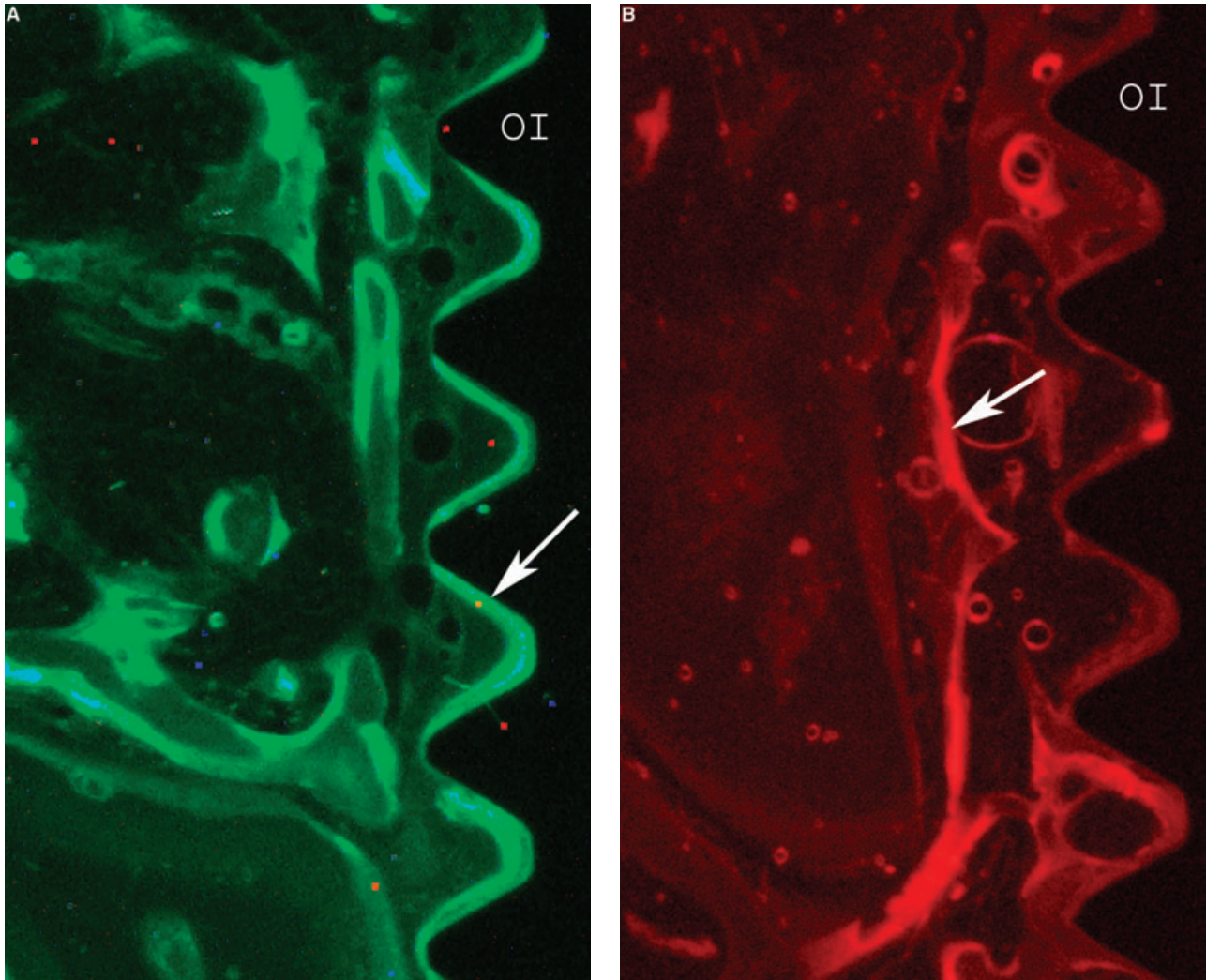


Figure 17 Light micrograph obtained from fluorescence microscopy slides. Distance between two threads = 600 μ m. *A*, Bone formation at the oxidized implant (OI) surface at 50 days after insertion (calcein labeling). The *arrow* points to bright green strips that indicate intense bone deposition. *B*, The *arrow* indicates bright red strips showing bone formation distant from the oxidized implant (OI) surface, 100 days after insertion (alizarin labeling).

in the BAR of the coagulum-alone or bone graft group were seen (Figure 20).

