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Radiographic alveolar bone changes following ridge preservation with two different biomaterials

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Abstract

Objectives: The aim of this randomized controlled trial was to evaluate radiographical bone changes following alveolar ridge preservation with a synthetic bone substitute or a bovine xenograft.

Methods: Alveolar ridge preservation was performed in 27 patients randomized in two groups. In the test group ($n=14$), the extraction socket was treated with Straumann bone ceramic® (SBC) and a collagen barrier membrane (Bio-Gide®), whereas in the control group ($n=13$) with deproteinized bovine bone mineral and the same barrier. Standardized periapical X-rays were taken at 4 time points, BL: after tooth extraction, GR: immediately after socket grafting, 4M: 16 weeks, 8M: 32 weeks post-operatively. The levels of the alveolar bone crest at the mesial (Mh), and distal (Dh) and central aspects of the socket were measured at all time points. All the radiographs obtained were subtracted from the follow-up images. The gain, loss and unchanged areas in terms of grey values were tested for significant difference between the two groups.

Results: In the test group, the Mh and Dh showed a mean difference ($\pm$ standard deviation) of 0.9 ± 1.2 and 0.7 ± 1.8 mm, respectively, among BL-8M. In the control group, the Mh and Dh showed a mean difference of 0.4 ± 1.3 and 0.7 ± 1.3 mm, respectively ($P>0.05$). Both treatments presented similar gain in grey values between BL-GR, BL-4M and BL-8M. The SBC presented less loss in grey values between BL-4M and BL-8M ($P<0.05$). Radiographic assessment underestimated the intrasurgical measurements (mesial and distal) of an average 0.3 mm (95% CI, 0.02–0.6).

Conclusion: Both types of bone grafts presented similar radiographic alveolar bone changes when used for alveolar ridge preservation.

Following tooth extraction, a significant alteration of the alveolar ridge contour takes place due to extended osseous resorption and remodelling (Amler 1969; Cardaropoli et al. 2003; Araujo & Lindhe 2005). As a result of these processes, post-extraction site dimensions are inferior to the dimensions of the alveolar bone before tooth extraction (Pietrovski & Massler 1967; Johnson 1969). In a recent study, Schropp et al. (2003) evaluated bone formation in the alveolar socket and quantified contour changes of the alveolar ridge following extraction of single tooth using study casts and standardized periapical radiographs. The authors reported a 5–7 mm reduction in the width of the alveolar ridge (a 50% of the pre-extraction alveolar ridge dimensions) that usually occured during the first three post-extraction months.

Modern aesthetic implant or tooth-supported prostheses, especially in the anterior region, require a complete ridge contour reconstruction in order to achieve an aesthetically pleasing immergence profile in the area of missing teeth. In order to preserve the original ridge dimensions following tooth extraction and promote bone regeneration of the residual alveolar socket, various bone grafts and substitutes used in combination or not with barriers for guided tissue regeneration (GTR) have been suggested (Becker et al. 1994, 1996; Gross 1995; Brugnami et al. 1996; Artzi et al. 2000; Froum et al. 2002; Feuille et al. 2003; Iasella et al. 2003; Serino et al. 2003; Barone et al. 2008). Among these grafting materials, deproteinized bovine bone mineral xenografts (DBBM) were able to promote bone regeneration and preserve the pre-extraction alveolar ridge dimensions when grafted in immediate extraction sockets, especially when combined with barriers for GTR (Artzi et al. 2000; Carmagnola et al. 2003). Furthermore, a randomized controlled clinical radiographic trial demonstrated that the post-extraction alveolar ridge resorption was significantly reduced when the extraction sockets were grafted with a deproteinized bovine bone in comparison with the sockets that were left to heal

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without any grafting (Nevins et al. 2006). According to the authors, the form of the residual alveolar ridge as evaluated in sagittal CT images was more favourable for subsequent implant placement when a socket preservation procedure occured. However, in another randomized controlled clinical trial comparing ridge dimensions and histological characteristics following socket preservation with two different techniques, the combination of deproteinized bovine bone and a collagen membrane was found inferior in terms of new bone formation to a combination of allograft ''putty'' combined with a calcium sulphate barrier (Vance et al. 2004), indicating that further research is necessary in order to identify the ideal grafting material for alveolar ridge preservation.

