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Nikos Mardas
Vivek Chadha
Nikolaos Donos

Alveolar ridge preservation with guided bone regeneration and a synthetic bone substitute or a bovine-derived xenograft: a randomized, controlled clinical trial

Authors' affiliations:
Nikos Mardas, Vivek Chadha, Nikolaos Donos, Periodontology Unit, UCL – Eastman Dental Institute, London, UK.

Corresponding author:
Prof. Nikolaos Donos, DDS, MS, FTHE, FDSRCS(Engl) PhD
Periodontology Unit
Department of Clinical Research
UCL – Eastman Dental Institute
University College London
256 Gray's Inn Road
London, WC1X8LD, UK
Tel.: +44 20 7915 1075
Fax: +44 20 7915 1137
e-mail: n.donos@eastman.ucl.ac.uk

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Abstract

Objectives: The aim of this randomized, controlled clinical trial was to compare the potential of a synthetic bone substitute or a bovine-derived xenograft combined with a collagen membrane to preserve the alveolar ridge dimensions following tooth extraction.

Methods: Twenty-seven patients were randomized into two treatment groups following single tooth extraction in the incisor, canine and premolar area. In the test group, the alveolar socket was grafted with Straumann Bone Ceramic® (SBC), while in the control group, Bio-Oss® deproteinized bovine bone mineral (DBBM) was applied. In both groups, a collagen barrier was used to cover the grafting material. Complete soft tissue coverage of the barriers was not achieved. After 8 months, during re-entry procedures and before implant placement, the horizontal and vertical dimensions of the residual ridge were re-evaluated and trephine biopsies were performed for histological analysis in all patients.

Results: Twenty-six patients completed the study. The bucco-lingual dimension of the alveolar ridge decreased by 1.1 $\pm$ 1 mm in the SBC group and by 2.1 $\pm$ 1 in the DBBM group ($P<0.05$). Both materials preserved the mesio-distal bone height of the ridge. No differences in the width of buccal and palatal bone plate were observed between the two groups. The histological analysis showed new bone formation in the apical part of the biopsies, which, in some instances, was in direct contact with both SBC and DBBM particles. The coronal part of the biopsies was occupied by a dense fibrous connective tissue surrounding the SBC and DBBM particles.

Conclusion: Both biomaterials partially preserved the width and the interproximal bone height of the alveolar ridge.

Tooth extraction normally results in a significant resorption of the alveolar ridge. The bone resorption process is initiated immediately after extraction, leading to an average 40–60% decrease in the horizontal and vertical dimensions of the alveolar ridge, during the first 2 years (Johnson 1969). The majority of postextraction bone loss is more evident on the buccal aspect of the ridge (Pietrovski & Massler 1967) and occurs mainly within the first 3 months (Johnson 1969; Schropp et al. 2003).

In order to preserve the original ridge dimensions following extraction, various bone grafts and substitutes have been suggested for grafting of the postextraction socket (Wang et al. 2004), such as autogenous bone (Becker et al. 1994), demineralized freeze-dried bone allograft (Becker et al. 1994, 1996; Froum et al. 2002), mineralized freeze-dried bone allograft (Feuille et al. 2003), deproteinized bovine bone (Artzi et al. 2000), alloplastic polymers (Gross 1995; Serino et al. 2003) and bioactive glasses (Froum et al. 2002).

Although some of these bone substitutes were able to preserve postextraction alveolar ridge dimensions to some extent, the quantity and the quality of the bone tissue formed in the socket have been variable and their presence often interfered with the normal healing process (Becker et al. 1994, 1996; Froum et al. 2002; Heberer et al. 2008). In recent preclinical studies in dogs, the placement of deproteinized bovine bone in combination with collagen in fresh extraction sockets demonstrated delayed initial socket healing in terms of new bone formation (Araujo et al. 2009) but also resulted in better preservation of the dimensions of the alveolar ridge than nongrafted sites after 6 months of healing (Araujo & Lindhe 2009).

The use of membranes according to the guided tissue regeneration (GTR) principle, either alone (Lekovic et al. 1998; Bartee 2001) or in combination with a bone substitute (Brugnami et al. 1996; Iasella et al. 2003; Barone et al. 2008), has also been evaluated for alveolar ridge preservation, with positive results. The combination treatment was based on the assumption that while a membrane will act as a barrier against the expected epithelial downgrowth into the extraction socket, the grafting material may be useful to prevent possible membrane collapse and to enhance new bone formation through osteoinduction and/or osteoconduction. Although current clinical trends support the use of resorbable membranes, specific combinations of membranes and bone substitutes that would have yielded optimal results in immediate socket preservation have not yet been identified. Cross-linked collagen barriers have been extensively used for guided bone regeneration due to the specific physicochemical properties such as haemostatic function that allows wound stabilization, chemotactic effect over gingival fibroblasts and permeability that allows nutrient transfer (Rothamel et al. 2004). The combination of resorbable porcine or bovine collagen membranes and bovine xenografts is one of the most promising combinations since it has been found to be effective for bone regeneration around titanium implants (Zitzmann et al. 1997; Hämmerle & Lang 2001), alveolar ridge augmentation (Zitzmann et al. 2001) and alveolar ridge preservation (Barone et al. 2008). However, in a recent randomized, controlled clinical trial comparing ridge dimensions and histologic characteristics, the above-mentioned combination was found to be inferior in terms of new bone formation to a combination of allograft ''putty'' combined with a calcium sulphate barrier (Vance et al. 2004).

Straumann Bone Ceramic® (SBC) is a new biphasic ceramic bone substitute, which is composed of a combination of hydroxyapatite (HA) and β-tricalcium phosphate (β-TCP). The HA constitutes the main mineral component of bone, and at physiological pH, is the least soluble of the naturally occurring calcium phosphate salts. For this reason, it is resistant to physiologic resorption (Govindaraj et al. 1999) and has been suggested for alveolar ridge augmentation (El Deeb & Holmes 1989; Mercier et al. 1992), ridge preservation (Quinn & Kent 1984), as well as fillers in periodontal defects (Kenney et al. 1986). Although HA is well tolerated, histological reports in biopsies have questioned its osteoconductive properties and its ability to promote bone regeneration on a predictable basis (Beirne et al. 1986; Stahl & Froum 1987). Unlike HA, tricalcium phosphate is resorbable (Breitbart et al. 1995). It has been suggested as an osteoconductive material able to provide a matrix where new bone can be deposited, and as it resorbs slowly, it is replaced by new bone (Bucholz et al. 1987; Niedhart et al. 2001). However, this replacement does not occur in a 1 : 1 ratio, resulting in less bone formation compared with the volume of tricalcium phosphate absorbed and often in soft tissue encapsulation (Froum & Stahl 1987). Therefore, the objective of combining the insoluble HA with β-TCP is that HA would maintain the space (scaffold function) while the β-TCP would resorb, while at the same time promoting bone regeneration. In recent human controlled trials, SBC has been found to produce similar amounts of newly formed bone when compared with a bovine xenograft for grafting of the maxillary sinus (Cordaro et al. 2008; Froum et al. 2008) or for periodontal regeneration (Zafiropoulos et al. 2007).

