The Effects of Resorbable Membrane on Human Maxillary Sinus Graft: A Pilot Study

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Purpose: *To investigate the effects of resorbable membrane on new bone formation in human maxillary sinus graft using anorganic bovine bone material histomorphometrically in a split-mouth study design.* ***Materials and Methods:*** *This prospective pilot study included six patients who required bilateral sinus augmentations prior to implant treatment. Each patient was grafted with anorganic bovine bone (Bio-Oss). The experimental side was covered with resorbable membrane (Bio-Gide) over the grafted sinus, and the control side was left uncovered. After 8 months of healing (range, 7 to 9 months), implants were placed. Biopsy samples were obtained from each side through the previously grafted sinus window and evaluated. Statistical analysis was performed using the Mann-Whitney* U *test at a significance level of* $\alpha = .05$. ***Results:*** *The control side appeared to have a significantly greater amount of soft tissue than the experimental side (*P = *.026), whereas no significant differences in the amount of new bone were observed (*P = *.937).* ***Conclusion:*** *Resorbable membranes significantly reduced the amount of soft tissue formed in the sinus grafted with anorganic bovine bone material but had no effect on new bone formation.* Int J Oral Maxillofac Implants 2009;24:73–80

Key words: *anorganic bovine bone, biopsy, histomorphometry, maxillary sinus, resorbable membrane*

Endosseous dental implants have been successfully used to treat partially[1,2] or completely edentulous patients.[3] However, patients with highly atrophic maxillae present considerable challenges for implant placement. The posterior maxilla with pneumatized sinuses often requires sinus augmentation prior to implant placement.[4]

Since Boyne and James[5] published the technique for maxillary sinus augmentation using autogenous bone in 1980, many different techniques[6–10] have been developed and used for the sinus graft procedure. Many studies have used autogenous bone,[11–13] which is considered to be the "gold standard" for grafting by many clinicians, but the morbidity and increased cost of hospitalization in harvesting autogenous bone have led clinicians to search for graft alternatives. Several studies have evaluated various bone grafting materials in maxillary sinus augmentation, such as freeze-dried demineralized bone,[14,15] resorbable hydroxyapatite,[14,16] nonresorbable hydroxyapatite,[14,15,17] and xenografts.[14,18–20] Anorganic bovine graft (Bio-Oss, Osteohealth, Newport Beach, CA) has been shown to be highly biocompatible and to fulfill the criteria of an osteoconductive grafting material.[21,22] This deproteinized bovine material has been proven a good bone substitute in maxillary sinus augmentation studies.[18–20]

Guided bone regeneration (GBR) with barrier membranes is a well-established therapy.[23–25] A membrane excludes nondesirable cells from populating the area of a defect, thus favoring wound healing with the desired type of tissue. There is considerable evidence indicating that a greater amount of bone regeneration occurs when membranes are used to protect the defect in GBR therapy.[26–28]

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Sinus augmentation surgery is considered to be an effective and predictable therapy.[29–31] However, there is limited evidence in the literature about the effect of membrane barriers on the antrostomy defect in sinus augmentation. There is still controversy regarding the need for barrier use in sinus augmentation. Resorbable and nonresorbable membranes placed over the antrostomy site in human maxillary sinus augmentations were well tolerated, without sign of soft tissue encleftation.[32] Tarnow et al[33] showed that placement of a nonresorbable membrane over the lateral window at the time of sinus grafting had positive effects on both new bone formation and implant survival rates. Tawil and Mawla[34] demonstrated that coverage of antrostomy sites with resorbable membranes improved the implant survival rate.

The purpose of this prospective split-mouth pilot study was to determine the need for a larger-scale study of maxillary augmentation with and without resorbable membrane. The null hypothesis was that there would be no histomorphometric differences in new bone formation in maxillary sinuses augmented using anorganic bovine bone graft (Bio-Oss) with and without a resorbable membrane covering the antrostomy.

