Bioactive Glass for Bone Replacement in Craniomaxillofacial Reconstruction

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Considerable investigation has been done to design alloplasts suitable for bone replacement in humans. During the last 10 years there has been increased use of biomaterials for bone replacement, particularly in facial reconstruction.1-3 Reasons for this include the increasing availability and ready usage of biomaterials, the long “shelf-life” of biomaterials, their increasing efficacy and safety, and their cost-effectiveness in reducing operating time.

Failure of most implants originates at the interface between the biomaterial and its host tissue.4 This problem makes surface activity of the alloplast critical in evaluating its suitability for bone replacement, particularly if the area to be reconstructed will be subject to stress-loading. Bioactive implants provide one potential solution to the problem of interface failure.4 A bioactive material is defined as one that elicits a specific biological response at the interface of the material that results in the formation of a bond between the tissues and the material.5 This process prevents formation of a fibrous capsule surrounding the implant by the adhesion of repairing tissues. Hench and colleagues6 reported the first bioactive material in 1971. This four-component glass was 45 percent silica dioxide, 45 percent sodium oxide, 5 percent calcium oxide, and 5 percent phosphate, and was first marketed as 45S5 Bioglass (USBiomaterials Corp., Alachua, Fla.). Since its introduction in 1971, 45SF Bioglass has subsequently been released as PerioGlas (Block Drug Co., Jersey City, N.J.), for periodontal bone regeneration, and NovaBone (Porex Surgical, Inc., Newnan, Ga.), for craniomaxillofacial applications.

BASIC SCIENCE

Bioactivity is initiated in glass particulates when they are mixed with saline or blood.7 The silicon-oxygen bonds are broken to release silicic acid, which condenses to form a negatively charged gel at the surface of the particles. This gel serves to hold the glass particles in a cohesive mass. Within several hours, calcium phosphate is produced within the gel to crystallize into a new surface apatite layer. Bioactivity is initiated within this surface layer when collagen, mucopolysaccharides, and glycoproteins from surrounding bone are incorporated into the apatite layer to mediate a direct chemical bond with the host bone, facilitating early bone formation at the biomaterial-bone interface. In vitro studies have shown a strong interface of type I collagen to glass particles embedded in the apatite layer. In vivo, this bioactive glass bonds to connective tissues and to bone.8 The growing apatite layer further serves to stimulate osteoprogenitor cells to produce transforming growth factor-β by release of silicon from the glass surface. Transforming growth factor-β serves as an osteogenic cytokine, leading to a rapid proliferation of bone in contact with the glass particles.9 Most biomaterials, including bioactive glasses, are osteoconductive, serving as a biocompatible interface along which bone cells migrate. In addition, bioactive glasses are osteoproducive, which is defined as the process whereby a bioactive surface
is colonized by osteogenic stem cells from the defect environment as a result of surgical intervention. Bioactive glass particles range in size from 90 to 710 μm. Resorption of particles of 150 μm or less occurs as silica is released within the apatite gel layer. Larger particles are incorporated in the growing bone matrix and are eventually broken down by osteoclasts. As a result of their bioactive properties, the interfacial bonding strength of most bioactive materials is equivalent to or greater than that of bone. Unlike the case with nonbioactive alloplasts, failure under mechanical stress does not occur at the bone interface but rather occurs in the host bone or within the biomaterial. This absence of failure at the bone interface is a unique and defining feature of bioactive materials.4

In an experimental study evaluating critical-sized defects in rabbit femurs reconstructed with either hydroxyapatite or bioactive glass particles, bone formation with the bioactive glass particles was found to be significantly greater and occurred at a much faster rate than that with hydroxyapatite reconstruction. Restoration of bone was observed within 2 weeks when the defect was packed with particulate bioactive glass, compared with 12 weeks when it was packed with particulate hydroxyapatite. The resulting substance filling the defects was observed to be trabecular bone when packed with bioactive glass, compared with a composite of bone reinforced by nonresorbable hydroxyapatite in the latter case. Furthermore, bone growth was reported to occur almost simultaneously throughout the implant, rather than gradually progressing from the margins of the scaffold. These observations are consistent with osteoproduction occurring in the bioactive glass reconstruction and osteoconduction occurring in the hydroxyapatite reconstruction.