The aim of this study was to clinically and histologically evaluate healing of fresh extraction sockets resulting from application of either SBC or deproteinized bovine bone mineral (DBBM) in combination with collagen membranes.

Material and methods

Study population

Thirty patients participated in this randomized, controlled, clinical trial, which took place in UCL Eastman Dental Institute, Clinical Investigation Center, during the period March 2006 to May 2008. The study was conducted in accordance with the ethical principles founded in the Declaration of Helsinki and the International Conference on Harmonisation (ICH) for Good Clinical Practice (GCP), awarded an ISO 14155 and approved by the relevant independent committee on the Ethics of Human Research of University College London.

The patients were evaluated for initial study eligibility during an initial screening visit. The study subjects were selected based on the following inclusion criteria: age between 18 and 75 years; good general health; the presence of a hopeless tooth in the mandibular or the maxillary incisor, canine or pre-molar region requiring extraction and would be suitable for replacement by a dental implant; the tooth to be extracted has at least one neighbouring tooth; and subject had voluntarily signed the informed consent.

In addition, patients were not admitted to the study or were excluded if any of the following exclusion criteria were present: pregnancy or lactating period; chronic treatment with any medication known to affect oral status and bone turnover or contraindicate surgical treatment within 1 month of baseline visit; concomitant anticoagulant therapy; any known diseases (not including controlled diabetes mellitus); infections or recent surgical procedures within 30 days of study initiation; HIV or hepatitis; administration of any other investigational drug within 30 days of study initiation; limited mental capacity or language skills or suffering from a known psychological disorder; heavy smoking (>10 cigarettes per day); uncontrolled or untreated periodontal disease; full-mouth plaque level (FMPL) >30% at the enrolment visit; severe bruxism; acute endodontic lesion in the test tooth or in the neighbouring areas; and major part of the buccal or palatal osseous wall damaged or lost following tooth extraction.

The subjects were randomly assigned to the test or the control group by a computer-generated table. A balanced randomly

permuted block approach was used to prepare the randomization tables in order to avoid unequal balance between the two treatments. The subjects were randomized according to smoking habits.

Baseline data and pre-surgical treatment

Demographic information, medical and dental history was recorded at the enrolment visit. Full-mouth plaque score (FMPS) to confirm FMPL of $<30\%$ was obtained at the enrolment visit. All subjects underwent a rigorous oral hygiene regimen including any periodontal treatment (when it was indicated) before study initiation.

The baseline data were collected just before tooth extraction and included probing pocket depth (PPD), gingival recession (REC) and bleeding upon probing (BOP) measured at six sites (mid-buccal, buccal, disto-buccal, lingual, mid-lingual and disto-lingual) adjacent to the extraction teeth by a single calibrated examiner using a UNC-15 probe with a light probing force.

Intrasurgical measurements of the alveolar ridge, surgical treatment and postoperative care

By means of intracrevicular incisions minimally extended to the neighbouring teeth, a full-thickness mucoperiosteal flap was elevated 3–4 mm from the buccal/lingual bone crest in the area of the tooth to be extracted. No vertical releasing incisions were used and an effort was made to preserve the interproximal papillae. The tooth was atraumatically extracted by means of periotomes, attempting to preserve the surrounding osseous walls as much as possible. The removal of residual pathology and granulation tissue was performed by means of bone curettes. In case a bony wall was severely damaged or completely lost during the extraction procedure, the patient was excluded from the study.

Following tooth extraction, the following intraoperative measurements of residual ridges dimensions were taken using a UNC-15 probe (Fig. 1a and b):

- Bucco-lingual/palatal width of the alveolar ridge at its most central part (B-L/P).
- Width of the buccal (Bbw) and the palatal/lingual (P/Lbw) bone plate at its most central part.
- Distance of the alveolar bone crest at the mesial-central (Mbh) and distal-central (Dbh) aspects of the socket relative to the cementum–enamel junction or the restoration margin of the neighbouring teeth.

After completion of the intrasurgical measurements, the randomization envelope was opened and the assigned treatment (test or control) was revealed to the surgeon. In the test group, the extraction socket was loosely filled with SBC (Straumann AG, Basel, Switzerland, granule size 400–1000 μm) (Fig. 2), while in the control group the extraction socket was filled with DBBM (Bio-Oss®; Geistlich Biomaterials, Wollhusen, Switzerland, granule size 250–1000 μm). Both grafting materials were previously rehydrated in blood and saline and the sockets were filled up to the level of the buccal and lingual/palatal bone plate. In both groups, a resorbable bi-layer collagen barrier (Bio-Gide, Geistlich, Basel, Switzerland) with a dimension of 25×25 mm was trimmed and adapted to cover the grafting material (Fig. 3). The membrane was placed with a double-layer technique. The first layer was placed with the rough side facing the entrance of the socket, followed by a second layer where the rough side was facing the upper smooth side of the first layer. The flaps were coronally replaced and secured by vertical mattress and horizontal cross mattress sutures (Gore-Tex®, W. L. Gore & Associates Inc., Flagstaff, AZ, USA) in order to cover the biomaterials as much as possible without, however, being able to achieve their complete coverage (Fig. 4).

Systemic antibiotics (amoxicillin 500 mg and metronidazole 400 mg) were administered three times per day for the first postoperative week. In case of a reported allergy to penicillin, 500 mg of erythromycin and metronidazole 400 mg were administered.

