

The Use of a Mineralized Allograft for Sinus Augmentation: An Interim Histological Case Report from a Prospective Clinical Study

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Abstract: A prospective clinical research study of various graft materials used for the augmentation of human maxillary sinuses is currently in progress at New York University Department of Implant Dentistry. This interim case report describes the healing response after a sinus augmentation procedure using a new mineralized cancellous bone allograft. The results after 9 months of healing demonstrated a vital bone content of 25.2% in the grafted sinus, as ascertained from a trephine core taken from the superior aspect of the lateral window area. Although the vital bone requirement for implant survival in an augmented sinus is unknown, the 25.2% vital bone demonstrated in this case compares favorably with that reported in the literature for other augmentation materials, including xenografts, alloplasts, and autogenous bone.

Augmentation of the maxillary sinus has been shown to be a predictable method of increasing posterior maxillary bone height, making it possible to place dental implants when the residual alveolar ridge is deficient in bone volume. The original protocol for this procedure used only autogenous bone from intraoral or extraoral sources.¹⁻⁵ Using autogenous bone required a second surgical site, increased the length of the surgical intervention, increased the surgical risk, and increased postsurgical morbidity by exposing multiple sites.

Bone replacement grafts are now used in sinus augmentation procedures to avoid the drawbacks inherent in the harvesting of autogenous bone. Their efficacy has been demonstrated by high implant survival rates in sinuses augmented with these materials.^{6,7} The graft materials for bone replacement include allografts,⁸ bovine-derived xenografts,⁹⁻¹⁵ and alloplasts.¹⁶⁻¹⁸

Mineralized cancellous bone allograft (MCBA) has been used as a grafting material in the treatment of periodontal bone defects, in oral surgery for extraction sites, and for ridge augmentation or sinus augmentation before, or concurrent with, implant placement.^{19,20} MCBA is a human bone product obtained from cadaver sources that has been processed and sterilized. A form of this graft material, Puros,^a prepared by a new processing and sterilizing procedure, Tutoplast,^b is currently being used as a bone replacement graft for sinus augmentation procedures in a prospective clinical study conducted by the NYU Department of Implant Dentistry. This processing and sterilization destroys the unwanted microbes but maintains the porous bone mineral structure as well as the natural extracellular collagen matrix proteins that are important for cell attachment and bone remodeling.²¹

After a careful review of the literature it was noted that there was no histologic verification of using this material in sinus augmentation surgery. Therefore the purpose of this interim report from the ongoing NYU study is

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Learning Objectives:

After reading this article, the reader should be able to:

- Discuss the origin and use of a new form of mineralized cancellous bone allograft (MCBA), Puros, for sinus augmentation.
- Describe the sinus lift procedure using Puros and autogenous bone.
- Describe the histological response around the particles of MCBA, 9 months after grafting the sinus Puros.

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Figure 1—Preoperative panoramic radiograph.

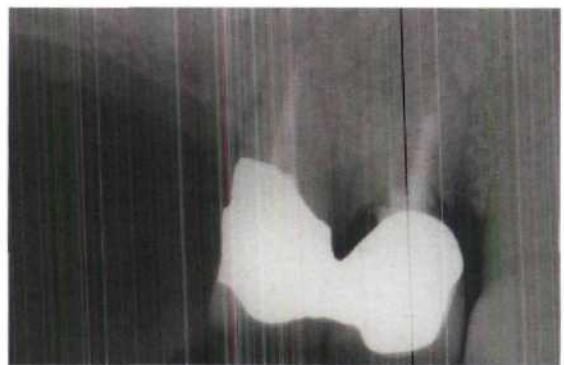


Figure 2—Periapical radiograph identifying hopeless teeth Nos. 4 and 5.

