VOLUMETRIC ANALYSIS OF REMODELLING PATTERN AFTER RIDGE PRESERVATION COMPARING USE OF TWO TYPES OF XENOGRAFTS.

A MULTICENTRE RANDOMIZED CLINICAL TRIAL.
Authors’ affiliations:
Antonio Barone, Paolo Toti, Fortunato Alfonsi, Ugo Covani, Department of Surgical, Medical, Molecular and Critical Area Pathology, University of Pisa, Pisa, Italy. Antonio Barone, Paolo Toti, Fortunato Alfonsi, Ugo Covani, Tuscan Stomatologic Institute, Versilia General Hospital, Lido di Camaiore (LU), Italy. Alessandro Quaranta, Department of Odontology and Specialized Clinical Sciences (DISCO), Marche Polytechnic University, Torrette di Ascona, Italy. Alessandro Cucchi, Department of Surgery, University of Verona, Verona, Italy. Jose L. Calvo-Guirado, Bruno Negri, Department of Implantology, University of Murcia, Murcia, Spain. Roberto Di Felice, Private Practice, Ascoli Piceno, Italy.

Corresponding author:
Dr Antonio Barone, DDS, PhD, MSc Department of Surgical, Medical, Molecular and Critical Area Pathology, University of Pisa, Piazza Dizia 10, 55041 Camaiore, Italy.
Tel.: +39 0584 6059888
Fax: +39 0584 6058716
e-mail: barosurg@gmail.com

Date Accepted 22 January 2015

© 2015 John Wiley & Sons A/S. Published by John Wiley & Sons Ltd
VOLUMETRIC ANALYSIS OF REMODELLING PATTERN AFTER RIDGE PRESERVATION COMPARING USE OF TWO TYPES OF XENOGRAFTS.

A MULTICENTRE RANDOMIZED CLINICAL TRIAL.

ANTONIO BARONE
PAOLO TOTI
ALESSANDRO QUARANTA FORTUNATO ALFONSI
ALESSANDRO CUCCHI
JOSE L. CALVO-GUIRADO
BRUNO NEGRI
ROBERTO DI FELICE
UGO COVANI

© 2015 John Wiley & Sons A/S. Published by John Wiley & Sons Ltd.
ABSTRACT

OBJECTIVES

The aim of this randomized clinical trial was to analyse and compare the volumetric changes after ridge preservation procedures using two different biomaterials and to evaluate associations between outcome variables and pristine three-dimensional aspects of the ridges.

MATERIALS AND METHODS

Twenty-eight patients subjected to single-tooth alveolar ridge preservation were enrolled in the present multicentre, single-blind, prospective and randomized clinical trial. Fourteen sites were randomly allocated to each experimental group. The experimental sites were grafted with pre-hydrated collagenated cortico-cancellous porcine bone (coll group) or with a cortical porcine bone (cort group) and a collagen membrane; a secondary soft tissue healing was obtained for all experimental sites. Plaster casts were scanned (preoperative, at 1 and 3 months postoperative). Analysis of volumes and areas was performed, and all measured variables were statistically compared.

RESULTS

Intragroup analyses at 3 months revealed that when examining changes related to three-dimensional features of remodelling patterns (volume, surfaces, height and shape), the two biomaterials showed similar behaviours with a minor loss in volume and ridge surface. Intergroup analysis at 3-month survey revealed that volume resorption of the coll group (244 mm$^3$) was significantly lower ($P = 0.0140$) than that of the cort group (349 mm$^3$). The reduction for basal surface appeared significantly different between the two groups at 1-month survey only ($P = 0.0137$), while the final basal surface reduction was 4.9 and 12.2 mm$^2$ for coll and cort group, respectively. The superior surface reduction was 40.8 mm$^2$ for coll and 50.7 mm$^2$ for cort group, with no significant difference between the two groups.

CONCLUSION

At the 3rd month analysis, coll group showed a significantly lower reduction of ridge volume and a significantly smaller shrinkage of the basal area when compared to the cort group; moreover, the coll group experienced a smaller superior surface shrinkage when compared to the cort group, even though no significance was evaluated.

Key Words: Alveolar bone loss, alveoloplasty, bone remodelling, heterografts, tooth sockets.
Tooth extraction and the subsequent alveolar healing process cause vertical as well as horizontal dimensional changes of the alveolar ridge (Pietrokovski & Massler 1967; Johnson 1969; Pietrokovski 1975). Several studies showed that horizontal bone resorption was as great as 63%, while the vertical bone resorption was 22%.

When soft tissue was considered with the hard tissue in the volumetric analysis, there was an increase in the vertical as well as in the horizontal resorption of the alveolar ridge (Covani et al. 2011; Ten Heggeler et al. 2011). These physiological hard and soft tissue changes might affect the outcome of dental treatment that aimed to restore the lost dentition, either by limiting the residual bone volume for implant placement or by compromising the aesthetic results of the traditional prosthetic rehabilitation.

Several ridge preservation treatments were performed with the aim to minimize the resorption of ridge volume and maximizing bone formation within the alveolar bone walls (Darby et al. 2009; Tan et al. 2012). In various studies, several regenerative biomaterials, such as autogenous bone, allografts, xenografts and growth factors, were used to preserve the volumetric dimension of the alveolar ridge after tooth extraction (Barone et al. 2008; Kim et al. 2011; Mardas et al. 2011; Gholami et al. 2012; Festà et al. 2013). The evaluation of these studies suggested that no biomaterial could completely prevent the physiological bone remodelling which follows a tooth extraction, although some biomaterials might limit the bone dimensional changes (Barone et al. 2008; Kim et al. 2011; Mardas et al. 2011; Gholami et al. 2012; Festà et al. 2013).

Furthermore, several randomized clinical trials showed that the extraction sockets grafted with xenografts significantly reduced ridge changes when compared with sockets that had a spontaneous healing (Fiorellini et al. 2005; Nevins et al. 2006; Misch 2010). Moreover, ridge preservation treatment improved the aesthetic outcome of implant rehabilitation (Irinakis & Tabesh 2007), while at the same time reduced the need for further bone augmentation at the time of implant placement (Barone et al. 2013, 2014).