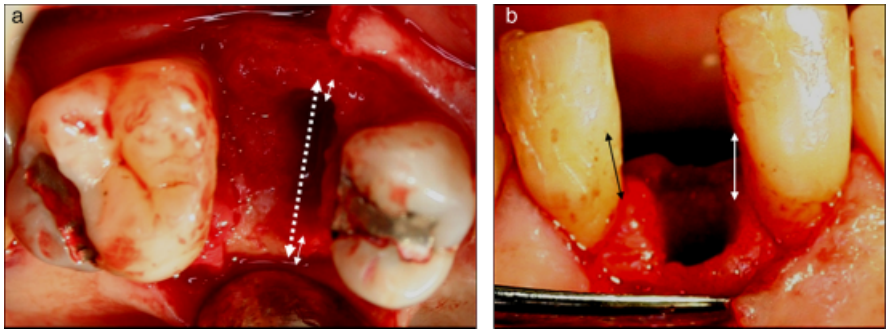

Fig. 1. (a) Intraoperative measurements of the residual ridge dimensions: B-L/P (white dotted line), Bbw and P/Lbw (small white arrows). (b) Intraoperative measurements of the residual ridge dimensions: Mbh (white arrow) and Dbh (black arrow).

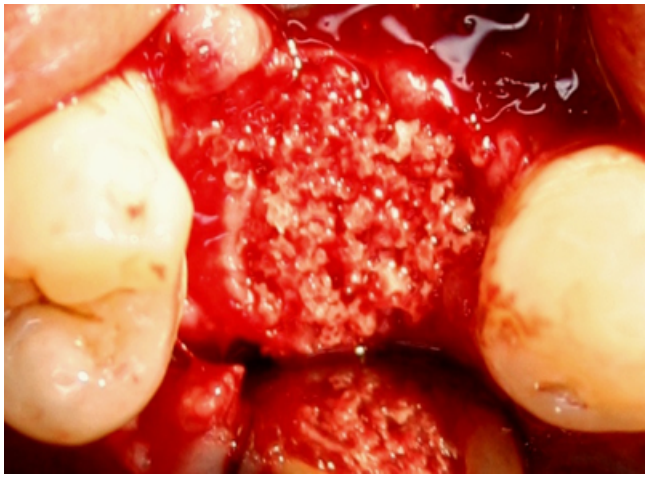

Fig. 2. Socket filled with SBC.

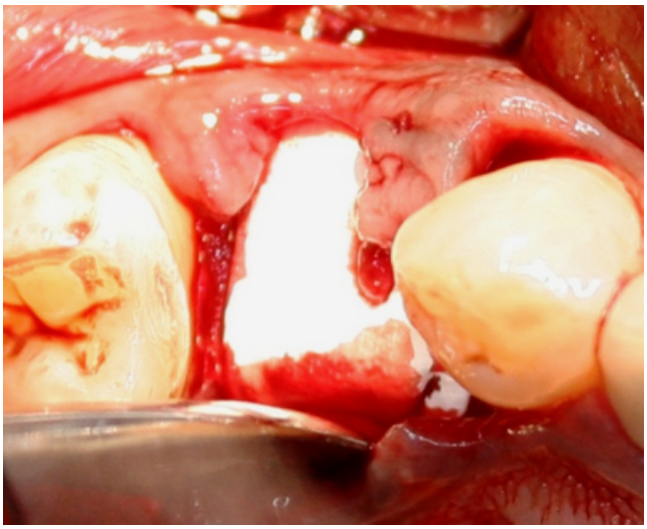

Fig. 3. Bilayer collagen membrane Bio-Gide® placed over the bone substitute.

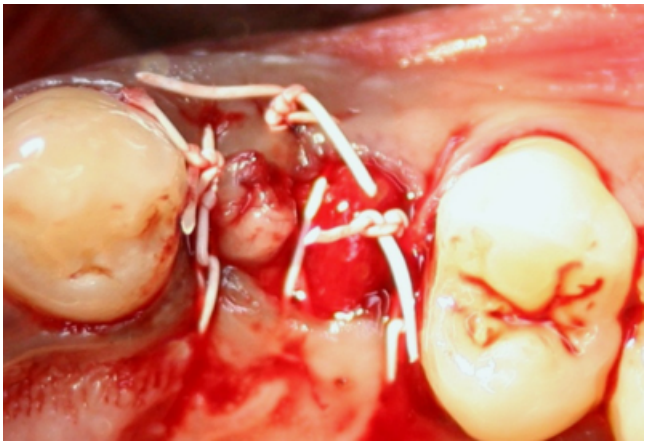

Fig. 4. Suturing with vertical mattress and horizontal cross mattress Gore-Tex® sutures. The barrier left partially exposed in the middle part of the defect.

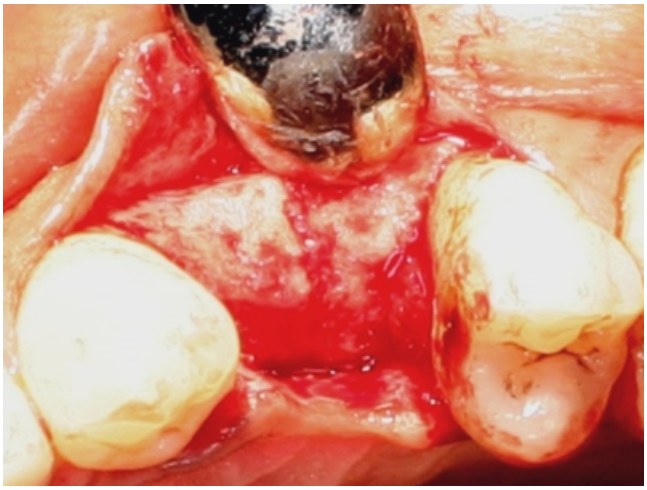

Fig. 5. Ridge preservation site at 8 months following the alveolar ridge preservation surgery.

For postoperative pain control, paracetamol 500 mg was subscribed upon patient discretion. All the patients were instructed to refrain from tooth brushing in the operated area and rinse with a 0.2% chlorhexidine-digluconate mouthwash, two times per day, for the first two postoperative weeks. Any removable temporary prostheses were not worn for the first 2–3 weeks and subsequently were adjusted to relieve any pressure elicited to the wound area. The sutures were removed after 14 days and wound-healing assessment together with prophylaxis were provided at 1, 2, 4, 8 and 16 weeks following the operation. In addition, the FMPS was reviewed at 16 and 32 weeks postoperatively.

