Clinical, Tomographic, and Histological Assessment of Periosteal Guided Bone Regeneration with Cortical Perforations in Advanced Human Critical Size Defects

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ABSTRACT

Background: Large osseous defects that fail to heal spontaneously require ridge augmentation prior to implant placement. The periosteum can act as an effective barrier membrane. Little is known about the influence of bone decortication in enhancing guided bone regeneration outcomes.

Purpose: The aim of the present study was a clinical, tomographic, and histological evaluation of bone healing in large defect sites treated with cortical perforations without the use of other membranes but the periosteum.

Material and Methods: Ten consecutive patients undergoing ridge augmentation on the pre-maxilla due to severe bone loss were followed for an average of 35 months. Recipient sites were cortico-perforated and augmented using a combination of autogenous particulate and block grafts. The periosteal membrane was preserved and it fully covered the autografts. Histological analysis was performed in four sites from a trephine core taken at the time of implant osteotomy preparation. Tomographic assessment (computed tomography [CT] scan) at baseline and post-augmentation evaluated graft volume maintenance.

Results: Recipient sites were re-entered for implant placement showing good incorporation of the grafts with minimal volume loss. Biopsy specimens showed viable bone rich in osteoblast-like cells with little or no inflammatory cells. Clinical exam revealed absence of implant transparency, mucosal recession, mobility, bleeding on probing, or suppuration at follow-up. CT scan evaluation showed an average increased bucco-lingual width at the recipient site of 8.1 mm $\pm$ 0.9 (2.5 fold) versus a 3.2 $\pm$ 0.9 at baseline ($p < .0001$; CI 95%: 4.04–5.71 mm), maintaining on average 98% of the augmented width at 2.9 years.

Conclusions: Periosteal preservation seems to be sufficient as a barrier membrane to protect particulate or block osseous grafts provided that good primary closure is achieved. Bone decortication may enhance clinical and histological outcomes. Graft viability (biopsy specimens) and volume maintenance (CT evaluation) remained stable 35 months post-augmentation.

KEY WORDS: bone grafting, bone histology, computerized tomography, cortical perforation, periosteal preservation, ridge augmentation

INTRODUCTION

Different surgical techniques have been developed to reconstruct sufficient ridge height and width for functional and esthetic implant therapy.[1–10] The principle of guided bone regeneration (GBR) has probably created most attention and it is based on the concept of excluding faster growing soft tissue cells into the treated bony

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defect, allowing the slower process of osteogenesis to take place without interruption.[1,2]

A recent prospective split-mouth study in 14 patients using iliac block grafts concluded that revascularization of the graft was sufficient after 3 months regardless of the graft coverage. The resorption rate seemed to be similar for grafts covered with the periosteum or a bioresorbable membrane.[11]

Lemperle and colleagues[12] studied the healing of large cranial and mandibular defects in an animal model evaluating bone regeneration with and without periosteal preservation. Defect protection by the periosteum alone seemed sufficient to allow for healing even in the critical size defects. When the periosteum was absent, spontaneous bone formation was limited. The concept of GBR can also be applied whenever the periosteal membrane remains intact over the graft material. Moreover, this natural membrane provides a source of blood supply and nutrients that artificial membranes lack.

A recent human study[13] evaluated the long-term influence of periodontal biotype on the volume maintenance of onlay grafts without the use of membranes to cover them. Computerized tomography assessment demonstrated that autogenous osseous transplants predictably maintained stable bone volume around implants at an average of 3.5 years. There is limited scientific documentation on the long-term healing response of autogenous bone grafts in large bony defects and the healing of human critical size defects. Moreover, little is known about the potential long-term influence of specific anatomical factors, such as the thickness or integrity of the periosteum, the underlying cortical plate, and the periodontal biotype, on the outcome therapy. Empirical evidence suggests that thick tissue is more resistant to trauma, promotes creeping attachment, improves implant esthetics and renders more predictable surgical procedures.[14–19]