Resonance Frequency Analysis

In general, implant placement resulted in good primary stability. The results from implant stability quotient measurements taken at placement and after 6 months are shown in Table 2.

DISCUSSION

The present experimental study was designed to evaluate bone formation and osseointegration at turned and oxidized implant surfaces placed simultaneously with maxillary sinus membrane elevation with or without adjunctive autogenous bone grafts. In general,

the histologic and histometric examinations revealed no apparent differences for bone formation or implant integration when comparing the two situations. However, both the clinical findings and the histologic examinations indicated a stronger bone response to oxidized implants than to turned ones; two of eight turned implants in membrane-elevated sites were removed because of mobility after 4 weeks, whereas no oxidized implants failed throughout the experimental period. Higher degrees of bone-implant contact and bone fill in the threads were seen for oxidized implants. The experimental findings give histologic evidence and confirm clinical experiences with sinus membrane elevation and simultaneous placement of oxidized implants.³³

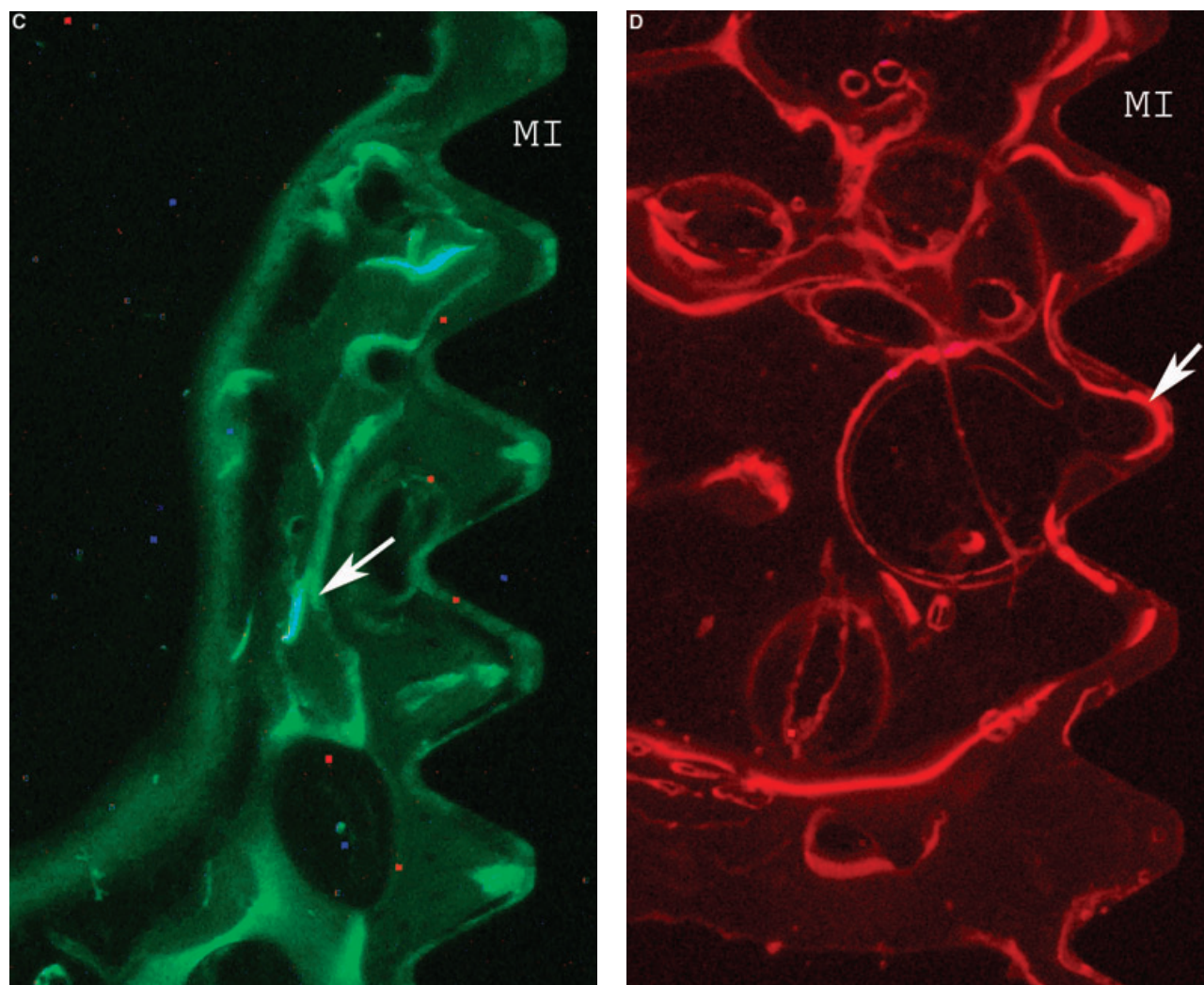


Figure 17 (*continued*) Light micrograph obtained from fluorescence microscopy slides. Distance between two threads = 600 μm . C, Low bone formation activity close to the turned implant (MI) surface 50 days after insertion, although some bone deposition can be detected toward the center of the augmented area (*arrow*) (calcein labeling). D, More intense bone deposition is identified closer to the turned implant (MI) surface at 100 days after insertion, indicated by bright red strips (*arrow*) (alizarin labeling).