The effects of ridge preservation with the use of different biomaterials have been widely investigated, and several studies have been performed comparing dimensional changes of grafted vs. non-grafted sockets. The mean width reduction for spontaneously healed sockets ranged between 3.79 and 3.87 mm, whereas the mean mid-buccal height loss ranged between 1.24 and 1.67 mm (Van der Weijden et al. 2009; Tan et al. 2012).

Conversely, the amount of ridge changes after socket grafting showed a great variation, which could depend on the type of biomaterials used and on the thickness of residual buccal bone plate. This might be caused by the different grafting materials that can affect the bone healing pattern and the bone quality of healed sockets (Horvath et al. 2013). Indeed, cortical and cancellous biomaterials showed their osteoconductive properties, with dissimilar healing patterns. It has been observed that cancellous bone heals with an initial bone formation followed by osteoclastic bone resorption, whereas on the other hand, cortical bone resorption precedes bone formation (Goldberg & Stevenson 1987; Virolainen et al. 1998; Taira et al. 2004).

The analysis of tissue remodelling was performed using two and/or three-dimensional analysis. While conventional radiographic analysis enabled a linear investigation of tissue remodelling, there is also the occurrence of distortion phenomenon which could create a bias (Roeder et al. 2011; Vazquez et al. 2011; Pfeiffer et al. 2012). Three-dimensional techniques, such as conventional or cone-beam (CB), multislice computed tomography (CT), were successfully employed for an in vivo observation of the alveolar bone dimensions and of the bucco-lingual bone surrounding dental implants (Braut et al. 2012; Katsoulis et al. 2012; Shiratori et al. 2012). Alveolar ridge dimensional changes after tooth extraction could be dependent on some factors: flap-raising during extraction (Barone et al. 2014), buccal plate thickness (Braut et al. 2010; Tomasi et al. 2010) or the involvement of a single- or multiple-rooted tooth (Moya-Villaescusa & Sanchez-Perez 2010). The purpose of this randomized clinical trial was to evaluate and compare the volumetric changes following ridge preservation with cortical and collagenated cortico-cancellous porcine bone.

The secondary aim was to determine whether there were any three-dimensional characteristics of the extraction sockets that could affect the superficial and volumetric changes occurring at the augmented experimental sites. This study is a preliminary report focusing on a volumetric analysis carried out up to 3 months after fresh extraction socket grafting.
PATIENTS AND METHODS

STUDY DESIGN/SAMPLE
Inclusion criteria were as follows:
• patients 18 years or older and, therefore, able to sign an informed consent form;
• patients requiring a single-tooth extraction with the presence of adjacent healthy teeth (tooth without failed dental restorative materials, restored cervical abrasion and abfraction); and
• patients requiring implant-supported restoration in a premolar or molar site. Exclusion criteria consisted of the following:
• history of systemic diseases that would contraindicate oral surgical treatment;
• long-term non-steroidal anti-inflammatory drug therapy;
• lack of opposite occluding dentition in the area intended for extraction and subsequent implant placement;
• absence of adjacent teeth;
• oral bisphosphonate therapy;
• pregnancy and lactating period;
• unwillingness to return for the follow-up examinations;
• sites with an acute inflammation;
• and cigarette consumption >10 per day. Subjects smoking fewer than 10 cigarettes per day were requested to stop smoking before and after surgery (without compliance monitoring).

Patients were recruited from June 2011 to April 2013, using similar and standardized procedures in university centres/private practices: (i) University of Pisa, Unit of Implantology, Versilia Hospital, Italy; (ii) University of Murcia, Unit of Implantology, Spain; (iii) University of Ancona, Department of Dental and Clinical Sciences, Italy; (iv) Private practice, Dr. Di Felice, S. Benedetto del Tronto, Italy; and (v) University of Verona, Unit of Implantology, Italy. This study was conducted in full accordance with expressed ethical principles, including the Declaration of Helsinki (as revised, amended and clarified in its version of 2008).

Moreover, the protocol of this study was approved by the Versilia Hospital Research Ethical Committee (ethical approval form 214/2011). Sample size was approximately calculated using the results of our previous rough linear analysis where the ridge changes were evaluated comparing ridge preservation vs. extraction alone. The primary parameters were changes in horizontal width (-2.5±1.2 mm and -4.5±0.8 mm, respectively, for the treated and control groups) and changes in mid-buccal vertical height (-0.7±1.4 mm and -3.6±1.5 mm, respectively, for the treated and control groups) (Barone et al. 2008). A power analysis suggested a sample size of 12 patients (Statistics Toolbox, Mat- Lab 7.11; The MathWorks, Natick, MA, USA); however, the sample was increased to 30 patients due to a lower rate of resorption of the investigated biomaterials compared to natural healing site.

In this restricted, multicentre, randomized, single-blind, parallel-group study, each centre contributed to the group comparisons according to the predetermined 1 : 1 ratio, using the alveolar ridge preservation procedure for single-tooth extraction; the fresh extraction socket was considered the unit of randomization. Corrections for balancing the two experimental groups regarding age,
gender and tooth position (bicuspids and molars) were not applied. All patients received thorough explanations and completed a written informed consent form prior to being enrolled in the trial. Patients who were enrolled in the study were carefully evaluated by examining diagnostic casts and periapical/panoramic radiographs; moreover, data were collected for each patient regarding age, gender, smoking habits, indications for tooth extraction based on both clinical and radiographic examination, location of tooth and the presence/absence of adjacent teeth.

After the informed consent had been signed, all patients underwent at least one session of oral hygiene prior to the extraction procedures, in order to provide an oral environment more favourable to wound healing. Impressions of the experimental sites were obtained from all patients before tooth extraction at baseline (T0), 1 month (T1) and 3 months (T2) after ridge preservation procedure. Impressions of the jaw were obtained in a one-step process with two viscosity polyvinyl siloxane impression materials (Precision, Denmat, Lompoc CA, USA). Within 24 h, model casts of the dental impressions were obtained using plaster of Paris.

