

Safety and performance of a novel collagenated xenogeneic bone block for lateral alveolar crest augmentation for staged implant placement

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Abstract

Objectives: To evaluate the performance and safety of placing a collagenated xenogeneic bone block (CXBB) graft for the lateral bone augmentation of the alveolar crest prior to implant placement.

Material & Methods: In patients with single or multiple tooth gaps and a severe horizontal collapse of the alveolar ridge, a ridge augmentation procedure was performed using CXBB fixated with osteosynthesis screws to the atrophic bone crest and complemented with deproteinized bovine bone mineral particles (DBBM) and a native bi-layer collagen membrane (NBCM). Patients were examined with CBCT prior to and 24 weeks after the augmentation. Twenty-six weeks postoperatively, a re-entry procedure was performed to evaluate the bone width and availability for adequate implant placement.

Results: Fifteen patients received 28 CXBB, and in 13 patients, a re-entry procedure was performed. Eleven patients (84.6%) gained enough bone volume for implant insertion without additional contouring or secondary bone augmentation. The mean crest width at baseline was 2.83 mm (*SD* 0.57), and the mean crest width at re-entry was 6.90 mm (*SD* 1.22), with a mean ridge width increase of 4.12 mm (*SD* 1.32). Soft tissue dehiscence occurred during the follow-up in 5 of 14 patients (35.7%) at various time points. In addition, there was a high incidence of early implant loss (30.8% [patient-based]).

Conclusions: CXBB achieved significant horizontal crestal width gains allowing a secondary implant placement in the majority of the patients. However, the occurrence of soft tissue dehiscence may notably affect the outcome of the subsequent implant therapy.

KEYWORDS

alveolar ridge augmentation, clinical trial, dental implants, heterografts, safety and performance

1 | INTRODUCTION

Adequate placement of dental implants requires not only a minimum amount of alveolar crest bone volume to provide anchorage

and primary stability, but also an adequate three-dimensional position guided by the prosthetic restoration. In light of the extensive hard and soft tissue changes, occurring after tooth extraction and the likely underlying pathology that caused tooth loss, bone augmentation

procedures either before or concomitant with implant placement are commonly needed (Sanz & Vignoletti, 2015). In a recent systematic review, significant bone gains were reported with the use of autogenous bone blocks staged to implant placement in non-contained and/or severe bone deficiencies (Sanz-Sanchez, Ortiz-Vigon, Sanz-Martin, Figuero & Sanz, 2015). This outcome is based on the excellent biological properties of autogenous bone (osteoconductivity, osteoinductivity, and osteogenicity) and the space maintaining effect of the blocks fixated to the defects (Jensen & Terheyden, 2009). In spite of these advantages, however, this regenerative approach has clear shortcomings due to the limited amount of intraoral bone available for harvesting (Cremonini, Dumas, Pannuti, Lima & Cavalcanti, 2010; Nkenke et al., 2004), the high degree of bio-absorbability of autogenous bone (Cordaro, Amade & Cordaro, 2002), and the morbidity associated with harvesting the graft (von Arx, Hafliger & Chappuis, 2005; Cordaro, Torsello, Miuccio, et al., 2011; Cordaro, Torsello, Morcavallo, et al., 2011; Nkenke et al., 2002). To overcome these limitations and complications, some authors have attempted extensive guided bone regeneration approaches using particulate bone (combining xenogeneic and autogenous bone) and barrier membranes (bioabsorbable or titanium reinforced non-bioabsorbable) (Simion, Fontana, Rasperini & Maiorana, 2007; Urban, Nagursky & Lozada, 2011). The use of particulate deproteinized bovine bone mineral (DBBM) has shown a high degree of biocompatibility and osteoconductivity with a slow or minimal bio-absorbability (Hammerle, Jung, Yaman & Lang, 2008), but it provides limited structural stability when used in severe crestal bone deficiencies (Mir-Mari, Wui, Jung, Hammerle & Benic, 2016). In spite of the good outcomes reported in a limited number of studies (Meloni et al., 2016; Urban, Nagursky, Lozada & Nagy, 2013), these interventions are very technique sensitive and require a high degree of surgical expertise. Another alternative for the treatment of severe bone defects has been the use of bone blocks of xenogeneic and allogenic origin, which have been evaluated in both animal and human studies (Acocella, Bertolai, Ellis, Nissan & Sacco, 2012; Dias et al., 2016; Moest et al., 2015; Spin-Neto et al., 2013). A collagenated xenogeneic bone block (CXBB) has recently been studied in dogs (Schwarz et al., 2010) (Benic et al., 2016) demonstrating bone ingrowth into the bone graft and the attainment of significant volume gains. In humans, a prospective single-arm study on single tooth defects with adjacent teeth has also reported promising results with a mean ridge width gain of 3.88 mm (*SD* 1.75) and a histologic homogeneous osseous organization (Schwarz, Mihatovic, Ghanaati & Becker, 2016). There is, however, no data on the outcomes of using CXBB in advanced horizontal defects. Therefore, the purpose of this single-arm study was to evaluate the safety and performance of CXBB for lateral bone augmentation in patients with severe crest atrophy prior to implant installation.

2 | MATERIALS AND METHODS

2.1 | Study design

This study was designed as a prospective, single-arm clinical study to assess the safety and performance of CXBB replacement

graft used for primary bone augmentation of advanced horizontal bone defects prior to implant placement and followed up to implant loading (up to 56 weeks after lateral bone augmentation).

This study was conducted at the Periodontal Postgraduate Clinic of the University Complutense of Madrid (Spain) by the ETEP (Etiology and Therapy of Periodontal Diseases) Research Group. Prior to its commencement, the protocol as well as the patient information sheet and the informed consent were approved (# 13/404-P) by the ethics committee of the Clinical San Carlos Hospital, Madrid. The investigators were trained in the surgical procedure and in the registration of outcome variables in accordance with ISO norm 14155:2011. The study was conducted from December 2013 to September 2016.

2.2 | Patients' sample

Adults (≥ 18 years of age) were screened on the bases of having single or multiple teeth absences and a severe horizontal collapse of the alveolar ridge in need of one or more implants for implant supported fixed prosthetic rehabilitation.

