Clinical and Histological Evaluation of Postextraction Platelet-rich Fibrin Socket Filling: A Prospective Randomized Controlled Study

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Objectives: *The aims were to investigate whether the use of platelet-rich fibrin membranes (PRF) for socket filling could improve microarchitecture and intrinsic bone tissue quality of the alveolar bone after premolar extraction and to assess the influence of the surgical procedure before implant placement.*

Material and Methods: *Twenty-three patients requiring premolar extraction followed by implant placement were randomized to three groups: (1) simple extraction and socket filling with PRF, (2) extraction with mucosal flap and socket filling with PRF, and (3) controls with simple extraction without socket filling. Implant placement was performed at week 8, and a bone biopsy was obtained for histomorphometric analysis.*

Results: *Analysis by microcomputed tomography showed better bone healing with improvement of the microarchitecture ($P < 0.05$) in group 1. This treatment had also a significant effect ($P < 0.05$) on intrinsic bone tissue quality and preservation of the alveolar width. An invasive surgical procedure with a mucosal flap appeared to completely neutralize the advantages of the PRF.*

Conclusions: *These results support the use of a minimally traumatic procedure for tooth extraction and socket filling with PRF to achieve preservation of hard tissue. (Implant Dent 2013;22:295–303)*

Key Words: alveolar bone, bone biopsy, surgical procedure, tooth extraction

Maintaining the original volume and architecture of the alveolar bone is essential obtaining esthetic and functional prosthetic reconstruction after implant therapy.[1,2] The residual alveolar ridge height and width is almost always reduced after dental extraction.[3,4] The reduction in width is usually greater than the loss in height,[5] and bone resorption is significantly larger at the buccal than at the lingual side.[6,7] Bone loss occurs generally in the first 6 months after extraction, but the resorption activity continues at a slower rate throughout life.[8] However, there are wide variations between individuals.

Most dental studies have assessed the alveolar ridge only in terms of bone geometry without focusing on its spatial distribution, microarchitecture, and intrinsic bone tissue quality. Analyzing these characteristics at the level of the newly formed trabecular bone inside the socket could improve the current knowledge on alveolar bone healing. Different procedures have been suggested to maintain width and height of the alveolar bone after tooth extraction. The aim of alveolar ridge preservation procedures is to limit maxillary and mandibular bone resorption and maintain enough alveolar bone for successful implant placement and esthetic soft tissue appearance.[1,9] Initially, such procedures were usually indicated when unassisted socket healing could compromise implant placement.[10]

Socket preservation procedures include the principles of guided tissue regeneration, minimally traumatic tooth removal, and the protection of the blood clot. Current methods include the use of autografts, allografts, alloplasts, or xenografts and naturally derived synthetic membranes that are either bioresorbable or nonresorbable.[7,11–19] However, the use

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of grafting materials in the fresh extraction socket has been questioned as they appeared to interfere with the normal healing process.[20]

Platelet-rich fibrin membranes (PRF) are a newly developed platelet concentrate allowing a simplified preparation without biochemical blood handling. The slow polymerization of the fibrin during PRF preparation creates a fibrin network very similar to the natural one with incorporation of the platelets in the fibrin meshes, which leads to efficient cell migration and proliferation. Platelets are also activated and this results in their massive degranulation with an important cytokine release (PDGF, TGF-beta, VEGF, TSP-1, EGF) during the fibrin matrix remodeling. PRF may remain exposed in the oral cavity and creates an accelerated tissue cicatrization due to its function in immune control, circulating stem cell trapping, angiogenesis, and wound-covering epithelialization.[21–26] Different surgical procedures using PRF or its precursor PRP (Platelet-Rich Plasma) as healing biomaterial or grafting material have been described in the literature, but with contradictory results.[27–33]

The aims of this study were to evaluate whether the use of PRF for socket filling could improve the microarchitecture and the intrinsic bone tissue quality of the alveolar bone and to demonstrate the influence of the surgical procedure on the final result for successful implant placement. Other aspects of this ridge preservation technique were also assessed, including clinical evaluation, vertical linear measurements on radiographs, and width of the alveolar crest. This study allowed also the development of a model to investigate the formation of new bone under the influence of a local manipulation in the socket and potentially offers the possibility to investigate the systemic treatment effects on that process.

MATERIAL AND METHODS

Study Design

The Ethics Committee of the Association of the Physicians of Geneva approved the study protocol. All patients received oral and written information about the study and provided informed written consent. The work was carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving human subjects.