A scanner for cone-beam computerized tomography (KODAK 9000 3D Extraoral Imaging System; Carestream Health, Inc., Rochester, NY, USA) was employed for 3D file acquisition of the three model casts of each patient (marked as T0, T1 and T2). For every acquisition, the scanner was set following identical parameters: 68 kV, 6.3 mA, 97.2° scan time, Voxel 200 µm and FOV Ø 102.4 mm x height 36 mm. During data acquisition, the model casts were fixed to the horizontal adjustment guide of the scanner by a soft pale-blue wax stick. Before area and volume analyses, the CBCT scan data were inserted into a Matrix Laboratory (Image Processing Toolbox, Mat- Lab 7.1; The MathWorks), and for each patient, positions of axial images related to time T0, T1 and T2 were elaborated in space in such a way that the residual teeth were superimposable (Sbordone et al. 2012a,b); the reorientation of the three-dimensional data led to the occlusal planes being parallel to each other.

A volumetric and area evaluation (V and A, respectively) of the study models in the site subjected to alveolar ridge preservation was performed with Segment and Planning tool of SimPlant Pro 12.02 (Materialise Dental Italia, Roma, Italy) according to Sbordone (Sbordone et al. 2009). The examinations were performed, for each patient, in a standardized volume of interest (VOI): an area between the two residual teeth in cross-sectional vision and extending 8 mm apical to the most coronal portion of soft tissue level at T0 (generally mesial or distal papilla in the site extraction). This study analysed modifications of a large region instead of analysing changes at different levels below the crest.

Therefore, as previously done in several studies, a chosen VOI of 8 mm included the overall set from two to four measurements of the width (Henriksson & Jemt 2004; Vera et al. 2012).

Even if a careful investigation of the alveolar crest was not performed, the set of introduced variables described superficial and volumetric outcomes, to clearly compare the two materials employed.

All model casts were sent to centre #1 for acquisition and analysis procedures; a blindfolded collector (PT), involved in neither surgical treatment and patient’s survey, nor healthcare maintenance, performed both acquisitions and measurements for all the sets of cast models, without any information related to the materials employed in the alveolar ridge preservation procedures. Regarding the interexaminer accuracy control, six operators (AB, AQ, RDF, AC, BN and FA) performed all the surgical procedures, each in his proper referring centre.

Accuracy among surgeons was controlled by a calibration meeting arranged in Pisa (in February 2011), in which digital images and videos of the surgical procedures were displayed.
SURGICAL METHODS

Extraction sockets were allocated to just one of the two groups using a computerized random allocation process.

A computer-generated restricted randomization list was created. Only one of the investigators, not involved in the selection and treatment of the patients, was aware of the randomization sequence and could have access to the randomization list. The randomized codes were enclosed in sequentially numbered, identical, opaque and sealed envelopes. All patients received prophylactic antibiotic therapy of 2 g of amoxicillin (or clindamycin 600 mg if allergic to penicillins) 1 h before the extraction procedure and continued to take the antibiotic postoperatively, 1 g amoxicillin (or 300 mg clindamycin) twice a day for 5 days. All patients rinsed for 1 min with chlorhexidine mouthwash 0.2% prior to the surgery (and twice a day for the following 3 weeks) and were treated under local anaesthesia using lidocaine with adrenaline 1 : 50,000. All the patients were treated with the same surgical technique, consisting of tooth extraction without raising a full thickness flap. Great care was taken to reduce the trauma on the buccal bone plate and to keep the integrity of the bone morphology. If necessary, the teeth were sectioned to allow for the least traumatic extraction possible. The extraction sockets were thoroughly debrided to remove all soft tissues. The randomization envelope was opened, and the surgeon followed the indications to include the extraction socket in one of the two groups considered, according to the randomization list that sorted the type of graft material employed: either in coll group, in which extraction sockets were grafted and slightly condensed with prehydrated collagenated cortico-cancellous porcine bone, with graft particle size between 600 and 1000 lm (MP3 OsteoBiol, Tecnoss, Coazze, Italy); or in cort group, in which the extraction sockets were grafted with cortical porcine bone alone, with particle size between 600 and 1000 lm (APATOS, OsteoBiol, Tecnoss, Coazze, Italy). The soft tissues were only undermined, and no releasing incisions were performed; the fresh extraction sockets were grafted up to the buccal and palatal alveolar bony walls. A collagen membrane (Evolution; OsteoBiol, Tecnoss) was used to completely cover the socket, left intentionally exposed to the oral cavity and stabilized with the use of sutures. Patients were instructed to continue with prophylactic antibiotic therapy, and naproxen sodium 550-mg tablets were prescribed as an anti-inflammatory to be taken two times a day, as long as required. Removable prostheses, if present, were not allowed to be used until they had been adjusted and refitted, which was no sooner than 3 weeks after surgery.

VARIABLES

Variables were divided into anatomical variables, dependent variables (which included both those describing the sample and those which allowed classification of patients into a finite number of subgroups) and outcome variables, and they were classified in Table 1. The analysis performed in the present trial was the same as that used by Sbordone for the analysis of the volume changes of augmented alveolar ridge by means of autogenous grafts (Sbordone et al. 2009). Additionally, outcomes for superficial features were also introduced. The metric used indexes for extracted areas instead of direct linear calculations performed by the blind-folded collector to reduce the error of measurement.

ANATOMICAL VARIABLES

Clinicians acquired several anatomical measurements, divided into variables related to volume, area and shape of the extraction socket site. The outcome variables were derived by processing data of anatomical measurements. All anatomical variables, such as those related to the volume, to the superficial layer and to the computed indexes, were positive in value.
Table 1. List and equation for all the primary and derived variables related to the anatomical sites.