Re-entry operation for implant placement and biopsy harvesting

Following 8 months of healing and before implant placement, the FMPS and the PPD, REC and BOP were measured at six sites (mid-buccal, buccal, disto-buccal, lingual, mid-lingual and disto-lingual) at the teeth adjacent to the extraction site using a UNC-15 probe with a light probing force. Following flap elevation, the same intraoperative measurements of the residual ridge dimensions were taken using a UNC-15 probe. By means of a trephine burr (diameter 2.6–2.8 mm, length: 6 mm), an intermediate osteotomy for placement of the dental implant (Straumann Standard Plus – SLActive) was performed in such a way that a tissue biopsy from the central part of the augmented alveolar ridge was harvested. At the same time, the resistance of bone tissue during the trephination process was evaluated by the operator and recorded according to three categories: (a) hard, (b) normal and (c) soft. The dental implant placement was then completed according to the standard procedures (Figs 5 and 6). If an osseous fenestration/dehiscence occurred during implant placement, guided bone regeneration was performed simultaneously using the same type of biomaterials as those used for socket preservation. The flaps were then coronally positioned to fully cover the regeneration materials by means of 5/0 and 6/0 non-resorbable sutures (Gore-Tex®, W. L. Gore & Associates Inc.).

According to local hospital protocols, systemic antibiotics (3 g amoxicillin) were administered 1 h before dental implant pla-

cement. In case of a reported allergy to penicillin, 3 g of erythromycin was administered 1 h before dental implant placement. Paracetamol was prescribed for pain control upon patient discretion. All the patients were instructed to refrain from tooth brushing in the operated area and rinse with a 0.2% chlorhexidine-digluconate mouthwash, two times per day, for the first 2 postoperative weeks. Temporary prostheses (if removable) were not used for the first 2–3 weeks and were adjusted subsequently to relieve any pressure from the wound area. The sutures were removed after 14 days and wound-healing assessment together with prophylaxis were provided at 2, 4 and 8 weeks following the operation.

Histological evaluation

The tissue biopsies were processed together with the trephine burr. All biopsies were placed in individual containers with 10% buffered formalin and fixated for at least 7 days. After fixation, the specimens were thoroughly rinsed in running water and dehydrated in ascending concentrations of ethanol (50%, 70% and 100%). After dehydration, the biopsy was embedded in methacrylate and the exact cutting–grinding technique (Donath & Breuner 1982) was used for the preparation of the histological specimens. One or two sections from the most central part of the trephine biopsy with an approximate thickness of 70–100 μm were obtained from the biopsy and stained with toluidine blue for histological analysis.

In the present study, a histomorphometric analysis was not applicable because the dimensions of the obtained biopsies varied, either due to destruction during the harvesting procedure or due to fracture of the apical border of the biopsy. In addition, the thickness of the obtained biopsy (together with the trephine burr) did not allow for more than one central section during the histological processing. Therefore, only a qualitative analysis of the biopsies was performed.

Sample size estimation, data collection and statistical analysis

The sample size was based on the assumption that a difference in the bucco-lingual/palatal width (the primary outcome) of 1.5 mm is clinically relevant. Based on a standard deviation of 1.2 mm (Vance et al. 2004), a size of 12 in each group will result in 80% power to detect such a difference in means (using an independent-sample *t*-test) at an α-level of 5%. A sample size of approximately 15 per group was selected to allow for drop-outs.

All the periodontal and intrasurgical measurements were made by a single, blinded previously calibrated examiner other than the surgeon, who was also not aware of the treatment assignment (test or control). The reproducibility of the examiner was verified by duplicate measurements in 10 randomly selected patients, with a minimum of a 15-min interval between measurements. A 98% agreement within ± 1 mm was achieved.

All data were entered into a computer database, proofed for entry errors and loaded in the SAS statistical software package for analysis. Significance was set to be at $P<0.05$. Differences between groups were assessed at each measurement interval and in particular at the final examination. This was achieved using parametric methods if the relevant assumptions (i.e. normally distributed data with approximately equal variances) were fulfilled. If the assumptions were not fulfilled, non-parametric tests were used instead. More specifically, these methods were applied as follows:

Parametric: Independent-samples *t*-tests for differences in means between groups at each measurement occasion or paired *t*-tests for the differences within each group between baseline and 8 months.

Non-parametric: Mann–Whitney *U*-test for differences in medians between the two groups at each measurement interval and the Wilcoxon test for the differences within each group between baseline and 8 months. Fisher's exact test was used for differences between groups in categorical or dichotomous variables (gender and smoking habits).

Results

Twenty-six out of the 30 patients who were initially enrolled completed the study. Two patients were excluded before randomization due to complete loss of the buccal osseous plate following extraction. One patient withdrew from the study before randomization and another who had been assigned to the test group quit the study before implant placement. The demographic data and smoking status of all the subjects who were enrolled and randomized in one of the treatment groups are presented in Table 1. The mean age of the subjects in the test group was 39.5 ± 7.8 years, whereas the mean age of the subjects in the control group was 34.9 ± 14.2 years. In the test group, 64.3% of the subjects were non-smokers, while 38.5% of the subjects in the control group were non-smokers. Only two out of 14 patients and one out of 13 patients were current

Table 1. **Summary of the demographic data and smoking status**

	SBC	DBBM	Total	*P*-value
Gender				
Male	2 (14.3%)	4 (30.8%)	6 (22.2%)	0.385[1]
Female	12 (85.7%)	9 (69.2%)	21 (77.8%)	
n	14	13	27	
Age (years)				
Mean	39.5	34.9	37.3	0.305[2]
Median	43	30	38	
SD	7.8	14.2	11.4	
Min	26	20	20	
Max	52	58	58	
Smoking				
Smoker	2 (14.3%)	1 (7.7%)	3 (11.1%)	0.501[1]
Non-smoker	9 (64.3%)	5 (38.5%)	14 (51.9%)	
Past smoker	2 (14.3%)	5 (38.5%)	7 (25.9%)	
Occasional	1 (7.1%)	2 (15.4%)	3 (11.1%)	

[1] *P*-values (statistically significant at the level of $P<0.05$) with Fisher's exact test for differences in means between groups in categorical variables.
[2] *P*-values (statistically significant at the level of $P<0.05$) with independent-samples *t*-tests for differences in means between groups.
SBC, Straumann Bone Ceramic®; DBBM, deproteinized bovine bone mineral.

smokers in the test and the control groups, respectively.

Each of the 26 patients who completed the study contributed one extraction site. The distribution of the extracted teeth between the two groups in these patients is presented in Table 2.