Twenty-three adult patients (14 women, 9 men) aged 22–75 years (mean age, 47 years; median, 46 years) who required the extraction of an upper or lower premolar before its replacement by a dental implant were enrolled in the study from 2008 to 2011. Patients older than 18 years were entered into the study independent of age or sex. Reasons for tooth extraction included endodontic treatment failures, root fractures, advanced caries lesions, and periodontally compromised teeth. Inclusion criteria were the presence of the buccal and palatal/lingual bony walls evaluated clinically by measuring the thickness of the alveolar ridge and radiologically by a periapical radiograph, and residual periodontal attachment of at least 6 mm.

Exclusion criteria were complicated tooth extraction, complicated implant placement, and any medical problem that could interfere with the mucosal and bony healing processes or contraindicating an implant placement, such as anticoagulation, antiaggregatory medication, radiotherapy, bisphosphonate therapy, diabetes, endocarditis risk factors, immunosuppression, and renal or hepatic failure.[34–38]

All patients were randomly assigned to 1 of the 3 following treatment groups by picking numbers out of a hat: (1) PRF (9; 39.1%): successful PRF collection, simple extraction of the premolar, socket filling with PRF, suture, follow-up controls, and delayed implant placement; (2) PRF-flap (6; 26.1%): successful collection of PRF, extraction of the premolar with a mucosal flap, socket filling with PRF recovering the alveolar crest, repositioning of the flap, suture, follow-up controls, and delayed implant placement; (3) controls (8; 34.8%): simple extraction of the premolar, suture, follow-up controls, and delayed implant placement.

PRF Preparation

For patients in the PRF and PRF-flap groups, PRF membrane preparation was performed immediately before the extraction procedure. A venous blood sample was taken in the forearm with a butterfly to fill four 8-mL tubes without anticoagulant or bovine thrombin or any other gelling agent. They were immediately centrifuged at 2700 rpm for 12 minutes. Blood centrifugation immediately after collection permitted the composition of a fibrin clot between the red corpuscles and acellular plasma. The membranes were then created by crushing the buffy coat from each tube between the compressions. This was a simple procedure without biochemical blood handling and was contamination free. The procedure has already been described in detail elsewhere.[21,26]

Surgical Procedure

A simple extraction procedure was retained: local anesthesia (4% articaine with epinephrine 1:100,000; Ubistesin; 3M ESPE AG, Seefeld, Germany); a scalpel for the syndesmotomy; a buccal and palatal/lingual mucosal flap without discharge for the PRF-flap group; use of dental elevators, extraction with forceps, curettage, and socket filling with PRF membranes for PRF and PRF-flap groups; placement of the PRF membranes over the alveolar crest for the PRF-flap group; hemostasis by compression; and suture with a point cross. An analgesic containing paracetamol was routinely prescribed to all patients, and they all agreed not to wear a partial removable denture during the healing phase. This technique was used to ensure the least damage possible to the alveolar bone or surrounding soft tissues. Follow-up was performed at week 1 with suture removal and at weeks 2 and 5. Implant was inserted at week 8 after extraction and corresponded to a type 2 delay according to the International Team for Implantology classification.[39]

Bone Biopsy Procedure

At week 8, an evaluation of the bony and mucosal healing was performed. The criteria for a good healing process were a surface of the wound completely re-epithelialized with minimal or no scar formation and radiographic evidence of bone formation inside the socket without any other bone healing pathology.[34,35,40] In that case, the surgical procedure for the implant placement (Standard Plus Implant Regular Neck; Straumann, Basel, Switzerland) was initiated as follows: local anesthesia (4% articaine with epinephrine 1:100,000; Ubistesin), mucosal flap, use of a core drill with external diameter of 3.5 mm (Straumann), and sample of a 3-mm-long minimum bone biopsy. Bone biopsies were placed in formalin 10% for 24 hours followed by 5 different baths of absolute ethanol for a minimum of 24 hours each. All surgical procedures for implant bed preparation were done without jeopardizing the treatment outcome.

Microcomputed Tomography Analysis

All investigations were performed blindly. Bone mass and architecture of the bone biopsy were analyzed in a high-resolution microcomputed tomography (μCT) system (μCT 40; Scanco Medical AG, Bassersdorf, Switzerland) as previously described.[41] In brief, bone biopsies were scanned in alcohol and the three-dimensional (3D) images were acquired with a voxel size of 12 μm in all spatial directions. The resulting gray scale images were segmented using a low-pass filter to remove noise, and a fixed threshold was used to extract the mineralized bone phase. The trabecular sections of the bone biopsies were separated on 200 slices with semiautomatically drawn contours. Only the new trabecular formed bone was retained. The remaining alveolar bone or septum was excluded. The distinction between new bone and compact bone was evident, and the selection was done manually (Fig. 1). Morphological analysis of the bone microarchitecture was determined for the new trabecular formed bone, including bone volume fraction (BV/TV), trabecular number (Tb.N), trabecular thickness (Tb.Th), trabecular separation (Tb.Sp), and bone mineral density.

