

# SINUS FLOOR AUGMENTATION USING A COMPOSITE GRAFT OF BONE MORPHOGENIC PROTEIN-2 AND ALLOGENIC CANCELLOUS BONE (PUROS): CASE REPORT

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## KEY WORDS

Bone morphogenic protein  
Osteoconduction  
Osteoinduction  
Mineralized bone

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Reconstruction of the atrophic maxilla is a difficult task. The gold standard for such reconstruction is autogenous bone. Presently, many excellent products are available to the dental surgeon to facilitate alveolar reconstruction in the absence of autogenous bone. This study describes the use of bone morphogenic protein in combination with allogenic bone substitute (Puros) to reconstruct the maxilla in preparation for dental implant placement.

## INTRODUCTION

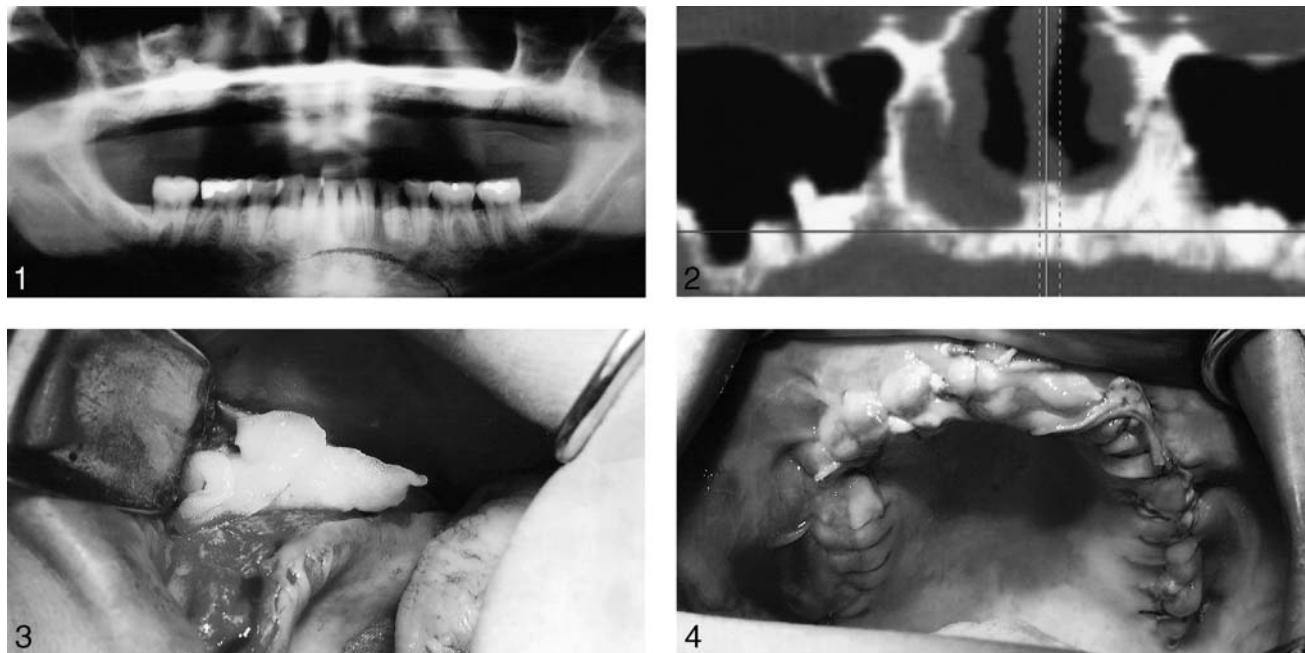
Dental reconstruction of patients with an atrophic maxilla is often a difficult task. These patients present with myriad challenges, including, but not limited to, insufficient quantity and quality of bone for the placement of dental implants, retro position of the maxilla secondary to bone resorption (acquired maxillary hypoplasia), pneumatization of the sinus cavity, and loss of lip support.

