CLINICAL ORAL IMPLANTS RESEARCH

Mariano Sanz
Jan Lindhe
Jaime Alcaraz
Ignacio Sanz-Sanchez
Denis Cecchinato

The effect of placing a bone replacement graft in the gap at immediately placed implants: a randomized clinical trial

Authors' affiliations:
Mariano Sanz, Jaime Alcaraz, Ignacio Sanz-Sanchez, Faculty of Odontology, University Complutense of Madrid, Madrid, Spain
Jan Lindhe, Sagralenska Academy, University of Goteborg, Goteborg, Sweden
Denis Cecchinato, Institute Franci, Padova, Italy

Corresponding author:
Mariano Sanz
ETEP Research Group
Facultad de Odontología – University Complutense of Madrid
Plaza Ramon y Cajal
28040 Madrid
Spain
Tel.: +34913942010
Fax: +34913941910
e-mail: marsan@ucm.es

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Abstract

Objective: To assess the added value of using a bone replacement graft in combination with immediate implants in reducing the bone dimensional changes occurring in the residual ridge.

Material and methods: Randomized parallel controlled clinical trial to study the efficacy of grafting with demineralized bovine bone mineral with 10% collagen (DBBM-C) in the gap between the implant surface and the inner bone walls when the implants were immediately placed in the anterior maxilla. The changes between implant placement and 16 weeks later in the horizontal and vertical crestal bone changes in relation to the implant were evaluated through direct bone measurements using a periodontal probe. Mean changes were compared between the experimental and control sites using parametric statistics.

Results: A total of 86 implant sites in 86 subjects were included in the analysis (43 in the test group and 43 in the control group). The horizontal crest dimension underwent marked changes during healing mainly at the buccal aspect of the alveolar crest where this reduction amounted to 1.1 (29%) in the test group and 1.6 mm (38%) in the control group, being these statistically significant ($P = 0.02$). This outcome was even more pronounced at sites in the anterior maxilla and with thinner buccal bone plates.

Conclusions: In conclusion, the results from this clinical trial demonstrated that placing a DBBM-C bone replacement graft significantly reduced the horizontal bone resorptive changes occurring in the buccal bone after the immediate implantation in fresh extraction sockets.

The dimensional changes occurring in the alveolar ridge after the tooth extraction have been documented in the experimental and clinical studies (Tan et al. 2012). Such reductions involve both the height (apicocoronal) and the width (buccolingual) of the residual ridge and may compromise the outcome of subsequent restorative therapy. Most of these dimensional changes will occur within the first 3 months of socket healing (Schropp et al. 2003b), and to counteract such early ridge contractions, the use of so-called immediate (type I) or early implant procedures (type II) was proposed (Chen et al. 2004; Hammerle et al. 2004).

In the type I protocol, the implant is placed in the fresh extraction socket with the aim of engaging the remaining socket walls to obtain the initial stability and to limit the ensuing bone resorption. This surgical approach may have other advantages, including the reduced exposure of patients to further surgical interventions or regenerative therapies. A recent systematic review (Lang et al. 2012), including 46 studies on 2908 immediately placed implants, reported high survival rates (2-year survival rate of 98.4% (97.3–99%)) and an estimated annual failure rate at the implant level of 0.82%. Most of studies included in the review, however, were short-term, with 5-year data limited to two studies (Bianchi & Sanfilippo 2004; Botticelli et al. 2008). Furthermore, in most of these studies, there were no data reporting the soft tissue changes or aesthetic outcomes. In fact, in the few studies where this outcome was assessed, marginal mucosal recession (≥1 mm) occurred in about 20% of the cases (Lang et al. 2012).

The crestal bone changes occurring after immediately placed implants have been

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evaluated in several clinical studies by comparing the bone architecture between implant installation and at second-stage surgery (usually 4 months later). A recent review publication concluded that immediately placed implants, in both clinical and experimental studies, failed to prevent the horizontal and vertical ridge dimensions (Vignoletti & Sanz 2014). Findings from a clinical trial comparing cylindrically and conically shaped implants placed in fresh extraction sockets in the maxilla (Sanz et al. 2010) reported similar outcomes in both implant designs, in terms of horizontal crestal bone changes, with 36% and 14% resorption at the buccal and palatal bone walls, respectively, and a mean vertical bone loss of approximately 1 mm. These resorptive changes were more accentuated in anterior maxillary teeth where the buccal bone plate is thinner (Ferrus et al. 2010). Using a multilevel multivariate analysis, the relevant factors influencing these dimensional changes included the thickness of the buccal bone wall for the horizontal changes and both the implant position and the thickness of the buccal bone for the vertical changes (Tomasi et al. 2010).

With the goal of counteracting the contraction of the residual ridge, different strategies have been tested, most of which have involved the combination of immediately placed implants and the use of different graft materials and barrier membranes. A randomized clinical trial (Chen et al. 2007) evaluated the outcome of immediate implants in the maxilla by comparing three treatment groups: one in which the gap (the void between the implant and the buccal-approximal bone walls) was left unfilled (control) and the other two in which the gap was filled either with deproteinized bovine bone mineral (DBBM) only or combined with a native bilayer collagen membrane (CM). Both experimental groups as compared with the controls showed similar outcomes, demonstrating a significant reduction (around 25%) in the extent of horizontal bone resorption. A recently published case series documented the soft tissue contour changes between implant placement and 1 year later of 26 single dental implants inserted in fresh extraction sockets and immediately provisionalized, where the bone-to-implant gap was grafted with a bovine bone mineral. No statistical differences were found between baseline and 1 year for all parameters, demonstrating that this surgical protocol was capable of maintaining the soft tissue contour and aesthetics compared to the pre-treatment status (Cardaropoli et al. 2015). These results are also consistent with the results from experimental studies, which have documented histologically that DBBM placed in this gap, modified the process of hard tissue healing and diminished the crestal bone resorption (Araújo et al. 2011).