<table>
<thead>
<tr>
<th>Primary anatomical variables</th>
<th>Derived anatomical variables</th>
<th>Outcome variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume $V_{TX}$</td>
<td>Superior surface (eq. 1: for $X = 0, 1, 2$) $SS_{TX} = TS_{TX} - BS_{TX} - mLST_{TX} - dLST_{TX}$</td>
<td>Volume change (eq. 4: from 0 to $X$) $\Delta V_x = V_{TX} - V_{T0}$</td>
</tr>
<tr>
<td>Basal surface $BS_{TX}$</td>
<td>Height index (eq. 2: for $X = 0, 1, 2$) $iH_{TX} = \frac{V_{TX}}{BS_{TX}}$</td>
<td>Basal surface change (eq. 5: from 0 to $X$) $\Delta BS_x = BS_{TX} - BS_{T0}$</td>
</tr>
<tr>
<td>Total surface $TS_{TX}$</td>
<td>Shape index (eq. 3: for $X = 0, 1, 2$) $iS_{TX} = \frac{V_{TX}}{SS_{TX}}$</td>
<td>Superior surface change (eq. 6: from 0 to $X$) $\Delta SS_x = SS_{TX} - SS_{T0}$</td>
</tr>
<tr>
<td>Mesial lateral surface $mLST_{TX}$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Distal lateral surface $dLST_{TX}$</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

VOLUMETRIC AND SUPERFICIAL LAYER VARIABLES

Volume of the alveolar ridge was obtained through standardized VOI for each patient, $V_{TX}$, for every operative follow-up time, $T_0$, $T_1$, and $T_2$ (Fig. 1).

Basal surface of the alveolar ridge was the area of the most apical axial of the standardized VOI for each patient, $BS_{TX}$, obtained for every operative follow-up time, $T_0$, $T_1$, and $T_2$.

Total surface was the area of the alveolar ridge within the standardized VOI for each patient, $TS_{TX}$, obtained for every operative follow-up time, $T_0$, $T_1$, and $T_2$.

Lateral surfaces were the areas of the extreme either mesial or distal cross-sectional image obtained in the VOI, respectively, for mesial ($mLST_{TX}$) or distal ($dLST_{TX}$) residual tooth, obtained for every operative follow-up time, $T_0$, $T_1$, and $T_2$.

Superior surface ($SS_{TX}$) was evaluated by subtracting the values of basal and lateral surfaces from that of the total surface for every operative follow-up time, $T_0$, $T_1$, and $T_2$ (eq. 1).

$$SS_{TX} = TS_{TX} - BS_{TX} - mLST_{TX} - dLST_{TX} \quad (for X = 0, 1, 2).$$

INDICES

Height index ($iH_{TX}$) was the ratio between the volume of alveolar ridge ($V_{TX}$) and the basal surface area ($BS_{TX}$) for every operative follow-up time, $T_0$, $T_1$, and $T_2$ (eq. 2); this index indicates a mean height of the VOI for all of the alveolar sites subjected to an extractive procedure.

$$iH_{TX} = \frac{V_{TX}}{BS_{TX}} \quad (for X = 0, 1, 2).$$

Shape index ($iS_{TX}$) was the ratio between the volume of alveolar ridge ($V_{TX}$) and superior surface area ($SS_{TX}$) for every operative follow-up time, $T_0$, $T_1$, and $T_2$ (eq. 3); this index indicates, for the alveolar site subjected to an extractive procedure, the mean distance between each point of the external surface in the VOI and the respective centroid, and for ridges with a regular contour, twofold shape index was, in good approximation, an estimate for the mean width.

$$iS_{TX} = \frac{V_{TX}}{SS_{TX}} \quad (for X = 0, 1, 2).$$
PRIMARY PREDICTOR AND DEPENDENT VARIABLES

- cortical porcine bone (cort group) or prehydrated collagenated cortico-cancellous porcine bone (coll group);
- gender: male (M) or female (F);
- smoking habit: smoker (S) or non-smoker (N);
- tooth position: bicuspid (Bd) or molar (Mr); and
- number of roots: single-rooted tooth or multiple-rooted tooth.

Outcome variables The outcome variables for alveolar ridge modification could be positive or negative. A negative number would indicate that the variable described a negative remodelling: a resorption in case of dimensional contour change and a reduction or shrinkage in case of surface measurements, and these are depicted as follows: Alveolar ridge volume changes, or $\Delta V_x$, were evaluated for all the postoperative follow-up analysis by subtracting the respective baseline value ($V_{T0}$) from both of the postoperative measurements (eq. 4)

$$\Delta V_x = V_{TX} - V_{T0} \tag{4}$$

therefore, it could be obtained $\Delta V_1$ and $\Delta V_2$.

Basal surface changes, or $\Delta BS_x$, were evaluated for all the postoperative surveys by subtracting the respective baseline value ($BS_{T0}$) from both of the postoperative measurements (eq. 5)

$$\Delta BS_x = BS_{TX} - BS_{T0} \tag{5}$$

therefore, it could be obtained $\Delta BS_1$ and $\Delta BS_2$.

Superior surface changes, or $\Delta SS_x$, were evaluated for all the postoperative surveys by subtracting the respective baseline value ($SS_{T0}$) from both of the postoperative measurements (eq. 6)

$$\Delta SS_x = SS_{TX} - SS_{T0} \tag{6}$$

therefore, it could be obtained $\Delta SS_1$ and $\Delta SS_2$.

STATISTICAL ANALYSIS

All patient-related data were entered into a database (Database Toolbox, MatLab 7.1; The MathWorks), allowing calculations to be performed automatically. All statistical analyses were performed using a statistical tools package of MatLab 7 (Statistics Toolbox, MatLab 7.11; The MathWorks). The two groups, employing biphasic and monophasic bone substitutes, were independent (one extraction site per patient) (Herrmann et al. 2005), but normal distribution for each variable was not confirmed by the Shapiro–Wilks test. Variable pairwise comparisons were performed by the Wilcoxon signed-rank test for matched samples (between times, obtaining times related P-value, $p_{wt}$) and by the Wilcoxon rank-sum test for unmatched data (between materials, obtaining material related P-value, $p_{wm}$). Spearman’s correlation ($r_s$) was used to assess the strength of the bivariate association between each outcome variable ($\Delta V$, $\Delta BS$ and $\Delta SS$) and the overall set of variables related to volume and area ($V$, BS and SS) and indices ($iH$ and $iS$). Two-dimensional scatter plots were employed to illustrate statistically significant associations obtained by correlation tests between outcome variables and specific anatomical variable values. Measurements in the text and tables are described as mean and standard deviations, m±SD, whereas median and interquartile ranges, m (iqr: the difference between 75th and 25th percentiles), are reported in the figures and tables. All measurements were rounded to the nearest decimal. To decrease false positive results between groups, the level of statistical significance was set at 0.05 for independent variables such as $V$, $\Delta V$, BS and $\Delta BS$; the level of statistical significance was set at 0.01 for derived variables such as $iH$, $iS$, SS and $\Delta SS$. The sample size was determined using a power of 90% based on measures of central tendency and measures of dispersion for all the anatomical and outcome variables’ data.

