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Hard tissue volume stability of guided bone regeneration during the healing stage in the anterior maxilla: A clinical and radiographic study

Xi Jiang DMD | Yu Zhang DMD | Ping Di MD | Ye Lin MD

Department of Oral Implantology, Peking University School and Hospital of Stomatology, Beijing, P.R. China

Correspondence
Ye Lin, Department of Oral Implantology, Peking University School and Hospital of Stomatology, No.22, Zhongguancun South Avenue, HaiDian District, Beijing, 100081, P.R. China.
Email: yorcklin@263.net

Abstract

Background: Guided bone regeneration (GBR) is currently the most widely used technique to reconstruct localized peri-implant bone defects.

Objectives: To evaluate hard tissue volume stability during the healing stage of GBR with particulate bone graft and resorbable collagen membrane.

Materials and methods: Twenty-eight patients who were missing a single maxillary incisor and required implant placement combined with GBR were randomly assigned to 2 groups: submerged (n = 14) and transmucosal (n = 14) healing groups. Cone-beam computed tomography (CBCT) was performed before, immediately after and 6 months post-surgery. The 3 sets of CBCT data were three-dimensionally reconstructed and superimposed. Horizontal hard tissue alterations at different vertical levels were recorded. The relative position and distances from the boundary line of the bony defect envelope to the outlines of the augmented ridge were determined immediately post-augmentation and 6 months after healing.

Results: Augmented ridge underwent horizontal volume reduction during the healing period. Vertical levels ($P = .000$) rather than healing strategies (submerged or transmucosal) ($P = .182$) had statistically significant impacts on the reduction width. The boundary line of the ridge defect envelope located within the bony profile immediately after surgery, but outside of the bony profile after 6 months.

Conclusions: GBR with resorbable membrane and particulate bovine bone would undergo horizontal volume reduction during the healing stage. New bone formation at the coronal site may only be predictable within the bony envelope.

KEYWORDS

alveolar bone regeneration, bone substitute, clinical study, cone-beam CT, instability, tissue pressure

1 | INTRODUCTION

Dental implant is currently the most common therapeutic strategy for the restoration of single missing teeth. However, traumatic, inflammatory, congenital reasons, and physiological ridge resorption after tooth loss often lead to unfavorable hard and soft tissue conditions in edentulous regions.[1] Augmentation procedures usually cannot be avoided. Furthermore, prosthetic driven implant placement requires precise and optimized three-dimensional positioning optimal for planned prosthetic restoration, which is often associated with peri-implant bone defects. In the esthetic zone, the reconstruction of sufficient bone volume around implant is a prerequisite for obtaining predictable long-term results and sound esthetic effect.[2]

Guided bone regeneration (GBR) with particulate deproteinized bovine bone mineral (DBBM) and covered with resorbable collagen membranes is currently the best documented and most widely

used method with which to augment peri-implant alveolar bone defects.[3,4] A large number of clinical evidence has revealed that the survival rates of dental implants placed simultaneously with GBR are similar to those of implants placed entirely into the native bone.[5–7] In the maxillary frontal area, a favorable esthetic outcome can be achieved with GBR of contour augmentation to reconstruct the facial bone wall supporting the soft tissue which is of esthetic concern.[8]

Despite these good clinical results of GBR, the major drawback of particulate bone grafting material and collagen membrane are their poor mechanical properties, which is a key issue in hard tissue regeneration, and their low resistance to tissue collapse.[9,10] Compressive forces may cause membrane collapse and displacement of parts of the grafting materials, thereby compromising the regeneration results.[11–13] This may occur at time of suturing of the soft tissue flap[14] or during the healing stage of GBR.[15,16]

Limited evidence is available regarding the hard tissue volume stability of sites that are augmented by GBR, especially at the buccal-coronal region in the anterior maxilla area where the tissue contour is esthetically significant. Well-designed clinical studies on the hard tissue alteration of the augmented region during the healing stage of GBR are lacking.

It has been reported that submerged and transmucosal healing of implants with simultaneous GBR are both successful clinical procedures. Similar predictable results have been achieved with respect to defect repair, marginal bone resorption and peri-implant soft tissue conditions.[17–19] However, to the authors' knowledge, whether the different healing patterns affect hard tissue volume stability during the healing stage of GBR has not yet been described.

