An Alternative Treatment for the Periodontal Infrabony Defect
A Synthetic Bioactive Resorbable Composite Graft

For the past 15 years emphasis has moved away from resective periodontal surgery toward regenerative periodontal surgery. Infrabony defects have been treated with guided tissue regeneration (GTR) with or without the placement of materials that are allogeneic (a graft between genetically dissimilar members of the same species) or alloplastic (a graft being biocompatible or inert). The addition of bone substitutes has been demonstrated to reduce the success rate of GTR procedures. This is a variation of the original protocol, which employed calcium sulfate alone or in combination with bone substitutes. Calcium sulfate is biodegradable, non-inflammatory, and readily available at a reduced expense compared to other regenerative materials. Calcium sulfate, useful as a binder, will harden when applied in periodontal defects and maintain its space by setting. However, CS does not induce bone regeneration due to rapid resorption and lack of chemotactic bioactivity.

In the case reports described in this article, calcium sulfate was mixed with a synthetic bioactive resorbable graft (SBRG) having a bioactive chemotactic response. This graft material has been used in a variety of bone augmentation cases alone or with DFDBA as a binder for sinus elevation procedures in which the material is well compacted. Results of one clinical and histologic study suggest that DFDBA alone may have little or no osteoinductive potential. Another study concluded that DFDBA does not induce bone regeneration, although it does show some definitional activity. After placement into a defect, the material maintains its sponge-like state and may act as an inhibitor to bone formation; thus it is not ideal for implant support. However, Gorg reported that allografts of DFDBA, which may be cortical or trabecular, have
to periodontal defect applications.\textsuperscript{13,14} The selection of synthetic materials (alloplasts), rather than organically derived materials, may be needed as a result of patients’ aversion to the use of human tissue and the risk of being infected with transmitted pathogens (ie, HIV, hepatitis) that escaped detection during testing and processing. DFDBA has been utilized in the treatment of periodontal defects for the past 15 years. Concerns have been raised about disease transmission, and the safety of human-derived materials has recently been questioned due to transmission of the hepatitis C virus by tissue transplantation.\textsuperscript{15} Transmission of HIV infection from seronegative organ and tissue donors has occurred,\textsuperscript{16} and other potential

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osteocductive and “possibly osteoinductive” properties, however, “they are not osteogenic.”\textsuperscript{13} In the particle size ranging from 150 to 1,000 \( \mu \text{m} \), “DFDBA [grafts] are more effective and limited
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normal disinfection or sterilization procedures. Although allogeneic or xenogeneic materials (human or bovine) used as grafts are treated with gamma radiation or by acid demineralization, the potential for disease transmission must be considered. This does not represent a problem for alloplastic graft material.

Synthetically derived materials have been utilized in periodontal surgery for more than 17 years. Although dense ceramic hydroxyapatite (CHA) (eg, OsteoGraf/N [CeraMed]) or bioactive glass (eg, Perioglass [Block Drug] or Biogran [Orthovita]) may be biocompatible, each material’s clinical efficacy has been questioned.20,21 For example, a recent report suggests that epithelial down-growth observed with high-density materials of CHA may be attributed to lack of material consolidation relevant to the material’s density and chemical complexities.22 Further, the use of CHA has been associated with a lack of material resorption, leading to irregular infiltration of new bone as well as fibrous tissue encapsulation.23 Because of their chemical structure and/or physical density, nonresorbable graft materials and membranes (plastics) break down, act as irritants, and sequester bone formation.24,25

Animal and human studies have demonstrated that fragmentation and transport of nonresorbable particulates spread into regional lymph nodes and other organs (lungs, spleen), which interferes with the function of these tissues and organs (and could compromise the immune system). In contrast, studies indicate that SBRG does not pose the problems that are associated with nonresorbable particulates. SBRG ionizes in situ into calcium and phosphate ions without transport by the cells. For example, the 6-week and 12-week in vivo bone responses of low-temperature SBRG were studied and compared to CHA coatings, sputtered CHA coatings, and smooth and roughened titanium surfaces. Implant materials were analyzed by x-ray diffraction and infrared spectrophotometry prior to implantation. The American Society for Testing and Materials has determined purity standards for ceramic hydroxyapatite. SBRG has almost twice the level of purity that is observed on ceramic materials. The analysis confirmed the presence of crystalline Ca₆₃(PO₃)₂(OH)₂ for SBRG particulates, which contained the hydroxyl groups (OH). This synthetic bioactive resorbable graft is chemically and crystallographically similar to human bone mineral and is different from high-temperature ceramic hydroxyapatite. Furthermore, it was found that there are no carbonate ions (CO₃²⁻) in CHA as is seen for human bone (approximately 4% to 6%) and SBRG (approximately 2% to 3%).26 Undecalcified specimens were examined by light microscopy and microangiography. At each time interval, bone growth into titanium implant chambers was significantly greater with SBRG than with other materials. In addition, Ricci concluded that the SBRG “materials showed bone directly surrounding and attaching to these materials without any visible interposing tissue.”26