Nanoindentation Test

Nanoindentation tests were performed using a nanohardness tester (NHT; CSM Instruments, Peseux, Switzerland) to evaluate the intrinsic mechanical properties of the newly formed trabecular bone. In this test, force-displacement data of a pyramidal diamond indenter pressed into the bone material were recorded. This technique has been described in detail elsewhere.[42,43] After μCt analysis, bone biopsies were placed in acetone for 24 hours and then embedded in polymethylmethacrylate (PMMA) (8.00590.2500; Merck, Darmstadt, Germany). The blocks were cut into 2 pieces transversally through the middle of the bone biopsy using a diamond wire saw (Well Mod 3242-3; Well Diamond Wire Saws SA, Le Locle, Switzerland). The face of one half of the transverse cuts was polished and finished with a 0.25-μm diamond solution. After this, specimens were kept at –4°C. Specimens were slowly thawed at 7°C in a saline solution overnight and then warmed to room temperature before nanomechanical testing. The tests included 5 indents in trabecular node situated in the newly formed trabecular bone (Fig. 2). Indents were set to a 900-nm depth with an approximate strain rate of $\epsilon = 0.066 \times 1/s$ for both loading and unloading. At maximal load, a 10-second holding period was applied. The limit of the maximum allowable thermal drift was set to 0.1 nm/s.

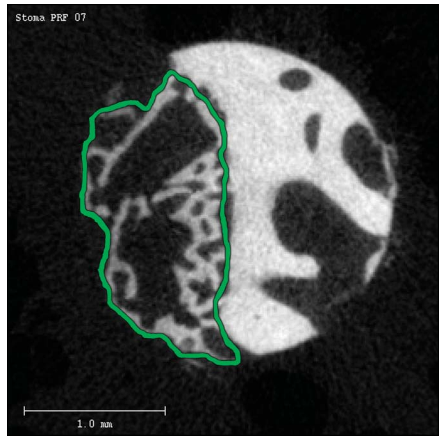

Fig. 1. Section of bone biopsy showing a portion of newly formed bone (marked in green) and a portion of compact bone.

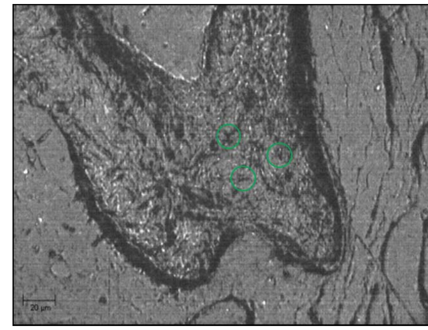

Fig. 2. Indentation location of the diamond indenter tip (green circles).

Clinical Evaluation

An assessment of the mucosal situation was performed before extraction and at week 8 before implant placement. These analyses included 3 different parameters: integrity of the soft tissues, the gingival biotype,[44] and the presence or absence of clinical symptoms. The presence of periapical radiolucencies corresponding to an active infection or a residual lesion was identified on the initial periapical radiograph. Control of the healing process was done on the second periapical radiograph before implant placement. Occlusal and lateral photographs were taken before extraction and then systematically at each visit.

The width of the alveolar ridge was measured before extraction and at week 8 using a caliper clamp (Leibinger GmbH, Mühlheim, Germany). The measurement was done perpendicular to the tangent of the dental arch at the midpoint of the extraction site approximately 4 mm under the level of the gingiva of the adjacent teeth and corresponded to the distance between the most prominent points buccally and orally (Fig. 3).

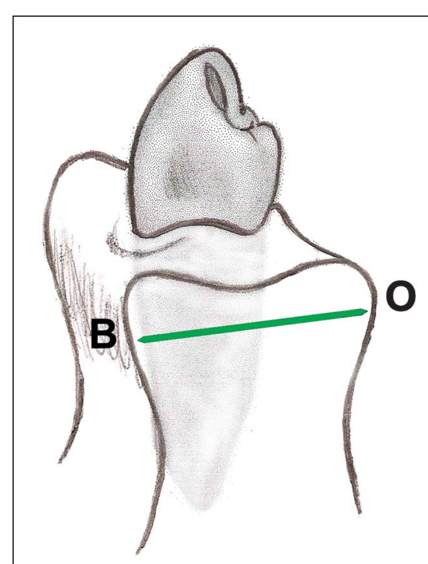

Fig. 3. Measurement of the width of the alveolar crest from buccal (B) and oral (O) points (green line).