Straumann bone ceramic® (SBC) is a fully synthetic bone graft substitute of medical-grade purity in particulate form composed of biphasic calcium phosphate – a mixture of 60% hydroxyapatite (HA), which is 100% crystalline, and of 40% of the beta form of tricalcium phosphate (β-TCP). The two mineral phases are mixed at an early stage of synthesis delivering blocks of a homogenous distribution of the two mineral phases and 90% porosity. The objective of combining the insoluble HA with the soluble β-TCP is that HA would maintain the space (scaffolding function) while the β-TCP resorbs promoting at the same time bone regeneration. The biocompatibility and osteoconductivity of the calcium phosphates have been demonstrated in recent human controlled trials where 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). In a randomized control clinical trial from our group (Mardas et al. 2010), these two biomaterials were tested clinically and histologically for alveolar ridge preservation in combination with collagen membranes for GTR. It was reported that following grafting of the socket with either SBC or DBBM, an equal preservation of the alveolar ridge dimensions was achieved and the same amount of bone regeneration was observed in the post-extraction sockets at 8 months following the ridge preservation surgery.

The aim of this study was to evaluate the radiographical bone changes following alveolar ridge preservation with a synthetic bone substitute or a bovine xenograft.

Materials and methods

Study population

Thirty patients participated in this randomized, controlled, single-blind, clinical trial that occured in UCL Eastman Dental Institute, Clinical Investigation Center during the period March 2006–July 2009. The study was conducted in accordance with ethical principles founded in the Declaration of Helsinki and the International Conference on Harmonisation for Good Clinical Practice, 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 based on the following inclusion criteria: age between 18 and 75 years old; good general health; presence of a hopeless tooth in mandibular or maxillary incisor, canine or premolar region requiring extraction; and the tooth to be extracted has at least one neighbour tooth.

In addition, patients were excluded from the studying in case of: pregnancy or lactating period; any known diseases (not including controlled diabetes mellitus) and the related medication, infections or recent surgical procedures within 1 month of baseline visit known to affect oral status or contraindicate surgical treatment; anticoagulant therapy; 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 >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 control group by a computer-generated table. A balanced random permuted block approach was used to prepare the randomization tables in order to avoid unequal balance between the two treatments.

Surgical treatment and post-operative care

The surgical protocol has been described in details elsewhere (Mardas et al. 2010). In summary, following the performance of minimally extended full-thickness mucoperiosteal flaps, the tooth was atraumatically extracted by means of periotomes, attempting to preserve as much as possible from the surrounding osseous walls. Following tooth extraction, the following intra-surgical measurements of residual ridges dimensions were taken using a UNC-15 probe:

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

In the randomly assigned test group, the extraction socket was loosely filled with SBC (Straumann AG, Basel, Switzerland) while in the control group the extraction socket was filled with and 0.25–1 mm in diameter DBBM particles (Bio-Oss; Geistlich Biomaterials, Wollhusen, Switzerland). In both groups, a bi-layer collagen barrier (Bio-Gide®, Geistlich, Switzerland) was used to cover the grafting material. The flaps were coronally replaced and secured by vertical mattress and horizontal cross mattress sutures (Gore Tex, Gore & Associates Inc., Flagstaff, AZ, USA) in order to cover as much as possible of the biomaterials without, however, being able to achieve their complete coverage.

Systemic antibiotics (Amoxicillin 500 mg and Metronidazole 400 mg) were administered three times per day for the first post-operative week and Paracetamol 500 mg was subscribed upon patient discretion for post-operative pain control. All the patients refrained from tooth brushing in the operated area and rinsed with 0.2% chlorhexidine–digluconate mouthwash for the first two post-operative weeks. Any removable temporary prosthesis was not worn for the first 2–3 weeks and subsequently was 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 regular intervals following operation.

Radiographic method

Standardized intraoral periapical radiographs were taken at the following observation periods:

- At baseline (BL)*:* immediately after tooth extraction.
- At grafting (GR)*:* immediately after socket augmentation.
- At 4 months (4M)*:* 16 weeks after tooth extraction visit.
- At 8 months (8M)*:* 32 weeks after tooth extraction just before dental implant placement.

The periapical radiographs were produced as described previously by Sewerin (1990), using the paralleling technique with an occlusal bite index, prepared from a silicone material and attached to the cone of the X-ray unit. The same bite index was used in all the visits (BL, GR, 4M and 8M). All the periapical radiographs were developed using the same type of film and were developed with the same automatic X-ray developer under standardized conditions. The radiographs were digitized using a slide scanner (SprintScan 35, CS-2700, Polaroid Scanner, Cambridge, MA, USA) after selecting constant scanning settings, 600 d.p.i. resolution, and 256 grey levels. The images were coded to preserve blinding of the recordings and stored in JPEG File Format without compression.