There are many methods the dental surgeon can pursue to reconstruct an atrophic maxilla. The gold standard has been autogenous bone procured from such places as the iliac crest, tibia, mandible, or skull.<sup>1-5</sup> The advantages of autogenous bone include availability of sufficient volume

of material, biologic safety, and its content of osteogenic cells. The disadvantages of host-procured bone are well known and include, but are not limited to, increased blood loss, donor site morbidity, increased instance of infection, and patient refusal.<sup>1-5</sup>

Current literature supports the use of allogenic substances for alveolar reconstruction in preparation for dental implants.<sup>6-10</sup> Allogenic bone-graft materials generally provide a scaffold across a defect or in a cavity into which host bone cells migrate to eventually generate bone via osteoinduction (demineralized graft) or osteoconduction (mineralized graft).<sup>6-10</sup>

Presently, many biocompatible allogenic and xenogeneic materials are available to the dental surgeon. Examples of these materials include demineralized



FIGURES 1–4. FIGURE 1. Panoramic radiograph at pregrafting. FIGURE 2. Simplant study of patient at presurgery. FIGURE 3. Surgery photograph showing bone morphogenetic protein graft in maxilla. FIGURE 4. Patient at 1 week postsurgery.

freeze-dried bone allograft (DFDBA), calcium carbonate coral (Bio-Coral, Inotek, St Gonner, France), bovine porous bone mineral (Bio-Oss, Osteo-health Luitpold Pharmaceuticals Inc, Shirley, NY), and PepGen-P-15 (Dentsply, Frialet, Ceramed Co, Lakewood, Colo). Each of these materials has beneficial properties that can produce successful results and are discussed elsewhere.<sup>7–11</sup> Although generally successful, drawbacks to these and most other bone substitute materials include unpredictable new quantity and quality of bone formation, patient acceptability, variable or slow resorption characteristics, and costs.<sup>7–11</sup>

Puros (Zimmer Dental, Carlsbad, Calif), a human mineralized cancellous bone substitute material, has been recently made available to the dental surgeon for alveolar reconstruction and preservation.<sup>1,12,13</sup> Its unique patented method of preparation is claimed by the manufacturer to ensure the preservation of the bone morpho-

genic proteins (BMPs) and minerals believed to be necessary for osteoinduction and to minimize the host cellular reaction to the product.<sup>12,13</sup> Additionally, the product has been shown to rapidly enhance bone formation and permit successful placement of dental implants in as little as 16 to 24 weeks.<sup>12–14</sup>

Recently, a member of the BMP family, recombinant human BMP (rhBMP-2), has gained favor for the reconstruction of bone defects in the maxillofacial skeleton.<sup>15–18</sup> It is one of the family of BMPs originally described by Urist and has been used in orthopedic surgery for many years to stimulate bone growth.<sup>15,16</sup> The various properties and characteristics of rhBMP-2 are described in detail elsewhere.<sup>8,17–19</sup> In summary, rhBMP-2 serves to predictably and quickly generate bone *de novo* by osteoinduction.<sup>17–20</sup>

This article will present a case of sinus floor augmentation using a combination of mineralized human bone allograft and

rhBMP-2 in preparation for placement of dental implants. Bone-core biopsies were used to evaluate the composite graft.

#### CASE REPORT

A healthy 50-year-old woman presented to the first author's office in July 2004 for consultation regarding dental implant reconstruction. She was currently wearing a complete upper denture and had been totally edentulous in her maxillary arch for 2 years. On examination, moderate alveolar atrophy was noted in the maxilla, and the soft tissue appeared normal. Review of the patient's panoramic radiograph revealed that there was less than 10 mm of bone available in the maxilla (Figure 1). It should be noted that slightly more bone volume was present in the right and left molar regions of the maxilla because of the previous grafting of the sockets at time of extraction by the general dentist some years ago.

A computerized tomography (CT) scan was obtained to more thoroughly evaluate the quantity and quality of bone present. A review of the scan with specialized software (Simplant 8.33, Columbia Scientific, Columbia, Md) demonstrated that there was insufficient height throughout the maxilla and insufficient width in selected areas to permit placement of dental implants (Figure 2).

During the preoperative consultation, various options of bone grafting, including use of autogenous bone, allogenic substances, and combinations thereof, were discussed with the patient with respect to reconstruction of the maxilla. After consideration of all options, informed consent was obtained for use of rhBMP-2, mineralized human bone allograft, and autogenous bone harvested from the mandibular symphysis to reconstruct the maxilla.