MATERIALS AND METHODS

This clinical study was approved by the Institutional Review Board at Loma Linda University. A total of seven patients who required bilateral sinus augmentation prior to implant placement were invited to participate in this study. To be included, subjects needed to be over 18 years old and able to read and provide written consent. They must have had no medical or psychological history that would complicate the outcome of the study and needed to be available for study monitoring and subsequent implant treatment. All patients were bilateral maxillary posterior edentulous patients who required sinus augmentation in both sides for implant placement. The patients could be partially or completely edentulous. The following patients were excluded from participation: those with medical or psychologic history that would contraindicate implant treatment, such as uncontrolled diabetes, blood dyscrasia, or head and neck radiation therapy; those with active sinus infection; subjects with poor oral hygiene; those who smoked; women who were pregnant; and those with drug and/or alcohol dependency issues.

Preliminary impressions were made with irreversible hydrocolloid impression material (Denstply, Milford, DE) and diagnostic casts were poured in type III dental stone (Whip Mix, Louisville, KY). The diagnostic casts were articulated with the use of a facebow on a Hanau H-2 semi-adjustable articulator (Teledyne Water Pik, Fort Collins, CO) with interocclusal record and record bases. Teeth were fabricated in diagnostic wax with wax pattern (Pro-Art, Williams, Amherst, NY) and then duplicated in type III dental stone. A vacuum-formed template (Polypropylene Coping Sheet, Ultradent Products, South Jordan, UT) was fabricated from this duplicated cast. This template was used in conjunction with the cast for identifying the desired locations of the dental implants.

Patients were given three choices of anesthesia for the sinus surgery as well as implant placement surgery: local anesthesia (LA) only, LA in conjunction with oral sedation, or LA in conjunction with intravenous (IV) sedation. On the day of surgery, twice the usual therapeutic dose of appropriate antibiotics (1 g amoxicillin, or 300 mg clindamycin for those allergic to amoxicillin) was administered at least 1 hour before the surgical procedure.[35] After appropriate LA was administered, a midcrestal incision was made and a vertical releasing incision was made anteriorly at the appropriate location. A full-thickness flap was reflected to expose the lateral wall of the sinus. The antrostomy was outlined with a no. 4 round bur, ensuring that the inferior border was at least 2 to 3 mm superior to the sinus floor. A chisel was used if the bony window was not completely separated from the surrounding bone. The sinus membrane was carefully elevated and space was created for the bone graft under the membrane. The inferior border of the antrostomy window was measured from the crest of the ridge with reference to the surgical template using a periodontal probe. Anorganic bovine grafting material (Bio-Oss) was gently packed into the sinus cavity. Control and experimental sides were determined randomly. On the control side, primary closure of the flap was performed. On the experimental side, a resorbable membrane (Bio-Gide, Osteohealth) was shaped and positioned to cover the antrostomy window. Four tacks were used to stabilize this membrane before the flap was closed, as on the control side, with sutures. Following the surgery, antibiotics were prescribed for 10 days and appropriate analgesia was prescribed for postoperative pain. Patients rinsed twice daily with 0.12% chlorhexidine gluconate for 2 weeks.

An average of 8 months of healing was allowed after the sinus surgery. A full-thickness flap was reflected, as in the grafting surgery. Previous antrostomy sites were located using the same surgical template. A trephine was used to collect biopsy specimens in dimensions of 2 × 8 mm from each

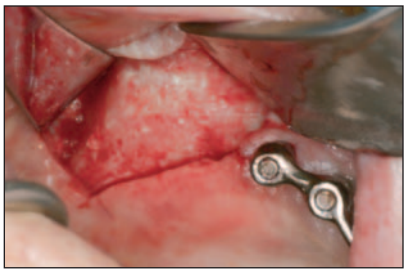

Fig 1 Subject #1, experimental side: Smooth and even surface.