The healing following the ridge preservation procedure was uneventful overall. Few patients in both groups reported minor postoperative pain or discomfort, localized oedema and in some cases exfoliated graft particles were observed. All the patients presented with membrane exposure at the first postoperative week that, in most cases, became larger during the second week. At the fourth postoperative week, most of the collagen barrier had been resorbed, and at the 16th postoperative week, complete closure of the postextraction socket was observed with newly formed keratinized mucosa.

***Table 2.* Tooth extraction distribution between the two groups**

	Central incisor	Lateral incisor	Canine	Premolars	Total
Maxilla SBC	6	1	1	1	9
Maxilla DBBM	7			5	12
Mandible SBC	1			3	4
Mandible DBBM				1	1
Total	14	1	1	10	26

SBC, Straumann Bone Ceramic®; DBBM, deproteinized bovine bone mineral.

***Table 3.* Periodontal clinical indices on neighbouring teeth: mean PPD and REC**

	Baseline	8 months	Difference	*P*-value**
PPD				
SBC	2.2 ± 0.2	2.2 ± 0.3	−0 ± 0.4	0.66
	$n = 14$	$n = 13$	$n = 13$	$n = 13$
DBBM	2.6 ± 0.4	2.2 ± 0.3	−0.3 ± 0.4	0.011**
	$n = 13$	$n = 13$	$n = 13$	$n = 13$
P-value*	0.003*	0.697		
REC				
SBC	0.4 ± 0.6	0.4 ± 0.5	−0 ± 0.1	0.54
	$n = 14$	$n = 13$	$n = 13$	$n = 13$
DBBM	0.3 ± 0.4	0.4 ± 0.5	0.1 ± 0.2	0.157
	$n = 13$	$n = 13$	$n = 13$	$n = 13$
P-value*	0.34	0.7		

*Statistically significant *P*-values (<0.05) with independent-samples *t*-tests (*) for differences in means between groups.
**Statistically significant *P*-values (<0.05) with paired *t*-tests (**) for the differences within each group between baseline and 8 months.
SBC, Straumann Bone Ceramic®; DBBM, deproteinized bovine bone mineral; REC, gingival recession; PPD, probing pocket depth.

***Table 4.* The bucco-lingual/palatal width of the alveolar ridge (mm; means/(median) ± SD)**

	Baseline	8 months	Difference	*P*-value**
SBC	8.1/(8) ± 1	7/(7) ± 1.1	−1.1/(−1) ± 1	0.0039**
DBBM	9/(9) ± 1.6	6.9/(7) ± 1.9	−2.1/(−2) ± 1	0.0002**
P-value*	0.117	0.809	0.017*	
N	13	13	13	

*Statistically significant *P*-values (<0.05) with the Mann–Whitney *U*-test for the difference in bucco-lingual/palatal width of the alveolar ridge between SBC and BDX groups.
**Statistically significant *P*-values (<0.05) with the Wilcoxon signed rank test for the differences within each group between baseline and 8 months.
SBC, Straumann Bone Ceramic®; DBBM, deproteinized bovine bone mineral.

Periodontal clinical indices and plaque levels

The periodontal clinical indices at the neighbouring teeth are presented in Table 3. At baseline, the mean PPD at neighbouring teeth was statistically higher in the control group. Moreover, at the 8-month visit, the PPD was significantly reduced in the control group but remained stable in the test group. No statistically significant differences in REC and BOP measurements were observed between the groups at any of the observation periods. Both treatments equally preserved the baseline level of the free gingival margin at the neighbouring teeth following the ridge preservation procedure.

Intrasurgical measurements of the alveolar ridge

The bucco-lingual/palatal width (B-L/P)

The mean and range values of the bucco-lingual/palatal width of the alveolar ridge are presented in Table 4. The baseline B-L/P of the alveolar ridge was comparable between the two groups, while a statistically significant reduction of this dimension was observed in both groups. In the SBC group, the mean B-L/P at baseline was 8.1 ± 1 mm and decreased to 7 ± 1.1 mm at 8-month follow-up, presenting a reduction of the B-L/P of 1.1 ± 1 mm. In the DBBM group, the mean B-L/P at baseline was 9 ± 1.6 mm and decreased to 6.9 ± 1.9 mm at 8-month follow-up, presenting a reduction of the B-L/P of 2.1 ± 1 mm. The mean reduction of the B-L/P from baseline to 8 months was statistically significantly lower in the SBC group ($P<0.05$).

Width of the buccal and palatal/lingual bone plate (Bbw, P/Lbw)

The mean and range values of the width of the buccal and palatal bone plate measured in the most central part are presented in Table 5. In 4/13 cases in the SBC group and in 3/13 cases from the DBBM group, the regenerated bone was completely integrated into the buccal and palatal/lingual bone plates and the examiner was unable to distinguish the borders between the augmented sites and the buccal bone plate. In the SBC group, the baseline Bbw and L/Pbw were 0.9 ± 0.3 and 1.3 ± 0.5 mm, respectively, while at 8-month follow-up, the Bbw and L/Pbw were 0.4 ± 0.5 and 1 ± 0.6 mm, respectively. In the DBBM group, the baseline Bbw and L/Pbw were 1.2 ± 0.6 and 1.2 ± 0.4 mm, respectively, while at 8-month follow-up, the Bbw and L/Pbw were 1.2 ± 1 mm and 1.3 ± 0.6 mm, respectively. The mean changes of Bbw and L/Pbw from baseline

Table 5. **Bbw, L/Pbw, Mbh and Dbh of the alveolar ridge (mm; mean (median) ± SD)**

	Baseline	8 months	Difference	*P*-value**
Bbw				
SBC	0.9 (1) ± 0.3	0.4 (0) ± 0.5	−0.4 (0) ± 0.5	0.125
	n = 13	*n* = 9	*n* = 9	*n* = 9
DBBM	1.2 (1) ± 0.6	1.2 (1) ± 1	−0.1(0) ± 0.7	1
	n = 13	*n* = 10	*n* = 10	*n* = 10
P-value*	0.096	0.097	0.317	
L/Pbw				
SBC	1.3 (1) ± 0.5	1 (1) ± 0.6	−0.3(0) ± 0.9	0.375
	n = 13	*n* = 13	*n* = 13	*n* = 13
DBBM	1.2 (1) ± 0.4	1.3 (1) ± 0.6	0.1 (0) ± 0.7	1
	n = 13	*n* = 13	*n* = 13	*n* = 13
P-value*	0.38	0.33	0.286	
Mbh				
SBC	3.4 (3) ± 0.8	3 (3) ± 1.2	−0.4 (−1) ± 1	0.312
	n = 13	*n* = 13	*n* = 13	*n* = 13
DBBM	3.1 (3) ± 0.9	3.3 (3) ± 1.1	0.2 (0) ± 0.7	0.687
	n = 12	*n* = 12	*n* = 12	*n* = 12
P-value*	0.328	0.775	0.09	
Dbh				
SBC	3.1 (3) ± 1.4	3.4 (3) ± 1.6	0.3 (0) ± 0.6	0.375
	n = 11	*n* = 11	*n* = 11	*n* = 11
DBBM	3.2 (3) ± 0.7	3.5 (3) ± 1.4	0.3 (0) ± 1.3	0.531
	n = 13	*n* = 13	*n* = 13	*n* = 13
P-value*	0.526	0.857	0.951	