On September 3, 2004, while under general anesthesia, the patient underwent bilateral sinus lifts as described by Block and Kent.<sup>21</sup> A combination of 8.4 g of rhBMP-2 on an absorbable collagen sponge prepared according to the manufacturer's instructions (rhBMP-2/ACS, Infuse bone graft, Medtronic Sofamor Danek, Memphis, Tenn) and 10 cm<sup>3</sup> of mineralized human bone allograft (Puros) was used as a graft material to fill the sinus cavity to create approximately 15 mm of additional height to the maxilla from the canine region to the first molar region (Figure 3). Additionally, bone harvested from the mandibular symphysis was grafted on the right and midline of the maxilla to provide additional width where indicated. The technique to obtain the grafted bone from the patient, prepare the host bone site for reception of the graft, and secure the graft to

the host bone is described in detail by Pikos.<sup>22,23</sup> To enhance soft tissue healing, 8 mL of platelet-rich plasma (PRP) was applied to the graft site. The method of generating and using PRP is described elsewhere by Petrunaro.<sup>24</sup>

The patient tolerated the procedure well and was discharged with an analgesic for pain control (mepergan fortis, Wyeth-Ayerst, Philadelphia, Pa), a prophylactic antibiotic (clindamycin, Pharmacia & Upjon, Peapack, NJ), and a steroid dose pack (Pharmacia & Upjon) to minimize postoperative swelling. She was asked to not wear her complete upper denture for 1 week and to rinse her mouth with salt water twice daily.

The patient was seen 1 week postoperatively. All wounds were primarily closed and there were no signs of infection (Figure 4). At this time the patient was permitted to wear her newly relined upper denture.

The patient was seen multiple times over the next 4 months to evaluate the healing of the surgical wounds. No signs of infection were evident and all wounds healed uneventfully.

Eight months after the initial surgery, the patient underwent placement of 7 SteriOss Replace Select (Nobel Biocare, Yorba Linda, Calif) dental implants (4.3 × 10 mm) in the maxilla in tooth positions 3, 4, 5, 7, 10, 14, and 15 as determined by the patient's existing denture.

During implant placement, a biopsy of the maxilla at this surgery was obtained. After elevation of a mucoperiosteal flap in the maxilla, the author (L.M.W.) could discern a clear demarcation in the bone, indicating the presence of graft material consistent with the location of the lateral window created previously during the sinus elevation surgery.

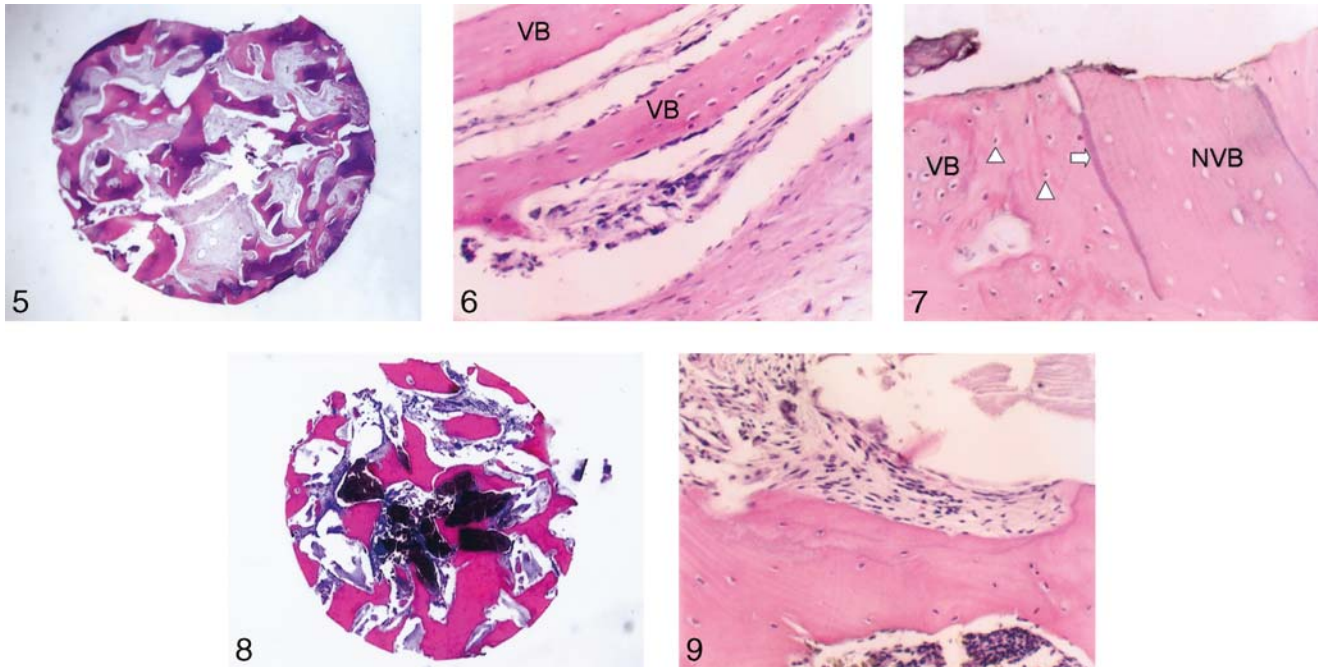
A biopsy specimen in the center of this area of grafted bone was taken from lateral to medial with a 2-mm trephine bur to a depth of approximately 6 mm. This 2- × 6-mm bone core was then immediately placed in 10% formalin for preservation.

