Human Autopsy Study of Peri-implant Dehiscence Defects with Guided Bone Regeneration: A Case Report

Jae-Kook Cha, DDS, PhD
Mariano Sanz, DDS, PhD
Ui-Won Jung, DDS, PhD

This report presents a histologic assessment of guided bone regeneration for dehiscence defects treated with bovine bone mineral or a combination of autogenous and synthetic bone. The samples were obtained from an autopsy specimen donated by a patient, which is a rare opportunity to evaluate long-term results of guided bone regeneration and osseointegration. The values for bone-to-implant contact were similar in both sites. The augmentation with bovine bone mineral demonstrated bone reconstruction after 1 year, whereas the augmentation with autogenous and synthetic bone failed to maintain the augmented volume, eventually leading to mucosal recession after 5.5 years.


Successful implant therapy requires sufficient bone to be available for placing implants in the ideal (prosthetically driven) position. However, this requirement is often not fulfilled due to resorptive patterns after tooth extraction resulting in bony dehiscence around the implants. These clinical situations have been successfully treated with different bone augmentation approaches performed either at the time of extraction, after soft tissue healing, or simultaneously with implant placement. Guided bone regeneration (GBR) has been the recommended technique for attaining predictable hard tissue around the implant surface.1–3 According to a recently reported randomized controlled clinical trial, GBR improved the stability of buccal bone and prevented vertical bone loss within 6 months after implant placement in control sites with spontaneous healing.4

A recent systematic review found that deproteinized bovine bone mineral (DBBM) in combination with a natural porcine bioresorbable collagen membrane was the most frequently used combination of bone replacement graft material for GBR, and that it significantly reduced the peri-implant defect height and width.5 Even though autogenous bone has unique osteogenic properties and is safe immunologically, its rapid resorption rate and increased
patient morbidity have limited its use in this clinical indication.

A combination of autogenous bone placed in contact with the implant surface and DBBM providing the space and stable maintenance of the clot under the bioresorbable membrane was proposed by Wang et al.⁶ This combination using two different layers of bone grafts covered with a bioresorbable membrane aims to combine the osteogenic potential of the autogenous bone, where it is most needed in contact with the implant surface, and the slow-resorption property of DBBM bone substitutes on the outside to maintain the lateral profile. Several clinical studies have found predictable bone augmentation in dehiscence defects using this technique,⁷,⁸ while a case series involving surgical reentry at 6 months found a bone height gain of 86.5⁹.

Although successful outcomes of GBR procedure have been demonstrated in various in vivo preclinical and clinical studies, a human autopsy study demonstrating long-term histologic outcomes is lacking, to the best of the present authors’ knowledge. It was therefore the aim of this case report to provide the clinical, radiographic, and histomorphometric findings for a human subject with sites where simultaneous lateral bone augmentation with placement of dental implants using different bone replacement grafts was used to treat buccal dehiscence defects.

Materials and Methods

This study was performed thanks to the generosity of a 62-year-old man who had died due to bladder cancer and donated his body to Yonsei University. This study received approval from the Institutional Review Board of Yonsei University (approval no. 2-2015-0046). This case report was written in accordance with the guidelines of the CARE checklist.¹⁰

Surgical Procedure

Maxillary Right First Premolar
The surgical procedures were performed by the same surgeon (U.W.J.). The tooth was extracted due to severe periodontitis, and 3 months later horizontal resorption of buccal bone could be observed clinically (Fig 1a). A submerged implant (diameter 4.1 mm, length 10 mm; Bone Level, Straumann) was placed with a final insertion torque of 50 Ncm.

Due to the narrowness of the ridge, a 5-mm-long dehiscence defect appeared on the buccal side of

![Fig 1 Maxillary right premolar.
(a) Intraoral image of the narrow ridge prior to implant surgery. (b–e) Surgical guided bone regeneration procedure. The dehiscence defect was treated with bovine hydroxyapatite and collagen membrane. (f) Intraoral image of the augmented ridge at 3 months postoperatively.](image-url)
the implant (Fig 1b). This defect was filled with DBBM (BioOss, Geistlich) (Fig 1c) and covered with a collagen barrier membrane (Biogide, Geistlich) (Fig 1d). After a periosteal releasing incision was made to produce tension-free flaps over the barrier membrane, sutures were applied to fully close the flaps (Fig 1e). Minimal crestal incisions were made without flap reflection at 3 months after the surgery (Fig 1f), and a healing cap with a diameter of 4.5 mm and a height of 3 mm was connected after checking that the implant was stable (value of –5 on the Periotest device [Siemens]). The final restoration was then placed, and the patient was followed up for 1 year in a supportive periodontal program.