Patients were selected on the bases of fulfillment of the following inclusion and exclusion criteria:

- Written informed consent
- Insufficient bone ridge width (< 4 mm) for implant placement measured on a cone-beam computed tomography (CBCT)
- Sufficient bone height for implant placement
- Healthy oral mucosa with at least ≥ 3 mm of attached keratinized mucosa

Patients were excluded if they had any of these conditions:

- General contraindications for dental and/or surgical treatments
- Inflammatory and autoimmune disease of the oral cavity
- Allergy to collagen
- Diabetes
- History of myeloma, respiratory tract cancer, breast cancer, prostate cancer, or kidney cancer requiring chemotherapy or radiotherapy within the past 5 years.

Concurrent or previous radiotherapy of head area

- Concurrent or previous immunosuppressant, bisphosphonate, or high-dose corticosteroid therapy
- Smokers
- Pregnant or lactating women.
- Women of child bearing age, who are not using a highly effective method of birth control
- Participation in an investigational device, drug, or biologics study within the last 24 weeks prior to the study start.

Before final inclusion, patients received meticulous verbal and written descriptions of the interventions and conditions and were

TABLE 1 Study chart and follow-up

Procedure	Enrollment	Surgery	Follow-up			Re-entry	Follow-up V6		Second stage	Implant loading
Visit	1	2	3	4	5	6	7	8	9	10
Days	-60 to -1	0	14 ± 4				14 ± 4		14 ± 4 V8	
Weeks				4 ± 1	13 ± 2	26 ± 4		13 ± 4		18 ± 4 V6
Adverse events	Continuously									

V6, Time from visit 6; V9, Time from visit 9.

requested to sign an informed consent form (directive 95/46/EC on data protection, in accordance with current legal provisions by the European Community).

2.3 | Description of investigational device

CXBB (Bio-Graft® Geistlich Pharma) is a bone substitute material in a natural block form. The dimensions of the Bio-Graft block are 10 mm in height, 10 mm in length, and 5 mm in width. It consists of a natural cancellous bone structure of hydroxyapatite and endogenous collagen type I and III. It has an equine origin, and it is considered a class III medical device according to the Medical Device Directive 93/42 EECs' definition (rule 8 implantable, bioabsorbable device).

2.4 | Outcomes variables

The study design and follow-up visits are summarized in Table 1. The primary outcome evaluated the performance of the CXBB by assessing if the final crestal ridge width after 6 months of healing is sufficient for implant placement. The ultimate goal is to have a dental implant placed in an adequate prosthetically driven position.

The following secondary endpoints were also evaluated:

Safety

- Adverse events (major complications, infections, and pain)
- Soft tissue healing: presence of dehiscence (yes/no). If present, soft tissue dehiscence was classified in type 0, 1, 2, 3, or 4 (0: No dehiscence; 1: from augmentation to 4 weeks healing; 2: from 4 weeks to 26 weeks; 3: from 26 weeks to implant abutment connection; 4: from implant abutment connection to implant loading)
- Implant loss (yes/no) and possibility of implant replacement (yes/no)

Performance

- Clinical ridge width gain (mm)
- Need of secondary augmentation (re-grafting)
- Need of contouring at time of implant placement (improvement of the buccal contour)
- Radiological linear ridge width gain in mm on CBCT
- Radiological volumetric ridge gain in mm³ on CBCT superposition

2.5 | Surgical procedure and Clinical measurements

A trained periodontal specialist (AOV) performed all the surgical procedures. One hour prior to the surgery, each patient received 750 mg of amoxicillin (or clindamycin 600 mg) and 600 mg of ibuprofen. Before anesthesia, the patient rinsed with chlorhexidine (0.12%) for 60 s. Under local anesthesia, a midcrestal incision was performed and a full-thickness flap was elevated extending at least 10 mm mesial and distal to the augmentation area and periosteal releasing incisions were performed to adequately expose the bone defect and to allow for tension free primary closure over the regenerated area. The horizontal width of the alveolar crest was measured 2 mm below the crest with a bone caliper (Ivanson Measuring Caliper® 0–10 mm, Stoma, Emmingen-Liptingen, Germany) to the nearest 0.1 mm. To enable the localization of this measurement point at re-entry, the horizontal mesio-distal distance from the measuring point to the root surface of the neighboring tooth was obtained and documented. Perforations of the cortical bone were performed to improve blood supply and allow for a good contact between the block graft and the underlying bone. Depending on the number of implants needed, 1–4 CXBB were used in a one-to-one ratio. The bone blocks were shaped, pre-drilled, and pre-hydrated for 5 min with sterile physiological saline before placement and fixed with one, titanium osteosynthesis, screw (1.5 mm × 9–12 mm; Medicon, Tuttlingen, Germany). Releasing incisions induced additional local bleeding and therefore blood soaking of CXBB. The spaces between the bone block and the surrounding bone were filled with DBBM particles (Geistlich Bio-Oss®, Geistlich Pharma AG, Wolhusen, Switzerland) and covered with a native collagen membrane (CM) (Geistlich Bio-Gide®, Geistlich Pharma AG) fixed to the underlying bone with titanium tacks (FRIOS Fixation-Set®, SYMBIOS, Mainz, Germany). The muco-periosteal flaps were then coronally advanced and sutured with crossed-horizontal internal mattress sutures combined with simple sutures until achieving a tension-free primary closure (Figure 1).

Patients were then instructed to brush gently the adjacent teeth and to rinse with a chlorhexidine-containing solution (0.12%), twice daily for 14 days. Standard post-surgical medication, consisting of 600 mg of ibuprofen and 750 mg of amoxicillin (or clindamycin 600 mg) every 8 hr for 7 days, was prescribed. Two weeks after the procedure, the patients were recalled and the sutures were removed.

Twenty-six weeks after the regenerative surgical procedure, the patient returned for the re-entry and dental implant installation procedure. Figure 2 describes this surgical intervention. After raising