The patient tolerated the procedure well and was discharged with appropriate antibiotics and analgesics. Healing was uneventful over the next 4 weeks. The patient is scheduled to begin the restorative phase of the treatment plan in 5 to 6 months.

#### MATERIALS AND METHODS

The bone cores were washed in running water for 30 minutes to remove fixative and were placed in formic acid and sodium citrate solution and allowed to decalcify for approximately 6 days.<sup>24</sup> After decalcification, samples were processed for routine embedding in paraffin, thin sectioning, and staining with hematoxylin and eosin. Digital images of the entire bone core were acquired with a digital spot camera (Spot Diagnostic Instrument Inc, Sterling Heights, Mich) attached to the stereo Zeiss dissecting microscope (Carl Zeiss, Wetzlar, Germany) with a ×20 magnification factor (10 × 2.0 optivar). Low-magnification (×2.5) digital images were acquired and used for the calculation of total bone volume in the samples. The higher-magnification images were used to calculate the volume of vital bone vs nonvital bone-graft materials in the samples. The images were then imported into a Bioquant Nova Prime Image Analysis software (Bioquant Image Analysis Program Co, Nashville, Tenn). Because all the histologic sections analyzed had the same thickness, the area fraction measurement (Aa) is equal to volume





FIGURES 5–9. FIGURE 5. Low-magnification view of right maxillary sinus bone core cross section stained with hematoxylin and eosin showing interconnecting bone trabeculae surrounded by connective tissue (magnification  $\times 2.5$ ). FIGURE 6. High-magnification view of right maxillary sinus bone core showing regenerated bone trabeculae with osteocytes and osteoblast covering its surface (magnification  $\times 20$ ). VB indicates vital bone. FIGURE 7. Photomicrograph of bone core from right maxillary sinus showing vital bone placed on Puros cancellous bone-graft remodeling lines. NVB indicates empty osteocytic lacunae. FIGURE 8. Low-magnification view of left maxillary sinus bone core showing bone trabeculae and dark-stained bone morphogenetic protein (arrows) (magnification  $\times 2.5$ ). FIGURE 9. High-magnification view of left maxillary sinus bone core showing regenerated bone with large number of osteocytes (magnification  $\times 20$ ).

fraction (Vv). The Vv of the total bone was measured and presented as a percentage of the total area of the core. At higher magnification, the Vv of vital bone (regenerated bone) and the Vv of nonvital bone (bone graft) were calculated and presented as a percentage of the total bone (Figure 5).