Autogenous grafting from intraoral sites is a predicable technique for successful osseous reconstruction and presents advantages such as short healing period, minimal bone loss, good volume maintenance, and high concentration of bone morphogenetic proteins.[3–7,20–24] The two main donor sites for this type of bone grafting are the mandibular symphysis and ramus.[5,6,13,20–24]

The aim of the present prospective study was to evaluate bone healing of large defect sites treated with cortical perforations and a combination of particulate and block autografts without the use of other membranes but the periosteum. A further aim was to provide clinical and histologic evidence of adequate transplant healing 4 to 6 months after augmentation at the time of implant placement. Moreover, a tomographic examination was done to assess transplant volume maintenance 35 months post-augmentation.

MATERIAL AND METHODS

Ten consecutive patients (6 males and 4 females) who underwent ridge augmentation due to insufficient bone prior to implant placement entered in this study. Residual ridges averaged 3.2 mm in width (Table 1). All

TABLE 1 Descriptive Analysis. Patients 1 to 10 Received Autogenous Bone Grafting for Ridge Augmentation. Etiologic Factors for Maxillary Collapse Included Endodontal, Periodontal, Combination, Trauma, and Peri-Implantitis Origin. Follow-up Listed in Months

	Age	Ethnicity	Donor	Recipient	BL Width* Baseline	BL Width Post-Augment	Follow-Up	Etiology
1	28	Caucasian	symphysis	#7 and #10	3.0	9.2	26	Endo
2	48	Caucasian	symphysis	#10	2.0	7.5	30	Peri-implantitis
3	38	Hispanic	symphysis	#8 and #10	4.1	8.3	24	Endo-perio
4	46	Caucasian	symphysis	#8	1.5	8.0	38	Trauma
5	37	Caucasian	symphysis	#7 and #9	4.3	9.0	32	Endo
6	69	Caucasian	symphysis	#10	2.8	7.6	30	Endo
7	41	Hispanic	symphysis	#8	4.0	8.2	66	Perio
8	68	Caucasian	symphysis	#8	3.5	9.6	53	Endo
9	39	Caucasian	ramus	#9 and #10	3.8	7.2	24	Trauma
10	27	Asian	ramus	#10 and #11	3.3	6.5	28	Trauma

*BL width: bucco-lingual width in mm.

patients presented unremarkable medical history and had an average age of 44 years (range: 27–69). Patients with uncontrolled diabetes, heavy smokers (more than $^1/_2$ pack per day), long-term corticosteroid therapy, history of intravenous bisphosphonates use, or uncontrolled hypertension were excluded from the study. Patients needed ridge reconstruction and had lost their teeth due to advanced periodontal disease (1), peri-implantitis (1), trauma (3), combined endo-perio lesions (1), or endodontic (4) reasons. They had an average of 26 teeth (range: 25–29) per person and probing depths ranging from 2 to 3 mm before the surgical phase. The recipient sites included six central incisors, eight lateral incisors and one canine.

Surgeries were performed between the years 2004 and 2007 in two private offices (Huntington Beach and Altadena, CA, USA, and Rome, Italy) by two surgeons with over 10 years of experience. Ethical approval was obtained from the University of Basque Country Ethics Committee. Patients were informed of the procedures and signed a written consent form.