Histologically, the oxidized and turned implants seemed to be integrated by following different paths. Whereas at oxidized implants, the bone contact was achieved through appositional and distance osteogenesis,³⁵ the bone tissue engaged turned surfaces through finger-like extensions of newly formed bone that grew from bone walls (appositional bone formation) toward the implant surface. The data from fluorescence analysis reveal that at 50 days postoperatively, mineralized bone was forming in contact with oxidized implants, and at 100 days postoperatively, the bone formation was displaced slightly further away from the implant surface. Most of the turned implant specimens showed very poor labeling at the surface at the same time periods. Typi-

cally, the oxidized implants were very often paved with mineralized tissue deep in the threads, in contact with the surface, even though no apparent neighboring bone projection could be found. In this respect, the interaction between growth factors or hormone and surface topography was demonstrated to modulate bone cell differentiation and mineralization through bone morphogenetic protein 2 expression *in vitro*.^{36,37} Such beneficial effects of surface roughness on implant osseointegration have been confirmed by a number of both experimental and clinical studies.^{27–29,38–40}

Primary implant stability in the present study was similar to that seen in a previous clinical study on sinus membrane elevation and implant placement.³³ The data

TABLE 1 Overall Mean \pm SD for Bone-Implant Contact, Bone Area in Threads, and Bone Area in Rectangle Values Comparing Oxidized and Turned Implants Inserted in Membrane-Elevated or Grafted Sites

Histometric Analysis (% (SD))				
Measurements, Mean (\pm SD)	Membrane Elevation		Membrane Elevation and Bone Graft	
	Turned	Oxidized	Turned	Oxidized
BIC	14.3 (15.1)	37.3 (8.5)	17.6 (10.1)	44.7 (12.9)
BA	28.5 (31.1)	42 (4.3)	17.2 (9.8)	36.5 (9.6)
BAR	45.4 (4.6)		38.5 (11.6)	

BA = bone area in threads; BAR = bone area in rectangle; BIC = bone-implant contact.