## RESULTS

Both vital and nonvital bone can be identified in the bone cores from the right and left maxillary sinuses (Figures 5 through 9). At lower magnification the regenerated vital bone could not be distinguished from the bone-graft materials. The Vv of total bone/total volume of bone core was 28.60% for the left maxillary sinus and 53.54% for the right maxillary sinus (Figure 10). The Vv of vital

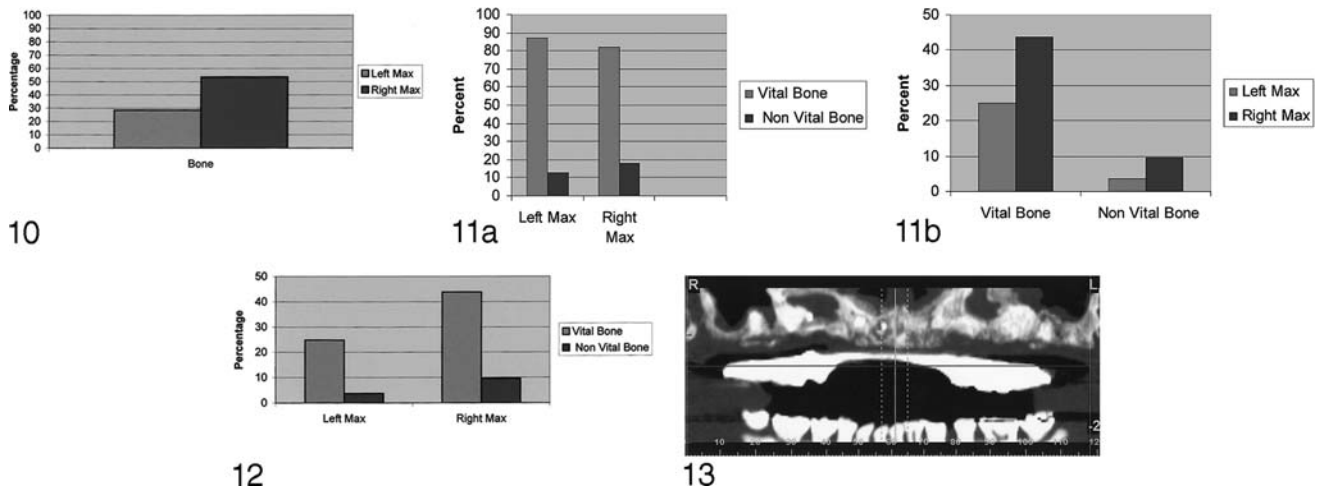
bone (bone with osteocytes) was 87% of the total bone in the left maxillary sinus bone core and 82% of the bone core of the right maxillary sinus (Figure 11). The Vv of vital bone/total bone core was calculated and expressed as 24.86% vital regenerated bone in the left bone core and 43.90% in the right bone core (Figure 12). Some of the vital bone could be seen either as trabeculae surrounded by connective tissue and lined with active osteoblasts or residual as a layer of new bone intimately associated with the nonvital mineralized bone allograft (Figures 6 and 9).

Comparison of the CT images before grafting with those 6 months postgrafting suggests the presence of suitable quantity and quality of bone. Figures 2 and 13 demonstrate that the grafting process yielded sufficient quantity of

bone. Hounsfield unit (HU) values of the approximated implant sites in the nongrafted maxilla ranged from an average low 168 HU at tooth position 15 to an average high of 1381 HU at tooth position 14 (Table). In the grafted maxilla the average low was 1160 HU at tooth position 5 and the average high was 1740 HU at tooth position 4 (Table). Normal bone in the maxilla considered suitable for dental implant placement typically has a value of 850 to 1250 HU (D1 or D2). Thus, the radiographic evidence supports the histologic findings of the formation of new bone suitable for dental implants.<sup>25</sup>

## DISCUSSION

Successful reconstruction of the atrophic maxilla and mandible has been reported after using



FIGURES 10–12. FIGURE 10. Percentage of total (vital and nonvital) bone volume (Vv) in total area of bone core. FIGURE 11. Relative proportion of vital bone vs remaining Puros bone graft (nonvital) calculated at high magnification. FIGURE 12. Percentage of vital bone vs nonvital bone in the total area of the bone core by using the proportions presented in Figure 7 against the total bone volume presented in Figure 6.