Radiographic Procedure

A recent panoramic radiograph (Scanora; Soredex, Orion Corporation Ltd, Helsinki, Finland) was requested for each case. A periapical radiograph (Kodak Ultra-speed; Carestream Health, Gland, Switzerland) of the tooth to be extracted was performed before extraction and implant placement. To obtain superimposable radiographs, a silicone bite of the patient (President Putty; Coltène AG, Altstätten, Switzerland) was carried out around the radiograph holder. After setting up the film and the bite in the patient's mouth, the film holder was secured to the radiograph tube (Heliodent MD; Sirona Dental GmbH, Salzburg, Austria) using a metal ring binding to the outer periphery of the tube. The material for this technique of superimposable radiographs was specifically designed for the University of Geneva Dental School and the technique is described in detail elsewhere.[45] All radiographs were digitized at a resolution of 600 dpi by a scanner with a transparency adapter (Epson V750 Pro, Kloten, Switzerland).

Radiological Linear Measurements

Vertical radiological measurements were performed on the digitized periapical radiographs using a program for linear measurements (Digora; Soredex, Orion Corporation Ltd). The level of the mesial and distal alveolar bone of the tooth to be extracted was determined by measuring the distance from a baseline drawn between 2 reproducible points on both radiographs to the bone level at these locations (Fig. 4). On the radiograph at week 8 after extraction, the level of the mesial and distal alveolar bone of the empty socket was measured from the same baseline (Fig. 4). To evaluate the loss of bone at the site of healing, the difference in the values at mesial and distal sites before extraction and at week 8 was calculated.

On the periapical radiographs before extraction, root length of the premolar to be extracted was determined by measuring the distance from a reference line drawn through the most coronal mesial and distal periodontal attachment points to the tooth apex (Fig. 5). If the tooth had 2 roots, the longest root was retained for measurement.

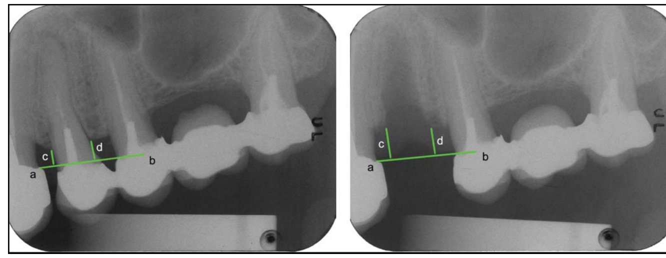

Fig. 4. Vertical linear radiographic measurements on superimposable periapical radiographs before extraction and at week 8 before implant placement from a baseline (green line: a–b) to crestal bone level: mesial measurement (green line: c) and distal measurement (green line: d).

All measurements were made twice by 2 different investigators (F.H. and L.V.). The average of these 4 values was selected for interpretation. The coefficient of variation of the method was also evaluated intraobserver and interobserver: mesial measurement = 2.66 ± 0.36 and 3.69 ± 063; distal measurement = 2.70 ± 0.38 and 2.95 ± 0.56; root measurement = 0.61 ± 0.09 and 0.82 ± 0.13, respectively.

Food Questionnaire

The surgical procedure of tooth extraction could be experienced as a trauma and induce a change in food intake. Because calcium and protein intake have an important influence on bone healing and wound healing[46–52] and could also influence the intrinsic bone tissue quality,[42,43] the differential intakes were measured in all patients. Protein and calcium intake were assessed before tooth extraction by filling out a food questionnaire conducted by the Division of Bone Diseases, Geneva University Hospitals, to exclude any confounding factors that could interfere with bone healing. The same food questionnaire was administered 8 weeks after extraction during the session of implant placement to highlight any intake changes resulting from the recent loss of teeth. A photographic guide was used as a support to allow assessment of the number of food portions.

Statistical Analysis

All results are expressed as means ± SEM. Significance of difference between the groups was determined by analysis of variance, followed by Fisher *post hoc* test and paired Student *t*-test, when appropriate.