In a sinus elevation study by Artzi, the author stated that all implants were successful. “Although rarely observed, fibrous encapsulation of some grafted (SBRG) particles could not be ruled out.” He also stated in his paper that implant studies by Fugazzotto had a 98% cumulative success rate over a 5-year period.

Due to a sintering process of CHA at high temperatures, it becomes OH-deficient (dehydroxylated) and is classified as an oxyapatite (Ca₅₀(PO₄)₂(OH)₂), not hydroxyapatite.27 In contrast, SBRG crystal growth and maturation is processed at lower temperatures and contains brushite (CaHPO₄•2H₂O) and CaHPO₄ monohydrate as a minor constituent. The chemical potentiality of brushite has been found to be the precursor phase to biologic hydroxyapatite in an embryonic environment, resulting in the first state of bone mineralization in situ.28,29 These bioactive precursor compounds induce the cytoplasmic activity of the osteoblast cells from pink color (at rest) to red, denoting cell excitation for the process of mineralization by a chemotactic response.7,25,26 The minimal connective tissue migration observed with the low-temperature SBRG material is due mostly to brushite. The crystallographic morphology of SBRG (rectangular and hexagonal) allows for faster crystal formation which permits controlled dissolution of the brushite. In a study by Fugazzotto and Meffert, it was observed that by grafting the crestal undercut portion of the implant neck, bone regeneration was observed. This technique was used to prevent apical migration of the epithelium due to the chemical potentiality of Osteogen (Impladent Ltd), a synthetic bioactive resorbable graft. Further, SBRG has been associated with bone fill in human clinical trials.10,30,31

Alloplastic graft materials are readily available and inexpensive. These materials can be utilized as an alternative to autogenous donor material or allografts, without the risk of disease transmission and morbidity. Utilization of alloplastic materials is not associated with an immunologic response to antigens. Numerous animal and human studies have demonstrated histologic and clinical efficacy of low-temperature SBRG.24,25 In one such study involving grafted human hydroxycarbonate implanted into the ileum of rats, the SBRG material demonstrated a significant increase in bone formation as compared to the control of other graft materials when implanted for more than 7 days. Further, this study demonstrated that SBRG was associated with enhanced bone formation in bony voids as compared to plastic graft material, and that bone fill progressed over time. It was concluded that SBRG also demonstrated a higher chemotactic response and cell-binding capacity when compared to other particulates. A study by Ruano compared the effect of ceramic hydroxyapatite versus non-ceramic hydroxyapatite (Osteogen) for cell growth capacity and procollogen synthesis of cultured human gingival fibroblasts. The study showed that “viable cells were significantly small in numbers for cultures grown with ceramic hydroxyapatite when compared to Osteogen.”

In one recent human clinical study, sinus elevations, cyst cavities, and tooth extraction sites were grafted with SBRG particulate.29 No failures were reported. In another study, periapical abscess repair, ridge contouring, and bone formation were demonstrated using SBRG mixed with small quantities of collagen (Avitene [Davol, a subsidiary of C.R. Bard]) as a binder. At 4 and 14 months, histology demonstrated progressive bone ingrowth concurrent with replacement of the SBRG particles; ie, the granules were gradually resorbed and replaced with bone. In one case in which a defect was filled with SBRG and then covered with CHA, it was observed histologically that the CHA particles migrated downward from the

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Figure 12. Radiograph 2.5 years postoperatively indicates bone fill.

Figure 13. Facial view preoperative-ly. Note the presence of deep pocketing mesial to the incisors.

Figure 14. Presurgical radiograph demonstrates osseous loss mesial to the incisors.

Figure 15. Pocket depth is clearly within acceptable limits 1 year postoperatively.

Figure 16. Radiographic view 2 years postoperatively confirms the osseous repair.