Fig. 1. Isometric views of the volume of interest (VOI) of healed post-extractive site. Basal surface in red, lateral surfaces in yellow and superior surface in green.
Thirty-seven patients were considered eligible for the study, but seven patients could not be enrolled in the trial for the following reasons: four patients showed a full buccal bone plate deficiency after tooth extraction, two patients were affected by chronic sinusitis in the area selected for the study, and one patient suffered from an acute infection which was widespread in the soft tissues at the time of tooth extraction.

Therefore, a total of thirty patients, who were enrolled and treated in the present multicentre, prospective and randomized clinical trial, had a single-tooth extraction and ridge preservation with the use of porcine bone to allow delayed dental implant insertion. Two patients (one for each of the two treatment groups) dropped out due to incompleteness of the set of model casts (before surgical procedure, at the 1st and 3rd month); therefore, the acquired data decreased to 28 surgical sites.

All the demographic data of the overall 28 patients were reported in Table 2. Fourteen patients in coll group received pre-hydrated collagenated cortico-cancellous porcine bone with a resorbable collagen membrane, while the remaining fourteen patients in cort group received cortical porcine bone and a resorbable collagen membrane.

No post-surgical adverse events (such as presence of oedema, inflammation or infection) were registered within 1 week post-surgery, and all postextraction sites healed without complications. At the end of the survey, 28 dental implants (BTEVO®Biotec, Povolano of Dueville (Vi), Italy) were placed without any further bone augmentation procedures.

All the anatomical variables, such as indexes (iH and iS), volume- and area-related measurements (V, BS and SS) and outcome variables (ΔV, ΔBS and ΔSS), are reported in Table 3 and Fig. 2, which also show descriptive statistical analysis of the two experimental groups. No significant differences were observed between the two groups, when examining the dependent variables (gender, smoking habit and tooth position). All anatomical variables – evaluated in the intragroup analysis – showed significant reduction between baseline (T₀) and post-surgery evaluations (T₁ and T₃), except for the basal surface reduction in the coll group.

Moreover, the cort group showed a significant superior surface reduction (from 38.0±26.0 mm² to 50.7±31.6 mm² with pWt = 0.0127) between T₁ and T₃, meanwhile, no significant difference was observed for the coll group. At the first month, the basal surface reduction was 9.4±10.0 mm² and 1.9±6.1 mm² for cort and coll group, respectively. At the 3-month (T₃) evaluation, the comparison of cort and coll groups showed a significant difference for volume loss with a mean value of 349±112 mm³ and 244±121 mm³, respectively.
Table 2. Demographic data for the two materials employed with descriptive variables: size, gender, smoking habit, age and bicuspids/molars ratio, Bd/Mr and single-/multiple-rooted tooth ratio

<table>
<thead>
<tr>
<th>Patient#</th>
<th>Age (years)</th>
<th>Gender</th>
<th>Smoking habits (no of cigarettes)</th>
<th>Position of the sockets</th>
<th>Single- or multiple-root tooth</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>28.7</td>
<td>F</td>
<td>N</td>
<td>36</td>
<td>M</td>
</tr>
<tr>
<td>4</td>
<td>33.0</td>
<td>F</td>
<td>N</td>
<td>46</td>
<td>M</td>
</tr>
<tr>
<td>6</td>
<td>61.0</td>
<td>M</td>
<td>N</td>
<td>16</td>
<td>M</td>
</tr>
<tr>
<td>7</td>
<td>64.1</td>
<td>F</td>
<td>N</td>
<td>14</td>
<td>S</td>
</tr>
<tr>
<td>8</td>
<td>44.8</td>
<td>M</td>
<td>N</td>
<td>15</td>
<td>M</td>
</tr>
<tr>
<td>9</td>
<td>54.5</td>
<td>F</td>
<td>N</td>
<td>16</td>
<td>M</td>
</tr>
<tr>
<td>11</td>
<td>52.8</td>
<td>M</td>
<td>N</td>
<td>26</td>
<td>M</td>
</tr>
<tr>
<td>13</td>
<td>39.5</td>
<td>F</td>
<td>Y (S)</td>
<td>36</td>
<td>M</td>
</tr>
<tr>
<td>16</td>
<td>49.1</td>
<td>M</td>
<td>N</td>
<td>16</td>
<td>M</td>
</tr>
<tr>
<td>21</td>
<td>66.5</td>
<td>F</td>
<td>N</td>
<td>34</td>
<td>S</td>
</tr>
<tr>
<td>22</td>
<td>34.6</td>
<td>F</td>
<td>N</td>
<td>16</td>
<td>M</td>
</tr>
<tr>
<td>26</td>
<td>48.1</td>
<td>F</td>
<td>N</td>
<td>14</td>
<td>M</td>
</tr>
<tr>
<td>27</td>
<td>31.7</td>
<td>M</td>
<td>N</td>
<td>26</td>
<td>M</td>
</tr>
<tr>
<td>28</td>
<td>49.0</td>
<td>M</td>
<td>N</td>
<td>16</td>
<td>M</td>
</tr>
</tbody>
</table>

**Coll Group: collagenated corticocancellous porcine bone**

<table>
<thead>
<tr>
<th>Age mean ± SD</th>
<th>Genders ratio (M/F)</th>
<th>Smoking habits (Y/N)</th>
<th>Bd/Mr ratio</th>
<th>Single/ Multiple ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>47.0 ± 12.2</td>
<td>5/9</td>
<td>1/13</td>
<td>4/10</td>
<td>2/12</td>
</tr>
</tbody>
</table>