Clinical studies have also reported that at immediate implant sites, there is a high percentage of spontaneous fill of this marginal gap; >90% of gaps wider than 2 mm were filled (Botticelli et al. 2004), and the median value representing the percentage fill was 100% (Sanz et al. 2010). Despite these observations, it was recently recommended that marginal gaps should be filled with a bone replacement graft in order to achieve the improved aesthetic outcomes (Chen & Buser 2014). There is, however, controversy on the clinical effect on such grafting, because only one clinical trial in a limited sample has tested this hypothesis. Hence, the purpose of this clinical trial was to evaluate the effect on the dimensional crestal bone changes after filling the gap in the immediate implant sites.

Material and methods

This study was designed as a prospective, randomized controlled parallel-group study documenting the response of implants immediately placed in the anterior maxilla in which a DBBM bone replacement graft was placed in the void between the implant surface and the inner bone walls. Three centers were involved, namely the ETEP Research Group at the Universidad de Complutense of Madrid (Spain), The Department of Periodontology at the Kings College Dental Institute (UK) and the Institute Franci from Padova (Italy). Prior to the commencement of the study, the human review boards from the respective participating institutions approved the protocol and informed consent forms.

Study population

Adult (≥18 years of age) subjects in need of one or more implants replacing teeth to be removed in the anterior maxilla (between 15 and 25) were included if they fulfilled the following criteria:

- The presence of at least 20 teeth with expected functional occlusion after the restoration
- The presence of an intact extraction socket following the removal of the natural tooth defined by:
  a. A marginal border of the facial bone crest that deviated ≤ 2 mm from that of the expected normal location of the site/region
  b. In the event of a potential facial fenestration, this should be no more than 3 mm apical from the marginal bone crest.

Subjects were excluded in the presence of any of the following:

- Untreated rampant caries and uncontrolled periodontal disease
- The absence of adjacent (mesial and/or distal) natural tooth root
- Uncontrolled diabetes or any other systemic or local disease or condition that would compromise post-operative healing and/or osseointegration
- Need for systemic corticosteroids or any other medication that would compromise post-operative healing and/or osseointegration
- Unable or unwilling to return for follow-up or unlikely to be able to comply with study procedures according to the investigators' judgement
- Smokers with cigarette consumption in excess of 10 cigarettes, or equivalent, per day during the healing period.

Treatments

Before the implant placement, the selected tooth was carefully extracted with the use of a periotome. Cylindrical dental implants (3.5 or 4.0 in diameter) were used (Fixture Microthread™ OsseoSpeed™; Dentsply, Mölndal, Sweden) in accordance with the guidelines described in the Dentsply Implants Manual™. Surgical placement of the implants always aimed for an ideal prosthetically driven implant installation.

After the implant insertion, a gap occurred between the implant surface and the hard tissue walls of the extraction socket. This defect could be present at the buccal, mesial, palatal and distal aspects of the implant. In order to assess precisely the size of the defect, the following landmarks were defined (Fig. 1d):

- Surface of implant (S)
- Rim of implant (R)
- Top of the bone crest (C)
- Inner border of the bone crest (IC), 1 mm apical of C.
- Outer border of the bone crest (OC), 1 mm apical of C.
- Base of the defect (D)

The following measurements were assessed by a blind examiner (JA) to the nearest millimeter using a periodontal probe (Hu-Friedy Diagnostic Probe UNC15 Qulix, Hu-Friedy Mfg. Co. Inc.) at both the buccal (B) and palatal (P) aspects (Fig. 1):