indicate that as little as 2.2 mm of marginal bone can give the implant adequate initial support, at least for oxidized implants. Interestingly, the stability of oxidized implants measured through RFA tended to increase from installation until sacrifice in nongrafted sites, whereas it diminished in bone graft sites. Considering that the BICs were almost equal at the sacrifice, the reason for the discrepancy might be that the implants gained stability from bone compaction at the graft site. Thus, the remodeling process seems to negatively affect implant stability mostly in bone-grafted compared with nongrafted sites. Indeed, when BAR is compared regarding the amount of bone found near the implants, the values of membrane elevation sites tended to be higher than in bone graft sites. This assumption may find explanation in the work of Xu and colleagues, who used a sinus floor elevation model in the rabbit.¹⁷ The authors

observed that a homologous graft was associated with significantly larger amounts of osteoclasts from 2 to 10 weeks after membrane elevation surgery than in the coagulum-alone group.

The histologic examination showed that the intact sinus membrane was mostly in contact with the apical surface of the implant, and from this point, it slightly collapsed into the space underneath to form a tent-shaped figure. The membrane-elevated site tended to exhibit larger marrow areas at the center of the elevated area. Both membrane elevation-alone and bone graft sites were characterized by the presence of trabecular bone formation close to implants, predominantly at the midthird. A strip of bone could be frequently seen near the uppermost part of the implant and downward, lining the elevated membrane. This finding is in accordance with descriptions made in a previous study with

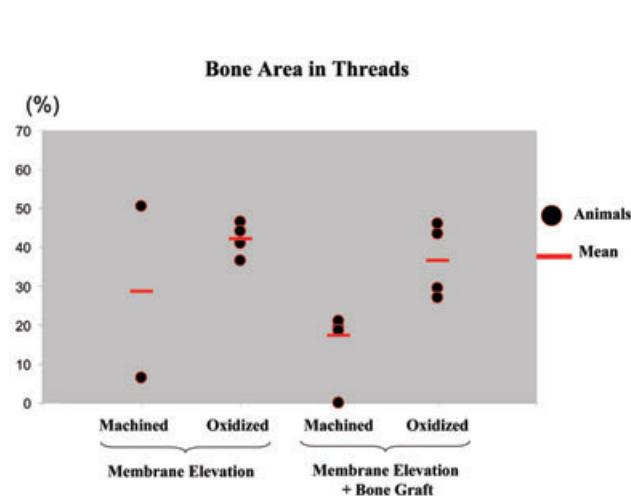


Figure 18 Diagram showing a plot of bone area values in the threads for oxidized and turned implants.

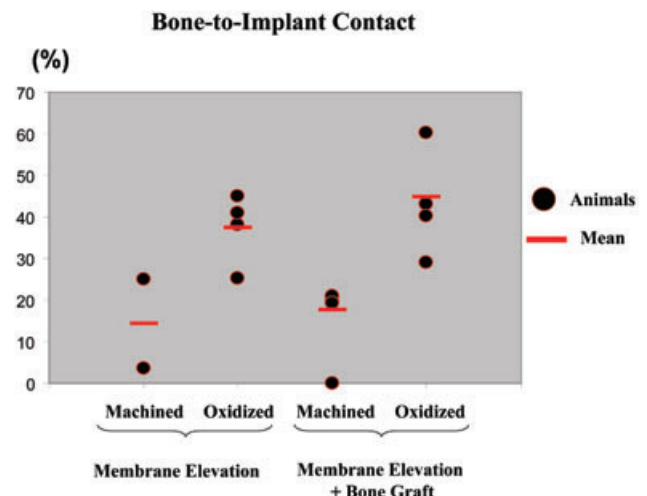


Figure 19 Diagram showing a plot of bone-implant contact values for oxidized and turned implants.