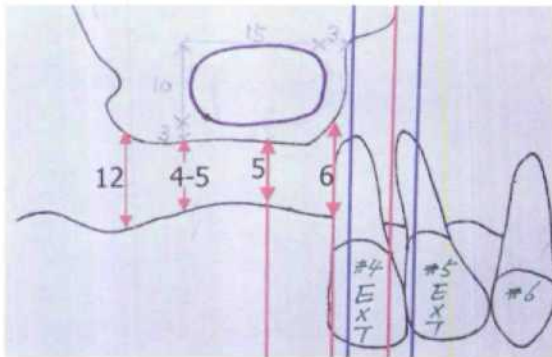


Figure 3—Preoperative planning from computer axial tomographic (CAT) scan with SIM/Plant analysis.

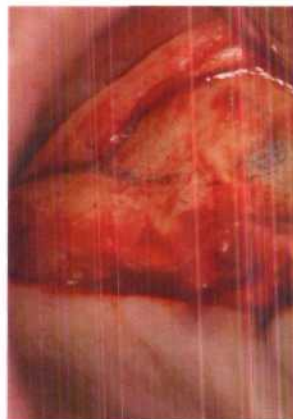


Figure 4—Mucoperiosteal flap elevated with window outlined.



Figure 5—Oval window elevated with membrane perforation visible.

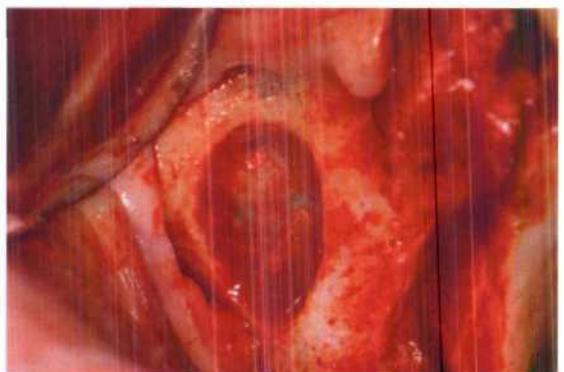


Figure 6—Collagen barrier membrane placed over perforation.

to histologically evaluate MCBA (Puros) in a sinus augmentation procedure after graft maturation.

Clinical Report

An 86-year-old woman presented to the Department of Implant Dentistry at NYU Dental Center after a 2 year absence to continue her implant treatment. Dental diagnosis included clinical and radiographic evaluation (Figure 1). Periapical, panoramic, and computer axial tomographic (CAT) scan radiographs were taken to evaluate the oral condition and develop a treatment plan. The maxillary right premolar teeth were deemed hopeless and extracted (Figure 2). Four implants at teeth

Nos. 11 through 14 had been placed 2 years earlier and remained unloaded.

The patient had 5 mm to 6 mm of crestal bone remaining below the sinus floor in the right molar area as determined by CAT scan and SIM/Plant evaluation^c (Figure 3). There were no medical or dental contraindications to treatment. Before surgery she was verbally informed of the alternatives to implant treatment and told of the benefits and risks of each treatment option. She wanted to avoid a removable prosthesis and agreed to a treatment plan that included sinus augmentation and implant placement to replace teeth Nos. 3 through 5. The patient consented to being included in NYU's

^cMaterialise NV, Glen Burnie, MD 21061; (443) 557-0121

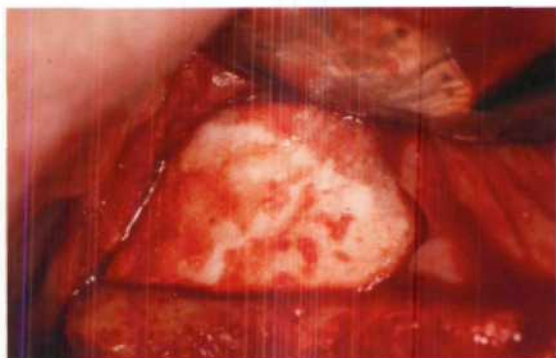


Figure 7—Collagen barrier membrane placed over lateral window.



Figure 8—Primary flap closure.