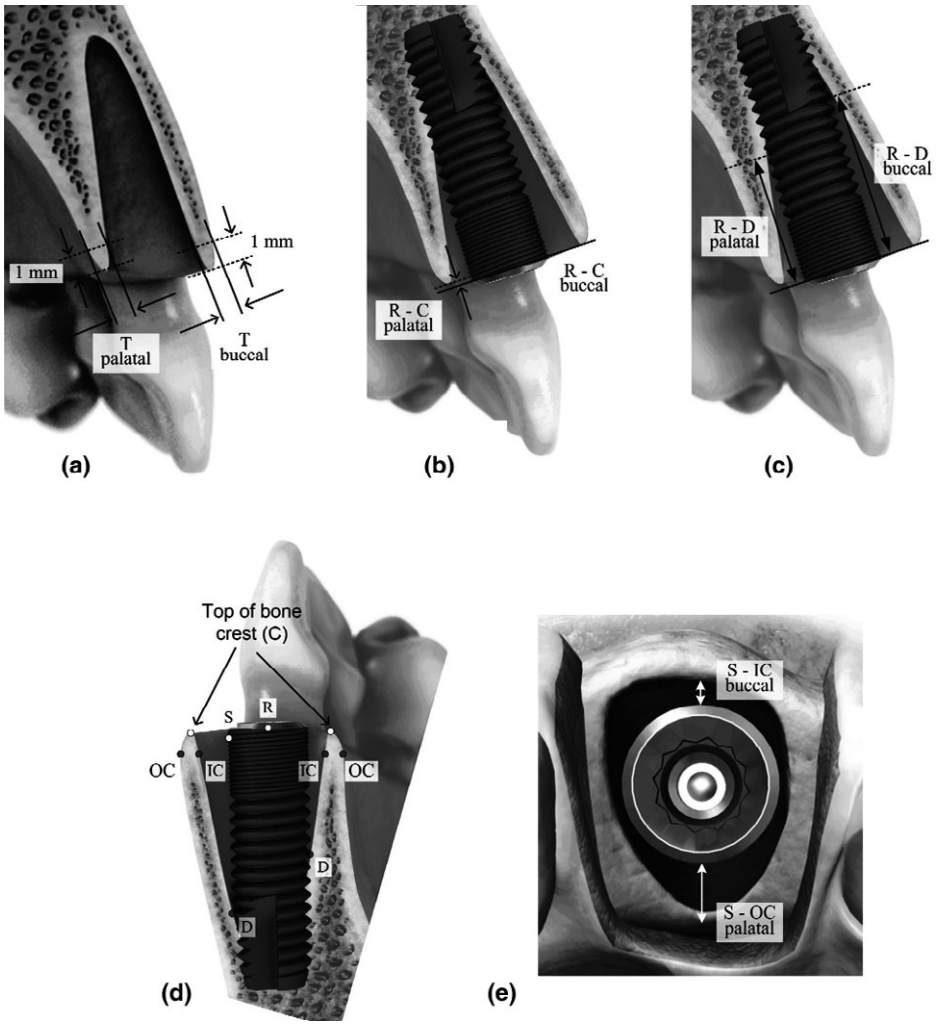

Fig. 1. Landmarks used to describe the dimension of the ridge as well as the size of the gap between the implant and the socket walls. (a) Assessment of the thickness of the crest (T) buccal/palatal. (b) Measurements performed to determine the relationship between the crest and the rim of the implant (R-C, buccal/palatal). (c) Measurements performed to determine the vertical defect dimension (R-D, buccal/palatal). (d) S, surface of implant; R, rim of implant; C, top of the bone crest; OC, outer border of the bone crest, 1 mm apical of C; IC, inner border of the bone crest, 1 mm apical of C; D, base of the defect. (e) Measurements performed to determine the size of the crest (S-OC) as well the horizontal defect dimension (S-IC).

- S to IC, constituting the horizontal defect distance, that is, the width of the gap between the implant surface and the bone crest (*S-IC buccal* and *S-IC palatal*) (Fig. 1e).
- S to OC, the horizontal distance between the implant surface and the outer surface of the bone crest (*S-OC buccal* and *S-OC palatal*) (Fig. 1e).
- R to D constituting the vertical defect distance from the rim of the implant to the base of the defect (*R-D buccal* and *R-D palatal*) (Fig. 1c).
- R to C, the vertical distance between the rim of the implant to top of the bone crest (*R-C buccal* and *R-C palatal*) (Fig. 1b). Although the implant placement was aimed to locate the rim levelled with the buccal bone plate, this measure could have a positive or negative value depending whether R was located apical of (positive) or below (negative) the bone crest (C).

The thickness of the buccal and palatal bone walls was measured 1 mm apical of the top of the bone crest (Fig. 1a). This was measured to the nearest half millimeter using a caliper (Iwanson caliper, DP720; Bontempi snc, Quirurgical Bontempi, Barcelona, Spain).

After these measurements and provided that the implants were stable and the extraction socket met the inclusion criteria, the site was randomly allocated to either treatment group A (test) or B (control). An independent randomization schedule was generated for each center in blocks and designed to ensure a balanced distribution of the tested interventions. In each center, the randomized treatment code was available in closed non-transparent envelopes. In treatment group A, the gap between the implant surface and the bone plates was filled with deproteinized bovine bone mineral with 10% collagen (DBBM-C) (Geistlich Bio-Oss® Collagen; Geistlich Pharma AG, 6110 Wolhusen, Switzerland). The material was pre-wetted in saline, inserted in the gap and once soaked in blood, it was gently pressed to the bone walls to completely fill the space (Fig. 2).

In treatment group B, no bone replacement graft material was used (Fig. 3).

Once the appropriate healing abutments were installed (Healing Abutment Zebra; Dentsply Implants, Mölndal, Sweden), the flaps were adapted and sutured to allow semi-submerged healing.

After surgery, mouth rinsing with a chlorhexidine-containing solution (0.1 or 0.12%), twice daily for 10 days, was prescribed together with the recommended standard post-surgical medication (such as analgesics, anti-inflammatory drugs or antibiotics). No implant-supported temporary restorations were used for the first 4 months. Seven days after the implant placement, the patients returned and the sutures were removed.

At 16 weeks after the implant placement, the patient returned for the re-entry procedure. The healing abutment was removed and the full-thickness flaps were elevated. Implant stability was examined and the remaining size of the defect was recorded in the same manner described following the implant installation (Fig. 1).

This study reports on the short-term hard tissue changes between the implant installation (baseline) and the 16-week re-entry procedure (re-entry).

Statistical methods

The null hypothesis was based on the assumption that crestal alveolar bone-level changes occurring following the immediate implant placement in the anterior maxilla were constant irrespective of whether the gap between the implant surface and the inner bone plate was filled with a bone replacement graft or not. The sample size was calculated on the assumption that the resulting residual gap size in the control group after 4 months would be 0.6 mm ± 0.7 mm and the introduction of the tested DBBM bone graft would result in almost elimination of the residual gap (0.15 mm) (Sanz et al. 2010). With this scenario, the needed number of patients (1 implant per patient) per group would be 50 (one-tailed test; $\alpha = 0.05$; $\beta = 0.10$).