Linear radiographic measurements

Linear measurements on the digitized radiographs were performed by means of a digital image analysis computer program for radiographic linear measurements (X-PoseIt, version 3.1.17, Image Interpreter System, Lystrup, Denmark). The distances from the alveolar BC at the mesial (MbhR), distal (DbhR) and central (CbhR) aspects of the socket to the cementum–enamel junction (CEJ) or restoration margin of the neighbouring to the extraction teeth were measured during all above-mentioned observation periods (BL, GR, 4M and 8M). For assessment of the bone-level changes at the extraction site, a reference line connecting the CEJ or restoration margin of the neighbouring to the extraction teeth was drawn in all the radiographs. The vertical distances from this reference line to the alveolar BC at the mesial (Mh), distal (Dh) and central (Ch) aspects of the socket were measured by a single calibrated examiner, other than the surgeon who was also not aware of the treatment assignment (test or control). The reproducibility of the examiner was tested previously in duplicated measurements taken within a week interval in 15 randomly selected digitized radiographs.

Subtraction radiography

Quantitative digital subtraction radiography was performed using the same digital analysis software (X-PoseIt, version 3.01). A region of interest (ROI) that corresponded to the alveolus of the extracted tooth and a region of control (ROC) that corresponded to an area expected not to be involved in bone changes were outlined in all the baseline radiographs immediately after the extraction (BL). The radiographs at the baseline were subtracted from the follow-up images taken at GR, 4M an 8M observation periods resulting in the subtraction images: BL–GR BL–4M, BL–8M, 4M–8M. Following the alignment and superimposition of digitized images (using 10 reference points drawn on both images) taken at two different time points (BL, GR, 4M and 8M), both ROI and ROC transferred automatically in the resulting superimposition image and the grey-shade pixel value within the ROI of each image was subtracted from the corresponding pixel value of the other image, resulting in the ''subtraction image'' that represented the differences in grey shades within the ROI between the two radiographs. Hard mineralized tissue was defined as pixels with a grey level more than 128 that appear bright in the subtraction image. Respectively, non mineralized tissue was defined as pixels with a grey level <128 that appeared dark in the image. Pixels with a grey scale within a conservative interval mean ± 3 SD for the ROC were defined as unchanged. Pixel values above this level were defined as hard tissue gain and values below as hard tissue loss. The mean grey values and the size of the gain, loss and unchanged areas were tested for significant difference between the two groups at the various observation periods.

Statistical analysis

All data were entered in a computer database, proofed for entry errors and imported into SPSS (version 17). Differences between and within the two treatment groups were assessed at each time interval (BL–GR BL–4M, BL–8M, 4M–8M) by using independent samples *t*-tests for differences in means between groups when the data were normally distributed and the Mann–Whitney *U*-test for differences in medians when the data were non-normally distributed. The differences between the repeated measures at each follow-up visit were evaluated with a non-parametric Friedman test for repeated measures. *Post hoc* comparisons between study groups at each visit were computed with Wilcoxon signed-rank tests and Bonferroni corrections. Non-parametric linear correlation analysis (Spearman) was performed between clinical (Mbh and Dbh) and radiographic linear measurements (MbhR and DbhR) (combining the mesial and distal measures at both visits) and intraclass correlation coefficient was reported. The differences between intrasurgical measurements and radiographic assessment were computed (normal distribution) and multiple linear regression models were created to ascertain the impact of additional intrasurgical measurements (B-L/P and Bbw, L/Pbw) on the validity of radiographic measurements. Significance level was set to be at $P<0.05$.

Results

Twenty-seven out of the thirty patients that have been initially enrolled participated in the radiographic part of the study. Two patients were excluded before randomization due to complete loss of the buccal osseous plate following extraction. One patient quit the study before randomization. One patient that had been assigned in the test (DBBM) group quit the study before implant placement. In this patient, only the radiographs corresponding to BL, GR and 4M were included in the analysis. The distribution of the treated sites treated is presented in Table 1.

The level of agreement between the duplicated radiographic linear measurements (Mh, Dh, Ch) performed by the single calibrated examiner is presented in Table 2. For the mesial linear measurements (Mh), both measurements were anticipated to fall within a ± 0.192 mm range on 95% of occasions (CR). Similarly, the CR for the distal measurements (Dh) was ± 0.164 mm and for the central measurements (Ch) was ± 0.388 mm.

Linear radiographic measurements

A comparison of the linear radiographic measurements was performed: (a) between treatment groups and (b) within treatment groups.

(a) *Between treatment groups:* The mean values of the three different linear radiographic

Table 1. **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®; DBMM, deproteinized bovine bone mineral.

