Volumetric Changes Following Lateral Guided Bone Regeneration

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Resorbable membranes are well described and employed for horizontal guided bone regeneration (GBR). However, the currently available literature does not provide information on the bone volumetric changes during the healing that follows GBR procedures and dental implant placement. Therefore, the aim of this pilot study was to initially analyze the volumetric bone changes after treating pristine edentulous mandibular defects with lateral GBR using freeze-dried bone allograft (FDBA) and collagen resorbable membrane. Six patients were selected for the analysis. Clinical changes in bone volume before and after GBR were measured. In addition, digital volumetric analysis of the augmented ridges was performed preoperatively, as well as 4 and 6 months after the GBR procedure. At the time of dental implant placement, bone cores were collected during the osteotomy for histologic analysis. Data on volume changes showed a mean of 297.5 ± 134 mm³ augmented bone volume at 4 months with 5% ± 3.78% resorption from 4 to ≥ 6 months. Histologic bone core analysis showed 44.9% ± 5.1% mineralization in the area of augmentation. Within the limitations of this pilot study, resorbable membranes exhibited reliability for GBR in intercalated mandibular defects, providing sufficient bone volume gain at ≥ 6 months for implant stabilization and limited resorption during graft healing. Int J Oral Maxillofac Implants 2020;35:e77–e85. doi: 10.11607/jomi.7524

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Increased use of dental implants for treating partially or completely edentulous patients has emphasized the need for augmenting alveolar ridges via guided bone regeneration (GBR) in order to enhance optimal implant placement and prosthetic treatment. The natural reduction of especially the horizontal dimension of jawbone following tooth extraction results in dimensional deficiencies that frequently prevent or complicate ideal implant placement.1,2 Indeed, Tan et al2 detected horizontal reduction of 32% and 29% to 63% at 3 and 6 to 7 months postextraction, respectively. The GBR procedure, by means of particulate bone grafts and membranes, has been shown to be a predictable way to regenerate bone. There is strong clinical and histologic evidence that GBR is an effective and reliable technique in bone augmentation of ridge deficiencies.3,4

Increasingly, implant positioning and placement is dictated by restorative needs. This contrasts with the former concept of placing implants in sites with favorable anatomy and bone quality, although this at times challenges the design of the future prosthesis. It is in this context that GBR can be employed to overcome lack of horizontal bone dimension and thereby achieve optimal implant positioning followed by improved function, esthetics, or prosthetic restoration of the edentulous sites.5,6

Several factors affect the success and predictability of lateral GBR, from defect morphology7 and biologic principles8 to the techniques3 and biomaterials employed.9 Membranes used for GBR require some basic characteristics, including biocompatibility, membrane stability, duration of barrier function, access of bone and bone-marrow–derived cells to the area of regeneration, blood fill of the space, and prevention of soft tissue dehiscence.9 Membrane type plays an important role, since it determines the space needed for osteogenic cells to repopulate for bone formation.10 Initially, nonresorbable membranes were considered the gold standard for bone augmentation procedures.11–14 These membranes benefit from resisting
breakdown by host tissues or microbes and their ability to maintain adequate space for bone regeneration. Maintaining space allows for undisturbed bone matrix deposition and mineralization and leads to more favorable clinical outcomes compared with resorbable materials under optimal conditions. However, membrane exposure is a rather frequent postoperative complication of both resorbable and nonresorbable membranes that may significantly affect the level of clinical success. It has been reported that the amount of bone formation is greater in patients where there has been no membrane exposure compared with situations of membrane exposure.