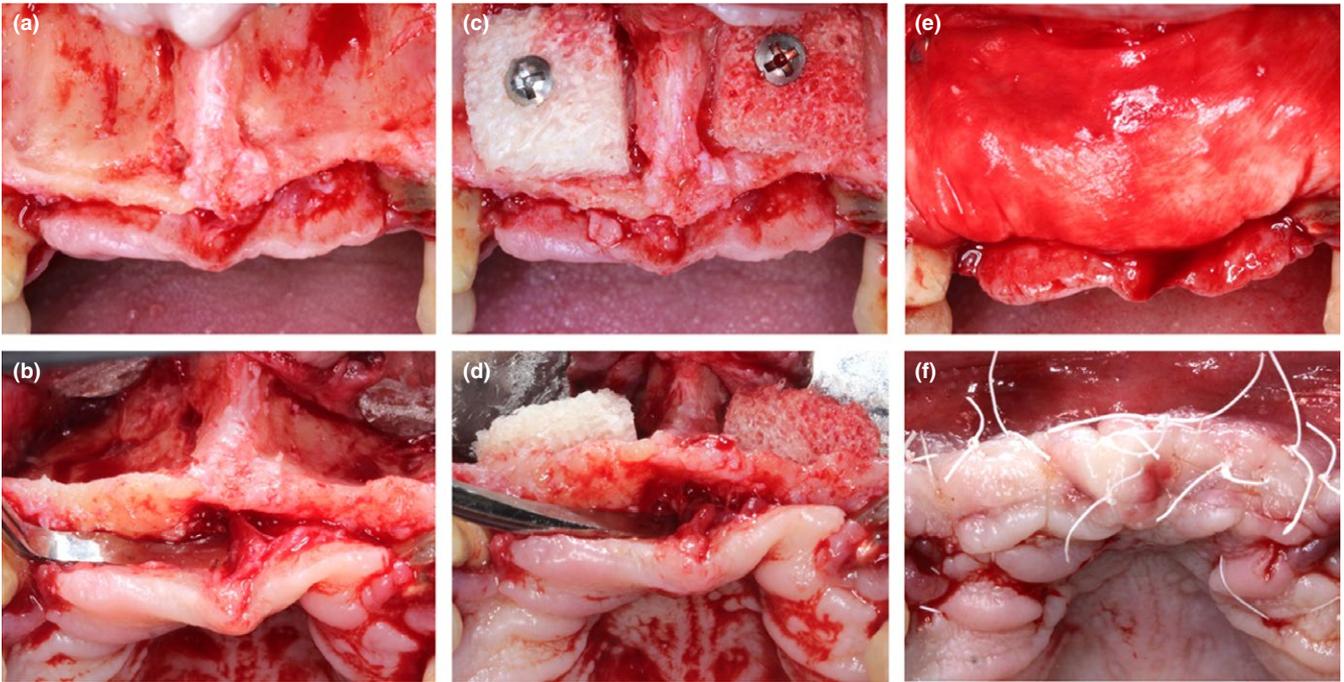


FIGURE 1 Lateral bone augmentation of the alveolar crest (a) Atrophic ridge. (b) Perforations and adaptation of the cortical layer. (c) Shaping, pre-wetting, and fixation of CXBB with titanium screws. (d) Horizontal contour and peripheral gap between CXBB and bone layer. (e) Outlying DBBM filling and NBCM stabilized with pins. (f) Tension-free primary closure

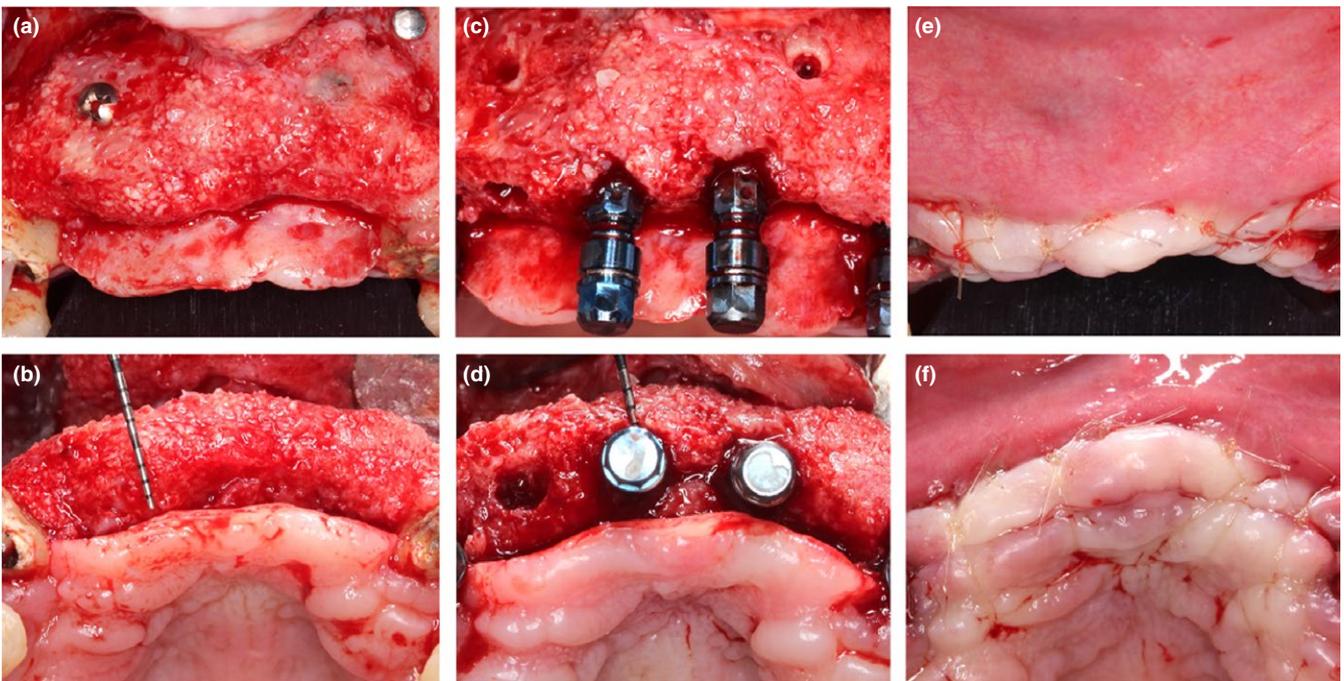


FIGURE 2 Re-entry procedure of patient in Figure 1. (a) Buccal aspect of the augmented region. (b) Horizontal bone augmentation. (c) Screws and pins removal and implants placement. (d) Buccal bone width from the implant shoulder. (e) Primary flap closure. (f) Implants submerged healing

full-thickness flaps to expose the augmented area, horizontal crestal width measurements were carried out using the same bone caliper at the same position 2 mm below the crest and in relation with adjacent teeth. The surgeon then evaluated the bone availability for implant placement, and the osteosynthesis screws and tacks were removed.

Commercially available titanium dental implants were placed in accordance with manufacturer guidelines. If the resulting buccal bone at the implant was thinner than 1.5 mm, a secondary simultaneous horizontal bone augmentation procedure (contouring) was performed through guided bone regeneration using DBBM particles and a NBCM.