*P-values (statistically significant at the level of $P<0.05$) with the Mann–Whitney U-test for the difference in the bucco-lingual/palatal width of the alveolar ridge between SBC and BDX groups.
**P-values (statistically significant at the level of $P<0.05$) with the Wilcoxon signed rank test for the differences within each group between baseline and 8 months.
SBC, Straumann Bone Ceramic®; DBBM, deproteinized bovine bone mineral.

Table 6. **Frequency distribution of treated sites according to the resistance of bone tissue during the trephination process**

	Hard	Medium	Soft	*N*
SBC	2 (15.4%)	6 (46.1%)	5 (38.5%)	13
DBBM	2 (15.4%)	6 (46.1%)	5 (38.5%)	13

SBC, Straumann Bone Ceramic®; DBBM, deproteinized bovine bone mineral.

to 8 months were not statistically significant between the two groups ($P>0.05$).

The mean and range values of the distance of the alveolar bone crest at the mesial-central (Mbh) and distal-central (Dbh) aspects of the socket to the relative cementum–enamel junction or the restoration margin of the neighbouring teeth are presented in Table 5. In 2/13 cases in the SBC group, the Dbh values were not available due to the absence of the relevant tooth distal of the extraction socket. In 1/13 cases from the DBBM group, the Mbh value was not available due to the absence of the relevant tooth mesial of the extraction socket. In the SBC group, the baseline Mbh and Dbh were 3.4 ± 0.8 and 3.1 ± 0.4 mm, respectively, while at 8-month follow-up, the Mbh and Dbh were 3 ± 1.2 and 3.4 ± 1.6 mm, respectively. In the DBBM group, the baseline Mbh and Dbh were 3.1 ± 0.9 and 3.2 ± 0.7 mm, respectively, while at 8-month follow-up, the Mbh and Dbh were 3.3 ± 1.1 and 3.5 ± 1.4 mm, respectively. The mean changes of the Mbh and Dbh from baseline to 8 months were not statistically significant between the two groups ($P>0.05$).

The resistance of bone tissue during the trephination process was similar in both groups (Table 6). In all patients in the SBC group, a dental implant of adequate dimensions was placed with satisfactory initial stability. In one patient from the DBBM group, implant placement was not possible due to insufficient primary stability. During implant placement, 9/13 implants in the SBC group and 8/12 implants in the DBBM group presented with either dehiscence or fenestration defects and required additional bone augmentation to allow implant placement in a predetermined prosthetically driven position (Table 7). Four implants in each group were placed without any additional bone augmentation procedure.

Histological analysis

Twelve specimens from each group were available for histological analysis. In one specimen from each group, it was not possible to perform the histological procedure.

In the SBC group, variable new bone formation was observed. The newly formed bone was observed mainly at the apical part of the biopsy and was mainly woven, with more lamellar bone occurring only in isolated instances (Figs 7 and 8). The amount of bone marrow differed significantly between individuals. In several specimens, the SBC particles were in direct contact with the newly formed bone (Figs 7 and 8). In the coronal part of the biopsy, the SBC particles were surrounded by dense connective tissue composed of various forms of fibroblasts, collagen fibres and blood vessels, with no signs of inflammation. In some specimens, areas of mineral apposition of the connective tissue fibres were seen (Figs 7 and 8). No active resorption of the SBC particles was observed.

Similar histological characteristics were observed in the biopsies at the DBBM group (Figs 9 and 10). New bone formation was mainly limited in the apical part of the biopsy, where newly formed bone of either the woven or the mature lamellar type was observed in direct contact with the DBBM particles. No signs of active resorption of the DBBM particles were observed. In the coronal part of the biopsies, the particles were surrounded by a dense connective tissue, with no signs of inflammation.

Discussion

The aim of the various ridge preservation procedures, involving grafting of immediate postextraction sockets, is to prevent alveolar ridge atrophy and maintain adequate dimensions of bone in order to facilitate implant placement in prosthetically driven positions or to maintain an acceptable ridge contour in areas of aesthetic concern. This randomized, controlled clinical trial compared the potential of a synthetic bone substitute (SBC) and a bovine-derived xenograft (DBBM), both in combination with a collagen barrier according to the GTR principle, to preserve alveolar ridge dimensions and promote osseous healing of postextraction alveolar sockets in the

Table 7. **Frequency distribution of residual peri-implant defects in the test and control group following implant placement**

	Pristine	Dehiscence	Fenestration	Failure	*N*
SBC	4 (31%)	6 (46%)	3 (23%)		13
DBBM	4 (31%)	7 (53.7%)	1 (7.7%)	1 (7.7%)	13

SBC, Straumann Bone Ceramic®; DBBM, deproteinized bovine bone mineral.

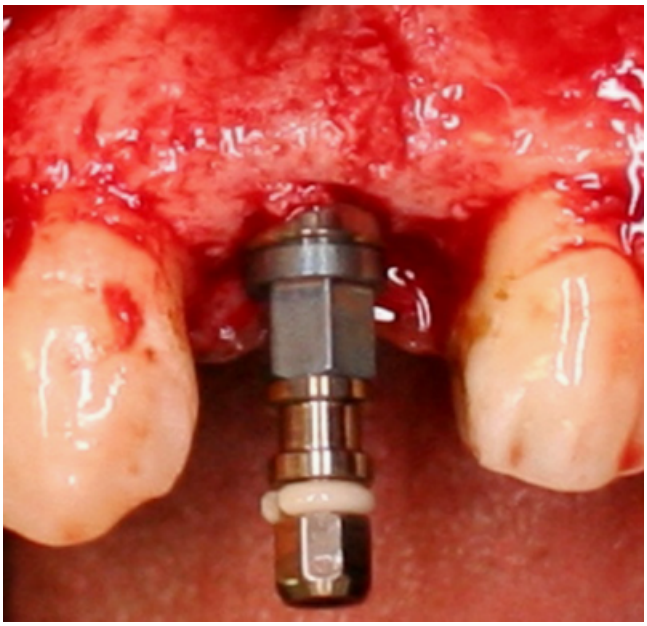

Fig. 6. Implant placement in the ridge preservation site at 8 months following the alveolar ridge preservation surgery.