Surgical Protocol

Subjects were medicated with 500 mg of amoxicillin three times a day starting the day before the surgical procedure for a total of 1 week. They were asked to brush their teeth immediately before the procedure for 2 minutes with a 0.2% chlorhexidine rinse (Corsodyl, Smithkline Beecham, Brentford, Middlesex, UK). Povidone-iodine 10% (Betadine, Purdue Pharma, Stamford, CT) was applied to the peri-oral skin to prevent contamination. Surgeries were carried out in a designated surgical operating room. The procedure has been explained elsewhere.[13] Briefly, local anesthesia was achieved through infiltrations of lidocaine 2% with 1:100.000 of epinephrine. A crestal and two vertical incisions were performed one to two teeth distant from the recipient site. A mucoperiosteal flap was elevated. After degranulation, intra-marrow penetrations were performed using a small $^1/_2$ round burr and cortical particles were placed to fill all voids around or underneath the fixated blocks (Figure 1, A–C). Block grafts were harvested from the symphysis or ramus and a safe scraper was used to collect the bone particles. All block grafts were fixated using 2 × 10 mm titanium mini-screws (Ace Surgical, Brockton, MA, USA). No membranes but the periosteum were used to cover the grafts. Interrupted 5-0 chromic gut sutures were used to close the flap. All patients received the same protocol of treatment: 4 to 6 months after ridge augmentation, implants were placed following a 2-stage approach (Figure 1, D–G). At that time, a biopsy specimen was taken using a 2 mm trephine from the same implant osteotomy site (Figure 1, H–I). Implants were uncovered and healing abutments placed 3 to 6 months after implant placement. Fixed provisional restorations were placed 4 weeks thereafter. Definitive screw retained restorations were delivered 1 to 3 months after healing abutment connection (Figure 2, A–B).

Computerized cone beam tomography (NewTom, QR sr 1, Verona, Italy) scans (computed tomography [CT] scan) were taken at an average of 35 months (Table 1; Figure 3, A–F) after augmentation to document bone volume maintenance and healing of the grafts.

Data Analysis

Descriptive analysis of data was expressed as mean ± SD. A commercially available software program (SPSS®, version 14.0, SPSS Inc., Chicago, IL, USA) was utilized to compare means and draw the box plot graphics. The *t*-test was used for paired observations to analyze values of bucco-lingual (BL) width at baseline and after augmentation. Statistical significance (SS) was set at $p < .05$.

RESULTS

Clinical examinations revealed absence of implant transparency or mucosal recession at an average of 35 months. Mobility, bleeding on probing or suppuration was not detected in any case. Probing depths ranged from 3–4 mm at implant or adjacent teeth sites.

Four to six months after grafting, all ten patients were re-entered for screw removal and implant placement. All cases showed good incorporation and blending of the blocks and particulate grafts with minimal volume loss (Figure 1, D–G). Biopsy specimens demonstrated, under light microscopy, viable bone rich in osteoblast-like cells with little or no infiltration of inflammatory cells at the regenerated sites. The sections revealed a core of tissue composed partly of immature woven bone with rims of mature lamellar bone. The supporting marrow was uninflamed and the marrow spaces generally showed no significant osteoclastic activity (Figure 1, I).

Patient's follow-up ranged from 24 to 66 months and averaged 35 months after augmentation.