**Cort Group: cortical porcine bone**

<table>
<thead>
<tr>
<th>Age mean ± SD</th>
<th>Genders ratio (M/F)</th>
<th>Smoking habits (Y/N)</th>
<th>Bd/Mr ratio</th>
<th>Single/ Multiple ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>44.9 ± 13.5</td>
<td>4/10</td>
<td>3/11</td>
<td>4/10</td>
<td>3/11</td>
</tr>
</tbody>
</table>

Associations between each outcome variable and all the anatomical variables were analysed (Table 4); only outcome variables that proved to be correlated with the pristine three-dimensional features were selected for further analysis. In the coll group, the superior surface shrinkage appeared to be significantly correlated with the superior surface \( r_t = -0.5374 \) with \( P = 0.0475 \) at the 1 month and \( r_t = 0.5545 \) with \( P = 0.0396 \) at the 3 month. On the other hand, in the cort group, the superior surface shrinkage was significantly associated with the shape index \( (r_t \text{ coefficient} = 0.8110 \) and 0.7143 with \( P = 0.0007 \) and 0.0056, respectively, at \( T_1 \) and \( T_2 \)). The aforementioned significant associations evaluated for the coll and cort groups were shown with two-dimensional graphs (Fig. 3a,b), which represented the metrics of those baseline anatomical variables affecting superficial dimensional contour changes. This indicates that the higher the superficial surface was, the higher the dimensional contour reduction was for the pre-hydrated collagenated cortico-cancellous porcine bone group; on the other hand, the lower the shape index was, the higher the superior surface resorption was for the cortical porcine bone group.
<table>
<thead>
<tr>
<th>Coll Group</th>
<th>Values for all variables</th>
<th>p&lt;sub&gt;Wm&lt;/sub&gt; between times</th>
<th>p&lt;sub&gt;Wt&lt;/sub&gt; between times</th>
</tr>
</thead>
<tbody>
<tr>
<td>collagenated cortical-cancellous porcine bone</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>V&lt;sub&gt;tx&lt;/sub&gt; (mm&lt;sup&gt;3&lt;/sup&gt;)</td>
<td>1033 ± 325 901 (424)</td>
<td>741 ± 278 671 (399)</td>
<td>726 ± 335 618 (437)</td>
</tr>
<tr>
<td>BS&lt;sub&gt;tx&lt;/sub&gt; (mm&lt;sup&gt;3&lt;/sup&gt;)</td>
<td>158 ± 38 157 (46)</td>
<td>156 ± 37 147 (50)</td>
<td>152 ± 40 146 (35)</td>
</tr>
<tr>
<td>SS&lt;sub&gt;tx&lt;/sub&gt; (mm&lt;sup&gt;3&lt;/sup&gt;)</td>
<td>250 ± 66 226 (61)</td>
<td>207 ± 49 190 (55)</td>
<td>199 ± 55 175 (60)</td>
</tr>
<tr>
<td>iH&lt;sub&gt;tx&lt;/sub&gt; (mm)</td>
<td>6.5 ± 0.8 6.8 (1.2)</td>
<td>4.7 ± 1.0 4.8 (1.2)</td>
<td>4.7 ± 1.2 4.8 (1.7)</td>
</tr>
<tr>
<td>iS&lt;sub&gt;i&lt;/sub&gt; (mm)</td>
<td>4.1 ± 0.5 3.9 (0.9)</td>
<td>3.6 ± 0.8 3.5 (1.1)</td>
<td>3.5 ± 0.8 3.5 (1.3)</td>
</tr>
<tr>
<td>ΔV&lt;sub&gt;x&lt;/sub&gt; (mm&lt;sup&gt;3&lt;/sup&gt;)</td>
<td>-231 ± 129 -176 (145)</td>
<td>-244 ± 121 -207 (169)</td>
<td></td>
</tr>
<tr>
<td>BS&lt;sub&gt;x&lt;/sub&gt; (%)</td>
<td>-1.9 ± 6.1 -1.0 (4.0)</td>
<td>-4.9 ± 7.1 -4.0 (7.0)</td>
<td></td>
</tr>
<tr>
<td>ΔSS&lt;sub&gt;x&lt;/sub&gt; (%)</td>
<td>-33.5 ± 29.3 -28.0 (18.0)</td>
<td>-40.8 ± 28.6 -31.5 (29.0)</td>
<td></td>
</tr>
<tr>
<td>Cort Group</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>cortical porcine bone</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>V&lt;sub&gt;tx&lt;/sub&gt; (mm&lt;sup&gt;3&lt;/sup&gt;)</td>
<td>1164 ± 239 1138 (286)</td>
<td>798 ± 273 764 (144)</td>
<td>745 ± 242 764 (280)</td>
</tr>
<tr>
<td>BS&lt;sub&gt;tx&lt;/sub&gt; (mm&lt;sup&gt;3&lt;/sup&gt;)</td>
<td>183 ± 31 182 (52)</td>
<td>171 ± 33 163 (52)</td>
<td>168 ± 34 165 (54)</td>
</tr>
<tr>
<td>SS&lt;sub&gt;tx&lt;/sub&gt; (mm&lt;sup&gt;3&lt;/sup&gt;)</td>
<td>260 ± 40 250 (69)</td>
<td>215 ± 42 210 (55)</td>
<td>199 ± 35 198 (48)</td>
</tr>
<tr>
<td>iH&lt;sub&gt;tx&lt;/sub&gt; (mm)</td>
<td>6.4 ± 1.0 6.5 (1.3)</td>
<td>4.6 ± 1.0 4.6 (1.8)</td>
<td>4.4 ± 0.9 4.3 (1.4)</td>
</tr>
<tr>
<td>iS&lt;sub&gt;i&lt;/sub&gt; (mm)</td>
<td>4.5 ± 0.9 4.2 (1.0)</td>
<td>3.7 ± 0.9 3.5 (1.0)</td>
<td>3.7 ± 0.9 3.5 (0.9)</td>
</tr>
<tr>
<td>ΔV&lt;sub&gt;x&lt;/sub&gt; (%)</td>
<td>-302 ± 100 -320 (166)</td>
<td>-349 ± 112 -345 (135)</td>
<td></td>
</tr>
<tr>
<td>BS&lt;sub&gt;x&lt;/sub&gt; (%)</td>
<td>-9.4 ± 10.0 -5.5 (10.0)</td>
<td>-12.2 ± 13.5 -10.0 (21.0)</td>
<td></td>
</tr>
<tr>
<td>ΔSS&lt;sub&gt;x&lt;/sub&gt; (%)</td>
<td>-38.0 ± 26.0 -31.5 (19.0)</td>
<td>-50.7 ± 31.6 -45.5 (24.0)</td>
<td></td>
</tr>
</tbody>
</table>