Table 2. **Reproducibility of the radiographic linear measurements**

Parameter	Lin's correlation coefficient	Bland and Altman's approach				
		Systematic error		Random error		Limits of agreement
		Mean difference	*P* (paired *t*-test)	Standard deviation	Coefficient of repeatability CR	
Mh	0.99	0.02	0.382	0.096	0.192	−0.166, 0.21
Ch	0.99	−0.01	0.838	0.194	0.388	−0.39, 0.369
Dh	0.99	−0.01	0.47	0.082	0.164	−0.176, 0.145

measurements (Mh, Ch, Dh) during all the observation periods (BL, GR, 4M and 8M) is presented in Tables 3, 4 and 5. At all observation periods, the Mh measurements were statistically higher in the SBC group ($P<0.05$) (Table 3). At GR and 4M observation periods, the Ch measurements were statistically significant higher ($P>0.05$) in the SBC group (Table 4).

The changes of radiographic hard tissue levels between different time intervals (BL–GR BL–4M, BL–8M, GR–4M, GR–8M) are presented in Tables 6, 7 and 8. The linear radiographic measurements in the mesial site of the socket (Mh) increased by approximately 0.9 mm in the SBC group for the period between BL and 8M, whereas in the DBBM group increased by 0.4 mm (Table 6). No statistical significant difference was observed between the two groups at any time interval ($P>0.05$) (Table 6).

The linear radiographic measurements in the central site of the socket (Ch) have been reduced by approximately 16 mm in SBC group and 18.6 mm in DBBM group for the period between BL and 8M (Table 7). No statistical significant difference was observed between the two groups at any time interval ($P>0.05$) (Table 7).

The linear radiographic measurements in the distal site (Dh) of the socket increased by 0.36 and 0.05 mm in the SBC and DBBM group, respectively (Table 8). The difference between the groups was not statistically significant at any time interval ($P>0.05$) (Table 8).

(b) *Within treatment groups*: The radiographic linear measurements changes within each group during the 8 month observation period are shown in Figs 1, 2 and 3.

In the SBC group, the Mh was increased by 0. 92 mm (Fig. 1) and the Dh by 1.03 mm (Fig. 3) between GR and 8M, while the Ch decreased by 16.05 mm between BL and 8 months (Fig. 2). The Mh and Dh values immediately after grafting of the socket were statistically significant lower than the relevant values at 8M indicating some progressive hard tissue loss in these sites treated with SBC ($P=0.03$ and $P=0.04$, respectively) (Figs 1 and 3). The Ch values immediately after extraction and before grafting (BL) were statistically significant higher than those values at 8M indicating radiographic socket fill in these sites treated with SBC ($P<0.0001$) (Fig. 2).

In the DBBM group, the Mh was increased by 0. 58 mm ($P=0.08$) (Fig. 1) and the Dh by 1 mm ($P<0.05$) (Fig. 3) between GR and 8 M, while the Ch decreased by 18.6 mm between BL and 8 months (Fig. 3). The Dh values at GR were statistically significant lower ($P<0.05$) than those values at 8 M indicating some progressive hard tissue loss in the distal sites treated with DBBM. In the mesial sites, although there was a trend for bone loss, it was not statistical significant ($P>0.05$). The Ch values immediately after extraction and before grafting (BL) were statistically significant higher ($P<0.0001$) than the Ch values at 8M indicating radiographic socket fill in these sites treated with DBBM.

Subtraction radiographic measurements

Seventeen radiographs from different observation periods were not available for subtraction radiography evaluation due to inadequate standardization or poor quality of the X-rays.

The grey-shade pixel value within the ROI corresponding to hard tissue gain, loss or unchanged areas is presented in Table 9. No statistical significant differences in grey-shade pixel values corresponding to hard tissue gain were observed between the two groups at any of the observation periods (BL–GR, BL–4M, BL–8M) ($P>0.05$). The sites treated with SBC presented with statistically significant lower ($P<0.05$) mean grey-shade pixel values corresponding to loss of hard tissue than the sites treated with DBBM at the observation period between BL and 8M. The unchanged areas were not different between study groups at each visit comparison ($P>0.05$).

Table 6. **Change in mesial height in mm (mean standard deviation) at different time intervals**

Change in Mh	SBC	DBBM	*P-value*
BL–GR	0 ± 0.5	0 ± 0.4	0.959
BL–4M	0.7 ± 1	0.4 ± 1.3	0.508
BL–8M	0.9 ± 1.2	0.4 ± 1.3	0.357
GR–4M	0.7 ± 1	0.6 ± 1	0.77
GR–8M	0.9 ± 1.2	0.6 ± 1	0.476

P-values with *t*-test for the difference in change in Mh between SBC and DBMM groups at different time intervals.
SBC, Straumann bone ceramics; DBMM, deproteinized bovine bone mineral; BL, baseline; GR, grafting; 4M, 4 months; 8M, 8 months.