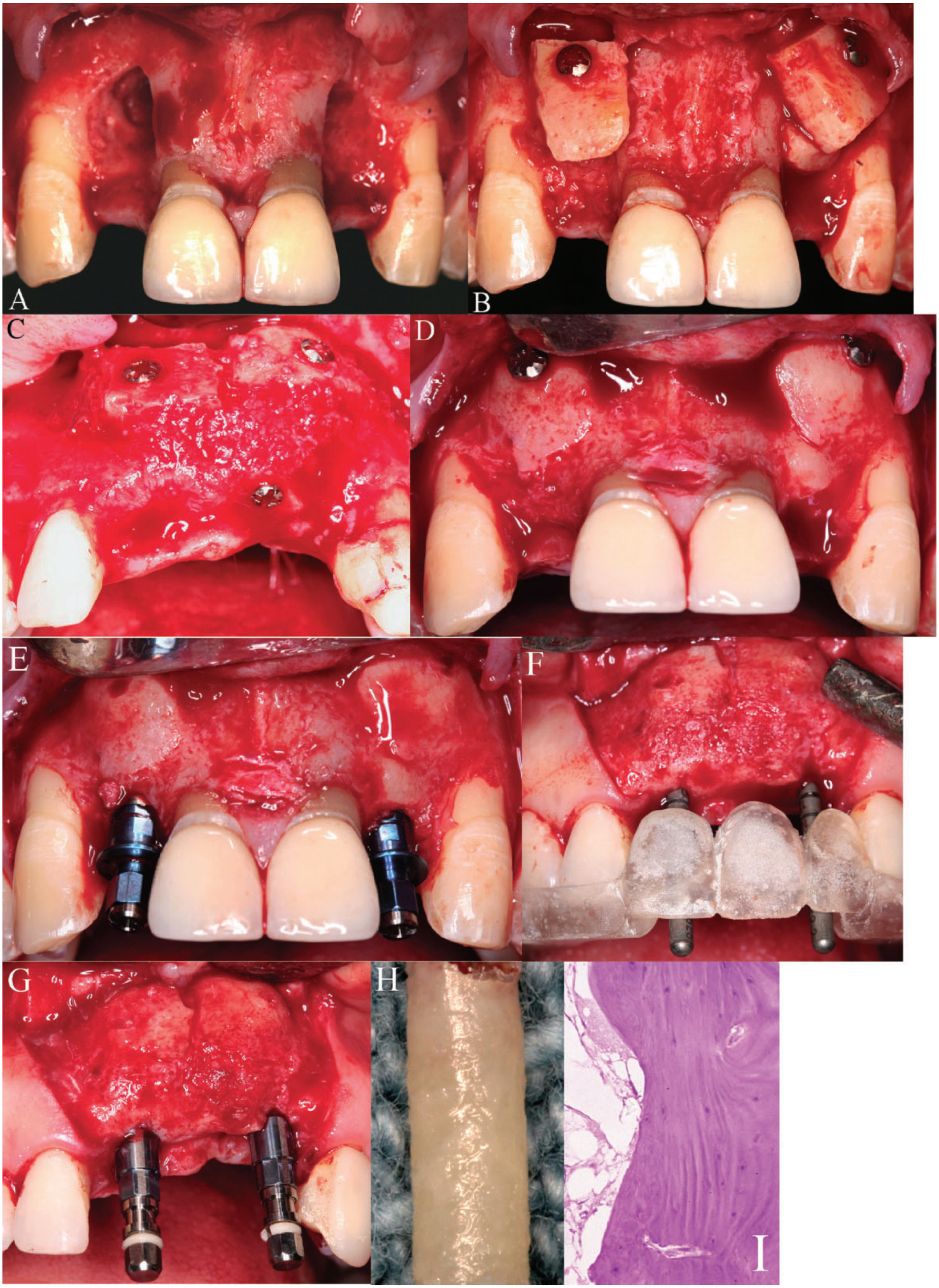

Figure 1 *A*, Pre-operative frontal view of patient 1 after degranulation and cortical perforation of bilateral 8 × 15 mm size defects. *B*, Buccal view of defect fill with particulate cortical graft and symphysis blocks partially covering bony defects. *C*, Symphysis graft on patient 3: buccal and oclussal blocks and cortical particles filling voids. *D*, Buccal view of patient in *A* and *B* at 5 months. Notice excellent graft incorporation and blending with adjacent osseous tissues. *E*, Buccal view of patient in *A*, *B*, and *D* at 5 months. Implant placement. *F*, Implant placement 4 months post-augmentation patient in *C*. *G*, Patient 3 from *C* and *F*: implant placement. *H*, Biopsy specimen taken in patient 1 at the time of implant placement. *I*, Light microscopy evaluation showing viable bone: osteoblast-like cells with no infiltration of inflammatory cells.

Figure 2 *A*, Pre-operative picture of recipient site in patient 1. *B*, Post-operative site at 26 months follow-up with definitive restorations.

Tomographic evaluation showed that the recipient site BL width average was 3.2 mm (SD 0.9 mm, range: 1.5–4.3) at baseline and 8.1 mm (SD 0.9 mm, range: 6.5–9.6) after augmentation (Table 1). This difference was statistically significant ($p < .0001$; CI 95%: 4.04–5.71 mm) (Figure 4). The average augmentation per site was 2.5 fold the initial BL width and maintained 98% of the augmented width after 2.9 years. All patient's functional and esthetic condition has been stable for the period of time followed. Moreover, the donor sites presented osseous repair ranging from 80 to 98% (Figure 3, E and F).