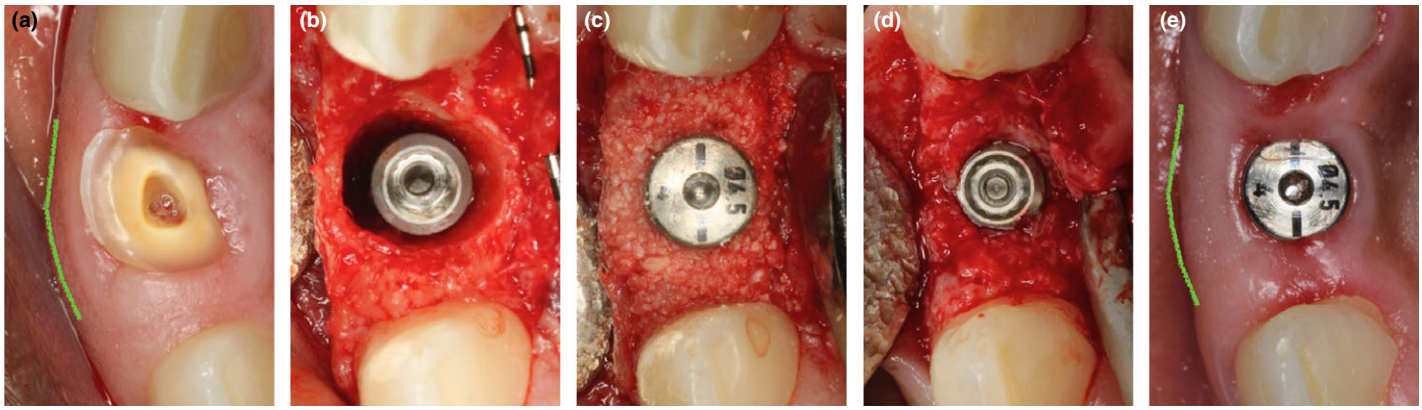

Fig. 2. Clinical case from the test group depicting (a) the tooth before the extraction; (b) the implant placed in the fresh extraction socket; (c) the site grafted with DBBM-C; (d) the site at the re-entry surgery (16 weeks); and (e) the final ridge profile.

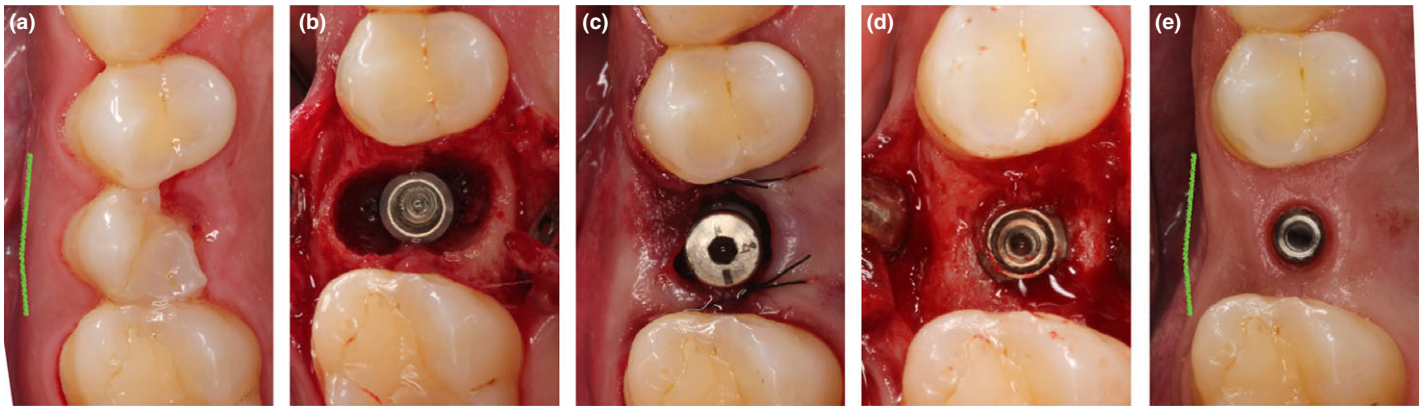

Fig. 3. Clinical case from the control group depicting (a) the tooth before the extraction; (b) the implant placed in the fresh extraction socket; (c) the site sutured without grafting; (d) the site at the re-entry surgery (16 weeks); and (e) the final ridge profile.

Demographics and other baseline characteristics were presented by means of descriptive statistics. Continuous variables were presented by means of the number of observations (*N*), mean and standard deviations (SD) and discrete variables by frequency and percentage. Inter-group comparisons were made by means of the Student's *t*-test. A two-sided *P*-value ≤0.05 was considered as being statistically significant.

Results

The study population consisted of 97 subjects that were screened for participating in this clinical trial from 2012 to 2013. Of these patients, three were excluded according to the criteria pre-established, two did not meet the inclusion criteria during the surgery and one refused to participate (see flowchart in Fig. 4). A total of 91 implant sites in 91 subjects were finally recruited, randomized and included in the clinical trial (45 in the test and 46 in the control group, respectively). At re-entry (16 weeks), two patients in the test group and three in the control group discontinued prior to the re-entry procedure at 4 months. Hence, a total of 86 implant sites in 86 subjects were included in the analysis (43 in the test group and 43 in the control group).