Maxillary Left First Premolar
The patient had been missing a tooth for more than 3 months due to the onset of periodontitis. A preoperative clinical photograph showed moderate horizontal and vertical bone loss (Fig 2a). A submerged implant (diameter 4.1 mm, length 10 mm; Bone Level, Straumann) was placed in the ideal position using a surgical guide with a final insertion torque of 30 Ncm. The implant placement resulted in a buccal dehiscence defect that was 5 mm long with four exposed threads (Fig 2b). The sandwich technique involving simultaneous lateral bone augmentation was chosen to treat this dehiscence defect.6 The inner layer of the autogenous particulated bone was obtained from the maxillary tuberosity and was applied to the entire surface of the exposed implant (Fig 2c). The outer layer consisted of biphasic calcium phosphate (BCP) (MBCP, Biomatlante) (Fig 2d). A bioresorbable collagen membrane (Bio-Gide, Geistlich) was then placed to cover the graft materials (Fig 2e). Tension-free flap closure was achieved by periosteal releasing incision and sutures. After 3 months, the augmented volume remained well maintained and complete defect filling was observed at the second-stage surgery (Figs 2f and 2g). The implant stability was confirmed (–6 on the Periotest device, Siemens), and healing abutments with a diameter of 4.5 mm and a height of 6 mm were placed. The final restoration...
was delivered 2 months later and the implant was checked periodically for 5.5 years (Fig 2h). During this follow-up period, there were no symptoms such as infection or inflammation.

**Clinical Observation**

The maxilla with the implants was gently extracted from the donated body. The amount of buccal recession was measured, and the contour of the soft tissue was observed.

**Radiographic Analysis**

The prosthetic restorations had been removed to prevent the likelihood of metal artefacts, and the specimen was scanned using a high-resolution microcomputed tomography system (SkyScan 1173, SkyScan) at a resolution of 14.91 mm (achieved using 130 kV and 60 mA). The scanned data were three-dimensionally (3D) reconstructed, and one experienced researcher (J.K.C.) evaluated the data using PC-based software (CT Analyzer 1.14, Bruker-CT). The overall augmented volume was color-coded and measured in the area at 5 mm mesiodistal from the center of the implants.

**Histomorphometric Analysis**

Each specimen was fixed in 10% neutral buffered formalin for 7 days, dehydrated in ethanol, and then embedded in methyl methacrylate without decalcification. The specimens were sectioned at a thickness of 20 µm in the buccolingual direction and stained with hematoxylin-eosin. For histometric analysis, the following parameters were recorded:

- Bone-to-implant contact (BIC) ratio: the length of implant surface boundary in direct contact with bone
- f-BIC (mm): distance from the implant platform to the most coronal level of BIC parallel to the axis of the implant

**Results**

**Clinical Observation**

Convex-shaped soft tissue contour was observed at the buccal side of both implants without any recession at the placement of final restorations. The buccal peri-implant mucosa around the maxillary right site was well maintained and convex, without any recession (Fig 3a). However, buccogingival recession that occurred during the 5.5 years of follow-up resulted in a 2-mm-long abutment exposure in the distal area of a maxillary left premolar (Fig 3b). Moreover, the soft tissue contour of the maxillary left site changed to a concave shape.

**Radiographic Analysis**

In the maxillary right site, the horizontally augmented volume was more than 3 mm from the implant platform, which indicates that the augmented bone volume was maintained successfully. The achieved lateral augmentation (root prominence–like shape) was still observed on the buccal surface of the implant (Fig 4a). On the other hand, the 3D-reconstructed image of the maxillary left site indicated that the augmented volume on the buccal implant surface had been gradually resorbed, and residual bone graft materials were barely observed (Fig 4b). The augmented volumes of the maxillary right and left sites measured at 145.11 and 11.75 mm³, respectively.
Histomorphometric Analysis

Maxillary Right First Premolar
In the histologic image, the buccal dehiscence defect was completely reconstructed, with newly formed bone that was tightly attached to the implant surface (BIC ratio = 79.62% and f-BIC = 0 mm) (Figs 5a and 5b). This newly formed bone represented residual bone replacement graft particles combined with new cortical bone (Fig 5c). The graft materials were well separated from the surrounding connective tissue by a periosteum-like structure with a uniform thickness of approximately 100 mm from the bottom of the defect to the sulcular epithelium (Figs 5d and 6). It appeared that bone remodelling was still progressing, with abundant osteoclasts surrounding the residual graft materials under this periosteum-like tissue coverage.