DISCUSSION

The present prospective study aimed to assess bone healing in large maxillary defect sites augmented with particulate and block autografts and the suitability of the periosteal membrane to contain the graft material. Furthermore, this study intended to provide clinical and histologic evidence of the osseous transplant healing 4 to 6 months post-augmentation at the time of implant placement. Moreover, a tomographic examination was performed on each patient to assess transplant volume maintenance 35 months after ridge augmentation. At the time of implant placement, recipient sites were re-entered to remove fixation screws. Digital pictures were taken at the time of augmentation and at re-entry. The particulate graft had blended in with adjacent osseous tissues maintaining nearly intact volume (Figure 1, D–G). The post-CT scan taken at an average of 2.9 years confirmed the volume maintenance of the transplanted bone (Figure 3, C–F). Lee and colleagues[25] reported a case series of reconstruction of orbital floor fractures using maxillary bone with no evidence of resorption of the graft. Their evaluation was done at an average of 1.7 years using a computerized tomography scan.

In an animal model, Berglund and colleagues[26] found different bone reactions to longstanding functional loading and compared this situation with unloaded control implants. Subsequent to loading, an increase in percentage of bone to implant contact compared with non-loaded controls was noted. The authors concluded that functional loading may enhance osseointegration and bone maintenance. A different paper confirmed this finding in human histological case reports.[27] Other researchers have found short-term conflicting evidence on the effect of onlay graft membrane coverage, suggesting that factors other than membrane GBR may play a more important role in grafted bone volume maintenance.[27,28]

Within the limitations of the present study, it was demonstrated that ridge augmentation was predictably achieved even in cases with a minimum BL width of 1.5 mm in large osseous critical size defects. The scaffold provided by the fixated block may have served as a tent to hold the space between the periosteum and the residual alveolar bone, allowing for minimal resorption of the particulate graft. Moreover, the dense microarchitecture of cortical block grafts has been shown to play an important role in maintaining the bone volume long term.[4,13]

Fonseca and colleagues[29] studied the histological healing of cortico-cancellous block transplants in primates showing an irregular pattern of trabeculae still evident at 3 months with occasional detection of osteoclasts and osteoblasts. At 6 months, the transplant was fully incorporated into the recipient site, however, the lamellar pattern of newly formed bone was still immature. This light microscopy observations and pattern of healing are in accordance with the biopsy specimens of the present study.