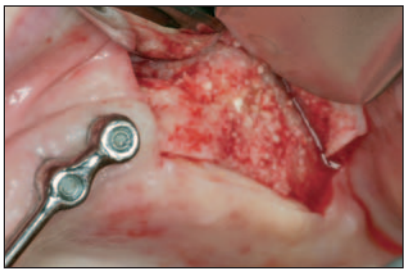

Fig 2 Subject #1, control side: A rough and grainy surface is apparent.

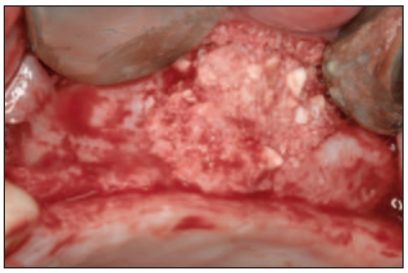

Fig 3 Subject #5, control side: Graft material protrudes beyond the neighboring sinus wall.

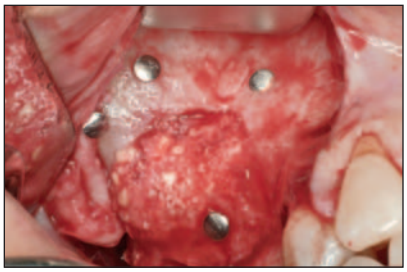

Fig 4 Subject #2, experimental side: Similar level to the adjacent sinus wall.

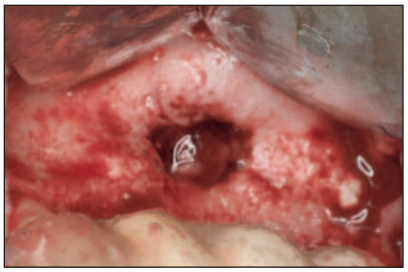

Fig 5 Subject #2, control side: A crater-like defect filled with soft tissue.

control and experimental side from the previous lateral window without interfering with implant placement. This biopsy approach ensured that the core sample included newly regenerated bone only and did not include any preexisting alveolar bone. The core sample was kept in the trephine in 10% buffered formalin and transported to the laboratory for the processing. The alveolar ridge was prepared for implant placement, in accordance with the conventional surgical protocol, and implants of appropriate dimensions were placed. Appropriate healing time for the implants was allowed for osseointegration, and definitive restorative prostheses were constructed accordingly.

Histomorphometric Analysis

The specimens were dehydrated with a graded series of alcohols for approximately 14 days. Following dehydration, the specimens were infiltrated with a light-curing embedding resin (Technovit 7200 VLC; Kulzer, Friedrichsdorf, Germany). Following approximately 14 days of infiltration with constant shaking at normal atmospheric pressure, the specimens were embedded and polymerized by 450-nm light, with the temperature of the specimens never exceeding 40°C. The specimens were then prepared by the cutting/grinding method of Donath and Breuner.[36,37] The specimens were cut to a thickness of 150 µ on an Exakt cutting/grinding system (Exakt Apparatebau, Norderstedt, Germany). Following this, the samples were polished to a thickness of 35 to 45 µ using the Exakt microgrinding system, and they were stained with Stevenel blue and van Gieson picric fuchsin. The specimens were analyzed using NIH Image, an image analysis software program developed by the National Institutes of Health, on a Power Macintosh.

The nonparametric Mann-Whitney *U* test, at a significance level of $\alpha = .05$, was used to make statistical comparisons of new bone formation, soft tissue, and residual graft materials on the control and experimental sides.

RESULTS

A total of 10 patients agreed to enroll in the study, but three participants were excluded from the study because of sinus pathology. A total of seven patients completed the bilateral sinus augmentation, but one patient elected to drop out of this clinical experiment after the sinus grafting because of unexpected personal problems. Four of the six subjects had uneventful healing until the implant surgery when biopsies were taken. Subject #2 had a crestal suture line that did not completely heal for 3 weeks on the control side only. Subject #4 had unexplained postoperative swelling on the control side 1 month after the surgery. This was resolved with antibiotic treatment. For the remainder of the study, there were no other complications.