Table 3. **Mesial height (Mh) in mm (mean ± standard deviation, *N* = number of X-rays evaluated)**

Mesial height	SBC	DBBM	*P-value*
BL	4 ± 2.2 (*N* = 13)	2.1 ± 1.5 (*N* = 12)	0.018*
GR	3.5 ± 1.4 (*N* = 12)	1.9 ± 1.5 (*N* = 13)	0.009*
4M	4.2 ± 1.5 (*N* = 12)	2.5 ± 1.8 (*N* = 12)	0.015*
8M	4.5 ± 1.8 (*N* = 12)	2.8 ± 1.6 (12)	0.022*

*Statistically significant at the level of $P<0.05$ with the *t*-test for the difference in Mh between SBC and DBMM groups.
SBC, Straumann bone ceramics; DBMM, deproteinized bovine bone mineral; BL, baseline; GR, grafting; 4M, 4 months; 8M, 8 months.

Table 4. **Central height (Ch) in mm (mean ± standard deviation, *N* = number of X-rays evaluated)**

Central height	SBC	DBBM	*P-value*
BL	22.1 ± 5.7 (*N* = 13)	21.83 ± 4.43 (*N* = 11)	0.895
GR	3.9 ± 1.8 (*N* = 12)	± 1.09 (*N* = 11)	0.041*
4M	5 ± 2.3 (*N* = 12)	3 ± 1.7 (*N* = 11)	0.025*
8M	4.8 ± 2.4 (*N* = 11)	3.4 ± 1.5 (*N* = 11)	0.123

*Statistically significant at the level of $P<0.05$ with the *t*-test for the difference in Ch between SBC and DBMM groups.
SBC, Straumann bone ceramics; DBMM, deproteinized bovine bone mineral; BL, baseline; GR, grafting; 4M, 4 months; 8M, 8 months.

Table 5. **Distal height (Dh) in mm (mean [median] ± standard deviation, *N* = number of X-rays evaluated)**

Distal height	SBC	DBBM	*P-value*
BL (N)	3.9 (2.8) ± 3.3 (*N* = 13)	1.9 (2.1) ± 1.33(*N* = 11)	0.224
GR(N)	3.5 (1.7) ± 3 (*N* = 12)	1.7 (2) ± 1.3 (*N* = 12)	0.623
4M (N)	4.3 (3.1) ± 3.4 (*N* = 12)	2.5 (2.7) ± 1.3 (*N* = 12)	0.194
8M (N)	4.7 (3.8) ± 3.8(*N* = 12)	2.9 (3.2) ± 1.1 (*N* = 11)	0.538

P-values with Mann–Whitney *U*-test for the difference in Dh between SBC and DBMM groups.
SBC, Straumann bone ceramics; DBMM, deproteinized bovine bone mineral; BL, baseline; GR, grafting; 4M, 4 months; 8M, 8 months.

Table 7. **Change in central height in mm (mean ± standard deviation) at different time intervals**

Change in Ch	SBC	DBBM	*P-value*
BL–GR	– 17.3 ± 4.2	– 19.3 ± 4.3	0.281
BL–4M	– 16.2 ± 4.1	– 18.8 ± 4.2	0.156
BL–8M	– 16 ± 4.3	– 18.6 ± 4.2	0.182
GR–4M	1.1 ± 1.2	0.5 ± 1.4	0.235
GR–8M	1 ± 1	0.9 ± 1.5	0.894

P-values with *t*-test for the difference in change in Ch between SBC and DBMM groups at different time intervals.
SBC, Straumann bone ceramics; DBMM, deproteinized bovine bone mineral; BL, baseline; GR, grafting; 4M, 4 months; 8M, 8 months.

Table 8. **Change in distal height in mm (mean ± standard deviation) at different time intervals**

Change in Dh	SBC	DBBM	*P-value*
BL–GR	0.3 (0.0) ± 1.1	0.1 (0.1) ± 0.5	0.954
BL–4M	0.5 (0.5) ± 1.6	0.5 (0.7) ± 0.8	0.839
BL–8M	0.7 (0.5) ± 1.8	0.7(0.8) ± 1.3	0.974
GR–4M	0.8(0.7) ± 1.1	0.8(0.7) ± 1.2	0.999
GR–8M	1 (1.3) ± 1.4	1 (1.2) ± 1.3	0.878

P-values with *t*-test for the difference in change in Dh between SBC and DBMM groups at different time intervals.
SBC, Straumann bone ceramics; DBMM, deproteinized bovine bone mineral, BL, baseline; GR, grafting; 4M, 4 months; 8M, 8 months.