Figure 17. Preoperative radiograph displays osseous loss to apex. Fural involvement is also apparent.

Figure 18. Radiograph of the site 1 year postoperatively indicates osseous repair.
mon name of plaster of Paris. However, calcium sulfate of the alpha phase hemihydrate/hydroxypropyl methylcellulose (hypromellose), when mixed with SBRG and hydrated with a limited solution of sterile water in a heavy consistency, will resorb in a controlled fashion.

**SURGICAL PROTOCOL**

With identification of an appropriate infrabony defect, local anesthesia is administered, and a full-thickness mucoperiosteal flap is reflected to visualize the defect. The area is debrided with hand and ultrasonic instrumentation to remove all granulomatous tissue and subgingival plaque and calculus. Based on studies that have demonstrated the potential of cementum and dentin to serve as reservoirs for tetracycline, it may be advantageous to treat the involved crestal to the apical region. The nonresorbable CHA was fibroencapsulated and surrounded by macrophages and multinucleated giant cells in the same defect site. No such activity was evident around the remaining SBRG particulates.37,38

Human clinical studies indicate the clinical efficacy of SBRG.39,40 This material is chemically and mechanically similar to natural bone and is physically similar to bone in regard to trabeculation and resorption rate. Several studies have demonstrated that the material is consistently radiolucent (at placement), however the material becomes radiopaque as progressive resorption and mineralization occurs (4 to 6 months postoperatively).10,41-44.

In summary, nonceramic SBRG material offers a reasonable and inexpensive alternative to the placement of bone allograft materials for individuals who have moral or religious reservations, concerns about disease transmission, and fears of donor-host cross-contamination associated with allograft materials. As described previously, calcium sulfate, and in particular Capset (Lifecore Biomedical), has been used extensively in many dental applications. However, it is not well known that the material functions as a containment barrier to maintain graft particles in a defect site. It will function as a cell occlusive protective barrier to prevent unwanted cells, bacteria, and debris from occupying the defect space before bone regeneration can take place. In particular, rapid resorption has been associated with the com-
An Alternative Treatment... continued from pageoot surfaces prior to placement of the composite graft. In addition, tetracycline may positively affect cell adhesion, migration, and proliferation of fibroblasts, and may also be effective in removing the smear layer and opening dentin tubules, which a resorbable bioactive crystal-like could fill.

Conditioning of the roots is performed by mixing one half of a 250-mg capsule of tetracycline with one half of a carpool (0.9 cc) of a local anesthetic that does not contain a vasoconstrictor (ie, epinephrine or Avitene). Avoid excessive bleeding, water, and empty spaces due to insufficient compacting of the material, as bone does not bridge such spaces.

Once the osseus defect is overfilled with a mixture of SBRG and calcium sulfate, the mucoperiosteal flaps are sutured. A protective periodontal dressing may be placed carefully over the surgical site without pressure to the graft; however, this is not mandatory. Postoperative instructions and a suitable analgesic are given to the patient; antibiotics and an antimicrobial mouthrinse (chlorhexidine) are also prescribed for 7 days. The patient is recalled the following week to remove the dressing and sutures. Patients are monitored for 1 month to prevent abberant healing, and maintenance therapy is continued every 3 months.

**CASE PRESENTATIONS**

**Case 1**
A 47-year-old male patient presented with deep pocketing in the interproximal area between the mandibular left first molar and the premolars (Figure 3). Upon reflection of the mucoperiosteal flap, the infrabony defect was visualized (Figure 4). Once debridement was completed using hand and ultrasonic instrumentation, tetracycline was applied according to the aforementioned protocol. This process resulted in a "milk glass" appearance of the root surface. The combination graft of low-temperature synthetic bioactive resorbable material (Osseogen) and calcium sulfate (Capsel) was mixed and placed firmly within the defect with a slight overfilling prior to flap closure (Figure 5). The tissues were subsequently coapted with resorbable sutures (Figure 6). Significant pocket reduction was observed 6 months postoperatively (Figure 7); the same trend continued over the course of a 2-year period of follow-up (Figure 8).

**Case 2**
A 51-year-old male patient was referred for treatment of a long-standing periodontal defect in the mandibular left cuspid. A deep pocket with exudate was seen at the examination (Figure 9). An infrabony defect with amalgam particles at the apical extent was seen radiographically (Figure 10). The defect was treated via open flap debridement; the extraneous amalgam particles were removed, and the composite graft was placed. Significant reduction of the periodontal defect was observed clinically and radiographically 2.5 years postoperatively (Figures 11 and 12).