The introduction of resorbable membranes has overcome the drawbacks of nonresorbable membranes regarding surgical morbidity, higher risk of tissue dehiscence, technique sensitivity, and need for a second surgical procedure for membrane removal. However, it is a shortcoming of resorbable membranes that they have less space-making capacity, shorter duration of barrier function, and a degradation process that varies according to biologic structure and physical properties. In terms of defect architecture, the type of edentulous bone defect varies among authors, and the potential for regeneration of bone defects depends not only on biomaterials and surgical technique, but also on its dimension and morphology. The heterogeneity of the defect could affect the final outcome since not all horizontal defects have the same regenerative potential. Garaicoa et al showed that the use of membranes and the horizontal bone ridge concavity plays a role in influencing GBR outcomes. It was reported that if crest angulation was higher than 150 degrees, the bone gain was significantly lower. Generally speaking, minor to moderate horizontal defects can be treated with resorbable membrane barriers, while severe horizontal defects or those with a vertical component may require a nonresorbable membrane. However, the multitude of studies regarding GBR seem to lack data on 3D mandibular defect morphology that may shed some light on graft behavior in time.

To the best of the authors’ knowledge, no studies have yet reported 3D volumetric changes between GBR procedures and implant placement including the intermediate interval. The primary aim of this pilot study was to provide a quantitative analysis of bone volume changes using digital technology, while the secondary aim was a qualitative histologic measure of the bone healing and mineral content in the augmented areas after GBR procedures.

**MATERIALS AND METHODS**

**Patient Selection**

This study included patients of a larger study who exhibited ridge deficiency and were in need of lateral ridge augmentation prior to dental implant placement. The protocol was approved by Tufts Health Sciences Institutional Review Board (IRB no. 11279).

Sixteen subjects were recruited based on the following inclusion criteria: ASA status I or II, at least 18 years of age, nonsmoker, and at least one pristine site with horizontal ridge deformity on a partially edentulous mandible. Specifically, the site should represent a residual horizontal ridge (width ≤ 6 mm) corresponding to one or two posterior adjacent missing teeth in an area contained by anterior and posterior teeth (Kennedy Class III).

Exclusion criteria included pregnant patients and patients with medical contraindications to the dental procedure and implant surgery, such as uncontrolled or poorly controlled diabetes, severe osteoporosis, treatment with immunosuppressant drugs, chemotherapy, chronic corticosteroids, previous or current head and neck radiation therapy, long-term steroid use, or a history of IV bisphosphonate therapy. The study outline and visits are listed in Fig 1.

**Clinical Measurements**

To assess the size of edentulous areas, the following measurements were taken. The mesiodistal edentulous span was measured with digital software (Meshmixer,}
Autodesk 2011) from the root distal margin of the mesial frontier tooth to the root mesial margin of the distal frontier tooth. The residual bone width was calculated as a mean between three points equally spaced mesiodistally on the edentulous areas by means of CBCT radiographs, when available, or clinically with a caliper upon flap reflection.

A baseline (preoperative T0) polyvinyl siloxane (PVS) impression of the edentulous area was taken and immediately poured with stone to generate a stone cast (Type IV). The model was scanned and digitalized with a 3D lab scanner (Activity 880, Smart Optics, Sensortechnik). On the same stone model, a customized resin stent was created (Fig 2).

Each stent contained two or three access holes depending on the extent of the edentulous area. These reference holes were prepared perpendicularly, 45 degrees and 0 degrees above the edentulous crest. The stent was used to measure the distance between the reference holes and the surface of the cast in the edentulous areas. It was decided not to measure it in the mouth of the patient since the probe could have compressed soft tissue and provided unreliable measurements.

**Surgical Procedure**

Each subject was treated with the GBR procedure according to standard principles by using freeze-dried bone allograft (FDBA; MinerOss BioHorizons) and resorbable membrane (RCM6, ACE Surgical Supply). If the subject had two qualifying sites, the one site used was selected randomly. After local anesthesia with lidocaine HCl 2% and epinephrine 1:100,000 was achieved, a full-thickness midcrestal incision was outlined in the keratinized gingiva with a surgical blade (no. 15). Mesially to the edentulous area, a sulcular incision included one or two teeth depending on the amount of access needed. The distal extension of the crestal incision continued with a sulcular approach and ended with a buccal vertical releasing incision past the mucogingival junction. If the surgical access was still limited, a mesiobuccal vertical releasing incision was achieved at least one tooth away, preferably two teeth away, from the surgical site.