Table 3. Anatomical (for time X, volume of alveolar ridge or V<sub>tx</sub>, basal surface or BSTX, superior surface or SSTX, height index or iHTX and shape index or iSTX) and outcome variables (alveolar ridge volume change or ΔV<sub>x</sub>, the basal surface changes or ΔBSTX and the superior surface changes, or ΔSSTX). All measurements were given by mean and standard deviations, ±SD, and by median and interquartile ranges, ~m (iqr). Wilcoxon rank-sum test significance (pWm) comparison between times were applied. Statistically significant values are in bold. Estimated effect size given for groups' comparisons were determined using a power of 90% based on all anatomical and outcome variables' data.
DISCUSSION

The aim of this multicentre and randomized clinical trial was to evaluate and compare the predictability of volume remodelling of extraction sockets when grafted with two porcine xenografts – collagenated cortico-cancellous or cortical.

Even though the CBCT radiation risk was reduced, the radiation dose for follow-up measurement is, in any case, both too high and not justified for a simple short-term multipoint survey (Covani et al. 2011); furthermore, some authors have underlined the accuracy and reliability of CBCT for the digital analysis of cast models (Fortin et al. 2002; Kobayashi et al. 2004; Kasaven et al. 2013). In the present study, to avoid X-ray radiation exposure, preoperative and postoperative CBCT scans of the cast models were acquired from the experimental sites, digitally superimposed and analysed, allowing a qualitative and quantitative evaluation of changes of the volume and contour at different time points.

The present study seemed to demonstrate that ridge preservation procedure with the use of two different biomaterials showed similar remodelling patterns: significant changes in volume between baseline and the 3-month evaluation were measured for both ridge preservation experimental groups. The coll group (collagenated cortico-cancellous porcine bone) had a volume decrease (ΔV) of 244 mm\(^3\), whereas the cort group (cortical porcine bone) had a 349 mm\(^3\) decrease with a statistically significant difference between the two groups. Moreover, basal area showed a significant reduction, even though the difference between the two groups after 3 months did not reach statistical significance; this was hypothetically due to the limited sample size of this study. Indeed, ridge preservation resulted in a loss of volume and surfaces in all experimental clinical cases.

Therefore, the use of a xeno graft seemed not to prevent the negative morphological remodelling after tooth extraction (Fig. 4); nevertheless, the collagenated cortico-cancellous porcine bone seemed to be more effective than the cortical porcine bone, because volume reduction was significantly higher in the cort than in the coll group (\(P = 0.0140\)).

The mean volume changes observed in the present study (reduction of 0.3 cc) appeared to be greater than those observed by Thalmair et al. (2013) (reduction of 0.033 cc). It should be considered that the Thalmair study measured changes occurring at the buccal side; conversely, our study measured the whole volume and contour area.

Moreover, in the Thalmair et al. study, a primary wound closure was performed using a gingival graft; this would account – according to the author’s hypothesis – for more favourable outcomes than those observed with secondary wound closure.

![Fig. 2. Box plots for all variables described for different times (time 0, preoperative; time 1 and 2, respectively, 1 and 3 months after surgery) and materials employed (collagenated cortico-cancellous porcine bone, coll group, vs. cortical porcine bone, cort group; (a) volumes V, basal surfaces, BS and superior surfaces, SS; (b) height and shape indexes (iH and iS) and outcome variables ΔV, ΔBS and ΔSS, respectively, the changes for alveolar ridge volume, basal surface and the superior surface. In box-and-whiskers plot the box line represents the lower, median and upper quartile values, the whisker lines include the rest of the data. Outliers were data with values beyond the ends of the whiskers.]

© 2015 John Wiley & Sons A/S. Published by John Wiley & Sons Ltd
Fig. 3. Two-dimensional scatter plots (a, b) showing: (a) for the coll group, the superior surface changes ($\Delta SS$) as a function of the baseline superior surface ($SST_0$) for both the postoperative surveys, $\Delta SS_1$ (red circle) and $\Delta SS_2$ (black circle); (b) for the cort group the superior surface changes ($\Delta SS$) as a function of the baseline index of shape ($iST_0$) for both the postoperative surveys, $\Delta SS_1$ (red circle) and $\Delta SS_2$ (black circle).

Table 4. Spearman’s correlation coefficients $r_s$ (with significance $P$, two-tailed) between outcome variables and overall anatomical variables for alveolar ridge conservation using collagenated cortico-cancellous porcine bone (coll) or cortical porcine bone (cort). Statistical significance (in bold) set at 0.05 level (two-tailed)

