Bio-Oss® Successfully Induces Bone Healing in a Segmental Mandibular Defect

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ABSTRACT

Objective: Increased understanding of the physiology of bone regeneration in clinically relevant animal models and the application of this information to patient care can potentially improve the long-term reconstructive success of patients with craniofacial defects. An osteoconductive graft material, Bio-Oss ®, is a natural bovine bone substitute. While commonly used in human dental procedures as an osteoconductive graft, its ability to heal segmental mandibulectomy defects has not previously been explored.

Objective: To test the osteoregenerative potential of Bio-Oss® in healing the critical size segmental mandibulectomy defect in the rat model in comparison to other biomimetic scaffolds.

Study Design: Prospective study using an animal model.

Methods: Sixteen Sprague-Dawley rats underwent segmental mandibulectomies with resultant 5 mm x10 mm critical-sized defects. The following were implanted into the defect sites: collagen sponge, PLGA scaffold with 5ug BMP-2, Bio-Oss®, and Bio-Oss® with 5ug BMP-2. The defects were spanned with titanium miniplates. Two months postoperatively, bone healing was analyzed with microcomputerized tomography (microCT) and histopathologic analysis.

Results: MicroCT analysis demonstrated that all scaffolds except for blank collagen healed the defects with various levels of bony regeneration. Combined Bio-Oss ® and BMP-2 showed the greatest increase in bone and total volume.

Conclusion: Bio-Oss ® is an effective osteoconductive graft agent in healing segmental mandibular defects. In combination with BMP-2, it showed the highest percentage of bone within healed tissue and total bone volume within the defect site when compared to the other biomimetic scaffolds.

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INTRODUCTION

Head and neck squamous cell carcinoma is the 8th most common cancer worldwide, presenting with 650,000 new cases annually. Currently, the preferred methods of reconstruction of segmental mandibular defects are bony vascularized flaps.[1] Free flaps, though reliable, necessitate prolonged operative time and can carry a 20.5% risk of perioperative medical complications.[1,2] Additionally, limited tissue availability and donor site morbidity have led to a search for alternate forms of reconstruction.[3]

Our previous work with bone morphogenetic protein (BMP)-2-impregnated biomimetic scaffolds showed successful bone healing in the marginal mandibular critical-sized defect in the rat.[3] The critical-sized defects of the mandible are those which will not heal spontaneously during the expected natural life of the animal.[3]

In this current study, we wished to determine the osteoconductive capability of Bio-Oss ®, a natural bone substitute material derived from the mineral portion of bovine bone, in a segmental defect. Bio-Oss's trabecular architecture, which has shown to promote invasion of blood and bone cells, allows it to function as a scaffold for osteogenic cells[4] and be commonly utilized in various oromaxillofacial procedures.[5]

METHODS & MATERIALS

Sixteen Sprague-Dawley rats were divided into four groups (collagen sponge, PLGA with 5ug BMP-2, Bio-Oss ®, and Bio-Oss® with 5ug BMP-2. The optimal 5ug concentration of BMP-2 was determined through a previous study.[3] Collagen and PLGA scaffolds were sized to 5 x 10 x 3-mm pieces which were inserted into the segmental mandibulectomy critical-sized defect sites. Bio-Oss ® was placed using a tuberculin syringe: 1.4 cc of granules in 30ul of sterile saline (25ul sterile saline +/- 5ul of 1ug/ml BMP-2). Two months postoperatively, the rats were sacrificed, and bone healing was analyzed with microcomputerized tomography (microCT).

SURGICAL TECHNIQUE

Using sterile technique, an incision was made parallel to the left mandible and carried down through the soft tissues. The ptergyomasseteric sling was exposed and divided. Subperiosteal elevation of the musculature revealed the lingual and buccal surfaces of the mandible. A high-speed cutting burr was used to create the 5 x 10mm bony segmental defect posterior to the incisor and contiguous with the inferior border of the mandible (Fig 1) The defect was then filled with scaffolds of the exact size or with consistent volumes of Bio-Oss® granules. (Fig 2)

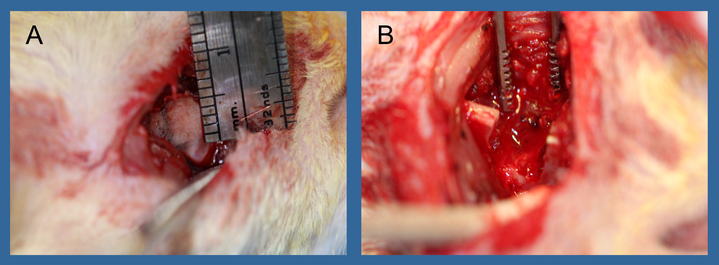


Figure 1: A) The left inferior border of the mandible is exposed, and a 5x10-mm segmental defect is outlined. B) The defect is created with a bone drill.