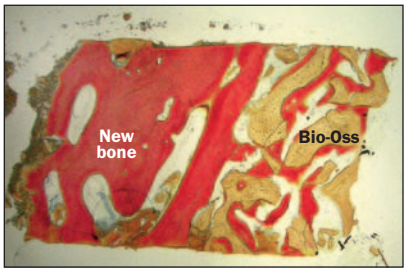

Fig 6 Subject #2, experimental side (magnification ×25).

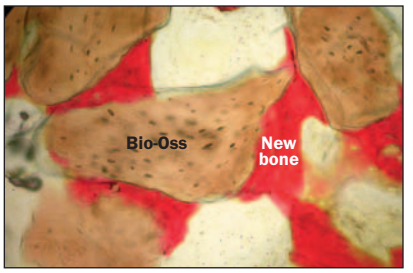

Fig 7 Subject #4, experimental side (magnification ×200).

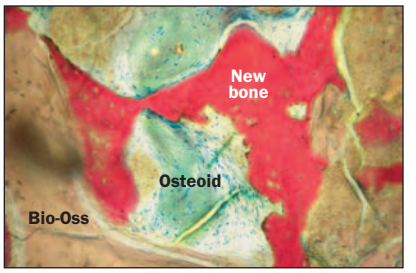

Fig 8 Subject #1, experimental side (magnification ×200).

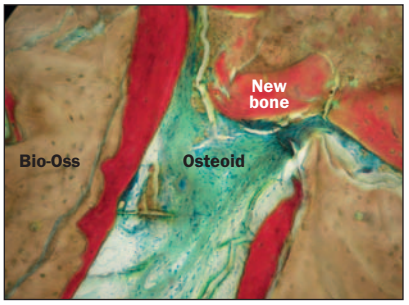

Fig 9 Subject #1, experimental side (magnification ×200).

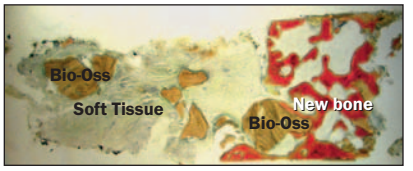

Fig 10 Subject #2, control side (magnification ×25).

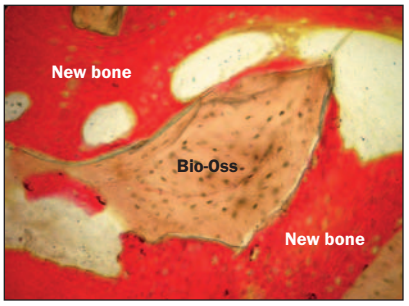

Fig 11 Subject #4, control side (magnification ×200).

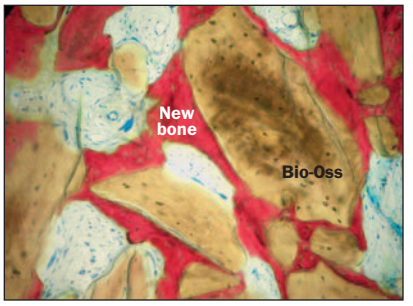

Fig 12 Subject #1, control side (magnification ×200).

Clinical Results

After an average of 8 months of healing (range: 7 to 9 months), the previous antrostomy sites were easily identifiable when the full-thickness mucoperiosteal flap was elevated to expose the grafted sinus wall. Particles of the grafting material (Bio-Oss) were still visible on both sides. However, there was no trace of the resorbable membrane (Bio-Gide) on the experimental side; it seemed to be completely resorbed. In comparison to the control side, where no membrane was used to cover the grafted antrostomy, the experimental side had a more even and smooth appearance (Fig 1). The residual particles of the control side appeared more coarse and grainy (Fig 2) and on occasion protruded out of the sinus wall boundary (Fig 3). The residual particles in the experimental side appeared less gritty and were at a similar level to the adjacent sinus wall (Fig 4).