The primary aim of this study was to evaluate the volume stability of hard tissue augmented with particulate bone graft (DBBM) and collagen membrane during the healing stage of GBR, in transmucosal (test) and submerged (control) groups, utilizing the three-dimensional virtual reconstruction and superimposition of cone-beam computed tomography (CBCT) data.

2 | MATERIALS AND METHODS

2.1 | Patient enrollment protocol

This study was carried out from November 2015 to April 2017 in the Department of Oral Implantology at Peking University School and Hospital of Stomatology. Subjects were selected from patients who were missing a maxillary central or lateral incisor for at least 6 months, and were seeking for single implant restoration. Twenty-eight patients (15 males and 13 females), ranging in age from 20 to 52 years (mean 36.85 ± 10.20 years) were enrolled in the present study. The inclusion and exclusion criteria were as follows:

Inclusion criteria:

1. At least 18 years of age
2. Single incisor missing in the maxilla (12–22) for at least 6 months
3. Healthy periodontal conditions of the neighboring teeth
4. Implant placement with simultaneous GBR is indicated
5. Willing to participate in this clinical study.

Exclusion criteria:

1. History of periodontal disease
2. Uncontrolled diabetes
3. Severe bone defect such that staged bone augmentation (BA) is needed.
4. Other systemic diseases or general health conditions that would contraindicate implant surgery and BA procedures

The study was conducted in accordance with the Helsinki Declaration of 1975 as revised in 2000, and the study protocol was approved by the local ethical committee (Institutional Review Board of Peking University School and Hospital of Stomatology, Approval Number: PKUSSIRB-201523074). Patients who met these criteria were informed about the study and asked to sign an informed consent. The patients were randomly assigned to test (transmucosal healing) and control (submerged healing) groups using sealed envelopes that were opened at the time of surgery. This study was supported by the "National Key Research and Develop Plan of China" (grant No. 2016YFC1102705).

2.2 | Surgical procedure

Prior to the surgery, prophylactic antibiotics (cefuroxime 0.25 g) were administered 1 hour before surgery. The patients were asked to rinse with a 0.2% chlorhexidine solution for 1 minute. The surgical area was anesthetized with Primacaine Adrenaline (Produits Dentaires Pierre Rolland, Acteon Pharma Division, Merignac, France) by local infiltration. Crestal incision was started at the edentulous area, and was followed by intrasulcular incisions of the neighboring teeth. A distal vertical releasing incision was then applied to facilitate the reflection of a triangular full thickness flap allowing complete visualization of the defect area and surrounding bone. After exposure of the alveolar ridge, sequential osteotomy and implant insertion were performed according to the manufacturer's guidelines (Ankylos, Dentsply implants, Mannheim, Germany). The implant shoulder was placed approximately 5 mm below the gingival margin of the neighboring teeth and 1–2 mm below the alveolar ridge according to the manufacturer's instructions. The bony defect around the implant was augmented by the GBR technique using DBBM (Bio-Oss; Geistlich Pharma AG, Wolhusen, Switzerland) and was covered with a resorbable collagen membrane (Bio-Gide, Geistlich Pharma AG, Wolhusen, Switzerland). In case of implant thread exposure (bone dehiscence or fenestration), autogenous bone chips collected by scraper from the surrounding bone were first used to cover the implant surface. At least 2 titanium fixation pins were used to stabilize the collagen membrane in the apical area, and additional pins were added at the coronal region if possible. Then, a periosteal incision apical to the full thickness flap was performed to facilitate tension-free soft tissue adaptation of the surgical area. For the control group, submerged healing was applied with primary soft tissue closure. In the test group, a healing abutment was connected to