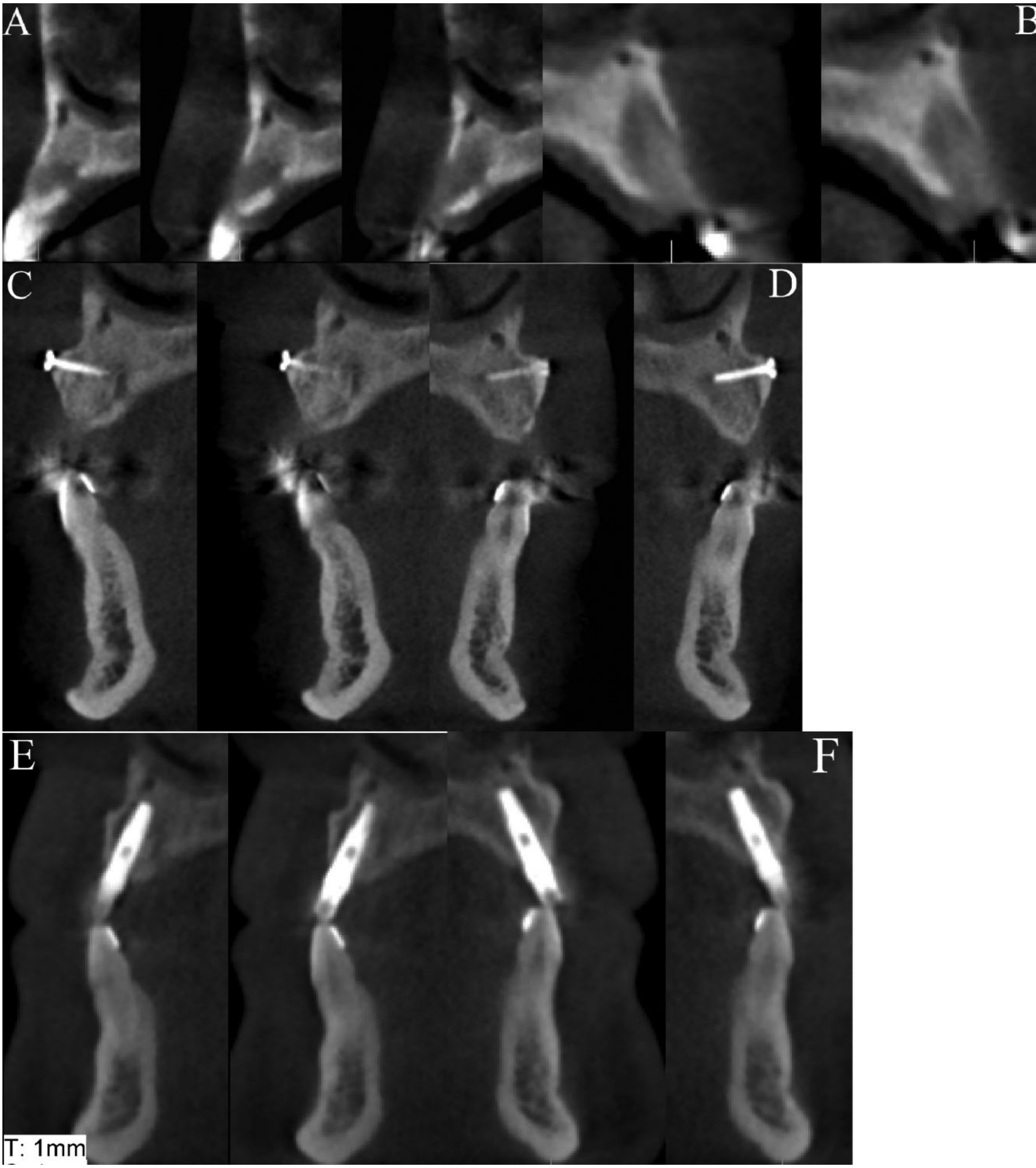

Figure 3 *A*, Pre-operative cross-sectional image of #7 area in patient 1 (Figure 1, A). Buccal wall is absent and palatal wall perforated. *B*, Pre-operative cross-sectional image of #10 area in patient 1 (from Figure 1, A). *C*, Post-operative cross-sectional image 5 months after augmentation #7 area (see *A*). *D*, Post-operative cross-sectional image 5 months after augmentation #10 area (see *B*). *E*, Post-operative cross-sectional image 26 months after augmentation #7 area (see *A*). *F*, Post-operative cross-sectional image 26 months after augmentation #10 area (see *B*).

A recent review paper found conflicting information on the role of bone decortication in enhancing outcomes for GBR. The authors suggested the need for clinical trials to elucidate the role of this variable in GBR procedures.[30] Cortical perforations at the recipient site may have enhanced the blood supply coming from the marrow spaces favoring the process of osteogenesis in the present study. Rapid vascularization of the