<table>
<thead>
<tr>
<th>Graft material</th>
<th>Coll group collagenated cortico-cancellous porcine bone</th>
<th>Cort group cortical porcine bone</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Outcome variables</strong></td>
<td><strong>$V_{T0}$</strong></td>
<td><strong>$BS_{T0}$</strong></td>
</tr>
<tr>
<td>$\Delta V_1$</td>
<td>$r_s$</td>
<td>-0.4374</td>
</tr>
<tr>
<td></td>
<td>$p$</td>
<td>0.1198</td>
</tr>
<tr>
<td>$\Delta V_2$</td>
<td>$r_s$</td>
<td>-0.2703</td>
</tr>
<tr>
<td></td>
<td>$p$</td>
<td>0.3491</td>
</tr>
<tr>
<td>$\Delta BS_1$</td>
<td>$r_s$</td>
<td>-0.1613</td>
</tr>
<tr>
<td></td>
<td>$p$</td>
<td>0.5816</td>
</tr>
<tr>
<td>$\Delta BS_2$</td>
<td>$r_s$</td>
<td>0.1189</td>
</tr>
<tr>
<td></td>
<td>$p$</td>
<td>0.6855</td>
</tr>
<tr>
<td>$\Delta SS_1$</td>
<td>$r_s$</td>
<td>-0.2863</td>
</tr>
<tr>
<td></td>
<td>$p$</td>
<td>0.3210</td>
</tr>
<tr>
<td>$\Delta SS_2$</td>
<td>$r_s$</td>
<td>-0.1628</td>
</tr>
<tr>
<td></td>
<td>$p$</td>
<td>0.5781</td>
</tr>
</tbody>
</table>
Fig. 4. Pictures of clinical case and CBCT scans of the model cast in cross-sectional and panoramic view: cortico-cancellous porcine bone (coll group): (a) view of the extraction socket, (b) exposed collagen membrane, (c) healed site and (d) implant positioned after socket preservation; CBCT scans at (e) baseline \( T_0 \), (f) 1 month post-surgery \( T_1 \), and (g) 3 months post-surgery \( T_2 \); cortical porcine bone (cort group): (h) view of the extraction socket, (i) exposed collagen membrane, (j) healed site and (k) implant positioned after socket preservation; and CBCT scans at (l) baseline \( T_0 \), (m) 1 month post-surgery \( T_1 \), and (n) 3 months post-surgery \( T_2 \).
Some other authors evaluated posterior alveolar sockets grafted with a xenograft (deproteinized bovine bone) and covered by an absorbable collagen membrane. After 3 months, the volume resorption was 193.79 ±21.47 mm\(^3\) in the augmented group and 252.19±37.21 mm\(^3\) in sites without grafting (Pang et al. 2014). It should be taken into consideration that the above reported study was performed on the basis of radiographic analysis, which evaluated the hard tissue changes; on the contrary, this study evaluated the soft and hard tissue changes on the basis of a cast evaluation at different time points. The ridge contour changes in the present study showed significant height and shape changes regardless of the two porcine xenografts.

The pattern of volume resorption for the experimental sites was confirmed by a height reduction of the alveolar crest. The height index (ih), which represents the mean height of the standardized volume, showed a reduction of 1.8 and 2.0 mm after 3 months for coll and cort groups, respectively. However, the present study took into consideration the whole volumetric analysis, which included hard and soft tissue changes together.

Moreover, the present values for height resorption (height index) reflected the general behaviour of all the parts of the alveolar ridge, as cumulative positive and negative remodeling for the overall set of voxels included in the VOI. Data from the present study seemed to be confirmed by other studies where sockets were grafted with bovine bone mineral; the clinical measurements showed a change of the alveolar ridge height ranging between +0.7 mm and -2.6 mm (Vance et al. 2004; Nevins et al. 2006; Mardas et al. 2011; Cardaropoli et al. 2014; Kotsakis et al. 2014). The shape index showed a reduction of 0.6 and 0.8 mm for coll and cort groups, respectively. All these changes could confirm a contour change for grafted sockets.

Moreover, the two biomaterials showed different healing patterns with a basal surface reduction of 9.4 and 1.9 mm\(^2\) for the cort and coll groups, respectively. These findings were in agreement with those reported by Thalmair et al.; after different ridge preservation procedures, the authors observed negative contour changes, which ranged between 0.79 and 1.45 mm (Thalmair et al. 2013).

The horizontal width reduction found in several studies ranged between 1.8 and 2.5 mm in grafted sockets (Barone et al. 2008; Festa et al. 2013). These data were confirmed by the present study where the grafted sockets showed a width reduction ranging between 1.2 and 1.6 mm (twofold shape index). All the augmented sockets had a volume reduction at 1- and 3-month evaluations, the absence of correlations between volume loss and the pristine anatomical features suggested that a volumetric healing pattern could be hypothesized but not predicted for the observed groups. One of the main limitations of this study is the restricted sample size.

A greater number of patients were scheduled to be enrolled, but some centres failed to take impressions of the experimental sites at the scheduled time points of the study. Therefore, a few clinical cases initially included in the study were considered as dropouts for the volumetric analysis, because it was not possible to complete the volumetric and contour analysis at all time intervals.

Another limitation of the study was the accuracy of the analysis method, which is highly influenced by the accuracy of the impression technique and cast production. Another possible source of bias could derive from standardization and projection of the geometry of the three dicom data matrices belonging to each patient. Moreover, the present findings in terms of loss and correlations could not be generalized for different surgical techniques: every modification of the procedure led to a possible alteration of the recorded behaviour.

Nevertheless, the present data, even if the number of treated sites should have been greater, may help predict the healing pattern after tooth extraction and socket filling. No data related to soft tissue biotype was acquired, so it was not possible to assume that different biotypes may result in different dimensional changes.

An innovation of the present trial was the analysis of three-dimensional data, comprising several features related to the alveolar ridge that could lead to the detection of even minimal differences between the healing patterns of the two different surgical procedures. In the present study, the cone-beam computed tomography (CBCT) is an alternative to the 3D optical scanners, due to the generation of high-resolution isotropic volumetric data that enabled researchers to analyze dicom files with conventional and more accessible dentascan softwares (Sbordone et al. 2012a,b; Dellavia et al. 2014).

The present description of the 3D remodeling phenomena after the filling with xenografts of the post-extraction alveolar sites does not reflect or predict further remodeling after dental implant placement; moreover, an increase of the sample size may increase the significance of the results. The present study has an explorative character; therefore, the findings from this study should be considered with caution and would need additional investigations before being incorporated into daily clinical practice.

In conclusion, the present findings showed that the ridge preservation procedures with porcine bone in two different forms (collagenated cortico-cancellous or cortical) were not able to maintain stable the pristine alveolar crest with a volume reduction, regardless of the grafting material, ranging between 244 and 349 mm\(^3\).

Therefore, this study supported the hypothesis that a pre-hydrated collagenated cortico-cancellous porcine bone showed better results, with significant smaller volume reduction and basal area shrinkage, when compared to the cortical porcine bone.
REFERENCES


Misch, C.M. (2010) The use of recombinant human bone morphogenetic protein-2 for the repair of extraction socket defects: a te-


All information and content (texts, graphics and images) are reported to the best of our knowledge, public knowledge, if unintentionally has been published or copyrighted material in violation of the law, please inform us and we will immediately remove it.