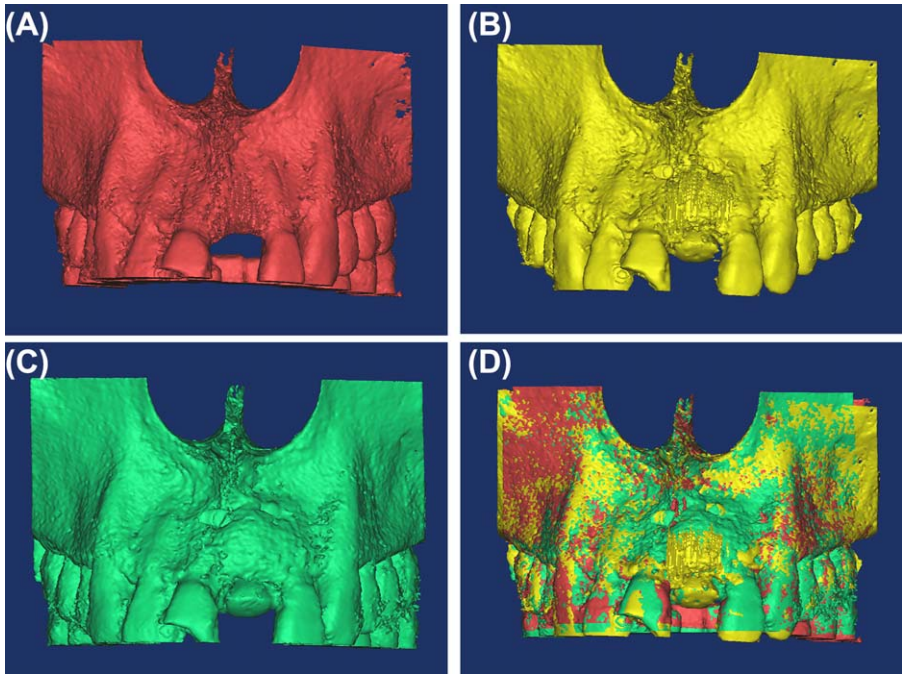

FIGURE 1 Three-dimensional virtual reconstruction and superimposition of the 3 sets of CBCT data. A, Before surgery, B, Immediate post-surgery, and C, after 6 months of healing. D, Superimposition of the 3 virtual models

the implant to facilitate transmucosal healing. The wounds were closed with horizontal mattress and interrupted 4-0 resorbable sutures (Vicryl Rapide, Ethicon, Sao Paulo, Brazil). All the surgical interventions were performed by the same surgeon (Dr Jiang).

All patients were prescribed post-surgical medications, including antibiotics (250 mg cefuroxime twice daily for 1 week, and 500 mg tinidazole once daily for 5 days), analgesics (300 mg ibuprofen, to be taken as required), and 0.2% chlorhexidine as a mouth rinse (3 times daily for 2 weeks). Dexamethasone (0.75 mg per day) was administered for 2 days to relieve post-surgical edema. The post-surgery healing process was monitored at recall visits, 1 week, 1 month, and 6 months post-surgery, the latter time point was set as the end point of the study. Subjects in the control group (submerged healing) had the reentry surgery at this time, and the test group (transmucosal healing) went to the prosthetic phase.

2.3 | Radiographic evaluation

All the patients underwent CBCT scanning before surgery, immediately after implant placement combined with GBR procedure, and 6 months after surgery using the same projection condition (Planmeca ProMax 3D, Planmeca Oy, Helsinki, Finland). The technique parameters were as follow: FOV diameter, 10 cm; FOV height, 5.6 cm; acceleration voltage, 90 KV; beam currency, 8.0 mA; and voxel size, 0.2 mm.

The 3 sets of Dicom data (before, immediately after, and 6 months post-surgery) were output and transferred to volumetric imaging software (Mimics 15.0, Materialise, Leuven, Belgium), in which virtual models of the upper jaw were three-dimensionally reconstructed and superimposed (Figure 1A-D). In the virtual pre-surgery jaw, a boundary line, connecting the most labially prominent point of the adjacent alveolar ridge at the vertical level of the bone zenith of neighboring teeth, was drawn and integrated into the virtual model before superimposition. This line defined the buccal-coronal boundary of the bony envelope (Figure 2A-C).