The antrostomy of control side on subject #2 had a moderate-sized crater that was filled with soft tissue (Fig 5). However, this did not prevent the placement of dental implants as planned. All six subjects had dental implants placed on both sides accordingly. When the osteotomies were prepared for the implants, the drill resistance on the experimental side felt slightly greater in comparison to the control side in most subjects.

Table 1 Histomorphometric Results

	New bone %		Soft tissue %		Remaining Bio-Oss %	
Patient no.	Control	Experimental	Control	Experimental	Control	Experimental
1	14%	17%	44%	28%	42%	55%
2	16%	32%	65%	32%	19%	36%
3	0%	12%	78%	42%	22%	46%
4	19%	10%	59%	18%	22%	72%
5	19%	7%	41%	38%	40%	55%
6	4%	2%	45%	59%	51%	38%
Average	12%	13%	55%	36%	33%	50%
P	.937		.026*		.093	

*Statistically significant ($P < .05$).

Table 2 Hard Tissue vs Soft Tissue vs Healing Time

	Hard tissue %*		Soft tissue %		
Patient no.	Control	Experimental	Control	Experimental	Healing time
1	66%	72%	44%	28%	9 mo 3 d
2	35%	68%	65%	32%	8 mo 12 d
3	22%	58%	78%	42%	8 mo 20 d
4	41%	82%	59%	18%	8 mo 3 d
5	59%	62%	41%	38%	8 mo 4 d
6	59%	40%	45%	59%	7 mo 17 d
Average	45%	64%	55%	36%	8 mo 10 d

*New bone + Bio-Oss.

Histomorphometric Results

Most of the biopsy samples demonstrated vital new bone formation in the sinus after grafting with an anorganic bovine bone graft material. Residual graft particles were still visible in all sites. Newly formed bone was found surrounding the Bio-Oss particles. New bone particles were firmly attached to the graft particles and bridged the residual graft particles (Figs 6 to 12). Table 1 presents the biopsy results of new bone, soft tissue, and residual graft material in the harvested specimens.

The average percentage of new bone formation in the control specimens was 12%, in comparison to 13% in the experimental sites. The difference was not statistically significant ($P = .937$). The average percentage of residual anorganic bovine bone graft (Bio-Oss) used in the study was 33% in control sides and 50% in experimental sides. This difference was not statistically significant either ($P = .093$). The average percentage of soft tissue in the specimens was 55% in the control side and 36% in the experimental side. This difference was statistically significant ($P = .026$).

Power analysis showed the probabilities of rejecting the null hypothesis to be .25 for new bone formation, .96 for soft tissue infiltration, and .95 for remaining Bio-Oss. To achieve a 95% confidence interval, a minimal sample size of 14 is recommended for future study.

DISCUSSION

The amount of new bone formed using anorganic bovine bone in the maxillary sinus in this study is slightly lower than other studies[18,38,39] in the literature which have used different approaches to obtaining biopsy samples. Since the graft material used in this experiment is considered to have only osteoconductive properties, the process of graft maturation is started from the periphery of the sinus walls, where osteogenic cells preside. It would take longer for osteoblasts to migrate from the border to the center of the maxillary sinus to form new bone and to bridge the graft materials. Therefore, the graft at the center of the maxillary sinus would be less mature than that at the border of the sinus.[40] The biopsy specimens in this study were accessed through the previous antrostomy site to the center of the sinus, rather than vertically from the alveolar ridge through the sinus floor, where more mature graft is present. The difference in new bone formation may be attributable to this different biopsy approach. It is likely that a higher percentage of new bone existed at the periphery of sites than in the area where actual biopsy samples were collected.