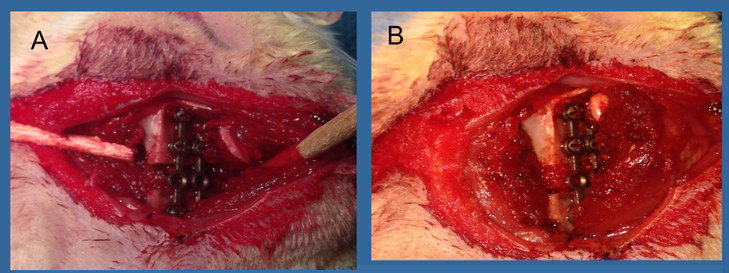


Figure 2: A) The segmental bony defect measuring 5x10x3 mm Is created, and the defect is spanned with titanium microplates. B) The bony defect in this rat mandible is filled with collagen sponge.

Figure 3: This a microCT reconstruction of a rat mandibular defect with collagen sponge (control). There is a nonhealed defect.

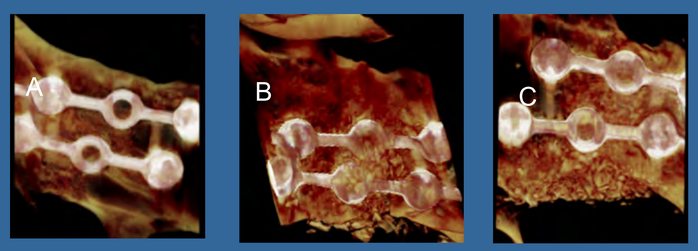
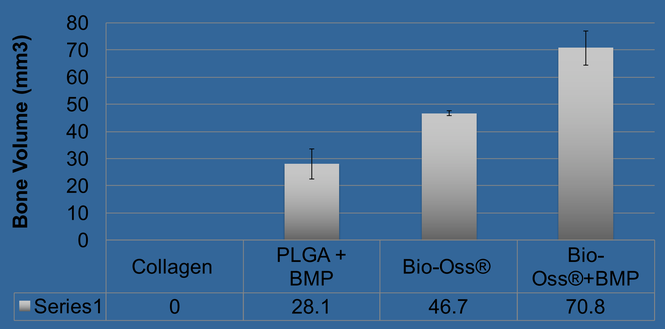


Figure 4: A) This is a microCT reconstruction of a rat mandibular defect with PLGA + BMP. There is non-uniform healing of the defect, with some areas of healing thinner than others. B) This is a microCT reconstruction of a defect with Bio-Oss® granules. There is complete segmental defect healing. C) This is a defect healed with Bio-Oss® and BMP. There is also complete segmental defect healing which appears more homogeneous and compact.



Level	Level	Std. Error	P-value
PLGA + BMP	Bio-Oss®	3.5	0.001
PLGA + BMP	Bio-Oss® +BMP	3.5	0.000
Bio-Oss®	Bio-Oss®+BMP	3.5	0.000

Figure 5: A) Graph depicting bone volume (BV) for all four groups. B) Tukey pairwise comparisons.

RESULTS

Quantification of bone regeneration was performed by evaluating new bone volume on post-mortem microCT analysis. (Fig 3,4). The defect volume (DV) remained constant at 150 mm^3; the new bone volume (BV), total volume (TV), and defect volume ratios (BV/TV) were evaluated. Tukey pairwise comparisons demonstrated that BioOss + BMP 70.80 mm^3) created significantly more bone than any of its counterparts (Bio-Oss® 46.7mm^3 ($p<0.0001$); PLGA + BMP 28.1 mm^3 ($p<0.0001$); and collagen. (Fig 5). MicroCT analysis revealed that bony defects were healed with all scaffolds except for collagen sponge; the amount of bony volume was greatest for Bio-Oss® and BMP.

DISCUSSION

While graft-based bone regeneration is currently utilized in settings to repair mandibular bone in the setting of trauma or tumor, reconstruction of segmental defects remains limited to autologous bone harvest. This carries increased patient donor site morbidity as well as prolonged operative time.

BMP-2 is known to induce cellular chemotaxis, proliferation, and osteogenic differentiation of both osseous and nonosseus mesenchymal cells.[3,6,7] It has previously been shown to heal marginal mandibular defects in the murine model at a concentration of 5ug.

This study evaluated the healing capability of Bio-Oss ® alone and in conjunction with BMP-2 to reconstruct a critical-sized segmental mandibular defect. Our data suggests that the defect is regenerated with the former and perhaps further strengthened with the growth factor.

CONCLUSIONS

Developing an alternative method to reconstruct segmental mandibular defects can be crucial in limiting the donor site morbidity and providing the flexibility to rebuild complex anatomic structures.

Further studies investigating the use of this natural bone substitute mineral may help realize the potential of BioOss ® to restore critical-sized osseous defects of the mandible, carrying promise as a platform for alternate, less invasive therapies.

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