After the primary incisions, periosteal elevators were used to reflect a full-thickness flap beyond the mucogingival junction and at least 5 mm beyond the bone defect. The lingual flap was elevated from the crest in order to decrease its tension. Decortications of the alveolar ridge were applied by means of a 0.14-mm round surgical drill mounted on a high-speed handpiece.

FDBA grafting material was placed on the defect to an extent that would take into consideration its resorption during healing. The membrane was placed following the manufacturer’s instructions and was immobilized with 2-mm titanium tacks on the mesiobuccal, distobuccal, apical portion in the central part of the defect and linguually. Primary passive closure was accomplished using periosteal release and conventional suturing procedures (Fig 3). After surgery, the patients were provided with verbal and written postoperative instructions and prescriptions for postoperative care (ibuprofen 800 mg three times a day for 3 days, then as needed, amoxicillin 500 mg three times a day for 7 days, ice pack, chlorhexidine 0.12% mouthwash). Subjects were followed and seen for regular surgical follow-up visits (including 1-week and 2-week postoperative visits).

**Implant Placement**

After ≥ 6 months of healing, implants were placed in the edentulous areas. After achieving adequate local anesthesia, a full-thickness flap was elevated. The customized acrylic stent was used to measure the soft tissue thickness in the same location as preoperatively. A trephine bur was used to obtain a standard-size (8 × 3 mm) bone core from the future implant sites for...
histomorphometric analysis. Before core collection, a dye was used to mark the mesial and coronal portion of the core. Subsequently, the osteotomy was completed in the same location of the core harvesting, and the implant was inserted according to the restorative treatment plan (Figs 4 and 5).

All implants (Institut Straumann and Nobel Biocare) placed registered torque values > 30 Ncm and primary stability. None of the implants required additional bone grafting, as all implants showed ≥ 2 mm of buccal bone thickness, measured linearly with a periodontal probe.

The labeled bone core specimens were immediately placed in a fixation solution containing 4% paraformaldehyde in phosphate-buffered saline (0.15 M NaCl, 0.05 M Na₂PO₄, pH 7.4) for 24 hours at 4°C or for 12 hours at room temperature. The specimens were then dehydrated in graded ethanol to 70%. Two blinded collaborators (D.Z.) supervised the preparation and handling of the specimens.

Volume Measurements
Stone cast models were obtained at baseline (T0), 4 months after the GBR procedure (T1), and at ≥ 6 months after the GBR procedure (T2) and then digitally scanned with a 3D desk scanner (Activity 880, Smart Optics). The resulting STL files were processed with dedicated software, and the volume was calculated (Meshmixer, Autodesk 2011; Fig 6). Two PVS impressions per site were taken in order to compensate for potential errors of impression taking and development.

Soft tissue linear measurements were obtained by using the same customized stent as for T0 and the stone model at ≥ 6 months (T2).

Histologic Analysis
Core biopsy specimens were embedded in blocks of methacrylate. The blocks were serially sectioned parallel to the longitudinal axis of the bone core up to the center of the bone core with a diamond saw microtome (1600, Leica); then, the remaining block was placed in a Reichert-Jung Autocut 1150 microtome (Nussloch) to obtain a series of 5-µm sections. The sections were

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**Fig 3**  (a) Preoperative site to be treated with GBR. (b) Full-thickness flap elevation to expose area to be treated. (c) After envelope opening and selection of membrane, decortications were applied as well as bone grafting to anticipate prosthetic dental implant placement location. (d) Resorbable membrane in place after stabilization with tacks. (e) Primary intention wound closure by passive flap release.

**Fig 4** Clinical sequence of the study surgical procedures after healing of GBR procedure. (a) Postoperative healing at > 6 months. (b) Full-thickness flap and bone core harvesting. (c) Trephine bur with core. (d) Flap closure after implant and healing abutment insertion.
Data from patients who completed the study were expressed as counts and percentages for categorical data and means and standard deviations for continuous data. Two sets of PVS impressions were poured and scanned. The impression that best reproduced the intraoral structures was selected for analysis. The examiners who analyzed and measured digital and histologic data were blinded to the procedure and group sample origin.