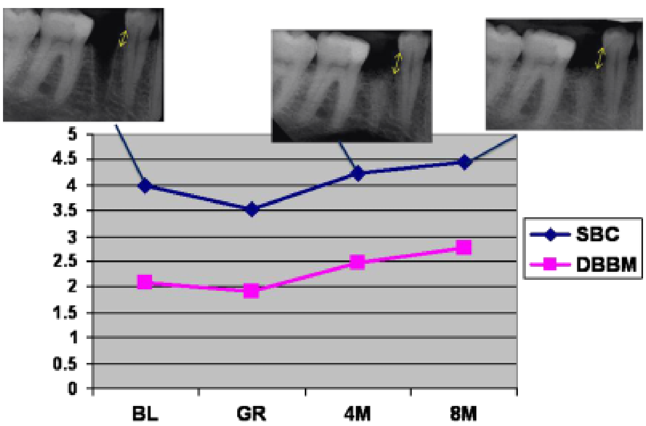

Fig. 1. Changes in Mh (yellow arrow) in Straumann bone ceramic® (SBC) and deproteinized bovine bone mineral group during the 8-month observation period together with the relevant standardized periapical X-rays from the SBC group.

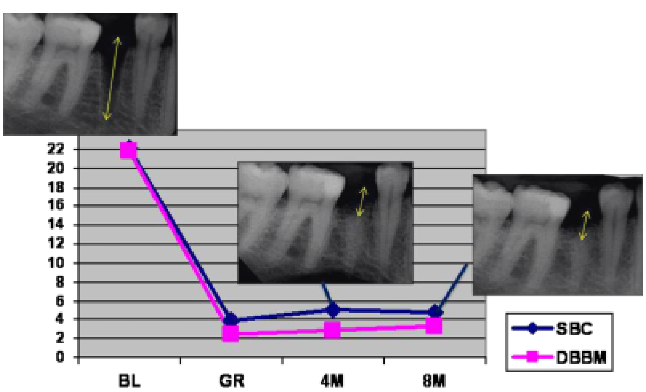

Fig. 2. Changes in Ch (yellow arrow) in Straumann bone ceramic® (SBC) and deproteinized bovine bone mineral group during the 8-month observation period together with the relevant standardized periapical X-rays from the SBC group.

Comparison between radiographic and clinical measurements

A positive albeit moderate linear association between clinical (Mbh and Dbh) and radiographic measures (MbhR and DbhR) was noted (Fig. 4). Both correlation coefficient ($R = 0.4$, $P < 0.0001$) and intraclass correlation coefficient (0.4, $P < 0.0001$) were statistically significant. No differences were noted if correlation analyses were performed at separate visits (data not shown). The mean difference between the intrasurgical measurement and radiographic assessment was of 0.3 mm (95% CI, 0.02–0.6). Multivariate analysis of this difference resulted in Bbw ($P = 0.004$) and L/Pbw ($P = 0.04$) widths as the only influential factors (linear regression model $F = 4.948$, $P = 0.009$, adjusted $R^2 = 0.78$).

Discussion

The present investigation indicated that alveolar ridge preservation with either SBC or DBBM resulted in similar radiographic bone-level changes. This is in agreement with the clinical results obtained in the study where the two biomaterials presented similar ability in preserving a significant portion of the pre-extraction clinical dimensions of the alveolar ridge and supporting bone formation (Mardas et al. 2010). In this first clinical study, the distance of the alveolar BC at the mesial and distal aspects of the socket to the relative CEJ or restoration margin of the neighbouring teeth were measured intrasurgically at baseline and at 8 months following tooth extraction and alveolar ridge preservation. The mean differences between the two groups were not statistically significant. In addition, within each group, the mean values taken at baseline were not statistical different to the values taken at 8M indicating that interproximal bone could be fully preserved following ridge preservation with both biomaterials. In the present investigation, the radiographic analysis on the same patients showed a small decrease in the interproximal radiographic bone levels at 4 and 8 months following operation in both groups. In the SBC group, the changes in Mh and Dh, representing possible radiographic hard tissue loss at the mesial and distal site, were 0.9 ± 1.2 and 0.7 ± 1.8 mm, respectively, at 8 months following tooth extraction (BL–8M). For the same period (BL–8M) in the DBBM group, the Mh and Dh showed a mean difference of 0.4 ± 1.3 and 0.7 ± 1.3 mm, respectively, indicating a mild interproximal bone loss of similar extent to that observed in the SBC group. On the other hand, caution should be taken in interpreting data on bone-level changes between different observation periods. Owing to the high number of statistical comparisons computed in this study, it may be possible that some of the results could be the result of statistical chance. In addition to that, it is questionable whether or not radiographic hard tissue changes at interproximal sites, of <1 mm present any significant clinical relevance.