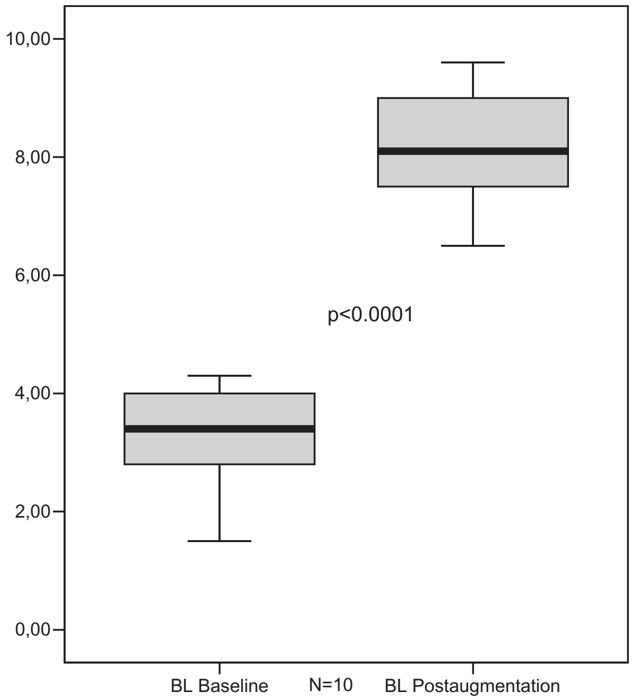

Figure 4 *A*, Box plot graphic depicting bucco-lingual width thickness of recipient site at baseline and post-augmentation ($p < .0001$).

transplant is paramount for successful neo-osteogenesis.[22] Cortical transplants could be penetrated by blood vessels in as little as 6 days and be fully revascularized in 1 to 2 months.[29,31] The cancellous transplant becomes revascularized by end-to-end vascular anastomosis. It would be plausible to speculate that cortical perforations could enhance phase 2 of the transplant healing process. Phase 2, or osteoinduction by osteoclastic secretion of promoter proteins, entails the release of bone morphogenetic proteins and osteogenin that will activate the transformation of pluripotent mesenchymal cells into osteoblasts.[20,29] Moreover, the normal cascade of physiologic healing events in response to injury might have favored the bone repair at the donor and recipient sites. This phenomenon was proposed by Frost[32] as a regional accelerated process of increased bone turnover in response to noxious stimuli. Further investigations are granted to evaluate the osseous repair potential of human critical size defects and assess the periosteum performance as compared with artificial membranes.

Flap management may also influence the degree of primary and collateral blood supply to underlying osseous grafts and ischemia could result from lack of adequate new angiogenesis.[33,34] In this regard, broad base mucoperiosteal flaps (Figure 1, A–C) may maintain better blood supply and undergo lesser trauma than small, one tooth wide, flaps. Some studies have suggested that thick biotype tissue promotes better blood supply to the underlying osseous structures affecting the early stages of wound healing.[35,36] A high volume of extracellular matrix and collagen as well as its increased vascularity would allow a surgical flap to withstand collapse and contraction. A more enhanced perfusion of oxygen could favor the elimination of toxic products during wound healing, enhancing growth factor chemotaxis. This entire process could promote a more desirable wound healing. Nonetheless, a recent human study has shown that the periodontal biotype has no influence on the long-term volume integrity of onlay grafts.[13]

Accurate diagnosis may be aided by the use of CT scans. Computerized tomography has been used as a non-destructive method to evaluate bone volume.[37–41] This technique was deemed highly accurate when measuring changes in bone stereology and micro-architecture in an animal model study.[37] There are multiple CT scan clinical applications, from diagnosis to treatment planning as well as assessment of regenerative therapy outcomes.[23,24,40,41] The tomographic evaluation at 35 months from the time of grafting validates the hypothesis that GBR with periosteal preservation and cortical perforations may have a positive effect on the healing and volume maintenance of transplanted autogenous bone long term. The above statement should be taken with caution due to the small sample size of the present study. Further prospective clinical trials with additional histological information are forthcoming.

CONCLUSIONS

Autogenous osseous transplants can predictably reconstruct function and esthetics in maxillary anterior severe critical size defects. Periosteal preservation appears to be a critical factor in maintaining long-term stable bone volume in transplanted bone grafts. Cortical perforations may enhance the transplant healing process of osteogenesis within the block and particulate graft by increasing revascularization and neo-angiogenesis from adjacent bone marrow spaces.

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None of the authors has any conflict of interest in this study.

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