RESULTS

The characteristics of the study group are summarized in Table 1. One patient in the control group withdrew from the study after the first appointment. Most sites were in the maxilla (20) and the remaining ones in the mandible (2). Only 2 patients presented acute symptomatology at the time of extraction. On the initial periapical radiograph, more than 50% of patients showed a well-defined apical radiolucency, which could correspond either to an active lesion or to a residual lesion. Most patients presented no defect on the gingiva. Only 1 patient (PRF-flap group) showed an asymptomatic chronic fistula on the vestibular side of the maxillary premolar. The gingival biotype was also assessed.

All surgical procedures were completed without any intraoperative complications. At first follow-up (week 1), patients reported minimal pain and swelling. Soft tissue healing occurred generally

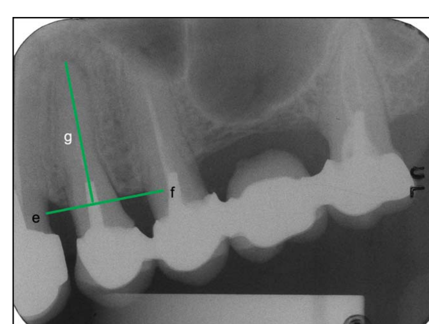

Fig. 5. Measurement of the root on periapical radiograph prior to extraction from a reference line (green line: e–f) through the most coronal mesial and distal periodontal attachment points to the apex of the root: length of the root (green line: g).

Table 1. Descriptive Statistics for the Demographic Characteristics of the Study Population, the Distribution of the Treated Sockets, the Prevalence of Symptoms, the Radiographic Findings, and the Gingival Biotype

	Control	PRF	PRF-Flap	Total
No. of cases	8	9	6	23
Age (yr)	45.62 ± 1.84	47.11 ± 5.57	50.33 ± 2.40	47.43 ± 2.30
Sex				
Male/Female	4/4	3/6	2/4	9/14
Socket No. (%)				
Maxillary first premolar	57.14	55.56	50	54.54
Maxillary second premolar	28.57	33.33	50	36.36
Mandibular first premolar	0	11.11	0	4.55
Mandibular second premolar	14.29	0	0	4.55
Symptomatology (%)				
Acute	14.29	11.11	0	9.09
None	85.71	88.89	100	90.91
Periapical lesion on x-ray (%)				
Apical radiolucency	57.14	55.56	83.33	63.64
Normal apex	42.86	44.44	16.67	36.36
Gingival biotype (%)				
Thick scalloped	14.29	22.23	16.67	18.18
Thick flat	42.85	33.33	66.66	45.46
Thin scalloped	28.57	33.33	16.67	27.27
Thin flat	14.29	11.11	0	9.09

Values are mean ± SEM unless otherwise specified in the table.

approximately 2 weeks postoperatively. Four patients presented a delayed healing of the soft tissue at week 2: alveolitis (PRF, 1; control, 1) and gingival necrosis following anesthesia (PRF, 1; PRF-flap, 1). At week 5, the soft tissue showed clinical characteristics of keratinized gingiva in all patients. Uneventful soft tissue healing was observed after this visit. At week 8 before implant placement, the healing process was still ongoing, but all patients showed enough keratinized attached gingival with no sign of infection or delayed healing. All extraction sites were still recognizable with only minor depression of the gingiva.

At the time of implant placement, the alveolar bone architecture was evaluated. All sites showed bone width and height sufficient for implant placement without supplemental bone augmentation and allowed the sampling of 21 bone biopsies. On one site, the bone biopsy (PRF-flap) broke during withdrawal. Good primary stability was obtained for all implants but one (PRF-flap). The stability of implants was measured by forceps and percussion.

Morphological Parameters

Among the 21 bone biopsies (control, 7; PRF, 9; PRF-flap, 5) sampled, the 2 sites with acute symptomatology at the time of extraction (control, 1; PRF, 1) presented bone healing with a density markedly lower compared with other cases at week 8, and these 2 bone biopsies were damaged during their sampling. These patients were removed from the analysis.

The μCT analysis performed blindly at biopsy demonstrated the significant effect of both the presence of PRF and technical surgery protocol. A tendency for higher value BV/TV was observed in the PRF group compared with the control (+12.9%) and PRF-flap (+42.6%) groups, but these values did not reach the level of significance. Tb.N was markedly increased in the PRF group compared to the control (+28.1%; $P < 0.05$) and PRF-flap (+22.2%; $P < 0.05$) groups. Tb.Th was not modified by either technique. Consequent lower Tb.Sp was observed in the PRF group compared to the control (–35.3%; $P < 0.05$) and PRF-flap (–26.6%; $P < 0.05$) groups. Representative μCT images of the bone biopsies are presented in Figure 6, and results are summarized in Table 2.