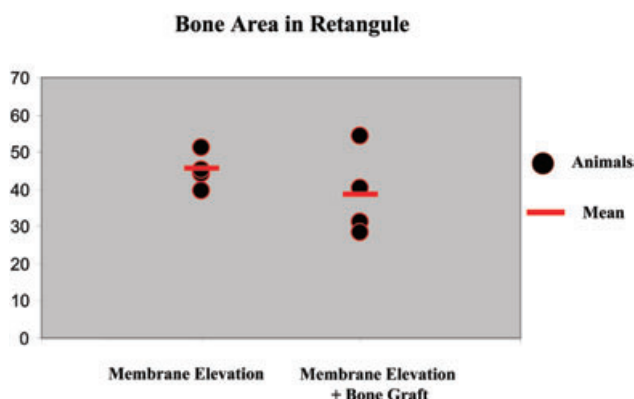


Figure 20 Diagram showing a plot of bone area in rectangle values.

maxillary sinus floor augmentation in the rabbit.¹⁷ In bone graft sites, the bone strips were mostly on the top of the implants, and in some cases, the bone showed a necrotic appearance, usually associated with the presence of sporadic Howship's lacunae and surrounded by fibrous tissue. Conversely, the bone tissue adhered to the membrane in coagulum sites exhibited healthy characteristics, showing a transition from woven to lamellar bone with secondary osteons. A recent *in vitro* study demonstrated that the sinus mucosa holds mesenchymal progenitor cells and cells committed to the osteogenic lineage,⁴¹ what in our study might explain the *de novo* bone formation in contact with the membrane. Altogether, these observations may suggest that despite the expected bone remodeling that takes place in all sites, bone deposition is a continuous process from the beginning at elevated sites without bone grafts, whereas a resorptive pattern of the bone particles predominates in bone graft sites. Undeniable by the evidence of the importance of coagulum and the endogenous growth factors it carries in the tissue regeneration field,^{32,33,42–47} it seems that the osteoinductive properties of the co-

agulum can be limited only by its inability to maintain space.

In a study by Haas and colleagues and in the present study, the sinus membrane was found partially collapsed in both the coagulum and bone graft groups.¹⁶ The progressive sinus pneumatization occurring following sinus floor augmentation procedures may require augmenting techniques that would enable the membrane to remain at the elevated place in the long term, which has been a justification for the growing application of grafting materials in these cases.^{2,7} On the other hand, the findings from Haas and colleagues¹⁶ and the present study showed that implant integration was well preserved in spite of a collapsing membrane.

CONCLUSIONS

Although bone formation following sinus floor augmentation without additional bone grafts has been observed by different authors,^{16,32,33,48,49} intentionally or not, the present study is the first to histologically describe this process and the integration of simultaneously placed implants with different surfaces in such circumstances. We conclude that

1. Membrane elevation of the sinus membrane and simultaneous placement of implants result in bone formation and osseointegration in the maxillary sinus.
2. The amount of bone tissue does not differ when comparing sinus membrane elevation with or without bone grafts.
3. Histologically, *de novo* bone was frequently deposited in contact with the Schneiderian membrane in nongrafted sites, confirming the osteoinductive potential of the membrane.
4. Oxidized implants show a stronger bone response in maxillary sinus floor augmentation procedures.

TABLE 2 Mean \pm SD for Implant Stability Quotient Values Measured during Installation and before Sacrifice at Oxidized and Turned Implants Placed in Coagulum-Alone and Bone Graft Sites

Measurements	RFA (ISQ (SD))							
	Membrane Elevation				Membrane Elevation and Bone Graft			
	Turned		Oxidized		Turned		Oxidized	
	Installed	Sacrificed	Installed	Sacrificed	Installed	Sacrificed	Installed	Sacrificed
Mean (\pm SD)	67 (2)	64 (2.8)	63.2 (4.6)	65.7 (2.4)	68 (2.6)	67.6 (12.5)	68 (1)	65 (4.6)

ISQ = implant stability quotient; RFA = resonance frequency analysis.

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