The demographic and key baseline characteristics of the study subjects are summarized in Table 1 and include the implant diameter, reason for extraction, smoking during healing and thickness of the buccal bone walls. All implant sites except two healed uneventfully. In one site, the patient reported pain after the implant surgery, but later improved and remained asymptomatic, and in the other site, the implant was lost during the healing period due to the failure in achieving osseointegration (Fig. 4). No complications were reported at the re-entry procedure.

The dimensional alterations that occurred during healing for all sites are reported in Table 2 and are presented individually according to the landmarks used for the measurement.

Buccolingual dimension of the socket (CC-BP)

The mean reduction in the buccolingual dimension between the buccal and lingual crests for the 16 weeks after the implant installation was 2.19 and 2.65 mm (test and control). This represented about 25% and 30% reduction, respectively, but these differences between the groups were not statistically significant (see Table 2).

Dimension OC-OC

The mean reduction in the alveolar crest width (buccolingual dimension 1 mm below the crest) for the 16 weeks after the implant installation was 1.3 and 1.7 mm (test and control). This represented about 11% and 16%, respectively, but these differences between the groups were not statistically significant (see Table 2).

Dimension S-OC (horizontal crest dimension)

The horizontal crest dimension underwent the marked changes during healing mainly at the buccal aspect of the alveolar crest where this reduction amounted to 1.1 (29%) in the test group and 1.6 mm (38%) in the control group. These differences between the two groups were statistically significant ($P = 0.03$) (see Table 2).

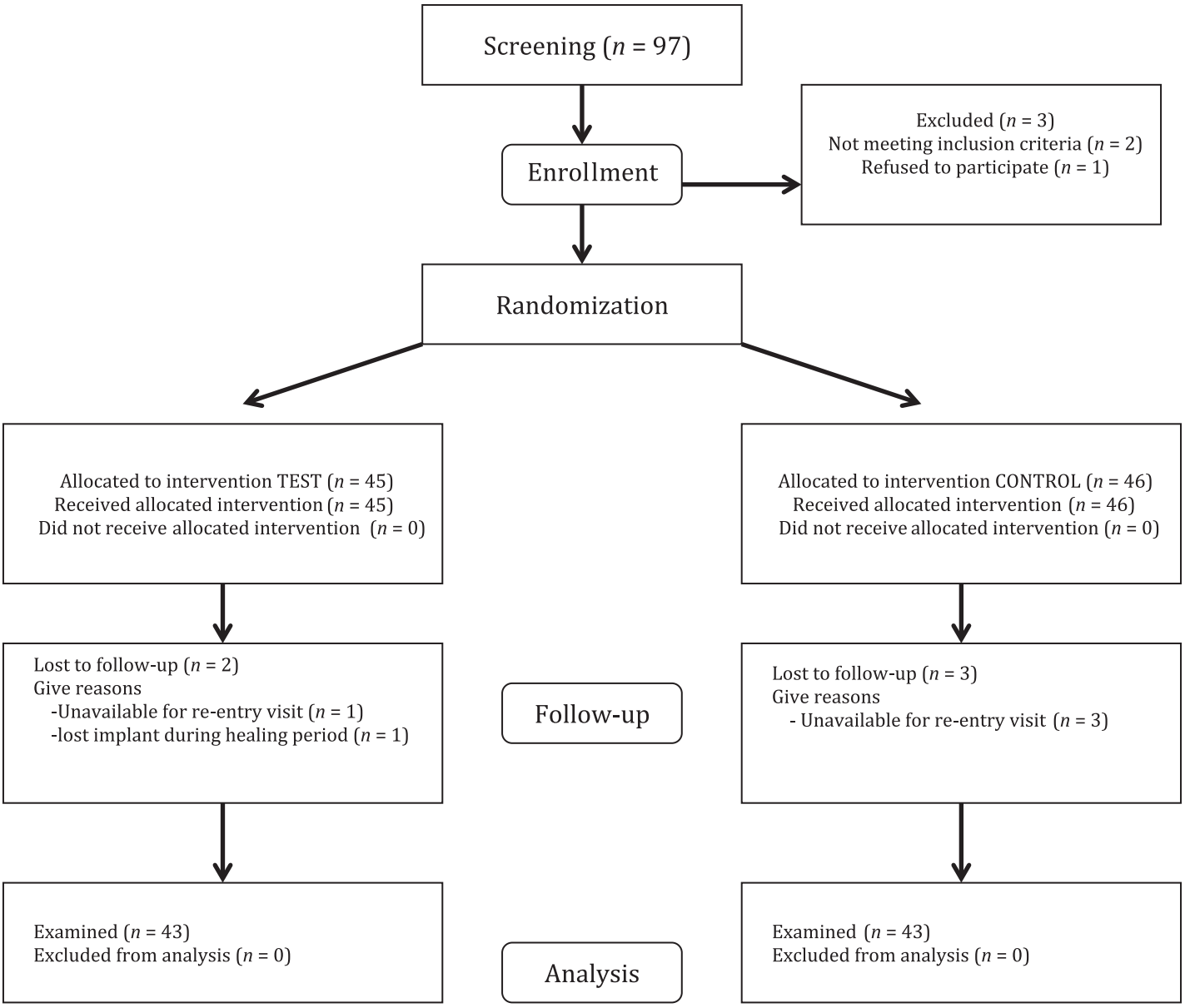

Fig. 4. Study flowchart depicting the randomization, treatment allocation and data set analyzed in the test and control groups.