After superimposition of the 3 reconstructed virtual jaws, a cross-sectional plane that along the implant long axis and perpendicular to the maxillary panoramic curve was used to evaluate the horizontal volume alteration during the healing stage of GBR. The profiles of the "hard tissue" (before surgery, immediately after augmentation and after 6 months of healing) were outlined (Figure 3A), and the following landmarks were identified:

The long axis of the placed implant was drawn as a reference line "r." Four lines perpendicular to line "r" at levels of 0, 2, 4, and 6 mm below the implant platform were buccally intersected with the 3 bony profiles. The following dimensions were measured using ImageJ software (ImageJ, version 1.47, NIH, Bethesda, Maryland) (Figure 3B):

1. The linear dimensions of "buccal bone" changes between different time points were recorded:
   a Bone augmentation (BA): the linear hard tissue dimension increase immediately post-surgery compared with the initial status.
   b Bone reduction (BR): the linear hard tissue dimension decrease at 6 months after healing compared with the value immediately post-surgery.
   c New bone formation (NBF): the linear dimension of regenerated bone, that is, after 6-month of healing compared with the initial status.

Each of the those 3 "buccal bone" alteration parameters was measured at the 4-aforementioned different vertical levels.

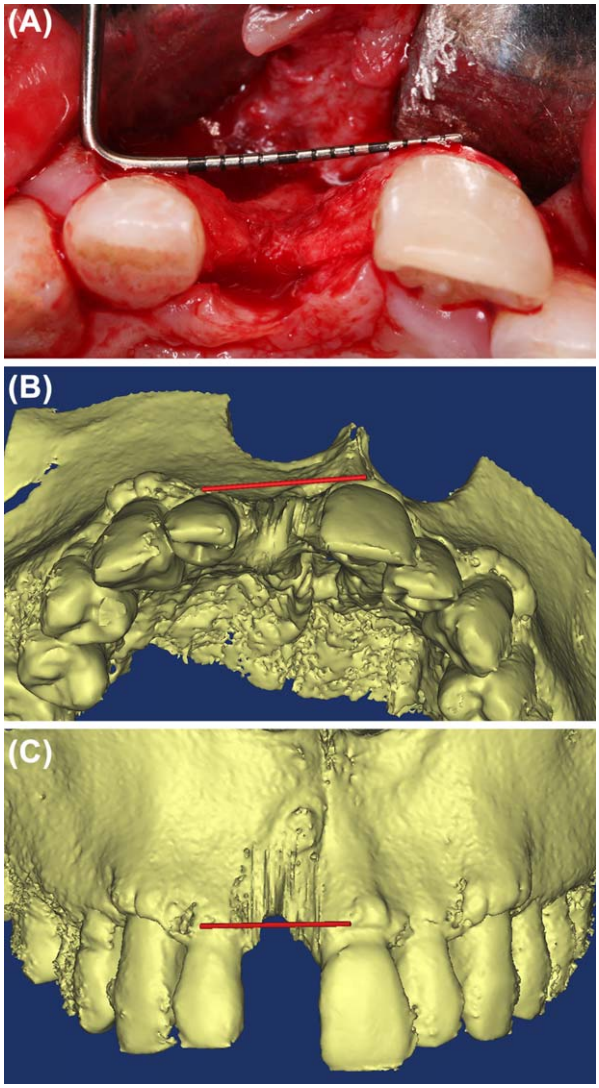

FIGURE 2 A, The bony envelope of the defect site. The probe connecting the most labially prominent point of the adjacent alveolar ridge at the level of the bone zenith of neighboring teeth, defined the boundary line of the bony envelope. B, Virtual simulation of this boundary line (red line), occlusal view. C, Frontal view of the boundary line (red line) in relation to the jaw bone

2. The alveolar ridge width at the most coronal level were measured at different time points: RW_{bef} (ridge width before surgery), RW_{imm} (ridge width immediately post-surgery), RW_{aft} (ridge width after 6-months of healing).
3. The distances from the boundary line, which appeared as a point in the cross-sectional image, to the hard tissue outline of the augmented ridge (BTA) immediately post-surgery and the newly formed bone (BTN) 6 months after healing (the distance from the point to the curve). If the point was located within the bony outline, the distance was recorded as a negative value.

2.4 | Statistical evaluation

All measurements were recorded in an Excel 2013 spreadsheet (Microsoft Corporation, Redmond, Washington), and transferred to SPSS version 13.0 (SPSS Inc, Chicago, Illinois) for statistical analysis. The measurements at the 3-time points (before, immediately after, and 6 months later) and the 4 different vertical levels (0, 2, 4, and 6 mm apically) were compared. If normally distributed data with approximately equal variances were present, parametric methods (Student's *t*-test or a multi-factor analysis of variance) were used. Otherwise, nonparametric tests (Mann-Whitney *U* test) were used. For all tests, a P value $< .05$ was considered significant.