Another interesting observation of this study was that the baseline linear measurements before grafting at mesial sites were found to be significantly different between the two groups. It was not possible to explain this discrepancy with any obvious biological or methodological reasons. The use of a strict randomization methodology and the masking of the examiner who performed the measurements have limited the possibility of introducing a systematic error able to create such a discrepancy in the baseline measurements. Therefore, we have to attribute this difference to an accidental fact.

Intraoral radiographic examination to assess bone levels following tooth extraction (Schropp et al. 2003; Munhoz et al. 2006; Aimetti et al 2007), or to detect changes in infrabony defects after regenerative treatment, has been used at previous clinical studies (Zybutz et al. 2000; Stavropoulos et al. 2003; Liñares et al. 2006). However, such type of analysis has specific limitations as an assessment tool, starting from the fact that periapical radiographs provide only two-dimensional images of three-dimensional structures. Furthermore, the radiographic image of interproximal bone loss may change with changing projection geometry. Therefore, it is important that the images are taken under standardized conditions (film type, time of exposure, film processing) at a standardized projection geometry (Wenzel & Sewerin 1991). In the present study, film type, time of exposure, film processing and radiographic equipment were fully standardized for all the radiographs taken. In addition, standardized projection geometry has been accomplished by using a customized bite index and the cone parallel technique. On the other hand, it should be emphasized that some degree of magnification is inevitable despite the fact that the intraoral radiographs were standardized. This magnification could be attributed to the contraction of the acrylic material, possible tooth migration or occlusal changes that in some cases have made an accurate and reproducible placement of the bite-index difficult or in some other occasions, the angulation of the cone and the bite index that may have slightly differed between the study visits. It is questionable, however, whether the utilization of other periapical film-positioning technique would have facilitated the repositioning of the films at the different observation periods and reduces this source of noise in the subtracted images (Ludlow & Peleaux 1994).

Besides standardization, the identification of anatomical landmarks in X-rays and the measurements of the distances between them represent a significant bias factor in all studies utilizing conventional radiography for evaluation of hard tissue changes. Both conventional methods (direct measurements on X-rays using magnifying means) and the use of computer assisted digital image analysis systems underestimate the true linear distances between reference anatomical landmarks such as CEJ or the BC to a varying degree when compared with the gold standard of intrasurgical measurements (Shrout et al. 1993; Eickholz et al. 1998). The mean difference of assessments of the CEJ–BC distance by means of computer-assisted radiographic analysis and direct surgical measurements, was reported to be between 0.3 and 1.4 mm (Eickholz et al 1999; Zybutz et al. 2000). In the present study, a direct correlation between radiographic linear measurements (MbhR and DBhR) and the intrasurgical measurements (Mbh and Dbh) between the CEJ–BC was performed to evaluate the validity of our linear radiographic measurements. Our findings are consistent with those reported previously with an average difference in radiographic measurements compared with the gold standard (intrasurgical) of 0.3 mm. Similarly, a moderate linear association between radiographic and intrasurgical measurements was found. Furthermore, the multivariate models suggested that the buccal and palatal widths of the alveolar crest (Bbw and L/Pbw) as measured intrasurgically, were the most influential factors in affecting the validity of radiographic assessment compared with gold standard. In particular, greater buccal and smaller palatal widths were associated with an overestimation and underestimation of the radiographic assessment of linear alveolar crestal bone heights, respectively.

The reproducibility of radiographic linear measurements may also be influenced by different factors. Wolf et al. (2001) tested the reproducibility of the radiographic linear measurements of interproximal bone loss at infrabony defects inter- and intraexaminer and reported that the radiographic measurements tended to overestimate the amount of bone loss as assessed by intrasurgical measurements and the reproducibility of the measurements found to be significantly influenced by the examiner. In the present study, one single, previously calibrated examiner, other than the surgeon who was also not aware of the treatment assignment (test or control) performed all the measurements. The reproducibility of the measurements obtained by this examiner was anticipated to fall within $< \pm 0.2$ mm in 95% of the measurements and was comparable to previous reports (Wolf et al. 2001).