Maxillary Left First Premolar
The histologic image demonstrated that the implant was...
osseointegrated with a high BIC ratio of 74.87% (Fig 7a). However, the lateral bone that had been augmented during implant placement had resorbed, and the implant showed recurrent coronal dehiscence. The f-BIC was 2.56 mm. At this dehiscence area, the implant surface was covered with connective tissue, showing tightly attached fibers without signs of inflammation (Fig 7b). The bone remodeling process was completed, and no traces were found of the bone replacement graft that had been used. The existing bone appeared mature, with no osteoclast or osteoblast activity. Although the augmented graft material had disappeared completely, the periosteum-like structure could be distinguished between the buccal bone and the connective tissue (Fig 7c). This periosteum-like tissue was formed at the original site of the collagen membrane, situated from the bottom of the dehiscence defect to the upper margin of the implant shoulder with a width of 100 to 200 µm. It was a highly vascularized tissue consisting of collagen fibers and blood clots, and in some areas the vessels clearly penetrated this periosteum-like membrane (Fig 7d).

Discussion

This human autopsy case report applied GBR technique to two dehiscence defects for lateral bone augmentation, which produced two outcomes: The augmented peri-implant dehiscence defect in the maxillary right site demonstrated complete bone reconstruction after
1 year, showing an f-BIC value of 0 mm. In the maxillary left site, the initial reconstructive outcome was not maintained, as after 5.5 years the f-BIC value was 2.56 mm and there was mucosal recession of 2 mm with exposed abutment.

The differences in clinical and regenerative outcomes between the two premolar sites could be attributed to various factors, such as the characteristics of the material, the flap tension, and the healing period. Since this study is a case report limited to a single patient and different healing periods, it would be impossible to evaluate the validity of the material and technique used for GBR. The present results should be interpreted conservatively.

Among these factors, the resorptive behavior of BCP might explain the differences. The resorption pattern could be influenced by the ratio of hydroxyapatite to calcium phosphate, which for MBCP is 60:40. A previous clinical radiographic and histologic analysis of tibial osteotomy found that the resorption rate of MBCP was more than 60% after 2 years. A recent in vitro study showed that the calcium phosphate in MBCP was selectively and rapidly dissolved within 1 day.

On the other hand, DBBM has been considered a nonresorbable material as demonstrated in previous human biopsy studies. The presence of a periosteum-like structure was one of the key findings of this human autopsy case report. This structure seems to have maintained the barrier function provided by the collagen membrane for more than 6 years postoperatively. The non–cross-linked nature of the collagen membrane used in this study typically degrades within 4 to 8 weeks. This usually occurs via an enzymatic process and seems to be inevitable, irrespective of the method used to prolong the membrane resorption pattern. After this degradation process has occurred, the connective tissue from the collagen membrane integrates with surrounding connective tissue, accompanied by a mononuclear cell-based tissue reaction and mild neovascularization.

Some authors have claimed that regenerative outcomes may be improved by prolonging the duration of barrier membrane resorption, but there is no evidence of improved outcomes when these bioresorbable barrier membranes exhibit slow resorption. Different methods have been applied to prolong the barrier membrane effect, from using the same membrane in double layers to modifying the collagen composition of the membrane by artificial cross-linking. However, the latter method may reduce the vascularization and tissue integration of the cross-linked collagen membrane and may induce significant inflammatory reactions with the presence of multinucleated giant cells.

The use of non–cross-linked collagen membrane in the present case seems to have successfully promoted bone regeneration, and it was replaced by a highly vascularized periosteum-like tissue that seems to have maintained the barrier effect even after the collagen membrane was resorbed, until the bone remodeling process ended.

Very few reported studies of ridge augmentation have observed regeneration of the periosteum after GBR. A recent clinical case series described that new periosteum had formed at 7 months after GBR using individualized ceramic sheets. In the present study, the new bone lined the lower border of the periosteum-like tissue that communicated with the outer connective tissue through small blood vessels. This observation suggests that the periosteum-like tissue allows angiogenesis within the structure and enhances wound healing until the end of the bone remodeling process. Although the periosteum-like tissue contained blood vessels and had a microscopic structure similar to that of the periosteum, the cellular activity could not be verified in this case report. This connective tissue structure should be characterized in future studies.

Conclusions

The augmentation of peri-implant dehiscence defects with DBBM in the present human autopsy study demonstrated bone reconstruction after 1 year, whereas the defect augmented with autogenous bone and BCP failed to maintain the augmented volume, eventually leading to mucosal recession after 5.5 years. However, it should be considered that this study is a case report of only two cases and the follow-up periods differed between the defects, which may have influenced the outcomes.
Acknowledgments

This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (Ministry of Science, ICT & Future Planning) (No. NRF-2017R1A2B2002537). The study was partially supported by the Osteology Foundation, Switzerland, with a research scholarship grant (16-004) to Jae-Kook Cha and the University Complutense of Madrid. The authors reported no conflicts of interest related to this study.

References