3 | RESULTS

All the 28 initially recruited patients completed the study. Fourteen subjects were randomly assigned to the control group (6 females and 8 males, mean age 37.50 years $\pm$ 9.29), and 14 patients were assigned to the test group (7 females and 7 males, mean age 36.21 years $\pm$ 11.00). Uneventful healing was achieved in all subjects, no signs of soft tissue dehiscence, secondary healing or infection were detected during the 6-month follow-up period. All the implants were successfully integrated, and the grafting material appeared to have healed and fused with the native alveolar bone based on the CBCT scans 6 months post-surgery.

No statistically significant differences were found between the test and control groups regarding the horizontal bone alteration parameters, namely, BA, BR, and NBF (Table 1). However, regarding the 4 vertical levels, the coronal region showed statistically significantly more BR ($P = .000$) and less NBF ($P = .005$) than the apical region. No statistically significant differences were found for the value of initial (BA) ($P = .465$) (Figure 4).

For the test and control group, alveolar ridge widths before surgery (RW_{bef}) were 4.73 $\pm$ 1.02 mm and 4.95 $\pm$ 1.20 mm, respectively; the width immediately after surgery (RW_{imm}) were 8.25 $\pm$ 0.82 mm and 8.34 $\pm$ 0.82 mm, respectively; and the width 6 months post-surgery (RW_{aft}) were 6.88 $\pm$ 0.86 mm and 6.92 $\pm$ 0.74 mm, respectively. No statistically significant differences were found between the groups (Table 2).

Initially, for the test and control groups, the distances from the boundary line of the bony envelope to the outline of immediately augmented ridge (BTA) were -0.82 ± 0.68 mm and -0.67 ± 0.60 mm, respectively, and the distances to the surface of the newly formed bone (BTN) were 0.16 $\pm$ 0.33 mm and 0.24 $\pm$ 0.46 mm, respectively. No statistically significant differences were found between the 2 groups ($P = .616$ and $P = .496$). The BTA measurements were statistically significant less than zero ($P = .000$), on the contrary, BTN measurement were statistically significant greater than zero ($P = .012$), indicating that the boundary line located within the outline of the augmented material immediate post-surgery and out of the profile of the regenerated bone 6 months after healing (Figure 5).

4 | DISCUSSION

Tooth loss often results in an unfavorable anatomic condition with tissue deficiency and esthetic compromise. GBR is used not only to reconstruct the peri-implant bone tissue, thus facilitating the placement

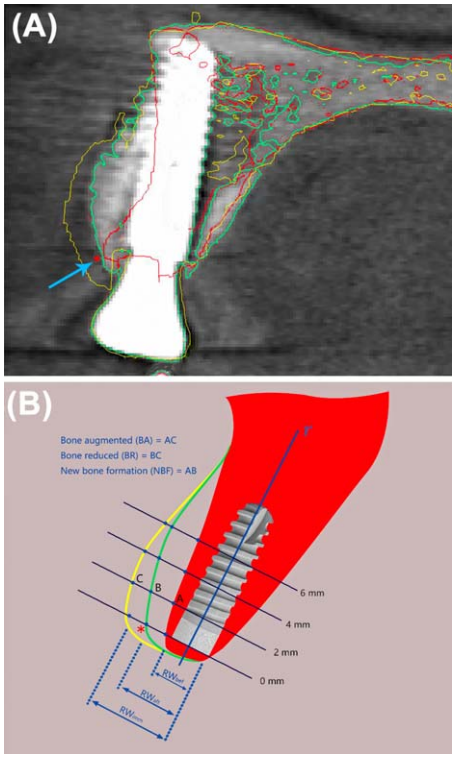

FIGURE 3 A, The cross-sectional plane along the long axis of the implant was used to evaluate horizontal bone alterations. Red line: bony profile before surgery; yellow line: bony profile immediately post-augmentation; green line: bony profile after 6 months of healing. Note that the boundary line appears as a point (blue array) located between the outlines of immediately post-surgery and after 6 months of healing. B, The Schematic drawing illustrating the landmarks used for measurements. Red area: alveolar ridge before surgery; yellow line: bony profile immediately post-augmentation; green outline: bony profile after 6 months of healing. The long axis of the placed implant is drawn as a reference line "r". Four lines perpendicular to line "r" at different vertical levels were buccally intersected with the 3 bony profiles (eg, with the 2-mm line at points A, B, and C; bone augmentation, *BA* = AC; bone reduction, *BR* = BC; new bone formation, *NBF* = AB). The red star indicates the boundary line