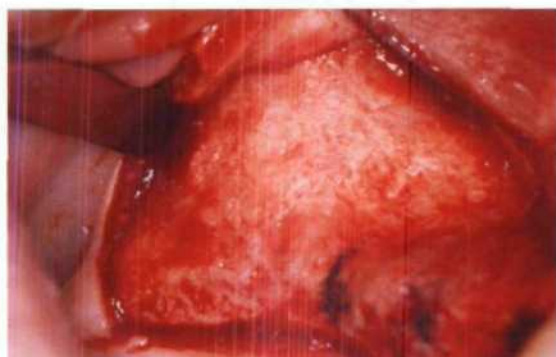


Figure 9—Re-entry at 9 months shows dense graft resistant to probing.

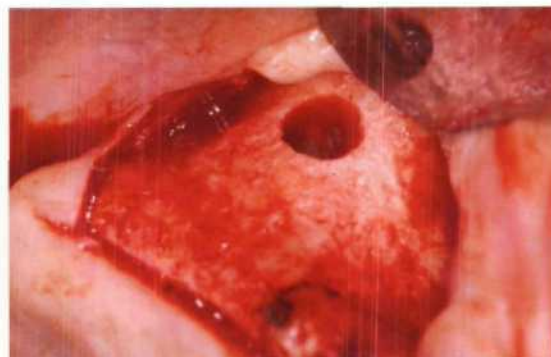


Figure 10—Site of trephine core is in distal, superior location in sinus.



Figure 11A—Three millimeter diameter core.

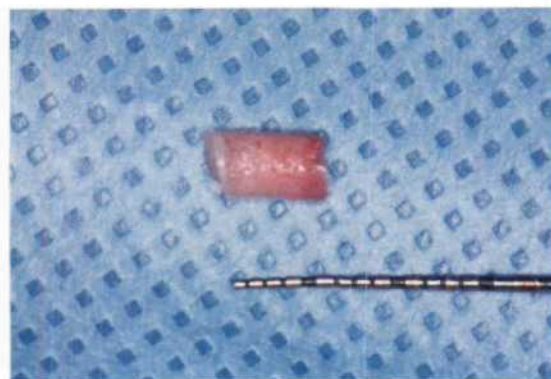


Figure 11B—Three millimeter diameter core.

clinical and histological study comparing graft materials used for sinus augmentation, and signed a consent form approved by the Institutional Board of Research Associates (IBRA), NYU School of Medicine.

The patient received 500 mg Augmentin^d 1 hour before surgery. The following surgical steps were then performed: administration of local infiltration anesthesia (lidocaine with epinephrine 1:100,000), a crestal incision from tooth No. 1 to tooth No. 6, reflection of a full thickness mucoperiosteal flap exposing the lateral wall of the sinus, and preparation of an oval window in the lateral sinus wall (Figure 4). The bony window was then elevated together with the sinus membrane (Figure 5). After ele-

vation, a small perforation of the Schneiderian membrane was observed and subsequently covered with a resorbable collagen membrane^a (Figure 6). Autogenous bone harvested from the tuberosity and window was added to the Puros graft. The graft mixture, consisting of 10% autogenous bone and 90% Puros, was hydrated in sterile saline and placed in the newly formed subantral compartment. The MCBA mixture consisted of 50% (3 mL) of .25 mm to 1 mm particle size and 50% (3 mL) of 1 mm to 2 mm particle size. More resorbable collagen membrane was hydrated for 1 to 5 minutes in sterile saline before placement, then contoured and placed over

^aGlaxoSmithKline, Middlesex England UK; (020) 8990 9000

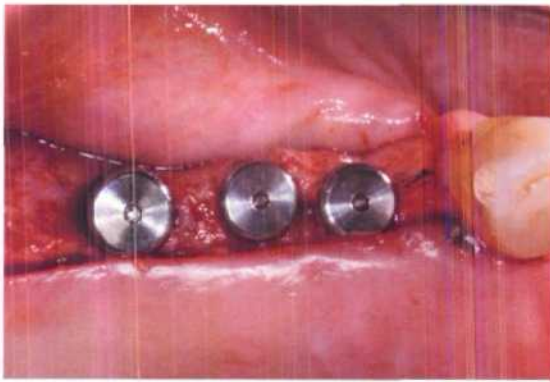


Figure 12—Implants placed anterior to and into sinus graft.