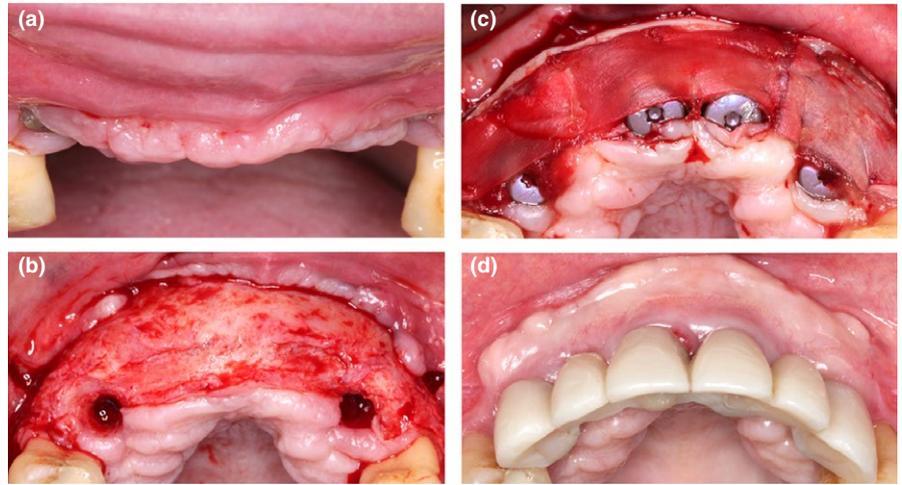


FIGURE 3 Second-stage surgery of patient in Figure 1. (a) Vestibular depth reduction after augmentation and implant placement. (b) Partial thickness and apical repositioned flap. (c) Implant abutment connection and CMX placement. (d) Implant loading

All sites underwent submerged healing, and sutures were removed 1 week later. Sixteen weeks after implant placement, a second-stage procedure was performed. As the mucogingival junction (MGJ) was moved coronally by advancing flaps during the regenerative surgical intervention, this second-stage surgery served not only to uncover the implants, but also to displace apically the MGJ. If there was a need to increase the width of keratinized mucosa and deepen the vestibule, a xenogeneic collagen matrix (CMX) (Geistlich Mucograft®; Geistlich Pharma AG) was stabilized with an external-crossed mattress and simple sutures. Eight weeks after the second-stage surgery implant loading was performed through fixed screw-retained restorations (Figure 3).

2.6 | Radiological analysis

Cone-beam computed tomography (CBCT) (i-CAT Classic, Imaging Sciences International, Hatfield, PA, USA) was obtained before inclusion

and 24 weeks after the augmentation procedure. A digital imaging software (SMOP®, Swissmeda Ltd.©, Zurich, Switzerland) was used to convert the DICOM files obtained from the pre- and post-augmentation CBCTs into STL files. Common anatomical reference points were used to perform the matching of the two surfaces. The software then used a series of mathematical algorithms to perform a “fine fit.”

Horizontal linear measurements were performed by selecting the center of the regenerated area with a longitudinal slice that divided the augmented area into two equal mesio-distal parts. Measurements were performed 2 mm below the baseline crest and assessed the baseline and post-regenerative crestal width. Horizontal gain was calculated by subtracting the post-op horizontal measurement to the baseline width. For the volumetric analysis, an area of interest was selected that corresponded with the augmented region. The software then calculated the volume, in cubic millimeters, enclosed between the two surfaces, which corresponded to the volume of augmented bone (Figure 4).

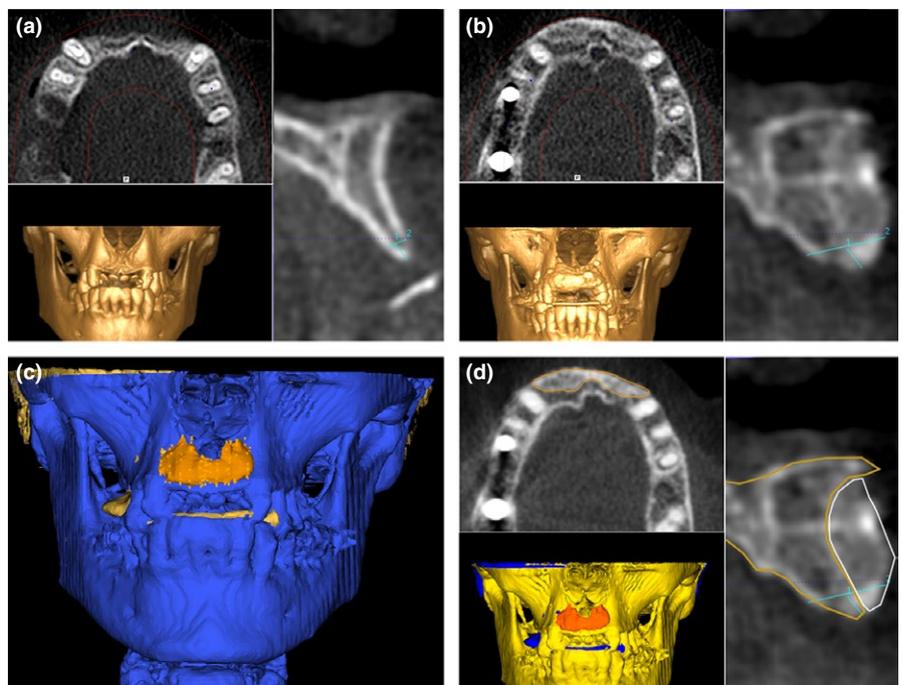


FIGURE 4 CBCT assessment of patient in Figure 1. (a) Baseline CBCT essential for inclusion. (b) CBCT 24 weeks after augmentation. (c) Pre- and postoperative CBCT matching (augmented area in orange). (d) Volumetric delimitation and quantification of the augmented region