Dimension of the Gap (Horizontal) SC-B

The mean reduction in the gap size during healing was at the buccal aspect 1.6 mm in the test group and 2.2 mm in the control group. These differences between the two groups were statistically significant ($P = 0.018$) and represented about 61% and 71% buccal gap fill, respectively (see Table 2).

Dimension R-D (vertical defect)

The vertical defect depth was markedly reduced on both the buccal and palatal aspects of the extraction socket. The reduction at the buccal aspect varied between 7.0 mm (92%) and 6.5 mm (88%) in the two groups. The difference between the groups was not statistically significant (see Table 2).

Dimension R-C (vertical crest reduction)

Similar vertical changes occurred at the buccal crest in the test and the control groups (0.3 mm). In the palatal aspect (R-P), the vertical crest reduction was twice as great in the control as the test group (1.1 mm vs. 0.6 mm), but this difference between the groups was not statistically significant ($P = 0.07$).

The sites at higher risk of losing bone (Tomasi et al. 2010) were analyzed independently, and data are presented in Tables 3 and 4.

Thin buccal sites (≤1 mm)

At the sites with a thin buccal bone wall, the reduction in the marginal buccolingual crest dimension was significantly less pronounced in the test than in the control sites (0.4 vs. 2.7 mm; $P = 0.03$) (Table 3). Similarly, the reductions in the horizontal crest dimension (OC_OC) were significantly greater in the test than in the control sites (0.7. vs. 2.3 mm; $P = 0.04$). The amount of horizontal gap fill, however, was greater in the control than in the test sites (2.3 vs. 0.9 mm; $P = 0.01$).

Anterior sites

At extraction sites in the anterior maxilla (from 1.3 to 2.3), there was a significantly smaller reduction in the horizontal crest dimension (S_OC_B) in the test than in the control sites (1.0. vs. 1.9 mm; $P = 0.01$), but with significantly less amount of horizontal gap fill (1.1 vs. 2.5 mm; $P = 0.00$) (Table 4).

Table 1. **Demographics and key baseline characteristics**

	Test (n = 43)	Control (N = 43)	Total (n = 86)
Sex (n and % of subjects)			
Male	22 (51)	19 (44)	41 (48)
Female	21 (49)	24 (56)	45 (52)
Implant diameter (n and % of subjects)			
3.5 mm	6 (14)	5 (12)	11 (13)
4.0 mm	37 (86)	38 (88)	75 (87)
Reason for extraction (n and % of subjects)			
Trauma	3 (7)	2 (5)	5 (6)
Caries/endodontic	15 (35)	14 (33)	29 (34)
Periodontitis	15 (35)	13 (29)	28 (32)
Other	10 (23)	14 (33)	24 (28)
Smoking during healing (n and % of subjects)			
Yes	5 (12)	9 (21)	14 (16)
No	38 (88)	34 (79)	72 (84)
Thickness buccal wall			
Mean (SD)	0.94 (0.67)	0.87 (0.97)	

Sites with a gap size of ≥ 2 mm

At sites with a large buccal gap, the reductions between the test and control sites were not statistically significant (Table 5).

Discussion

The present study demonstrated that the placement of DBBM-C in the void between the implant and the walls of the fresh extraction socket to some extent counteracted the diminution of the buccal (facial) hard tissue plate that normally occurs during healing. Thus, in the grafted sites, the distance between the implant and the buccal bone plate was decreased to about 1.1 mm, while in the non-grafted controls the corresponding contraction amounted to about 1.6 mm. Furthermore, it was observed that the reduction in the entire buccal–palatal ridge dimension tended to be less pronounced in the grafted (−11%) than in the non-grafted (−16%) sites. Grafting, however, did apparently not improve the gap closure. On the contrary, the "horizontal" gap was reduced more in the control than in the test sites (2.2 mm vs. 1.7 mm), while the vertical component of the gap in both categories of sites was reduced similarly, about 90%.

Ridge dimension

The findings from studies in humans (Pietrokovski & Massler 1967) (Schropp et al. 2003a) (Araujo et al. 2015) and experiments in dogs (Araujo et al. 2005) (Araujo et al. 2006b; Blanco et al. 2008) have demonstrated (i) that following tooth extraction, a marked contraction of the ridge dimensions occurs and that this change is more pronounced at buccal than at palatal/lingual aspects and (ii) that implant placement in the fresh extraction socket may not counteract such change (Botticelli et al. 2004; Araujo et al. 2006a). The amount of diminution of the buccal ridge dimension observed in the non-grafted sites of the current study (1.7 mm; 16%) is essentially in agreement with the findings from similar studies. Botticelli et al. (2004) reported that the buccal ridge dimension of the marginal portion of the edentulous ridge in "immediate implant" sites after 4 months was reduced to 1.9 mm (56%), while the decrease described by Sanz et al. (2010) was limited to 1.1 mm (36%). The more advanced diminution of the buccal aspect of the healed crest presented by Botticelli et al. (2004) is most likely related to the number and size of the implant sites included in the studies. Thus, while Botticelli et al. (2004) included only a small number of extraction sites (21 incisor, canine or premolar sites) from both the maxilla and the mandible, the current material as well as the sample by Sanz et al. (2010) (i) had a much large number of sites (4–5 times), which (ii) were confined to the maxilla and (iii) the majority of which had a premolar location.