Figure 13—Radiograph of implants in Figure 12.

the prepared window.²² The membrane extended 3 mm beyond the limits of the prepared window and was placed in close apposition to the bone (Figure 7). Primary closure of the flap was achieved with interrupted 4-0 silk sutures (Figure 8). The patient was placed on antibiotics (Augmentin 500 mg 3 times a day for 10 days after surgery), an anti-inflammatory (Medrol Dose Pack[®]), and analgesics (Tylenol with Codeine #3[†]). Rinses with .12% chlorhexidine digluconate twice daily for 2 weeks were prescribed. Healing was within normal limits 7 days after surgery, and the sutures were removed.

Nine months later, at stage I surgery, 3 implants were placed and a trephine core sample (10 mm in length and 3 mm diameter) was retrieved from the lateral window area in a manner that did not compromise implant placement (Figures 9 through 13). This method of core retrieval is consistent with previously published NYU sinus studies.¹⁰ Both the lateral wall and implant osteotomy sites presented resistance when the drill was used. The patient was placed on antibiotics (amoxicillin 500 mg 3 times a day) for 10 days after surgery beginning 1 hour before surgery and was given a prescription for analgesics. Rinses were prescribed with .12% chlorhexidine digluconate twice daily for 2 weeks. The sutures were removed 7 days after surgery. The patient was seen for follow-up at 1 week, 4 weeks, 8 weeks, and 16 weeks after implant placement surgery. All implants appeared to be healing within normal limits.

Histological Report

The retrieved core was sent to the Hard Tissue Research Laboratory for histological

analysis. The histologist was blinded to the nature of the bone graft material in the sample.¹⁰ The specimen was fixed in 10% neutral buffered formalin. The specimen was then dehydrated with a graded series of alcohols for approximately 14 days. After dehydration, the specimen was infiltrated with a light-curing embedding resin[®]. After approximately 14 days of infiltration with constant shaking at normal atmospheric pressure, the specimen was embedded and polymerized by 450 nm light with the temperature of the specimens never exceeding 40°C. The specimen was prepared by the cutting/grinding method of Donath and Rohrer,^{23,24} and cut to a thickness of 150 μm on an EXACT[®] cutting/grinding system. Then the slide was polished to a thickness of 35 μm to 45 μm on the EXACT micro grinding system, and was stained with Stevenel's blue and Van Gieson's picric fuchsin. Microphotographs were taken, scanned, digitized, and analyzed using the public domain National Institutes of Health image program (developed at the US National Institutes of Health and available on the internet at <http://rsb.info.nih.gov/nih-image/>). Three sections were analyzed from the core. The percentage of vital bone, connective tissue, and residual graft material was determined by an average of these 3 sections.

Results

The average percentage in the 9 month post sinus lift core of vital bone was 25.2%. The average percentage of connective tissue and marrow was 58%. There remained 16.8% of residual graft material in the core. However, the MCBA graft particles were in apposition to

[†]Pfizer, New York, NY 10017; (212) 573-2323
[®]Ortho-McNeil Pharmaceutical Inc, Raritan, NJ 08869; (908) 218-6000

[®]7200 VLC, Heraeus Kulzer, Germany, Gruner Weg 11, Hanau D-63450; 49.6181.3540.16

[®]Esakt Apparatebau GmbH & Co, Norderstedt, Germany

the new bone and in many cases nearly indistinguishable. Representative histologic examples are presented in Figures 14, 15, and 16.

Discussion

To the authors' knowledge, this is the first human case report to histomorphometrically evaluate vital bone production in the maxillary sinus using Puros bone replacement graft. The analysis was made 9 months after grafting of the maxillary sinus. The cadaver bone processed into Puros is obtained from a certified (American Association of Tissue Banks) tissue bank. Donor material is deemed suitable based on medical, social, and sexual history inquiry, physical examination, autopsy findings (if performed), medical history/records review, and laboratory tests. Tissue is procured aseptically and held in approved storage until preservation and sterilization processes are performed.