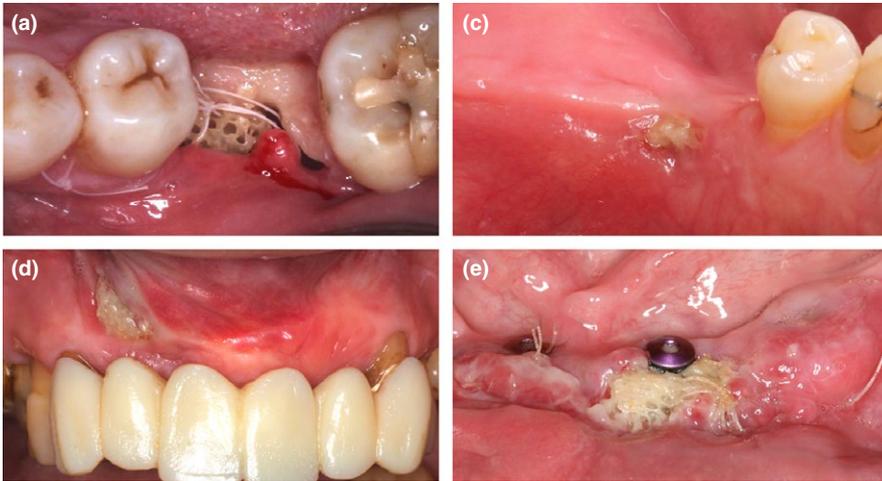


FIGURE 5 Complications. (a) Major complication requiring CXBB removal. (b) Dehiscence type 1 requiring a secondary augmentation procedure. (c) Dehiscence type 2 leading to a posterior implant loss. (d) Dehiscence type 4 after second-stage surgery deriving in to implants loss

2.7 | Statistical analysis

Data were entered into an Excel (Microsoft Office 2011) database and were proofed for entry errors. The software package (IBM SPSS Statistics 21.0; IBM Corporation, Armonk, NY, USA) was used for the analysis. A subject-level analysis was performed for each outcome measurement, and data were reported as mean values, standard deviations, medians, 95% confidence intervals (CI), and frequencies. Shapiro–Wilk goodness-of-fit tests were used to assess the normality and distribution of data. Differences between baseline and re-entry were evaluated using the paired sample *t* test. Results were considered statistically significant at $p < .05$.

3 | RESULTS

Twenty-one patients were screened for participation in this clinical study from December 2013 to October 2015. From these, five did not meet all exclusion criteria and one did not meet all inclusion criteria, and therefore, a total of 15 patients that fulfilled the selection criteria (12 women and 3 men) with a mean age of 54.5 (*SD* 8.34) were recruited to participate in this prospective single-arm study. In these 15 patients, 28 CXBB were placed and in 13 patients a re-entry procedure was performed. One patient refused to continue the study and denied to proceed with implant placement after suffering from a dehiscence type 1 complication. Another patient was excluded from the study due to the occurrence of an adverse event related to an allergic reaction. Although the patient was subject to extensive allergic testing, no confirmation was possible on the allergen causing the complication.

This patient suffered from intense pain and a soft tissue dehiscence 3 days after the regenerative procedure. The graft material had to be immediately removed (Figure 5a).

Minor adverse events occurred in three patients postoperatively in relation with pain, which were treated with pain and anti-inflammatory medication. Soft tissue dehiscences, with graft exposure, developed at different time points in 5 of 15 patients (33.3%) (Table 3). Apart

from the dehiscence type 1 in the patient that was withdrawn from the study, the rest were type 2 and 4 dehiscence types, which could be treated by remodeling the graft and allowing the soft tissues to heal in 2–4 weeks (Figure 5). There was no dehiscence in any patient where only one bone block was placed.

Total of 13 of 15 patients (86.7%) were scheduled for the re-entry procedure. Eleven of 13 patients (84.6%) attained enough bone volume for implant insertion without the need for additional contouring procedure. Two of 13 patients (15.4%) needed an additional contouring with DBBM and NBCM simultaneously with implant placement (Table 2).

A total of 24 implants were placed in 13 patients. Table 3 depicts the data on implant survival. Three implants were lost in three patients at the time of loading, and one patient presenting very narrow ridge at baseline (<3 mm) lost all four implants. All implants except one could be replaced with subsequent implants without additional grafting procedure. Implant loading was performed in 12 of 15 patients (80%); all the restorations were screw-retained, and in total, five single crowns and seven short-span bridges were delivered.

From the 13 patients completing the study, the mean ridge width was 2.78 mm (*SD* 0.55) at baseline and 6.90 mm (*SD* 1.22) at re-entry, demonstrating a statistical significant mean alveolar crest width gain of 4.12 mm (*SD* 1.32) (Table 2). Radiological mean width at baseline on the selected clinical area measured 2 mm apical to the crest was 2.98 mm (*SD* 0.56) and 7.13 mm (*SD* 1.28) 24 weeks after augmentation, resulting in a statistically significant width gain of 4.15 mm (*SD* 1.33) and a mean bone volumetric augmentation of 386 mm³ (*SD* 79) (Table 4).

4 | DISCUSSION

The purpose of this prospective clinical study was to evaluate the safety and performance of using CXBB for staged lateral bone augmentation in patients with severe atrophy of the alveolar crest. Six months after healing from the regenerative intervention dental implants were placed in 11 of 15 patients (73.3%) without the need of contouring and the mean alveolar ridge width increased 4.12 mm.

TABLE 2 Clinical alveolar crest assessment, secondary augmentation, and implant placement

Patient	CBW Baseline (mm) 0 weeks	Number of blocks	CBW Re-entry (mm) 26 weeks	CBW Gain (mm)	NSA	Implant	Site(s) of Implant(s)
1	3.1	2	5.7	2.6	No	Yes	34-36
2	3.75	2	6.5	2.75	No	Yes	45-46
3	3.5	1	7.5	4	No	Yes	36
4	2	1	6.5	4.5	No	Yes	46
5	2.5	3	6	3.5	No	Yes	44-46
6	3.5	2	–	–	Yes	No	–
7	3	2	7.55	4.55	No	Yes	11-13
8	2.85	2	6.75	3.9	Yes	Yes ^a	13-15
9	2.35	2	4.50	2.15	Yes	Yes ^a	23-26
10	2.9	1	–	–	Yes	No	–
11	2	2	7.60	5.6	No	Yes	11-21
12	2.6	1	6.20	3.6	No	Yes	21
13	2.75	4	7.87	5.12	No	Yes	44-42-32-34
14	2.25	2	9.35	7.1	No	Yes	45-46
15	3.5	1	7.8	4.4	No	Yes	36
Mean/%	2.83	1.85	6.90	4.12 ^b	Yes: 26.7%	Yes: 86.7% No: 13.3%	
SD	0.57		1.22	1.32	No: 73.3%		
95% IC	2.43; 3.12		6.17; 7.64	3.32; 4.93			
SS				$p < .01$			

CBW, clinical bone width; NSA, need of contouring or secondary augmentation; SD, standard deviation; SS, statistical significance.

^aImplant placement was possible simultaneous to contouring.

^bMean clinical gain width excluding patient 6 and 10 due to dehiscence type 1.