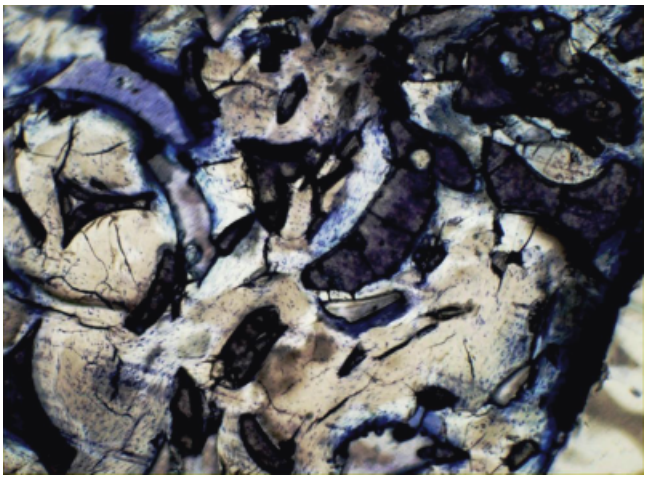

Fig. 7. Photomicrograph of a test specimen [Straumann Bone Ceramic® (SBC)] at the apical portion of the socket. Residual SBC particles are integrated into newly formed bone. Toluidine blue staining, original magnification × 10.

incisor, canine and bicuspid areas. Although a decrease in the bucco-lingual dimension of the alveolar ridge was observed in both groups, both materials equally preserved all the other clinical dimensions of the site and supported new bone formation in postextraction sockets, allowing the placement of dental implants. The results of this study are in agreement with previous controlled studies where similar combinations of bone grafts or substitutes with resorbable barriers were successfully used for alveolar ridge preservation (Iasella et al. 2003; Vance et al. 2004; Barone et al. 2008). However, complete preservation of the pre-extraction ridge dimensions should not be anticipated, even when alveolar ridge preservation techniques involving postextraction socket grafting are applied. In the present study, a bucco-lingual width reduction of the alveolar ridge was observed in both groups, confirming previous clinical and preclinical reports that postextraction healing is always characterized by osseous resorption and significant contour changes especially in the horizontal plane of the residual alveolar ridge (Schropp et al. 2003; Araujo & Lindhe 2005). These changes may be limited but not avoided when grafting of the socket is utilized (Iasella et al. 2003; Barone et al. 2008; Araujo & Lindhe 2009; Araujo et al. 2009).

In our study, the bucco-lingual dimension of the coronal part of the socket decreased by 1.1 ± 1 mm in the SBC group and by 2.1 ± 1 mm in the DBBM group. Similar postextraction alveolar ridge resorption was observed in previous randomized, controlled clinical trials where extraction sockets were treated with either a porcine xenograft and a collagen barrier (Barone et al. 2008) or freeze-dried bone and a collagen membrane (Iasella et al. 2003) and compared with the healing of ''empty'' untreated extraction sockets (for a review, see Darby et al. 2009). One of the limitations of the present study is the absence of a negative control group including patients in whom unassisted socket healing would have been followed for a similar period of time and therefore the lack of a negative control group does not allow a complete evaluation of the overall effectiveness of the two biomaterials.

In the present investigation, full-thickness buccal and palatal/lingual muco-periosteal flaps were raised to facilitate the placement of the barrier membranes over sound alveolar bone. It has been previously advocated that in full-thickness muco-periosteal flaps, the bone–periosteum continuity is disrupted and a marginal bone resorption of approximately 1 mm should be anticipated (Moghaddas & Stahl 1980). Based on this, it has been suggested that in cases of postextraction ridge preservation, flapless techniques should be utilized, because flap reflection may initiate further bone resorption in addition to that naturally occurring in the bundle bone of the

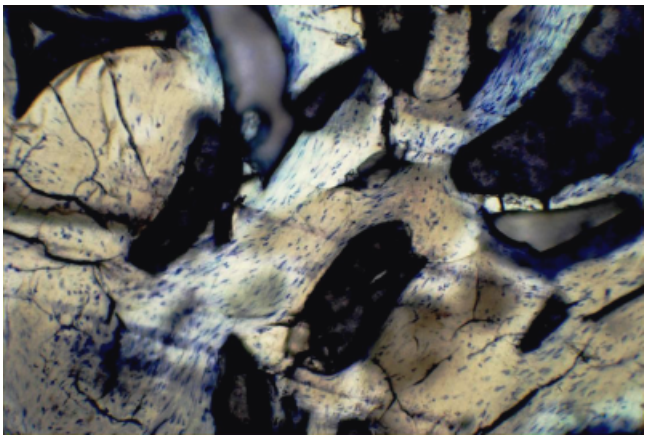

Fig. 8. Higher magnification of the same test specimen [Straumann Bone Ceramic® (SBC)]. Residual SBC particles are integrated either into newly formed woven bone or into connective tissue. Toluidine blue staining, original magnification × 20.

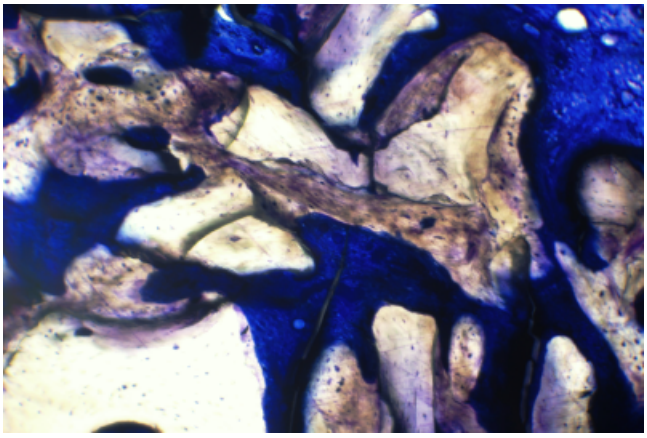

Fig. 9. Photomicrograph of a control specimen [deproteinized bovine bone mineral (DBBM)] at the apical portion of the socket. Residual DBBM particles are integrated into newly formed bone and dense connective tissue. Toluidine blue staining, original magnification × 10.