Investigators have also demonstrated a higher cellular density and osteoblast proliferation rate with bioactive glass than with hydroxyapatite cement paste, and they have obtained results comparable to those found when using autogenous bone graft for the repair of skeletal defects. In an in vitro study, similar histologic findings were noted when osteoblasts were cultured with bioactive glass particles, compared with osteoblasts cultured with titanium, steel, or hydroxyapatite particles.

Clinical Applications

Most clinical reports of bioactive glasses deal with the repair of periodontal defects and alveolar ridge defects. There is more limited experience with reconstruction of other areas of the head and neck. Clinical applications are discussed below.

Periodontal Reconstruction and Alveolar Ridge Augmentation

Bioactive glass and demineralized, freeze-dried bone allograft produced similar results within 6 months for moderate to deep osseous periodontal defects. Bioactive glass was also found to be efficacious in alveolar ridge augmentation and for the repair of immediate tooth extraction sites. The material can be used alone or mixed with autogenous bone particles. Many authors use bioactive glass as an adjunct to conventional surgery for the treatment of osseous periodontal defects, and it has also been used as an adjunct to guided bone regeneration for such defects in conjunction with placement of polytetrafluoroethylene barriers. However, other studies suggest equivocal new bone growth when bioactive glasses are used in periodontal defects and for augmentation of the alveolar ridge. Despite these findings, the authors have attributed nonsseous benefits to the use of bioactive glass, including improved gingival attachment following third molar extraction and prolonged survival of dental implants placed in these areas.

Orbit and Facial Skeleton

Implants of bioactive glass have been used successfully for the repair of orbital floor fractures, with good maintenance of globe position in follow-up of up to 1 year. Bioactive glass ceramic implants have also been used for contour restoration of the facial skeleton. However, extrusion was reported in 20 percent of cases, requiring reoperation with implant size reduction or revision of soft-tissue cover.

Maxillary Sinus Augmentation and Frontal Sinus Obliteration

Bioactive glass particles have been applied to modify the facial sinuses. A composite consisting of 80 to 90 percent bioactive glass particles and 10 to 20 percent autogenous iliac bone was compared with 100 percent autogenous iliac bone particles for elevation of the maxillary
sinus floor. Using histomorphometric analysis, the authors found that the composite bioactive glass mixture accelerated healing time for bone regeneration to 6 months, compared with 12 months for bone graft alone. Both treatment regimens resulted in stable bone at the reconstructed site. Accelerated bone healing for elevation of the maxillary sinus floor can allow for simultaneous bone augmentation of the sinus floor and placement of titanium implants for dental restoration in patients who would otherwise have insufficient maxillary bone for implant placement. Utilizing this technique for 27 implants, with a 4:1 ratio of bioactive glass particles to autogenous bone, Cordioli et al. found all implants to be stable at second-stage surgery 9 to 12 months later, with a mean increase in mineralized tissue height of 7.1 mm.

Peltola and colleagues have reported on the use of bioactive glass particles to obliterate the frontal sinus in 30 patients over a 10-year period. Although there was some decrease in radiologic density of the obliteration material over time, they reported the material to be well tolerated with no loss of volume.

**Calvarial Defects**

We have reported on bioactive glass particles (NovaBone, from Porex Surgical, Newman, Ga.) mixed with autogenous bone particles harvested from cranial burr holes as an adjunct to cranial vault reconstruction. This was done to reconstruct full-thickness defects in two patients aged 5 years and older, when minimal spontaneous bone regeneration was expected. On follow-up computed tomography scans, these patients demonstrated conversion of the majority of the reconstructed defect to bone density within 6 months. At 4-year follow-up, both patients had stable reconstruction, and there has been no need for reoperation or biopsy of the biomaterial.

**Summary**

Bioactive glass particles are an important consideration when choosing the optimal biomaterial to be used as a bone substitute in craniomaxillofacial applications. The bioactive properties of these particles allow for an osteo-productive environment in which the bone–biomaterial interface is uniquely stronger than it would be with other forms of biomaterials. A review of the present literature supports clinical applications of bioactive glasses in particu-

late form, preferably mixed with 10 to 20 percent autogenous bone particles. This protocol has been highly successful for dental and periodontal reconstruction, augmentation of the alveolar ridge, and elevation of the maxillary sinus floor in preparation for titanium implant placement in the atrophic maxilla. A similar protocol may prove useful in reconstruction of full-thickness calvarial defects. However, present experience with prefabricated implants made of bioactive glass ceramics, as has been used for augmentation of the facial skeleton, does not support an additional advantage of this biomaterial over alternate forms of prefabricated implants.

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