Grafting

The placement of DBBM-C in the void between the implant and the socket walls resulted in an apparent clinical benefit. Thus, in the grafted sites, the amount of buccal hard tissue loss was significantly smaller than in the non-grafted controls. This outcome was recognized in the total sample as well as at sites representing the "aesthetic zone," that is, the anterior maxilla. This observation in some respects is in agreement with the findings reported by Araujo et al. (2015) from a clinical study using CBCT scans to evaluate the dimensional changes in the ridge following the tooth extraction. These authors reported that DBBM-C at most sites retarded/prevented the ridge diminution and hence maintained the width and cross-sectional area of the residual ridge. The results of the current study are also consistent with the results by Nevins et al. (2006), who grafted fresh extraction sockets with DBBM and observed that the

Table 2. **Changes between baseline and 4 months in horizontal and vertical measurements**

All Data	TEST				Control				
Difference (Baseline – 4 months)	*N*	Mean	SD	% Red	*N*	Mean	SD	% Red	Sig (two-tailed)
Marginal Width CC_BP	42	−2.19	2.10	24.6%	40	−2.65	1.81	30.2%	0.149
OC_OC	43	−1.26	1.75	11.0%	42	1.71	1.36	16.4%	0.187
Crest Dimension S_OC_B	43	−1.07	1.10	28.8%	43	1.59	1.05	37.8%	0.029
Gap (Horizontal) SC-B	43	−1.57	−1.27	61.2%	43	−2.23	1.22	71.9%	0.018
Gap (Vertical) R_D_B	43	−6.97	2.68	92.2%	43	−6.45	3.24	88.1%	0.432
Crest Position RC_B	39	0.26	1.21	42.8%	37	0.26	1.36	53.2%	0.980
Crest Position RC_P	39	0.58	1.15	88.2%	37	1.05	1.17	115.6%	0.07

In yellow, statistically significant differences between test and control ($P < 0.05$).
Blue and green are only test and control groups.
C_C_BP: Buccolingual dimension of the socket.
OC_OC_: From outer crest to outer crest 1 mm below the crest (B_L).
S_OC_B_: Buccolingual dimension from implant to buccal bone plate 1 mm below the crest.
RC_B__: From implant rim to bone crest buccal.
RC_P__: From implant rim to bone crest palatal.
SC_B_: Internal horizontal GAP size (buccal).
R_D_B_: Internal vertical GAP distance (palatal).

Table 3. **Changes between baseline and 4 months in horizontal and vertical measurements in sites with buccal thickness ≤1 mm**

Sites with buccal thickness ≤1 mm	TEST			Control			
Difference (Baseline – 4 months)	*N*	Mean	SD	*N*	Mean	SD	Sig (two-tailed)
Marginal Width CC_BP	15	−0.35	1.97	11	−2.65	1.88	0.010
OC_OC	15	−0.65	2.17	11	−2.32	1.69	0.040
Crest Dimension S_OC_B	15	−0.89	1.34	11	−1.61	0.85	0.130
Crest Position RC_B	15	0.55	1.30	11	0.09	2.01	0.480
Crest Position RC_P	15	0.83	1.14	11	1.68	1.06	0.07
Gap (Horizontal) SC-B	15	−0.91	1.16	11	−2.25	1.17	0.010
Gap (Vertical) R_D_B	15	−7.86	3.34	11	−6.68	2.99	0.360

In yellow, statistically significant differences between test and control ($P < 0.05$).
Blue and green are only test and control groups.
C_C_BP: Buccolingual dimension of the socket.
OC_OC_: From outer crest to outer crest 1 mm below the crest (B_L).
S_OC_B_: Buccolingual dimension from implant to buccal bone plate 1 mm below the crest.
RC_B__: From implant rim to bone crest buccal.
RC_P__: From implant rim to bone crest palatal.
SC_B_: Internal horizontal GAP size (buccal).
R_D_B_: Internal vertical GAP distance (palatal).

Table 4. **Changes between baseline and 4 months in horizontal and vertical measurements in anterior teeth sites (1.3–2.3)**

Anterior sites 1.3-2.3	TEST			Control			
Difference (Baseline – 4 months)	*N*	Mean	SD	*N*	Mean	SD	Sig (two-tailed)
Marginal Width CC_BP	14	−1.38	1.52	12	−2.45	2.01	0.160
OC_OC	14	−0.86	1.51	12	−1.91	1.71	0.120
Crest Dimension S_OC_B	14	−0.96	0.72	12	−1.88	0.88	0.010
Crest Position RC_B	14	0.68	1.15	12	0.89	1.43	0.720
Crest Position RC_P	14	0.82	0.56	12	1.00	1.12	0.67
Gap (Horizontal) SC-B	14	−1.07	0.51	12	−2.46	1.32	0.000
Gap (Vertical) R_D_B	14	−7.86	3.34	12	−6.68	2.99	0.360

In yellow, statistically significant differences between test and control ($p < 0.05$).
Blue and green are only test and control groups.
C_C_BP: Buccolingual dimension of the socket.
OC_OC_: From outer crest to outer crest 1 mm below the crest (B_L).
S_OC_B_: Buccolingual dimension from implant to buccal bone plate 1 mm below the crest.
RC_B__: From implant rim to bone crest buccal.
RC_P__: From implant rim to bone crest palatal.
SC_B_: Internal horizontal GAP size (buccal).
R_D_B_: Internal vertical GAP distance (palatal).