These results are comparable with those published in a recent systematic review with the use of intraoral autogenous bone blocks reporting a mean width increase of 3.90 mm (*SD* 0.38) (Sanz-Sanchez et al., 2015), with those obtained with bone block allografts 4.50 mm (*SD* 1.3) (Dias et al., 2016) and with those reporting the outcome of using the same CXBB in single tooth bone defects (Schwarz et al., 2016). Schwarz et al. (2016) performed a pilot study on 10 patients and reported that in eight patients (mean baseline alveolar ridge of 4.38 mm [*SD* 0.92]) treated with CXBB, a mean crestal width gain of 3.88 mm (*SD* 1.75) was achieved. At the re-entry, implant placement was possible in 8 of 10 (80%) patients. In the current study, one step further was taken and patients with narrower ridges (mean of 2.78 mm [*SD* 0.57]) were treated using staged bone augmentation procedure.

In terms of safety, one patient suffered an adverse event 3 days after the regenerative intervention. This patient suffered from acute pain and soft tissue dehiscence, which could only be solved by re-intervention and removal of the graft. Pain remitted after 2 days and complete soft tissue healing was achieved within 2 weeks. This patient was excluded from the study and underwent testing for a variety of allergens. Other authors have reported the possibility of allergy to the xenogeneic collagen (Fadok, 2013; Marti et al., 2015), although this fact could not be confirmed in this patient.

Soft tissue dehiscence at a later healing time was a frequent complication occurring in 35.7% of the patients with different degree of severity. This secondary dehiscence was treated by reshaping the graft material and allowing the soft tissue to heal by secondary intention. Similar complication rates have been reported in other studies (37.5%) using autogenous bone blocks combined with DBBM + NBCM (Cordaro, Torsello, Miuccio, et al., 2011; Cordaro, Torsello, Morcavallo, et al., 2011), (33.3%) with allogenic bone blocks covered with DBBM + NBCM (Dias et al., 2016), and (25%) with allogenic bone blocks alone (Spin-Neto et al., 2014), and even a higher percentage of dehiscence (70%) was reported when using the same xenogeneic bone block (Schwarz et al., 2016). This high exposure rate could be also related to the macroscopic structure of the bone graft composed of natural cancellous xenogenic bone. When using autologous bone block grafts alone, the reported incidence of soft tissue dehiscence has been lower (11% versus 37.5%) but with a statistically significant greater graft resorption (22% versus 5.5%) (Cordaro, Torsello, Miuccio, et al., 2011; Cordaro, Torsello, Morcavallo, et al., 2011).

The high number of complications occurring in this clinical study may also be explained by the extreme narrow crestal defects (mean crestal width of 2.78 mm [*SD* 0.57]) treated, what needed in many cases to use more than one block graft. In fact, there was no incidence of

Patient	Major complication	Dehiscence	Dehiscence type ^a	Implant loss	PIR
1	No	No	0	No	-
2	No	Yes	2	Yes	Yes
3	No	No	0	No	-
4	No	No	0	No	-
5	No	No	0	Yes	Yes
6	No	Yes	1	-	-
7	No	Yes	4	No	-
8	No	No	0	No	-
9	No	Yes	2	No	-
10	Yes	-	-	-	-
11	No	No	0	No	-
12	No	No	0	Yes	No
13	No	Yes	4	Yes	Yes
14	No	No	0	No	-
15	No	No	0	No	-
Percentage	No: 94.3% Yes: 6.7%	No: 64.3% Yes: 35.7%	0: 64.3% 1: 7.1% 2: 14.3% 3: 0% 4: 14.3%	No: 69.2% Yes: 30.8%	No: 25% Yes: 75%

PIR, possibility of implant replacement prior to visit 10.

^aDehiscence type: 0 (No dehiscence); 1 (Primary dehiscence); 2 (Secondary dehiscence); 3 (Tertiary dehiscence); 4 (Late dehiscence).

TABLE 3 Complications (i.e., dehiscence, secondary augmentation, implant loss)

Patient	RBW Baseline (mm)	RBW Re-entry (mm)	RBW Gain (mm)	RBW Volumetric (mm ³)
1	3.2	5.8	2.6	377
2	3.9	6.8	2.9	415
3	3.6	8	4.4	474
4	3.6	7.2	3.6	335
5	2.5	6.1	3.6	418
6	3.2	-	-	-
7	3.1	7.9	4.8	327
8	2.9	7	4.1	305
9	2.5	4.6	2.1	229
10	2.8	-	-	-
11	2.1	7.6	4.5	358
12	2.5	6.1	3.6	378
13	2.8	8.1	5.3	498
14	2.5	9.6	7.1	511
15	3.6	8	4.4	388
Mean	2.98	7.13	4.15	386
SD	0.56	1.28	1.33	79
95% IC	2.79;3.27	6.36;7.91	3.34;4.96	338;434
SS			$p < .01$	

TABLE 4 Radiological alveolar crest assessment (Linear and volumetric)

RBW, radiological bone width 2 mm apical to the bone crest; SD, standard deviation; SS, statistical significance.

soft tissue dehiscence when only one bone block graft was placed and there was a positive correlation between the number of blocks used and the incidence of soft tissue dehiscences. The use of large grafts or more than one graft may have hindered an appropriate blood supply or colonization of the graft material with bone forming cells (Gruber, Stadlinger & Terheyden, 2016).

Dehiscence type 2 was clinically manageable but tended to compromise the implant osseointegration, as we observed a correlation between this type 2 and implant loss. This may be due to early contamination of the exposed bone block that may have jeopardized bone ingrowth. Similar complications have been observed in previous studies using particulated DBBM and NBCM over autogenous bone blocks (von Arx & Buser, 2006; Cordaro, Torsello, Miuccio, et al., 2011; Cordaro, Torsello, Morcavallo, et al., 2011) and over allogenic bone blocks (Dias et al., 2016; Nissan, Ghelfan, Mardinger, Calderon & Chaushu, 2011). Type 4 dehiscence, however, occurred in two patients after implant abutment connection and may be due to the thinning of the flap, and the mucogingival procedures aimed to increase the amount of keratinized tissue and vestibule deepening. Similar tissue shrinkage has been reported after the reconstruction of the mucogingival tissues secondary to major bone regenerative procedures (Urban, Lozada, Nagy & Sanz, 2015).