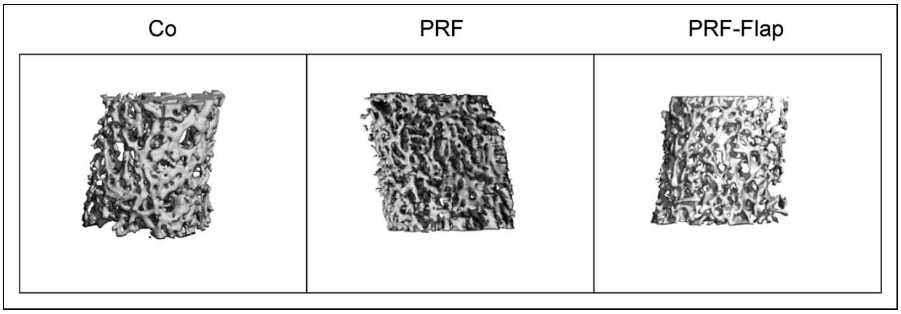

Fig. 6. Representative μCT images of the bone biopsies: the 3D reconstruction of the PRF group showed a bone healing with a density higher compared to the 3D reconstruction of the PRF-flap and control groups.

Intrinsic Bone Tissue Quality

Intrinsic bone tissue quality of the trabecular bone formed in the PRF group displayed better properties compared to

Table 2. The Effects of PRF Membranes and Technical Surgery Protocol on the Microarchitecture of the New Trabecular Formed Bone Analyzed by μCT: The BV/TV, Tb N ($P < 0.05$), and Tb.Sp ($P < 0.05$) Were Higher in the PRF Group Compared With PRF-Flap and Control Groups

	Control	PRF	PRF-Flap
BV/TV (1)	0.249 ± 0.037	0.281 ± 0.037	0.197 ± 0.027
Tb.N (1/mm)	4.34 ± 0.34	5.56 ± 0.37*	4.55 ± 0.32
Tb.Th (mm)	0.067 ± 0.005	0.065 ± 0.003	0.059 ± 0.003
Tb.Sp (mm)	0.234 ± 0.019	0.173 ± 0.016*	0.219 ± 0.012
Density (mmHA/ccm)	780 ± 10†	820 ± 23	832 ± 18

Results are bone volume to total volume (BV/TV), trabecular number (Tb.N), trabecular thickness (Tb.Th), trabecular separation (Tb.Sp), and density. Values are means ± SEM.
*$P < 0.05$ compared with control.
†$P = 0.0577$.

Table 3. The Effects of PRF Membranes and Technical Surgery Protocol on the Intrinsic Bone Tissue Quality of the New Trabecular Bone Formed: The PRF Group Displayed Better Elastic Modulus ($P < 0.05$) and Working Energy ($P < 0.05$) Compared With PRF-Flap Group

Parameters	Control	PRF	PRF-Flap
Modulus (Gpa)	6.92 ± 0.36	7.01 ± 0.33	5.97 ± 0.20*
Hardness (Mpa)	226.25 ± 12.58	238.68 ± 13.85	214.79 ± 11.43
Working energy (mN*nm)	2425.89 ± 90.59	2515.10 ± 71.43	2264.92 ± 78.49*

Values are mean ± SEM.
*$P < 0.05$ compared with PRF group.

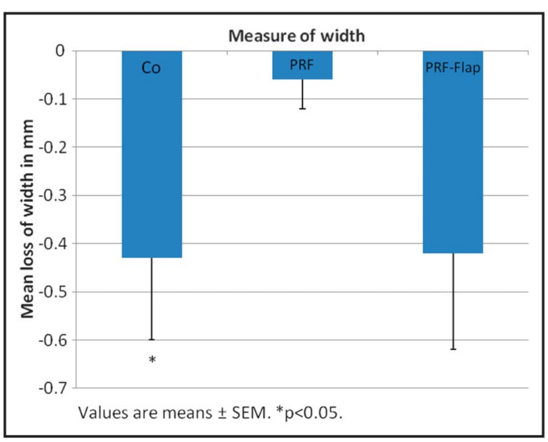

Fig. 7. The measurements of the alveolar crest width before extraction and at week 8 showing the mean loss: the control group had the highest mean loss ($P < 0.05$) compared with PRF and PRF-flap groups.