FIGURE 13. Simplant scan at 6 months postgrafting.

allogenic bone either alone or in combination with autogenous bone.<sup>1,7,8,11,13,17</sup>

Human mineralized allograft is often used in alveolar bone reconstruction before the insertion of dental implants. It can be used in the cortical or cancellous form. The preservation of the mineral component of the bone and its associated BMPs is paramount to the product working to successfully stimulate bone formation in the grafted site.<sup>12–14</sup>

A genetically engineered product, rhBMP-2 has been shown to induce bone formation de novo.<sup>11,15,18,20</sup> It appears to induce undifferentiated mesenchymal cells to differentiate into osteoblasts, which are necessary for bone formation.<sup>11</sup>

For many years the orthopedic literature has reported the benefits of BMPs vs other types of grafting materials for the repair of bony defects.<sup>15,16</sup> More recent reports in the maxillofacial literature have detailed some of the benefits and successes of BMP use in regeneration bone in the alveolus for placement of dental implants.<sup>17,18</sup> Schwartz et al<sup>20</sup>

demonstrated that rhBMP-2 can be added to DFDBA to yield superior results vs DFDBA alone. Boyne and Shabahang<sup>11</sup> showed that rhBMP-2 in combination with Bioplant HTR (Sybron Dental Specialties, Kerr Corporation, Newport Beach, Calif) or Bio-Oss or Bio-Coral produced adequate repair of the alveolar bone for placement of dental implants.

Some of the benefits of rhBMP-2 as a bone-regeneration product include the elimination of disease transmission risk, the ease of use with many commonly used carriers, and the ability to rapidly generate new bone. Disadvantages

of rhBMP-2 are few but include its relatively high cost and difficulty of obtaining the product.<sup>16–21</sup> Currently, rhBMP-2 is approved for orthopedic use only; however, multiple studies support its off-label use in reconstructing the maxilla and mandible.<sup>15,17–20</sup>

The combination of mineralized human bone allograft and rhBMP-2 as a composite graft for sinus floor augmentation proved to be an excellent method to gain sufficient quantity and quality of bone in the atrophic maxilla while minimizing the need for autogenous bone. The bone-core biopsy showed new bone formation in

TABLE  
Measure of Hounsfield units of grafted maxilla\*

Tooth Position	Pregrafting			Postgrafting		
	Inside Dental Implant	Outside Dental Implant	Average	Inside Dental Implant	Outside Dental Implant	Average
3	811	880	846	1790	1124	1457
4	927	576	1189	1828	1651	1740
5	1297	1080	1189	1218	1102	1160
7	1131	813	972	1501	1354	1428
10	850	627	739	1302	1054	1178
14	1472	1290	1381	1644	1446	1545
15	160	175	168	1196	1243	1220

\*As measured by Simplant 8.33 program (Columbia Scientific, Columbia, Md).

direct contact with the allogenic bone, which apparently acted as a scaffold. The percentage of vital bone differed with respect to the right and left sinuses but was clinically adequate and appeared similar to that of normal bone in either case.

The question naturally arises as to the rationale of using a combination of products vs a single product in similar cases. By itself, rhBMP-2 has been shown to be capable of inducing bone in situ.<sup>15,18</sup> Multiple literature reports support the sole use of either of these products for successful bone grafting.<sup>1,12,13,17,18</sup> In this particular case, the author (L.M.W.) elected to use both human mineralized bone-graft material and BMP in an attempt to generate a superior quality and quantity of new bone. Although BMP produces excellent new bone, the typical method in which it is carried to the patient (ie, collagen sponge) means that the anticipated volume of new bone may be less than desired, as the collagen sponge compresses in the maxillary sinus. The addition of human mineralized bone to the rhBMP-2 added volume and acted as a space-maintaining carrier and scaffold for the formation of new bone, thus potentially permitting more bone volume to be generated.

The frontier of bone reconstruction is vast and full of opportunities. This single case provides the dental surgeon with a scientific basis for the use of new materials to regenerate sufficient quantity and quality of bone in the atrophic maxilla for the dental implant patient. Of course, additional studies on the combination of human mineralized graft material with BMPs will be needed to further support these data.

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