

NONMETALLIC MATERIALS FOR BONE SUBSTITUTES

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INTRODUCTION:

Bone loss frequently results from high-energy trauma, birth defects, infection, tumour resection and harvesting of bone graft. Bone grafting using autogenous cancellous bone, cortical bone, allograft and heterograft are common clinical procedures. Cancellous bone graft has a high content of osteogenic stem cells but lacks stability and must be used with stable internal fixation. High morbidity of the donor site is yet another drawback of this procedure. Cortical bone graft has a low content of osteogenic stem cells, poor vitality and serves rather as a bridge-forming splint. Immune defence, potential for HIV infection and prions contamination are disadvantages of the use of allo- and heterografts. Bone defects are also treated using bone segment transport, vascularized bone graft, bone marrow aspirates and demineralized bone powder. Alternative treatment modalities involve growth factors, cytokines, gene therapy, tissue engineering and bone graft substitutes.

Non-metal materials for bone substitutes can be of inorganic or organic origin. The first include synthetic ceramics such as hydroxyapatite, tricalcium phosphate, carbonated hydroxyapatite, calcium sulphate, coral and ceramic cements. The second group comprises bioresorbable natural and synthetic polymers. Composites based on polymers and ceramics provide another option.

There are many commercial bone substitutes available at present and their number is continuously growing. Typical examples are *ProOsteon* and *ProOsteon500R* from Interpore. These consist of coral converted into hydroxyapatite and carbonated hydroxyapatite. A preserved porous coralline structure acts as a scaffold for new bone. The material is used in the treatment of metaphyseal fractures of long bones and cervical spine fusions. *Ostoglass* from US Biomaterials is bioactive glass which, it is claimed, binds collagen and promotes bone formation between the implant, collagen fibres and old bone. Present applications are for periodontal defects, facial bones and bones in the middle ear. Foreseen applications include long bone fracture fixation, spinal fusion and joint replacement. The *Norian Skeletal Repair System (SRS)* is injectable, mouldable cement that hardens *in vivo* forming a

carbonated apatite. It is used as an adjunct to fracture stabilization and for low impact unstable metaphyseal radius fractures. ETEX Corporation *α-BSM* is synthetic, crystalline, nanosized calcium phosphate paste and putty that undergoes endothermal hardening at body temperature. It can also be formed into prehardened blocks. Intended applications include dental and periodontal treatments. *Bi-Ostetic*, *Cem-Ostetic* from Berkeley Advanced Biomaterials are hydroxyapatite - tricalcium phosphate compounds in a form of porous granules, blocks, putty and nanocrystals. *Vitoss* and *Crotoss* from Orthovita are cortical bone void fillers based on a terpolymer of bisphenol- α -glycidyl dimethacrylate, bisphenol- α -ethoxy dimethacrylate and triethylene glycol dimethacrylate reinforced with bone-bonding glass-ceramic particles. It is used as an injectable cement for cranial repair, and as a bone defect filler for the spine and pelvis.

BoneSource from Orthofix (Stryker-Howmedica) is a ceramic cement based on nonceramic hydroxyapatite, which hardens over 20-30 minutes and converts into hydroxyapatite in 4 hrs. It is used to repair cranial defects and as a bone void filler in some non-load-bearing orthopaedic indications. *ChronOs* from Mathys (*chronOs* granules; *chronOs* cylinder; *chronOs* block; *chronOs* wedge) are materials based on β -tricalcium phosphate. Resorption time 6 to 18 months. Foreseen applications for filling of bone defects (cranial, maxillofacial, metaphyseal) and spinal fusion. *Collagraft* from Zimmer consists of hydroxyapatite-tricalcium phosphate granules and bovine fibrillar collagen and finds application in total joint replacement, spinal fusion, fracture repair, as an autograft extender and as a harvest site filler. *Grafton* from Osteotech is banked human tissue-demineralized bone matrix suspended in glycerol. Used adjunctive to spinal and joint fusions and for the repair of osseous defects and arthroplasties. *DynaGraft* of GenSci is demineralised bone matrix with collagen in the form of a gel, putty or a sponge for oral and craniofacial applications. *Osteoset*, *Ballomatrix* and *Allomatrix* from Wright Medical are surgical-grade calcium sulphate and bone putty containing demineralized bone matrix and cancellous bone chips in calcium sulphate, to be used in spine and pelvis, respectively. *Healos* from Orquest is a

collagen sponge coated with a nonceramic, fully resorbable form of synthetic hydroxyapatite used as replacement for autograft in spinal fusion.