**RESULTS**

Six subjects were enrolled in the study. The mean age of the participants was 50.7 ± 15.5 years with a male-to-female ratio of 2:5. Six subjects completed the study and received seven dental implants in the augmented edentulous areas, with no additional graft needed. One
A case was excluded from analysis due to major membrane complications and graft failure. Only one subject experienced a minor complication. A circular soft tissue dehiscence on the edentulous crest determined a 2 × 2-mm membrane exposure that did not compromise graft healing and GBR outcome.

The duration of follow-up after implant placement ranged from 48 to 60 months. No radiographic signs of bone loss, biologic or technical complications, or implant loss were noted.

Bone Volumetric Changes

The initial bone defects are described in Table 1. The longest mesiodistal span was 18.5 mm, and the shortest was 7 mm. The narrowest and widest ridges measured 4.3 ± 0.3 mm and 6 ± 0.3 mm, respectively. All edentulous areas presented a concavity on the central portion of the defect with the most apical portion of the defect being more buccally extended.

The mean volume gain from baseline (T0) to 4 months (T1) was 297.5 ± 134 mm³. Between 4 months (T1) and ≥ 6 months (T2), a mean volume loss of 60.2 ± 44.3 mm³ (4.9% ± 3.7%) was recorded. Analysis of volumetric changes between baseline (T0) and time of implant placement (T2 at ≥ 6 months) resulted in a mean gain of 247 ± 144 mm³ (Table 1). The mean ± SD soft tissue thickness at baseline was 1.26 ± 0.44 mm. The change in soft tissue thickness at the time of implant placement (visit 4) was −0.02 ± 0.38 mm (Table 2).

Histologic Analysis

Light microscopic evaluation at 2.5×, 10×, and 20× magnifications was used to identify vital bone, residual graft, and connective tissue/nonmineralized tissue. Residual graft particles were defined by regions of lamellar bone with the absence of osteocytes in lacunae, while vital bone was identified by the presence of osteocytes in lacunae. It was common to observe vital bone in direct contact with residual graft material in both groups. All of the specimens had some areas of well-defined organized lamellar structures with or without osteocytic lacunae, a presentation consistent with vital bone and residual allograft particles, respectively. The ESEM analysis resulted in a total mean of 44.9% ± 5.1% as measured with ImageJ software (Table 3). Six specimens were available since one patient moved away before implant placement but after digital measurements at ≥ 6 months, and one bone core was not suitable for analysis due to fracture during harvesting.

DISCUSSION

The principal aim of this pilot study was a quantitative and qualitative analysis of bone changes in terms of volume gain in mandibular regions treated with lateral ridge augmentation procedures. The present paper reports a novel approach to calculate volumetric changes after a GBR procedure in pristine sites prior to implant placement. To the best of the authors’ knowledge, no data on volume changes have appeared in
the literature on this specific topic. Digital techniques for volume measurements are not new to dentistry. Different authors employed this technique to calculate soft and hard tissue changes after surgical procedures.\(^{19-22}\) A recent study from Elnayef et al\(^{17}\) reported different degrees of graft resorption regardless of the material used for regeneration. The authors reported a linear overall net bone gain of 2.86 ± 0.23 mm. The estimated mean ± SD resorption after 6 months was 1.13 ± 0.25 mm, with 0.75 ± 0.59 mm for the block graft technique and 1.22 ± 0.28 mm for GBR. The main difference with the present study is that the present study provided volumetric data as well as percentages. The most noticeable outcome is that all implants placed in the augmented defects demonstrated uneventful healing 6 months after ridge augmentation. All edentulous areas presented a concavity on the central portion of the defect. The importance of defect morphology must not be underestimated since it affects containment of the bone graft and blood clot. A concave topography is