of dental implants in the prosthetically correct position, but also to augment the buccal contour of the implant site and achieve sufficient soft tissue support in the esthetic zone.[20]

Clinical studies had demonstrated that submerged and transmucosal surgical technique with GBR yield similar good results with regard to degree of defect repair, implant survival, marginal bone levels, peri-implant soft tissue parameters and patient satisfaction.[19,21,22] The results of the present study further revealed that submerged and transmucosal healing have similar effects on hard tissue volume stability during the healing process as evaluated by CBCT.

One principle of GBR is to apply the tissue exclusive membranes. Compared with nonresorbable membranes, resorbable membranes have lower risks of surgical complications such as premature exposure and infection[23]; however, resorbable membranes have been criticized for their unfavorable mechanical properties and volume instability due to their soft consistency and low resistance to pressure from the

TABLE 1 Bony contour alterations at 4 different vertical levels in the test and control groups

Vertical levels	0 mm			2 mm			4 mm			6 mm		
Groups	BA	BR	NBF	BA	BR	NBF	BA	BR	NBF	BA	BR	NBF
	Mean ± SD (mm)											
Test	3.42 ± 1.17	1.63 ± 1.02	1.79 ± 1.30	3.69 ± 1.09	1.55 ± 1.05	2.14 ± 1.38	3.90 ± 0.97	1.25 ± 0.75	2.65 ± 1.23	3.48 ± 0.77	0.91 ± 0.64	2.58 ± 1.13
Control	3.43 ± 0.85	1.82 ± 0.92	1.61 ± 1.07	3.53 ± 0.94	1.29 ± 0.89	2.24 ± 1.20	3.67 ± 1.26	0.83 ± 0.74	2.84 ± 1.27	3.31 ± 1.10	0.54 ± 0.71	2.77 ± 0.98
P value	.968	.600	.693	.67	.490	.851	.604	.159	.694	.638	.169	.633

BA, bone augmentation immediately post-surgery; BR, bone reduction after 6 months of healing; NBF, new bone formation after 6 months of healing.

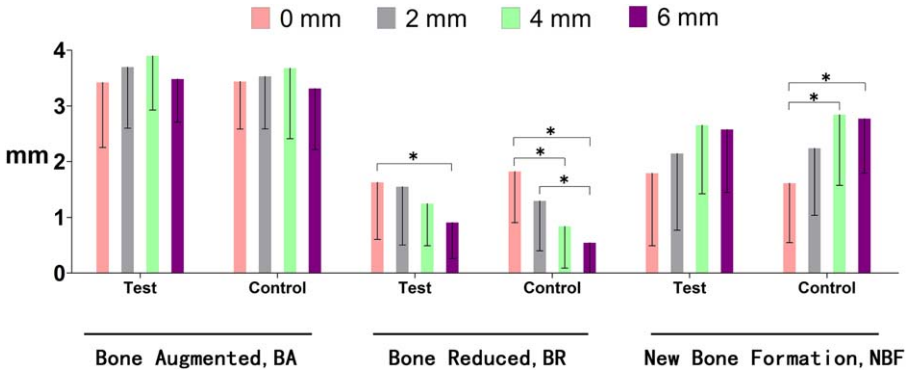

FIGURE 4 Horizontal bone alteration parameters BA, BR, and NBF at different vertical levels in the test and control groups. The coronal region shows significantly more bone reduction and less new bone formation than the apical region. *$P < .05$

surrounding tissue, which may result in membrane collapse and the compromise of NBF due to the loss of tissue volume during the healing stage of GBR procedure.[10,11] Therefore, osteoconductive bone graft materials are considered necessary to mechanically support the membranes and to avoid collapse of the resorbable membranes. However, particulate graft materials combined with resorbable membranes still cannot stably maintain the original grafted area. In an animal study, standardized buccal dehiscence defects around implants were surgically created. The defects were then filled with particulate bone graft material and covered with collagen membranes. After 9 weeks, histological findings revealed the dislocation of the membranes and the bone graft granules in the apical direction.[10]