Table 5. **Changes between baseline and 4 months in horizontal and vertical measurements in sites with gap size ≥ 2**

GAP SIZE ≥ 2 mm	TEST			Control			
Difference (Baseline – 4 months)	*N*	Mean	SD	*N*	Mean	SD	Sig (two-tailed)
Marginal Width CC_BP	32	−2.18	2.22	40	−2.62	1.87	0.370
OC_OC	32	−1.37	1.92	40	−1.67	1.35	0.440
Crest Dimension S_OC_B	32	−1.34	0.95	40	−1.68	1.02	0.160
Crest Position RC_B	32	0.34	1.17	40	0.19	1.38	0.650
Crest Position RC_P	32	0.66	1.09	40	1.15	1.15	0.09
Gap (Horizontal) SC-B	32	−1.92	1.16	40	−2.34	1.18	0.130
Gap (Vertical) R_D_B	32	−7.56	2.29	40	−6.84	2.98	0.260

Blue and green are only test and control groups.
C_C_BP: Buccolingual dimension of the socket.
OC_OC_: From outer crest to outer crest 1 mm below the crest (B_L).
S_OC_B_: Buccolingual dimension from Implant to buccal bone plate 1 mm below the crest.
RC_B__: From implant rim to bone crest buccal.
RC_P__: From implant rim to bone crest palatal.
SC_B_: Internal horizontal GAP size (buccal).
R_D_B_: Internal vertical GAP distance (palatal).

buccal hard tissue wall of the grafted sites, in comparison with non-grafted controls, was slightly reduced.

The gap

The findings from studies in humans showed that the void that often occurs between an "immediate implant" and the hard tissue walls of the socket, after a rather short period of healing (4 months), will exhibit a high degree of bone fill (Botticelli et al. 2004) (Sanz et al. 2010). Furthermore, this "closure" of the gap seems to be independent of the original size of the defect (Tomasi et al. 2010). The results of the present study are in good agreement with the aforementioned data and showed that the horizontal component of the gap was reduced to about 60% and its vertical counterpart to about more than 90%. The findings of the current study, however, also demonstrated that the placement of a bone replacement graft (DBBM-C) in the void between the implant and the socket walls failed to further improve the hard tissue fill. On the contrary, in the marginal portion of most of the grafted sites, a narrow band of soft tissue was almost consistently observed to be present in direct proximity to the implant. This soft tissue "capsule" was removed prior to the *in situ* measurements at the re-entry procedure and apparently included mineralized particles, judged by the clinicians to be remnants of the graft material. This hypothesis is supported by the findings from an animal experiment (Araujo et al. 2008), in which the influence of DBBM-C on socket healing was evaluated in the biopsies sampled after 3 months. The authors reported that graft particles that were located outside the newly formed bone in the socket site consistently were surrounded by the connective tissue. Based on these findings, it seems reasonable to suggest that the graft material placed in the marginal gap in an "immediate" implant site should be protected with a barrier (membrane) that will allow the optimal stabilization of the coagulum in which the biomaterial resides and will prevent the ingrowth of connective tissue cells from the mucosa. This suggestion agrees with previous clinical studies reporting that the amount of the osseous fraction increased when DBBM-C was covered with a GTR membrane (Perelman-Karmon et al. 2012).

Among the foreseen advantages of using immediate implants is the achievement of improved aesthetic outcomes. Chen & Buser (2014) have recently reviewed systematically the outcome after this intervention based on 50 studies (6 RCTs, 6 cohort, 5 cross-sectional and 33 case series) and have reported acceptable aesthetic outcomes, although recession of the mid-facial mucosa may be a risk. Improved aesthetic outcomes have also been reported in studies when combining immediate implants with the use of DBBM

grafting of the gap and placement of an immediate provisional restoration (Cosyn et al. 2012), although there are currently no RCTs evaluating the specific role of either filling the gap or the immediate provisionalization. Chen et al. (2007) studied the added value of filling the gap with DBBM and/or placing a collagen barrier membrane in immediately placed single-tooth implants in the anterior maxilla. The sample consisted of 30 patients where in 10 the gap was filled with DBBM, in 10 the gap was filled with DBBM and covered with a bioabsorbable collagen membrane and in 10 the gap remained unfilled. When direct bone measurements were made 6 months after the implant placement, there were no significant differences in the amount of the gap filled, both horizontally and vertically, although the grafted sites were able to preserve significantly better the horizontal contour of the buccal crest (15% in DBBM sites vs. 48% reduction in control sites). These results are fully coherent with those obtained in this clinical trial, in which there was a significant benefit in filling the gap with DBBM-C to partially prevent the horizontal bone resorptive changes, although there was no significant difference in the vertical crest changes or the filling of the gap. Similarly, in this clinical trial, the changes in gap size were unrelated to gap size because in sockets with gaps >2 mm, grafted sites behaved similar to the control sites in terms of gap closure. In spite of the clinical recommendation by some authors to use the bone replacement grafts when gaps are greater than 2 mm (Wilson et al. 1998; Paolantonio et al. 2001), the results from this investigation do not justify this assertion.

In conclusion, the results from this clinical trial demonstrated that placing a bone replacement graft consisting of DBBM-C significantly reduced the horizontal bone resorptive changes occurring in the buccal bone after the immediate implantation in fresh extraction sockets.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Appendix S1 CONSORT 2010 checklist of information to include when reporting a randomised trial*