As with any implantable materials there are advantages and drawbacks to ceramic bone substitutes. Thus, the fact that substitutes expand the volume of autogenic graft, serve as scaffolds, enhance the stability of fixation and protect against the infiltration of soft tissue, which promotes graft consolidation is advantageous. On the other hand, ceramic bone substitutes occupy space in the fusion mass that would otherwise be filled with viable bone, they introduce stress concentration and may impede vascularization. These are claimed to be drawbacks of ceramic materials. Hence, the question arises: What is *an ideal bone substitute*? It should: be porous with interconnected pores of adequate size; allow for the ingrowth of capillaries, perivascular tissues and osteo-progenitor cells; attract mesenchymal stem cells from the surrounding area; promote their differentiation into osteoblasts; be bioresorbable - biodegradable, complex calcium ions from the body fluids, be radiolucent and mechanically strong. The latter feature is much dependent on the intended application of the substitute.

For a number of applications polymeric bone substitutes could be options and/or supplement ceramic substitutes. These could be produced from natural or synthetic bioresorbable-biodegradable polymers used alone, or as composites with calcium salts. Polymers with a potential for application as bone substitutes are polyglycolide, polylactides, copolymers of glycolide with lactides, polydioxanone, tyrosine polycarbonates, terpolymers from hydroxyacids, poly(glycolide-co-trimethylene carbonate), poly(lactides-co-trimethylene carbonate), biodegradable polyurethanes, and protein-based polymers to mention but a few.

Bone substitutes can be sponge-like with an interconnected open-cell structure, sponge-like with a closed-cell structure or in fibrous form as a fleece or nonwoven mat. They can have the form of 3-D blocks, chips, beads or microfibrils. The factors, which affect the properties of polymeric implants, include the material quality, the technique used for production and post-treatment. Interaction with cells and tissues is determined by the surface chemistry, surface texture and contamination.

Porous polylactide sponge-like scaffolds support the attachment, growth, migration and differentiation of bone forming cells.^{1,2}

Impregnated with bone marrow and implanted in critical-size segmental defects in the sheep tibiae³ and human femur,⁴ they promote bone regeneration. Biodegradable polyurethane sponges with varying hydrophilicity implanted in unicortical and tricortical defects in the sheep iliac crest induce the formation of new cancellous bone of higher density than the original bone.⁴ A similar healing pattern was also observed in sheep with osteopenia.⁵

CONCLUSIONS: Resorbable porous scaffolds from synthetic polymers promote the healing of large defects in long bones, in the iliac crest and craniofacial skeleton. Impregnation with autogenic bone marrow facilitates healing. Seeding scaffolds with bone-forming cells or loading them with osteogenic drugs can enhance healing. Scaffold's osteoconductivity can be improved by loading or coating with calcium phosphate salts. Scaffolds induce hydroxyapatite deposition, a required property of bone substitute materials. Scaffolds are radiolucent which allows for radiographic follow-up of bone healing process. Resorbable polymeric scaffolds are promising candidates for cancellous bone substitutes. Modified biologically and/or pharmacologically they may in a number of situations replace autogenic cancellous bone graft.

REFERENCES: ¹ Gugala Z, Gogolewski S, The growth and activity of sheep osteoblasts on the 3-D porous polylactide scaffolds, *Transactions*, 24th Annual Meeting of Society for Biomaterials, San Diego, California, USA, 21, 417, 1998; ² Gugala Z, Gogolewski S, Growth, differentiation and activity of rat bone marrow stromal cells on resorbable poly(L/DL-lactide) membranes with defined surface characteristics, *Transactions*, 25th Society for Biomaterials Annual Meeting and 31st International Biomaterials Symposium, Providence, RI, USA, 22, 115, 1999; ³ Gogolewski S, Rahn B, Wieling R, Bone regeneration in critical-size segmental diaphyseal defects implanted with bioresorbable polylactide bone substitute, *Transactions*, 27th Society for Biomaterials Annual Meeting, Saint Paul, MN, USA, 24, 572, 2001; ⁴ Ip W, Gogolewski S, to be published; ⁵ Gogolewski S, Gorna K, Rahn B, Wieling R, Biodegradable polyurethane cancellous bone graft substitute promotes bone regeneration in the iliac crest defects, *Transactions*, 27th Society for Biomaterials Annual Meeting, Saint Paul, MN, USA, 24, 573, 2001.