The dimensional stability of GBR during the healing stage with the use of particulate graft materials and resorbable membranes was investigated in another animal study. The ridge width immediately after GBR procedure was used as the reference values, as in the present clinical study, to assess volume alteration at the grafting site during the healing period. Histologically, a continuous reduction in dimensions was detected in most augmented alveolar ridges, and the most pronounced reduction was found during the first 4 weeks post-surgery.[16] To the best of the authors' knowledge, no previous clinical studies evaluated the volume stability of bone substitute during the healing stage of GBR. It is difficult to compare the results of these animal studies with those of the present clinical study. However, the general trends of volume alteration during the healing stage of GBR seem to be the same. GBR with resorbable membranes and particulate bone substitutes exhibited volume instability, which would result in the shrinkage of grafted area and the alteration the ridge contour. The coronal region may be the most vulnerable site, where the most obvious ridge width reduction occurred.

TABLE 2 Buccal-palatal ridge width before surgery (RW_{bef}), immediately post-augmentation (RW_{imm}) and after 6 months of healing (RW_{aft}) in the test and control groups

Group	RW_{bef}	RW_{imm}	RW_{aft}
Test	4.73 ± 1.02 mm	8.25 ± 0.82 mm	6.88 ± 0.86 mm
Control	4.95 ± 1.20 mm	8.34 ± 0.82 mm	6.92 ± 0.74 mm
P value	.60	.77	.89

For ethical reasons, no additional CBCT scans were obtained during the healing period, therefore, we cannot evaluate the stage at which the graft site had the most pronounced hard tissue volume change. The augmented area was presumed to be most vulnerable in the initial healing stage, that is, immediately post-surgery, and exhibited a decrease in volume. As the healing process went on, the blood clot and network of fibrin may contribute to the stability of the particulate bone graft material. However, the collagen membrane was resorbed due to biodegradation within 4 weeks,[24] which may jeopardize the stability of the augmented area.

The reasons for the contour reduction of the augmented site by GBR have rarely been investigated. Due to the slow resorption of particulate bovine bone and the rapid alteration of tissue volume, mechanical rather than biological factors may play a more important role. In an animal study, Strietzel mentioned that pressure from the overlying soft

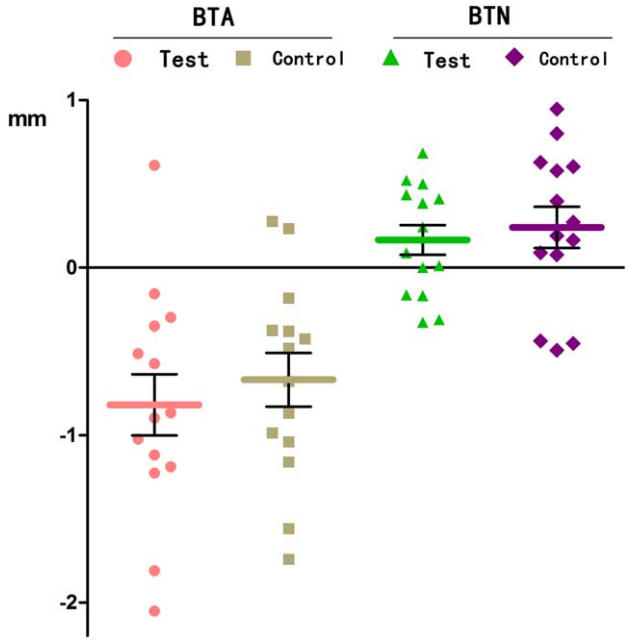

FIGURE 5 The distance from the boundary line of the bony envelope to the hard tissue profile of immediately post-augmentation (BTA) and after 6 months of healing (BTN) in the test and control groups