Table 4. The Vertical Linear Measurements on Superimposable Radiographs Showing the Reduction of the Alveolar Crest Height at the Mesial and Distal Sites: The Control Group had a Significant Loss ($P < 0.05$) and It Seemed the PRF Membranes had a Preventive Effect

	Mesial	Distal
Control	−0.77 ± 0.17*	−2.07 ± 0.81
PRF	−1.21 ± 0.40	−0.76 ± 0.25
PRF-Flap	−0.86 ± 0.34	−2.15 ± 1.05

Values are mean (mm) ± SEM.
*$P < 0.05$.

the PRF-flap group. Specifically, elastic modulus (+17.42%; $P < 0.05$) and working energy (+11.05%; $P < 0.05$) were significantly increased compared with the PRF-flap group. The results of the PRF group were not significantly different from the control group (+1.30% and +3.68%, respectively). The tissue hardness was not altered by treatment or surgical technique. The results are summarized in Table 3.

Clinical Evaluation

Measurements of the alveolar crest width before extraction and at week 8 showed differences between the 3 groups. The PRF group showed a markedly lower percentage of loss of width (–0.48%) compared with the PRF-flap (–3.70%) and control (–3.68%; $P < 0.05$) groups. The control group had the highest mean loss (0.43 mm; $P < 0.05$) compared with the PRF (0.06 mm) and PRF-flap (0.42 mm) groups (Fig. 7).

Vertical Linear Measurements on Radiographs

On the periapical radiograph at week 8, the bone healing process was ongoing with a tooth socket still visible for all patients. All apical radiolucencies disappeared, and no other bone healing pathology was observed. The technique used to obtain superimposable radiographs was difficult to achieve. Thirteen patients were excluded from the statistical analysis because of poor radiological recording reproducibility. Results are described for the remaining 9 patients (control, 3; PRF, 3; PRF-flap, 3).

A general observation of bone changes in the extraction sites showed that bone formation took place in the extraction sockets simultaneously to loss of alveolar crest height. The reduction of the crest height at week 8 was confirmed in all patients at the mesial and distal sites (Table 4). All initial periapical radiographs were reincluded for the statistical analysis of the measurement of root length; mean length was 11.55 ± 0.47 mm.

Food Questionnaire

In all groups, calcium and protein intake was in accordance with current recommendations of the Swiss Society of Nutrition, 2002. Premolar extraction did not change patient food intake, which remained within recommended standards.

DISCUSSION

The present prospective, randomized controlled study demonstrates that the use of PRF membranes to fill the socket without mucosal flap after tooth extraction is associated with improved alveolar bone healing and a better preservation of the width of the alveolar crest and bone architecture. Socket healing analyzed by μCT showed that sockets filled with PRF without a mucosal flap presented the highest number of newly formed trabeculae (Tb.N) and a smaller separation between these trabeculae (Tb.Sp), together with an overall improvement in the 3D bone architecture. There was no significant difference in the bone mass (BV/TV), but there was a higher tendency in the PRF group. Intrinsic bone tissue quality (ie, elastic modulus and working energy) was improved in the PRF group compared to the PRF-flap group but was not significantly different from the control group. This beneficial effect disappeared at the time of investigation when a more invasive surgical procedure was performed. The results of the intrinsic bone tissue quality are difficult to interpret because the maturity level of the newly formed bone was not known. However at 8 weeks after extraction, there were significant differences.

These results could be explained by the growth factors contained in the PRF membranes (PDGF, VEGF, EGF, TSP-1, TGF-β [BMP]) and their slow release, which stimulated the cicatrization for at least 1 week after extraction. These growth factors acted on the 4 fundamental events of cicatrization: angiogenesis, immune control, circulating stem cell trapping, and wound-covering epithelialization.[23,24,53] The improvement in the 3D bone architecture and the positive effects on intrinsic bone tissue quality might be explained by the fact that the newly formed bone structures in the sockets could be influenced by these growth factors.

By contrast, the mucosal flap seemed to completely neutralize the advantages of the PRF membranes with a bone mass and trabecular thickness slightly reduced. Thus, the surgical procedure seems to play a role as important as the type of filling placed inside the socket with repercussions on the bone microarchitecture. The mucosal flap represented an invasive procedure for the soft tissue with a negative impact on bone healing inside the socket, which could potentially reduce or cancel the benefits of a filling material placed in the socket or on the alveolar crest and influence the final outcome. The healing signals induced by the mucosal flap appeared to be of great importance with a lower bone healing and an increased surrounding bone resorption. This local trauma on the soft tissue probably induced local factors for bone resorption, which succeeded in overcoming the growth factors released by the platelets. These local factors could negatively influence the bone modeling and remodeling in the socket and could lead also to an altered intrinsic bone tissue quality and a difference in the maturity of the newly formed bone, but this requires further investigation.