In addition to linear radiographic measurements, the present study evaluated hard tissue

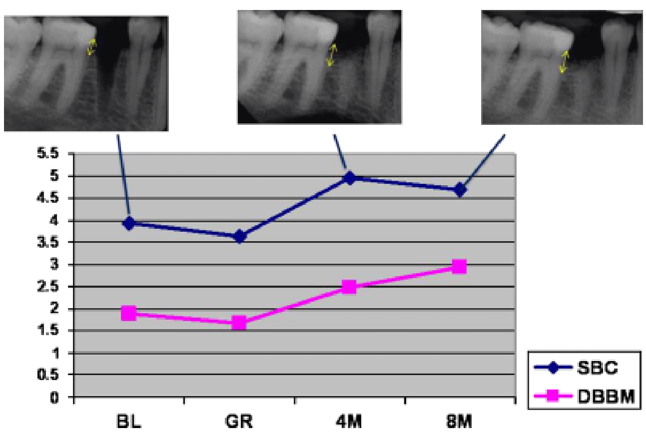

Fig. 3. Changes in Dh (yellow arrow) in Straumann bone ceramic® (SBC) and deproteinized bovine bone mineral group during the 8-month observation period together with the relevant standardized periapical X-rays from the SBC group.

***Table 9*. Grey shade pixel value within the ROI corresponding to hard tissue gain (G), loss (L) or unchanged areas (U)**

Tx	G BL–GR	G BL–4M	G BL–8M	L BL–GR	L BL–4M	L BL–8M	U BL–GR	U BL–4M	U BL–8M
SBC	168.4 ± 22.4	130.7 ± 73.1	110 ± 74.1	26.7 ± 46.5	48.6 ± 47.1*	32.5 ± 37.7*	129.5 ± 13.3	134.1 ± 17.9	128 ± 16.3
DBBM	150.2 ± 71	172.5 ± 24.3	140.3 ± 68.6	56.1 ± 54.9	60 ± 40.2*	65.4 ± 39.4*	134.8 ± 18.3	132 ± 24.2	134 ± 21.9

*Statistically significant at the level of $P<0.05$ for multiple comparisons between the groups with Wilcoxon signed-rank tests conducted with Bonferroni corrections.
SBC, Straumann bone ceramic®; DBMM, deproteinized bovine bone mineral, BL, baseline; GR, grafting; 4M, 4 months; 8M, 8 months.

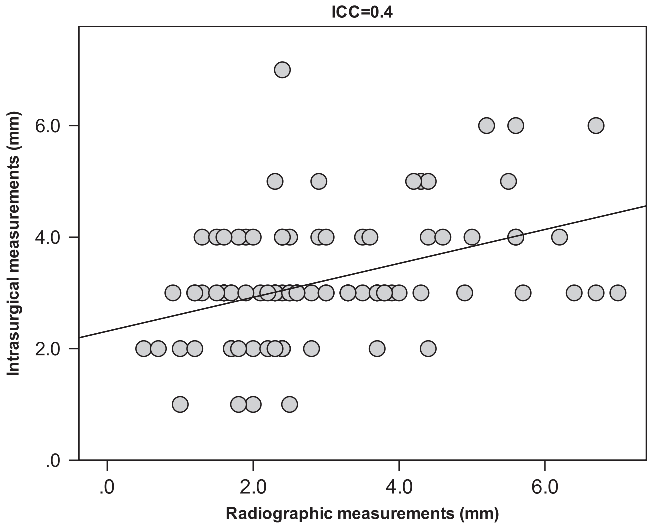

Fig. 4. Scatter plot for the correlation between radiographic assessment and intrasurgical measurements.

changes using subtraction radiography where the grey-shade pixel value within the ROI corresponding to hard tissue gain, and unchanged areas were compared between the two groups. The analysis showed that grey-shade pixel values corresponding to hard tissue loss were significantly lower in the SBC group. However, changes in grey-shade pixel values may not necessarily depict the ''real'' healing events that occur into the socket at the different observation periods. This is due to the fact that subtraction radiography is not able to distinguish between changes in the mineralized connective tissue and the presence of residual radiopaque biomaterial. In our study, grey-shade pixel values within the ROI corresponding to hard tissue gain maybe explained not only by the addition of a radiopaque biomaterial into an empty socket but also by an ongoing bone formation process during the healing period. In a similar way, the difference in grey-shade pixel values corresponding to hard tissue loss observed between the two groups could be explained by either an increased bone resorption process in the sockets grafted by DBBM or an increased resorption rate of the DBBM material or a combination of these biological processes resulting in all cases in reduced radiopacity. An initial correlation of subtraction radiographic data with the qualitatitive histological analysis performed in the first part of this study, (Mardas et al. 2010) supports the assumption that part of the radiographic hard tissue gain observed in the subtraction images taken can be attributed to ongoing new bone formation, especially at the base of the socket. However, the amount and location of bone formation or bone resorption cannot be estimated with the methodology applied in this study.

Conclusions

Taking into consideration the limitations of this study, alveolar ridge preservation with either a synthetic bone substitute, or a bovine-derived xenograft, both in combination with a collagen barrier will equally preserve radiographic bone levels up to 8 months following the grafting of the sockets.

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