tissue pushed the resorbable membrane into the bone defect, resulting in the formation of fibrous connective tissue plugs instead of new bone.[11] In another animal study using rabbit calvarium, the authors suggested that even the calvarium is considered as free of pressure and movement, but some typical behaviors and gestures of the animal can cause an undesirable effect on the stability of the grafted regions.[25] A recent in vitro study based on CBCT, revealed that soft tissue wound closure and suturing resulted in an evident grafting material displacement and partial collapse of the collagen membrane. The coronal region of the grafting site (implant shoulder) had the most pronounced volume instability and the greatest tendency to collapse into the previously grafted portion. The apical portion exhibited less collapse of the membranes.[14] The use of fixation pins and block grafts can significantly improve the horizontal volume stability of the augmented region during wound closure.[26]

In a clinical study on ridge preservation, Jiang and colleagues fixed a rigid micro-titanium stent onto the facial bone wall of extraction socket serving as pressure bearing device. They found that, the middle portion of the micro-titanium stent, which was overlaid on the coronal buccal bone of the extraction socket, underwent deformation and migrated palatally during the healing period.[27] This study provided evidence of the existence of pressure from the facial soft tissue and showed that if the pressure is properly managed (counteracted), better tissue stability can be achieved and more bone volume preservation (87.61% vs 55.09%) can be expected.

The results of horizontal hard tissue reduction of GBR procedure in the present study may also be explained by the soft tissue pressure applied from the labial side. It is reasonable to assume that labial soft tissue, such as the upper lip, needs support from the tooth and alveolar ridge. Meanwhile, the labial soft tissue obviously places pressure on the underlying hard tissue. GBR was performed on the buccal side of the residual ridge using particulate bovine bone and collagen membrane, which have low stability even when using fixation pins. Furthermore, the buccal-coronal region, which always has the most prominent shape after augmentation procedure against the soft tissue of the lip, may suffer a higher soft tissue pressure, resulting in subsequent grafting material dislocation during the healing period and comprised NBF at the coronal level.

To compensate the volume reduction during the healing stage of GBR, over-augmentation has been recommended by some clinicians.[22] In our study, following this protocol, the defect sites were always over-grafted by placing more DBBM beyond the bony envelope, as confirmed by CBCT analysis, that is, the boundary line was located within the outline of grafting material immediately post-surgery, resulting in negative BTA values. However, after 6 months of healing, the bony profile of the regenerated bone showed contour shrinkage, which resulted in the boundary line being located outside (in most cases) but close to the hard tissue outline, regardless of how buccal-coronally the over-augmentation was in the initial stage. The boundary line, which defined the bony envelope of the defect side, seemed able to predict the buccal-coronal bony outline after 6 months of healing after GBR procedure. In other words, at the buccal-coronal site, GBR with bovine bone particle and collagen membrane may only able to augment and guarantee NBF within the bony envelope in the single-tooth edentulous ridge of maxillary anterior region. Based on this result, we may need to reconsider whether over-augmentation can benefit more hard tissue regeneration and better esthetic results. In addition, to the authors' knowledge, no solid clinical evidence had proven the advantages of the over-grafting procedure.

The results of this investigation should be interpreted with caution due to the small number of subjects and the short follow-up time. Although all implants were placed by 1 surgeon, consistency in insertion depth and angulation cannot be guaranteed between subjects due to the free hand nature of the surgery, which may influence the CBCT measurements. Regenerated hard tissue, determined by radiographic scans, may not be the true new bone in histological sense. However, this might be the first clinical study to report the volume stability of GBR with particulate bone graft and collagen membrane during the healing phase. The results also implied that the coronal boundary of the bony envelope may be a predictor of how buccal-coronally we can regenerate new bone with this technique.

5 | CONCLUSIONS

1. GBR with resorbable collagen membrane and particulate bovine bone would undergo some horizontal volume reduction during the healing stage. Greater deduction was expected at the coronal region. The use of different implant healing strategies (transmucosal or submerged) did not make significant differences.
2. In the coronal region, NBF may be predictably expected only within the bony envelope of the defect side, although further studies are needed to confirm this result.

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CONFLICT OF INTEREST

The authors report no conflicts of interest related to this study.

ORCID

Xi Jiang DMD http://orcid.org/0000-0001-5811-1780

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