The procedure with PRF membranes without mucosal flap showed a better preservation of the alveolar crest width with a smaller mean loss observed in fewer patients. The highest reduction of the alveolar crest width was observed in the control group, which was statistically significant.

Due to the inclusion criteria, all cases were low-risk patients with the bony walls present around the tooth before extraction. In addition, all patients had previously undergone oral health care to remove all active pathologies. The removed teeth were exclusively premolars, and the socket size of the sockets was therefore smaller than multiple-root teeth and the bone healing faster.[10] All these factors influenced the final outcome of the alveolar ridge, explaining the overall small losses of width and the good rate of healing. It would be interesting to reproduce these tests when one of the bony walls is missing at the time of tooth extraction. However, bone loss is also known to be more pronounced when more than 1 adjacent tooth is extracted.[54]

Although the method for intraoral radiographs was standardized, some degree of variation is inevitable, and 13 patients were excluded from the statistical analysis because of poor recording reproducibility. These results could be explained by a different angle of radiographs, which is a common problem in studies with superimposable radiographs.[55] However, the retained radiographs showed good recording reproducibility. A statistically significant loss ($P < 0.05$) of bone height was found in the control group, but the variability was large. It seemed that the PRF membranes prevented the loss of bone height in an improved manner with a simple extraction and in a less effective way when a mucosal flap was performed. The control group was also compared with the combined PRF and PRF-flap groups to evaluate the overall effect of the PRF membranes. Although the number of patients is too limited to draw definitive conclusions from the statistical analysis, it is nevertheless tempting to suggest that the PRF membranes seemed to reduce the loss of bone height. However, linear measurement of the roots confirmed the residual periodontal attachment of 6 mm necessary to sample a bone biopsy of at least 3 mm of newly formed bone in all cases.

Malnutrition or undernourishment is a highly prevalent disease, particularly among the elderly, and could lead to a low bone mass or negatively influence bone healing by altering bone turnover and significantly delaying bone healing.[46–52] It was therefore important to exclude such confounding factors with bone microarchitecture. In this study, patient food intake did not influence the results. In the case of malnutrition, it is probably important to correct the calcium and protein intake to improve bone healing and eventually implant osseointegration.

The study has several limitations, such as the small number of patients. However, despite the small number of cases included, statistically significant values have been found. The initial selection of low-risk patients can be considered as a limitation, but it has provided a study model with a reduced variability. The suboptimal recording reproducibility for superimposable radiographs is a common problem in clinical trials, but due to the technical difficulty, it cannot be considered as a primary end point. By contrast, the coefficient of variation of the measurement of intraobsrever and interobserver are poorly described in the literature and showed a good reproducibility in our study. Compared with the current literature on PRF,[27–31] there are some discrepancies showing some great benefits and at other times no effect.

Other dental studies on alveolar ridge preservation procedures have only focused on bone geometry and the width of the residual alveolar crest after tooth extraction, but without giving any information on bone microarchitecture and intrinsic tissue quality of the healing socket.[7,10–13,55–59] It has already been demonstrated in animals that the quality of bone at the implant placement site plays a major role in osseointegration.[60] Some studies with histological analysis showed that filling the socket with grafting material could provide controversial results with no improvement or enhanced bone healing.[16,61,62]

The principal target of this study was the alveolar bone using a precise measurement tool (μCT) on bone biopsy to highlight the morphological parameters, such as the microarchitecture, which has not been analyzed by most other studies. This new model could be used in the future to analyze bone healing with local or systemic treatment.

Conclusions

The results of this study indicate that the use of PRF membranes to fill the socket after tooth extraction led to improved alveolar bone healing with a better preservation of the alveolar crest width. Of note, the surgical procedure seems to be as important as the grafting material. These data could have a major impact on the recommended surgical procedure for tooth extraction before implant placement given the important role played by the surrounding bone microarchitecture in the process of implant osseointegration.[60] It would have been interesting also to have an additional control group with a mucosal flap without PRF alveolar filling. In conclusion, the minimally traumatic procedure for extraction without mucosal flap appears to be appropriate to preserve the hard tissue, but these results should be confirmed by clinical studies in a larger patient population.

Disclosure

The authors claim to have no financial interest, either directly or indirectly, in the products or information listed in the article.

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