The incidence of dehiscence was also correlated with the need of contouring and secondary augmentation, which is also in agreement with previous studies reporting a mean bone gain of 3.1 mm (WMD) when comparing dehiscence *versus* non-exposed sites (Penarrocha-Diago, Aloy-Prosper, Penarrocha-Oltra, Guirado & Penarrocha-Diago, 2013; Sanz-Sanchez et al., 2015). In the present study, we augmented the peripheral contour of the CXBB with DBBM particles, which may have contributed to the soft dehiscence, as it has been reported by other authors (von Arx & Buser, 2006; Cordaro, Torsello, Miuccio, et al., 2011; Cordaro, Torsello, Morcavallo, et al., 2011).

The rate of implants loss reported in this study (29.2%) is significantly higher than previously reported evaluating dental implants in regenerated bone (<5%) (Aloy-Prosper, Penarrocha-Oltra, Penarrocha-Diago & Penarrocha-Diago, 2015; Sanz-Sanchez et al., 2015). When analyzing the patient distribution, 30.8% of the patients had early implant loss: three patients (75%) lost one implant, and one patient (25%) lost four. Of the four patients affected by early implant loss, new implants were successfully inserted in all of them and only one required additional bone re-contouring. These numbers are higher than those recently published in a Swedish population reporting early implant lost in 4.4% of the subjects and in 1.4% of implants (Derks et al., 2015). These differences could be explained by the challenging baseline clinical situation with the patients in this study, presenting very narrow alveolar ridges with a mean width of 2.83 mm (SD 0.57). Early implant loss may also be related to dehiscence of the soft tissues during healing and bacterial contamination of the CXBB, thus altering bone ingrowth and appropriate healing.

The clinical and the CBCT radiological results had a high degree of concordance both for measuring alveolar bone widths and volumes, which is in agreement with previous studies comparing both diagnostic methods (Jacobs & Quirynen, 2014). Regarding the volumetric analysis, the present results with a mean augmentation of 386 mm³

(79 SD) are in agreement with a similar protocol using allograft bone blocks (529.51 mm³) (SD 275) but with a larger standard deviation maybe due to the heterogeneity in the results using allogenic bone grafts (Dias et al., 2016).

This prospective single-arm study has clear limitations to evaluate the effectiveness of this bone regenerative procedure, due to the lack of a control group and a sufficient sample population (Berglundh & Giannobile, 2013), but this investigation was aimed for evaluating the safety of this procedure and its performance, by assessing the incidence of adverse events and the possibilities of subsequent successful implant therapy.

In conclusion, the use of CXBB in combination with DBBM particles and a native bilayer collagen membrane for staged lateral bone augmentation achieved significant horizontal crestal width allowing for secondary implant placement in the majority of the patients. The occurrence of soft tissue dehiscence lesions may notably jeopardize the outcome of the subsequent implant therapy. Further investigations are needed to identify the best indications and surgical approaches for the successful use of xenogeneic bone blocks in lateral bone augmentation procedures.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

REFERENCES

- Acocella, A., Bertolai, R., Ellis, E. 3rd, Nissan, J., & Sacco, R. (2012). Maxillary alveolar ridge reconstruction with monocortical fresh-frozen bone blocks: A clinical, histological and histomorphometric study. *Journal of Craniomaxillofacial Surgery*, 40, 525–533.
- Aloy-Prosper, A., Penarrocha-Oltra, D., Penarrocha-Diago, M., & Penarrocha-Diago, M. (2015). The outcome of intraoral onlay block bone grafts on alveolar ridge augmentations: A systematic review. *Medicina Oral Patología Oral y Cirugía Bucal*, 20, e251–e258.
- von Arx, T., & Buser, D. (2006). Horizontal ridge augmentation using autogenous block grafts and the guided bone regeneration technique with collagen membranes: A clinical study with 42 patients. *Clinical Oral Implants Research*, 17, 359–366.
- von Arx, T., Hafliger, J., & Chappuis, V. (2005). Neurosensory disturbances following bone harvesting in the symphysis: A prospective clinical study. *Clinical Oral Implants Research*, 16, 432–439.
- Benic, G. I., Thoma, D. S., Munoz, F., Sanz Martin, I., Jung, R. E., & Hammerle, C. H. (2016). Guided bone regeneration of peri-implant defects with particulated and block xenogenic bone substitutes. *Clinical Oral Implants Research*, 27, 567–576.
- Berglundh, T., & Giannobile, W. V. (2013). Investigational clinical research in implant dentistry: Beyond observational and descriptive studies. *Journal of Dental Research*, 92, 1075–1085.
- Cordaro, L., Amade, D. S., & Cordaro, M. (2002). Clinical results of alveolar ridge augmentation with mandibular block bone grafts in partially edentulous patients prior to implant placement. *Clinical Oral Implants Research*, 13, 103–111.