The effect of the membrane on the new bone formation in the maxillary sinus in this experiment is inconsistent with the results of others[33,41] who used

the same biopsy approach but used nonresorbable (expanded polytetrafluoroethylene) membranes to cover the sinus windows. A significantly greater amount of new vital bone was produced in the human maxillary sinus when nonresorbable membrane was used, compared to the no-membrane side. However, those studies did not include information regarding the amount of soft tissue in the obtained biopsy cores; nor was this factor compared in the individuals using the same graft material. The theoretical function of the barrier membrane covering the lateral window of the grafted sinus is to inhibit graft particle displacement and to prevent proliferation of connective tissue into the maxillary sinus. By excluding the nonosteogenic connective tissue that competes with the osteogenic cells, bone formation inside the sinus may become more favorable for graft maturation. The significantly smaller amount of soft tissue formation in the experimental side in this study suggests that the resorbable membranes (BioGide) used were effective in stabilizing graft particles and preventing soft tissue infiltration.

The appearance of the nonmembrane side was coarse and grainy, and sometimes the graft particles protruded beyond the boundary of the neighboring sinus wall. This may be explained by the direct contact between the connective tissue and the graft particles in the control side, which allowed immediate tissue proliferation and infiltration into the anorganic bovine graft, resulting in soft tissue adherence to the graft particles. The presence of the resorbable membrane on the experimental side, on the other hand, delayed such events, contributing to the different surface appearance.

The soft tissues adhered to the particles had to be detached during the mucoperiosteal flap elevation for the biopsy sampling. During the mucoperiosteal flap elevation, more effort was required to reflect the flaps on the control side than on the experimental sides. A higher degree of connective tissue infiltration to the graft on the control side may have manifested itself in the greater effort to reflect flaps during the biopsy procedures on the grafted sinus window. The histomorphometric results show that there was a greater amount of connective tissue infiltration in the control sites than in the experimental sites Tables 1 and 2).

The resorbable membrane had the additional effect of stabilizing the graft particles. This effect was apparent on the experimental side, where solidified graft was contiguous with the adjacent sinus wall. Control side grafts sometimes protruded beyond the neighboring sinus wall boundary. This may explain the delayed suture line healing on the control side in subject #2. This subject reported that she found graft particles occasionally during the healing period. It is likely that the soft tissue that was in direct contact with protruding graft particles had a significantly greater effect in disturbing and mobilizing the graft particles on the surface of the sinus window. These loose particles eventually moved toward the suture line, preventing the healing of the soft tissues. In this particular patient, the soft tissue invagination on loose graft particles was so great that a moderate-size crater defect resulted (Fig 4); this was completely filled with connective tissue. Similar soft tissue encleftation also has been reported in the literature.[32,41,42] In contrast, the experimental side had a barrier that helped immobilize the graft particles in the sinus by preventing direct soft tissue contact with the graft particles.

The overall amount of hard tissue (new bone and residual graft particles) was higher in the experimental side than in the control side (64% vs 45% in Table 2). It is possible that a greater amount of hard tissue can provide improved implant success rates in human maxillary sinuses grafted with anorganic bovine bone, since implant survival rates are strongly affected by the bone density.[43,44] A recent meta-analysis of the literature[45] concluded that implant survival rates were higher when a membrane was placed over the lateral window in sinus augmentation. As seen in the present biopsy samples (Figs 6 to 12), residual anorganic bovine graft particles were surrounded by new bone. It has been found that these residual anorganic bovine bone graft particles do not interfere with the osseointegration process, and they are not in direct contact with dental implants.[21,46,47] This would mean that residual graft material increases the mineral content of the implant placement site, which can help to improve implant survival rates. This higher bone density achieved by an increase in mineral composition in the grafted sinus would explain the higher drilling resistance experienced on the experimental side than on the control side during implant placement.

CONCLUSION

Within the limits of this study, it can be concluded that the placement of resorbable membranes over augmented sinuses does not present any additional risks. While the resorbable membrane had no effect on the amount of new bone formation within sinuses grafted with anorganic bovine bone material, it significantly reduced the amount of soft tissue formed in grafted human maxillary sinuses.

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