| Table 1 Bone Volume Changes Before and After Augmentation in Resorbable Group (Group 1): Values at Baseline, After 4 months (T1), and After 6 months (T2) of Healing and the Difference Between 4 and 6 months Compared with Baseline |
|---------------------------------|------------------|------------------|------------------|------------------|------------------|
| Subject | Length and width of edentulous areas (mm) | Volume of edentulous areas (mm\(^3\)) | Reduction (%) | Age (y) |
| | L | W ± SD | T0 Baseline | T1 4 ± 1 mo | T2 ≥ 6 mo | Volume differences (mm\(^3\)) | |
| S01 | 18.5 | 4.8 | 0.2 | 1,726.5 | 2,281.2 | 2,208.4 | −72.8 | 3.2 | 69.0 |
| S04 | 7 | 4.7 | 0.3 | 864.2 | 1,011.3 | 996.8 | 147.1 | 132.6 | −14.5 | 46.0 |
| S09 | 11 | 5.5 | 0.5 | 977.6 | 1,316.3 | 1,300.0 | 338.7 | 322.4 | −16.3 | 56.0 |
| S11 | 9 | 4.3 | 0.3 | 884.6 | 1,190.1 | 1,121.4 | 305.6 | 236.8 | −68.7 | 55.0 |
| S13 | 9.3 | 5 | 0.2 | 615.7 | 791.4 | 715.8 | 175.6 | 100.0 | −75.6 | 24.0 |
| S14 | 10.7 | 6 | 0.3 | 849.1 | 1,195.3 | 1,160.4 | 311.4 | 346.2 | −34.9 | 65.0 |
| S16 | 14.3 | 4.6 | 0.3 | 1,079.27 | 1,328.8 | 1,188.1 | 249.6 | 108.8 | −140.8 | 40.0 |
| Mean | | | | 986.3 | 1350.1 | 1281.8 | 297.5 | 247.0 | −60.2 | 50.7 |
| SD | 381.9 | 657.0 | 563.3 | 134.1 | 144.1 | 44.3 | 4.8 | 15.5 |

| Table 2 Soft Tissue Thickness and Soft Tissue Thickness Change |
|---------------------------------|------------------|------------------|------------------|------------------|
| Soft tissue thickness | Mean (mm) | SD (mm) | |
| T0 | 1.26 mm | ± 0.44 mm | |
| T2 | 1.24 mm | ± 0.32 mm | |
| Soft tissue thickness change | | | −0.02 mm | ± 0.38 mm |

The mean soft tissue thickness measured with a custom stent at baseline (T0) when the GBR procedure was performed. The soft tissue difference between T0 and T2 (at the time of implant placement), considering the 45- and 90-degree angles of entrance of the probe on the customized stent.

| Table 3 Mean Mineralized Tissue Core Content for Group 1 |
|---------------------------------|------------------|------------------|------------------|------------------|
| Subject | Group 1 (%) | |
| S01 | 50.4 | |
| S04 | 48.3 | |
| S09 | 39.7 | |
| S11 | 42.6 | |
| S13 | 49.6 | |
| S14 | 38.8 | |
| Mean | 44.9 ± 5.1 | |

Calculations were made by measuring mineralized tissue comprising residual graft, newly formed bone, and existing bone from the ESEM imaging.
considered a favorable condition compared with a convex structure. The treated defects were not extended to more than two molar-size teeth. The reduced length of the edentulous area helped to decrease the defect vertical component that would have compromised the predictability of the graft. The results of this study demonstrated and confirmed that resorbable membranes provided sufficient bone volume gains for implant therapy. A literature review showed that if soft tissue dehiscence did not occur, the volume of regenarated bone generally is more substantial with nonresorbable membranes than with resorbable membranes. However, an extended volume of data on resorbable membranes used for GBR seems to support comparable results with nonresorbable membranes. The results obtained from the present investigation confirm stability of the bone regenerated by procedures employing resorbable membranes. From this limited pool of patients, it can be suggested that resorbable membranes may be comparable to nonresorbable membranes in terms of volume gain since no additional bone graft was needed to place a prosthetically driven implant presenting 2 mm of buccal bone.