**Case 3**
A 63-year-old female patient presented with discomfort in the area of the maxillary right central incisor. Upon clinical evaluation, deep pocketing on the mesial aspect was detected (Figure 13). Endodontic evaluation confirmed the presence of a combined endodontic-periodontal lesion, which was successfully treated with root canal therapy (Figure 14). Treatment of the residual defect was performed with placement of the composite graft following open debridement. The complete eradication of the infrabony defect was demonstrated clinically at 1 year and radiographically at 2 years (Figures 15 and 16).

**Case 4**
A 63-year-old male patient with diabetes mellitus presented with pain and swelling in the area of the mandibular right first molar. Bone loss to the apex was noted in the preoperative radiograph (Figure 17). Fureation involvement was also noted. Following administration of local anesthesia, the area was debrided, and the composite graft was placed. An antibiotic was prescribed for 7 days. One year postoperatively the patient no longer exhibited painful symptoms, and marked resolution of the infrabony defect was evident (Figure 18).

**CONCLUSION**
Guided tissue regeneration (GTR) therapy has been described to treat periodontal infrabony defects. A new surgical technique adapts the principle of GTR therapy utilizing a synthetic bioactive graft (SBRG). Instead of using freeze-dried bone allograft and a membrane barrier, SBRG (Osseogen) is used, which is mixed with calcium sulfate (Capsel) in a 4-to-1 ratio, respectively. The advantages of this technique compared to more traditional techniques include a simplified surgical procedure, easy delivery, and a significant decrease in treatment time and cost without the risks associated with a second surgery, which is required if a nonresorbable GTR membrane is used. The treatment described in this article is also risk-free to the patient and doctor in terms of disease transmission associated with placement of organic bone substitutes (human or bovine).

References
18. FDA. Strenghthens Tissue Transplantation Regulations. AAO/AMS Digest, February (5); 1994.
Continuing Education
Test No. 74.x

To submit Continuing Education answers, use the answer sheet on page xx. On the answer sheet, identify the article (this one is Test 74.x), place an X in the box corresponding to the answer you believe is correct, detach the answer sheet from the magazine, and mail to Dentistry Today Department of Continuing Education.

The following 8 questions were derived from the article An Alternative Treatment for the Periodontal Infrabony Defect: A Synthetic Bioactive Resorbable Composite Graft by Stuart R. Epstein, DDS, and Maurice Valen on pages xx through xx.

Learning Objectives

After reading this article, the individual will learn:

• a predictable surgical guided tissue regeneration procedure using cost-effective synthetic material and timesaving techniques, and
• not all hydroxyapatites are created equal: in scientific terms, ceramic hydroxyapatites, dense, or nonresorbing bone graft materials have no comparison to human physiology and they are abusive to the host.

1. Epithelial downward migration will interfere with the regeneration of
   a. bone
   b. cementum
   c. mandibular hydroxyapatite
   d. all of the above

2. Which of the following combination materials may be used as a barrier for guided tissue regeneration?
   a. calcium hydroxide and ammonium hydroxide
   b. calcium sulfate and SBRG
   c. both a and b
   d. none of the above

3. Recent studies question the ability of demineralized freeze-dried bone to be
   a. osseocoductive
   b. osseoinductive
   c. both a and b
   d. all of the above

4. Which material is radiolucent the day of placement and the site is radiopaque in 4 to 6 months?
   a. ceramic hydroxyapatite (CHA)
   b. synthetic bioactive resorbable graft
   c. bioactive glass
   d. bovine hydroxyapatite

5. Chemical treatment of the involved roots may be done using ______.
   a. ceramic hydroxyapatite
   b. saline
   c. calcium sulfate
   d. tetracycline

6. Root conditioning may affect fibroblasts by increasing______.
   a. cell adhesion
   b. cell migration
   c. cell proliferation
   d. all of the above

7. The composite graft is obtained by mixing________.
   a. 4 parts of bone to 1 part of ceramic hydroxyapatite
   b. 4 parts of calcium sulfate to 1 part of DFDBA
   c. 4 parts of synthetic bioactive resorbable graft to 1 part calcium sulfate
   d. 4 parts of ceramic hydroxyapatite to 1 part of DFDBA

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Disclosure: Mr. Valen is the president of Implant Ltd and is the manufacturer of Osseogen.

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