The allograft material consisted of human cancellous donor bone that was treated for biological safety through a 5-step proprietary (Tutoplast) process that included delipidization (defatting), osmotic contrast treatment, oxidation with hydrogen peroxide, solvent dehydration, and limited-dose gamma irradiation (17.8 Gy).^{25,26}

This method of processing has been shown to inactivate the HIV virus and the agent responsible for Creutzfeldt-Jakob disease.²¹ Reports of bovine spongiform encephalopathy (BSE) in humans²⁷ and the finding that viable HIV viruses have survived in allogenic bone tissue after freezing, washing, and freeze-drying²⁸ have raised concerns about disease transmission from xenografts and allografts. International standards define sterility as the absence of any viable pathogen.²⁹

Common methods of inactivating pathogens (bacteria, viruses, fungi, protozoa) in heterogeneous tissues before sterilization include the application of ultraviolet light, heat, irradiation, and/or chemical energy to change the conformation of proteins by altering chemical bonds, or to fragment the DNA/RNA strands. With changed conformation, proteins can no longer work properly. When the proteins in the capsid or envelope of viruses is changed in their conformation, viruses can no longer infect cells.³⁰ If

DNA/RNA is changed through low-dose irradiation, natural ultraviolet light, strong alkali (pH > 12) or low pH (pH < 3), bacteria die or can no longer replicate.

Proteinaceous infectious particles called prions have been identified as the agents that cause and transmit BSE and related encephalopathies. Prions are extremely resistant to conventional inactivation procedures, including irradiation, boiling, dry heat, and chemical treatment (formalin, betapropiolactone, alcohols).^{27,31-42} Denaturing organic solvents (phenol), chaotropic agents (guanidine isothiocyanate), or alkali (NaOH as used for solvent dehydration in the Tutoplast process) have been shown to effectively inactivate prions.⁴³⁻⁴⁷

Most tissue bank processing techniques effectively minimize the risk of disease transmission from dangerous pathogens in their products. Screening of potential tissue donors is also imperative to rule out health and lifestyle factors that could engender susceptibility to such pathogens as the HIV viruses.^{28,48,49} Sterility validation studies and adherence to good manufacturing practices help to ensure product safety.

Since the advent of the sinus elevation procedure, researchers have been evaluating various bone replacement grafts to determine which are best suited for the successful placement of endosseous implants. Many bone replacement grafts have been used and evaluated histologically. These include allografts,⁸ alloplasts,⁵⁰⁻⁵⁵ and xenografts.^{10,56-60} The use of an ideal material should result in the formation of a high percentage of vital bone after reasonable graft maturation. The literature shows a wide range of results using these different grafting materials, with vital bone content ranging from 14% to 44%.^{10,51}

Implant survival rates with mineralized xenografts and alloplasts have been reported to be as high as or higher than those achieved with autogenous bone grafts.^{6,7} While a significant percentage of these mineralized graft materials may not be resorbed,^{14,57-59} there is no evidence that this residual graft material adversely affects osseointegration and, ultimately, implant survival. In fact, the high implant survival rates reported with mineralized bone

replacement grafts may be due in part to the increased stability (greater density) that they provide.

On the other hand, reports on the use of mineralized and demineralized human allografts have not been as promising.⁶¹⁻⁶³ The only positive report occurred when crestal bone heights were greater than 4 mm.⁸

Conclusion

This case describes the healing response after a sinus augmentation procedure using the mineralized cancellous bone allograft, Puros. The results after 9 months of healing demonstrated a vital bone content of 25.2% in the grafted sinus, as ascertained from a trephine core taken from the superior aspect of the lateral window area. Although the vital bone requirement for implant survival in an augmented sinus is unknown, the 25.2% vital bone demonstrated in this case compares favorably with that reported in the literature for other augmentation materials including xenografts, alloplasts, and autogenous bone. The remaining Puros particles (16.8%) were in close apposition to the new bone. It might be reasonable to assume that, over time, these particles will be absorbed and replaced by new bone, which would result in the formation of a greater percentage of vital bone. However, one must note that more extensive research is required.

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