- Cordaro, L., Torsello, F., Miuccio, M. T., di Torresanto, V. M., & Eliopoulos, D. (2011). Mandibular bone harvesting for alveolar reconstruction and implant placement: Subjective and objective cross-sectional evaluation of donor and recipient site up to 4 years. *Clinical Oral Implants Research*, 22, 1320–1326.
- Cordaro, L., Torsello, F., Morcavallo, S., & di Torresanto, V. M. (2011). Effect of bovine bone and collagen membranes on healing of mandibular bone blocks: A prospective randomized controlled study. *Clinical Oral Implants Research*, 22, 1145–1150.
- Cremonini, C. C., Dumas, M., Pannuti, C., Lima, L. A., & Cavalcanti, M. G. (2010). Assessment of the availability of bone volume for grafting in the donor retromolar region using computed tomography: A pilot study. *International Journal of Oral Maxillofacial Implants*, 25, 374–378.
- Derks, J., Hakansson, J., Wennstrom, J. L., Tomasi, C., Larsson, M., & Berglundh, T. (2015). Effectiveness of implant therapy analyzed in a Swedish population: Early and late implant loss. *Journal of Dental Research*, 94, 445–515.
- Dias, R. R., Sehn, F. P., de Santana Santos, T., Silva, E. R., Chaushu, G., & Xavier, S. P. (2016). Corticocancellous fresh-frozen allograft bone blocks for augmenting atrophied posterior mandibles in humans. *Clinical Oral Implants Research*, 27, 39–46.
- Fadok, V. A. (2013). Update on equine allergies. *Veterinary Clinics of North America Equine Practice*, 29, 541–550.
- Gruber, R., Stadlinger, B., & Terheyden, H. (2016). Cell-to-cell communication in guided bone regeneration: Molecular and cellular mechanisms. *Clinical Oral Implants Research*, 1–8. <https://doi.org/10.1111/clr.12929>.
- Hammerle, C. H., Jung, R. E., Yaman, D., & Lang, N. P. (2008). Ridge augmentation by applying bioresorbable membranes and deproteinized bovine bone mineral: A report of twelve consecutive cases. *Clinical Oral Implants Research*, 19, 19–25.
- Jacobs, R., & Quirynen, M. (2014). Dental cone beam computed tomography: Justification for use in planning oral implant placement. *Periodontology 2000*, 66, 203–213.
- Jensen, S. S., & Terheyden, H. (2009). Bone augmentation procedures in localized defects in the alveolar ridge: Clinical results with different bone grafts and bone-substitute materials. *International Journal of Oral and Maxillofacial Implants*, 24(Suppl), 218–236.
- Marti, E., Wang, X., Jambari, N. N., Rhyner, C., Olzhausen, J., Perez-Barea, J. J., ... Alcocer, M. J. (2015). Novel in vitro diagnosis of equine allergies using a protein array and mathematical modelling approach: A proof of concept using insect bite hypersensitivity. *Veterinary Immunology and Immunopathology*, 167, 171–177.
- Meloni, S. M., Jovanovic, S. A., Urban, I., Canullo, L., Pisano, M., & Tallarico, M. (2016). Horizontal ridge augmentation using gbr with a native collagen membrane and 1:1 ratio of particulated xenograft and autologous bone: A 1-year prospective clinical study. *Clinical Implant Dentistry and Related Research*, 19(1), 38–45.
- Mir-Mari, J., Wui, H., Jung, R. E., Hammerle, C. H., & Benic, G. I. (2016). Influence of blinded wound closure on the volume stability of different gbr materials: An in vitro cone-beam computed tomographic examination. *Clinical Oral Implants Research*, 27, 258–265.
- Moest, T., Wehrhan, F., Lutz, R., Schmitt, C. M., Neukam, F. W., & Schlegel, K. A. (2015). Extra-oral defect augmentation using autologous, bovine and equine bone blocks: A preclinical histomorphometrical comparative study. *Journal of Craniomaxillofacial Surgery*, 43, 559–566.
- Nissan, J., Ghelfan, O., Mardinger, O., Calderon, S., & Chaushu, G. (2011). Efficacy of cancellous block allograft augmentation prior to implant placement in the posterior atrophic mandible. *Clinical Implant Dentistry and Related Research*, 13, 279–285.
- Nkenke, E., Radespiel-Troger, M., Wiltfang, J., Schultze-Mosgau, S., Winkler, G., & Neukam, F. W. (2002). Morbidity of harvesting of retromolar bone grafts: A prospective study. *Clinical Oral Implants Research*, 13, 514–521.
- Nkenke, E., Weisbach, V., Winckler, E., Kessler, P., Schultze-Mosgau, S., Wiltfang, J., & Neukam, F. W. (2004). Morbidity of harvesting of bone grafts from the iliac crest for preprosthetic augmentation procedures: A prospective study. *International Journal of Oral and Maxillofacial Surgery*, 33, 157–163.
- Penarrocha-Diago, M., Aloy-Prosper, A., Penarrocha-Oltra, D., Guirado, J. L., & Penarrocha-Diago, M. (2013). Localized lateral alveolar ridge augmentation with block bone grafts: Simultaneous versus delayed implant placement: A clinical and radiographic retrospective study. *International Journal of Oral Maxillofacial Implants*, 28, 846–853.
- Sanz, M., & Vignoletti, F. (2015). Key aspects on the use of bone substitutes for bone regeneration of edentulous ridges. *Dental Materials*, 31, 640–647.
- Sanz-Sanchez, I., Ortiz-Vigón, A., Sanz-Martin, I., Figuero, E., & Sanz, M. (2015). Effectiveness of lateral bone augmentation on the alveolar crest dimension: A systematic review and meta-analysis. *Journal of Dental Research*, 94, 1285–1425.
- Schwarz, F., Ferrari, D., Balic, E., Buser, D., Becker, J., & Sager, M. (2010). Lateral ridge augmentation using equine- and bovine-derived cancellous bone blocks: A feasibility study in dogs. *Clinical Oral Implants Research*, 21, 904–912.
- Schwarz, F., Mihatovic, I., Ghanaati, S., & Becker, J. (2016). Performance and safety of collagenated xenogeneic bone block for lateral alveolar ridge augmentation and staged implant placement. A monocenter, prospective single-arm clinical study. *Clinical Oral Implants Research*, 1–7.
- Simion, M., Fontana, F., Rasperini, G., & Maiorana, C. (2007). Vertical ridge augmentation by expanded-polytetrafluoroethylene membrane and a combination of intraoral autogenous bone graft and deproteinized anorganic bovine bone (bio oss). *Clinical Oral Implants Research*, 18, 620–629.
- Spin-Neto, R., Landazuri Del Barrio, R. A., Pereira, L. A., Marcantonio, R. A., Marcantonio, E., & Marcantonio, E. Jr (2013). Clinical similarities and histological diversity comparing fresh frozen onlay bone blocks allografts and autografts in human maxillary reconstruction. *Clinical Implant Dentistry and Related Research*, 15, 490–497.
- Spin-Neto, R., Stavropoulos, A., Coletti, F. L., Faeda, R. S., Pereira, L. A., & Marcantonio, E. Jr (2014). Graft incorporation and implant osseointegration following the use of autologous and fresh-frozen allogeneic block bone grafts for lateral ridge augmentation. *Clinical Oral Implants Research*, 25, 226–233.
- Urban, I. A., Lozada, J. L., Nagy, K., & Sanz, M. (2015). Treatment of severe mucogingival defects with a combination of strip gingival grafts and a xenogeneic collagen matrix: A prospective case series study. *International Journal of Periodontics and Restorative Dentistry*, 35, 345–353.
- Urban, I. A., Nagursky, H., & Lozada, J. L. (2011). Horizontal ridge augmentation with a resorbable membrane and particulated autogenous bone with or without anorganic bovine bone-derived mineral: A prospective case series in 22 patients. *International Journal of Oral and Maxillofacial Implants*, 26, 404–414.
- Urban, I. A., Nagursky, H., Lozada, J. L., & Nagy, K. (2013). Horizontal ridge augmentation with a collagen membrane and a combination of particulated autogenous bone and anorganic bovine bone-derived mineral: A prospective case series in 25 patients. *International Journal of Periodontics and Restorative Dentistry*, 33, 299–307.

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