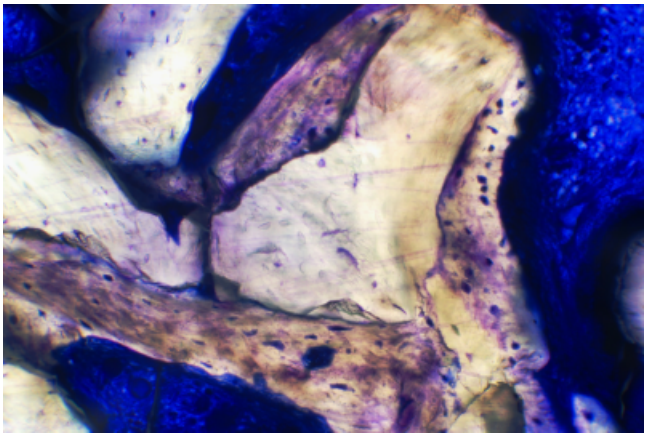

Fig. 10. Higher magnification of the same control specimen [deproteinized bovine bone mineral (DBBM)]. Residual DBBM particles are integrated into newly formed woven bone. Toluidine blue staining, original magnification × 20.

alveolar socket as a result of postextraction healing. Whether or not the adaption of a less extensive flap elevation or even a flapless approach would have resulted in further reduction of postextraction bone resorption remains to be investigated; therefore, further research is necessary to define the most effective surgical protocol for alveolar ridge preservation.

Although all the other alveolar ridge dimensions were similar between the two groups, SBC was associated with statistically significantly less reduction of the bucco-lingual width. A sound biologic explanation for the observed difference remains unknown, but it should not be attributed solely to a different ability of the two biomaterials to promote bone formation because no other clinical or histological parameter differed between the two groups. Pre-operative factors such as the different distribution of the extraction sites (four mandibular teeth in the SBC group versus one in the DBBM group), together with possible differences in the condition of soft and hard tissues immediately after tooth extraction that were not evaluated in this study, may be responsible for this observation.

At 8 months following an alveolar ridge preservation operation, the bucco-lingual width was 7 ± 1.1 mm and 6.9 ± 1.9 mm in the SBC and DBBM groups, respectively. Considering that an alveolar ridge width between 7 and 8 mm is usually necessary for the placement of a standard diameter implant, such postextraction ridge dimensions allowed implant placement in all but one case. However, in nine out of the 13 cases in the SBC group and in eight out of 12 cases in the DBBM group guided bone regeneration to treat residual dehiscence or fenestration defects around the implants was necessary. These findings were not in agreement with Barone et al. (2008), where implant placement was uncomplicated in the sockets that were treated with a porcine xenograft and a collagen barrier. Different implant and augmentation materials and implant placement protocol, as well as the intraoral distribution of the treated sites, may be responsible for this different outcome.

To our knowledge, this is one of the few prospective randomized, controlled trials (Barone et al. 2008) in which clinical and histological data are correlated following comparison of two different grafting materials for alveolar ridge preservation according to the GTR principle. From the histological point of view, both biomaterials promoted new bone formation, possibly by osteoconduction at the apical and the middle part of the socket while the

coronal and central part of the socket was mainly occupied by graft particles surrounded by dense connective tissue, even at 8 months following the alveolar ridge preservation surgery. The histological results of the present study corroborate previous preclinical reports in dogs, where it was concluded that both DBBM and SBC are potential osteoconductive scaffolds to support GBR for the treatment of dehiscence peri-implant defects (Schwarz et al. 2007). However, previous human histological reports presented similar or even better healing response after grafting of the socket with deproteinized xenografts in combination (Vance et al. 2004; Barone et al. 2008) or not (Artzi et al. 2000; Heberer et al. 2008) with barrier membranes. Similar promising human histological results have been published when SBC was used for sinus augmentation (Cordaro et al. 2008; Froum et al. 2008). Although the moderate histological results of the present study cannot be directly compared with previous human histological reports, as histomorphometric analysis was not applicable in this study, several factors may have contributed to the lack of complete osseous regeneration of the alveolar socket. The early membrane exposure that took place in our study may have compromised bone formation in the event that these barriers became infected at a later stage (Nowzari et al. 1995). However, no obvious clinical signs of infections such as suppuration were observed in this study or in any of the above-mentioned studies where the central part of the membrane was also left uncovered. Although the membrane was still visible in both groups at the second postoperative week, at the fourth postoperative week, most of the collagen membrane had been resorbed and possibly had lost barrier function (Donos et al. 2004). Whether or not an early resorption of the collagen barrier has influenced bone formation in the coronal part of the socket is an issue that needs further investigation. However, it is logical to assume that the use of barriers with delayed resorption time would provide an elongated barrier function that would have promoted further new bone formation in the extraction socket by inhibiting the connective tissue proliferation into the socket area for a longer period of time (Mardas et al. 2003; Donos et al. 2005).

In the present study, no effort was made to select a predetermined type of socket (Juodzbalys et al. 2008). The extraction sockets in this study presented with different soft tissue quantities, qualities and gingival tissue biotypes as well as with different anatomical and dimensional characteristics of the hard tissue compartment. Obviously, some of these characteristics, together with several other factors (e.g. smoking, reason for extraction, tooth location, etc.), may influence the final outcome of any socket preservation procedure and may be important in making the decision of whether or not a ridge preservation technique is indicated. Although many of these factors were evaluated in this study, the small unequal numbers of subjects in each category (Tables 1 and 2) did not allow any conclusions from this set of data. Additional studies based on large patient samples are necessary in order to identify the specific trends and risk parameters that should be evaluated before any alveolar ridge preservation procedure as prognostic factors of their effectiveness.

Conclusion

Both biomaterials partially preserved the width and the interproximal bone height of alveolar ridge. Both biomaterials supported implant placement at 8 months following the ridge preservation procedure.

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Supporting Information

Additional supporting information may be found in the online version of this article:

The Consort E-Flowchart Aug. 2005

Table S1. Supporting information in accordance with the CONSORT Statement 2001 checklist used in reporting randomized trials.

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