This study presents several drawbacks. First, and as may be anticipated between patients, there was heterogeneity between the residual ridge thickness and mesiodistal extension of the edentulous ridges treated. To overcome this heterogeneity, the authors calculated the percentage reduction between grafted areas in the middle of healing (4 ± 1 month) and after completion of healing at ≥ 6 months. This helped to compensate the data of extremely resorbed ridges that needed a greater net increase of volume compared to eligible sites with less need for augmentation. When this study was initially designed in 2012, intraoral digital scanners were not as common as in 2020, and this explains the decision to analyze volumes with a traditional technique based on PVS dental impression. The procedure steps of pouring and development process to determine volumetric alterations might have been avoided with the use of a digital intraoral scanner.

The statistical analysis for a pilot study such as the present study does not include the same level of statistical hypothesis testing and number of subjects treated or a strict power calculation as for a randomized clinical trial. The results deriving from a larger number of subjects enrolled in a prospective controlled study would be required to confirm the results from the present study. It should be noted that volume values reflect changes in both soft and hard tissues. It was not possible to calculate soft and hard tissue volumes as single entities, as preoperative and postoperative CBCT analysis was denied by the IRB. However, to compensate for this limitation, linear average measurements taken showed that the majority of the measured volume changes are accounted for by increases in bone and not by a thickening of soft tissue. Another important consideration regards soft tissue thickness and quality after regeneration therapies. Data derived from this investigation show a loss of soft tissue thickness at 6 months of healing, as reported in the literature. It is possible that the membrane or graft might have interfered with the soft tissue vascularity during healing. The values deriving from the bone volume calculations at ≥ 6 months show lower values compared with 4 months of healing. Simon et al in 2000 showed a loss in width of grafted bone after 4 months of healing ranging from 52.1% to 58.0% 3 mm from the crest, 47.6% to 67.4% 5 mm from the crest, and 39.1% to 46.7% 10 mm from the crest. Soft tissue changes demonstrated a 0.4- to 0.5-mm gain of thickness at 6 months on the buccal and lingual aspects.

One could argue that there was no calculation of graft resorption from immediately after GBR and 4 months. Without a CBCT analysis, it was not feasible to capture a realistic volume impression. First, the primary closure and reduction of vestibule in the area of surgery would have falsified the true graft volume. The result would have been a much higher value than the real augmentation. Second, the impression could have displaced and altered the flap position. The implant diameter selected for placement was > 4 mm. More than 2 mm of bone thickness was calculated lingually and buccally at the time of implant placement. The resorption that occurred during healing was not enough to preclude a prosthetically driven implant with respect to biologic requirements. Histology

The secondary aim of this study was to histologically evaluate the quality of the regenerated tissue, particularly the mineralized content of the cores. The result of mineralized content was inferior compared with other studies using GBR with resorbable membranes. Urban et al demonstrated that autogenous or regenerated bone represented a mean of 31.0% of the specimens with 25.8% of residual graft material. These differences may be due to the location of the biopsy specimens and the timing of their collection. Also, the present study only utilized FDBA and not an anorganic bovine bone–derived mineral (ABBM) mixed 1:1 with autogenous bone. The authors assume that the faster degradation of FDBA compared with ABBM determined the lower percentage of residual graft and then less overall mineral content in the core. Other authors investigated the presence of vital bone and residual graft after ridge preservation techniques. They demonstrated that the FDBA group showed a mean of 24.08% vital bone and 22.96% residual graft material. The location
of harvesting could have possibly included some native bone. The difference in bone density from subject to subject may have contributed in decreasing or increasing the total amount of mineralization of the core.

CONCLUSIONS

Within the limitations of this study, resorbable membranes confirmed their reliability for lateral ridge augmentation, providing a sufficient amount of bone to allow implant placement and primary stability as prosthetically planned and showing minimal (5%) resorption after healing. This investigation provided a technique to measure 3D volume changes during GBR healing phases and calls for a full-scale randomized controlled clinical trial to confirm these findings.

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