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Repair of Bone Defects using Various Biomaterials

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A significant proportion of clinical orthopaedic surgery involves attempts to stimulate bone healing. Although the results of fracture repair and reconstructive surgery usually good, complications of skeletal repair occur frequently enough that surgeons often need bone graft or a skeletal substitute material. Bone grafts and synthetic skeletal materials are being used with increased frequency worldwide, but there are many unanswered questions concerning the basic processes of graft immunology, incorporation and remodeling. Clinical and basic science data do not yet provide sufficient information to choose the most appropriate synthetic materials to be used as skeletal substitutes, alone or in combination with autogenous bone grafts. Experience to date suggests that grafting materials and composites will become progressively specialized for use in specific applications.

1) Bone graft materials classified by composition

A. Autograft

1. Aspirated bone marrow or processed osteogenic cells
2. Cancellous bone
3. Nonvascularized cortical bone
4. Vascularized bone

B. Allograft

1. Graft anatomy: cortical, cancellous, osteochondral
2. Graft processing: fresh, frozen, freeze-dried, demineralized
3. Graft sterilization: sterilely processed, irradiated, ethylene oxide
4. Handling properties (packaged products): powder, particulate, gel, paste or putty, chips, strips or blocks, massive

C. Synthetic skeletal materials

1. osteoconductive granules or blocks
2. osteoconductive cements
3. osteoinductive protein
4. composites

2) Scaffold Biomaterials

Scaffold materials for making matrices for bone tissue engineering include several classes of biomaterials: synthetic polymers, ceramics, native polymers, and composites

A. Synthetic polymers

Both organic and inorganic synthetic polymers are used in a wide variety of biomedical applications. The polymers can be biodegradable or nondegradable. Polylactic acid, polyglycolic acid and copolymers thereof are broken down in the body hydrolytically to produce lactic acid and glycolic acid, respectively. Other biodegradable polymers currently being studied for tissue engineering applications include polycaprolactone, polyanhydrides, ande polyphosphazenes. Polymethylmethacrylate(PMMA), polytetrafluoroethylene(PTFE), and PMMA/ polyhydroxyethyl-methacrylate(PHEMA) may be described as alloplastic, synthetic, nonbiodegradable polymers. PMMA has considerable versatility. It is used for dentures, arthroplasties, cranioplasties, and as a cement for many orthopedic prostheses. PTFE has been used for augmentation and guided bone regeneration. The principle of guided bone regeneration is that new bone formation will occur by providing a "passageway" for osteoblast lineage cells and osteoblasts. Precluding soft tissue prolapse into an osseous deficit provides the underpinning to guide bone, thereby deterring scar formation. Physiologically, fibroblasts are more likely to populate an intraosseous deficit than osteoblasts; therefore, by sustaining a zone for migration of osteoblast lineage cells, the clinical outcome should be bone and not connective tissue scar.

PMMA/PHEMA is commercially prepared under the name hard tissue replacement (HTR-MFI) as blocks and particulates. The block format is for augmentation whereas particulates have periodontal applications to restore deficient alveolar bone

B. Ceramics

Ceramics are also widely used in dental applications, and are being examined for bone tissue engineering applications. Two common ceramics used in dentistry and hip prostheses are alumina and hydroxyapatite. Alumina (Al2O3) has excellent corrosion resistance, good biocompatibility, high strength, and high wear resistance, and has been used for over 20 years in orthopedic surgery.

Hydroxyapatite (HA) is a calcium-phosphate based ceramic and has also been used for over 20 years in medicine and dentistry. HA is a major component of the inorganic compartment of bone. HA prepared commercially is biocompatible with biodegradability either absent or protracted (a timeline spanning years. Interpore Cross International has established the reputation as a company that produces laboratory modified HA. Through a technique of phosphoric acid

processing and hydrothermal exchange, calcium carbonate from species of marine coral becomes HA. A porous, "bone-like" morphology of the resulting structure provided investigators with a unique-looking structure, when implanted into bone defects, supported bone growth through the pores. Marshal Urist has defined the term osteoconduction as bone growth into and through a porous structure.

The degradation of hydroxyapatite can be controlled by varying the chemical structure. Tricalcium phosphate degrades much more quickly than HA. Medical grade tricalcium phosphate (TCP) was envisioned as an autograft expander. Plaster of Paris is the common name for the composition described chemically as calcium sulfate. The capacity to be fashioned and molded into the desired contour for the craniofacial complex is an asset. Unfortunately, unpredictable clinical outcome has been the track record for plaster of Paris. Contemporary calcium sulfate known as Osteoset (Wright Medical Corporation) is produced for orthopedic application in non-stress bearing sites, such as the tibial plateau. The aspirin-sized tablet of Osteoset may find utility in the craniofacial skeleton to fill bone voids. Biocompatibility and biodegradability of this new generation calcium sulfate may enliven clinical enthusiasm. A combination product of calcium sulfate and tricalcium phosphate (Hapset) has been suggested for dental applications; however, dental extraction sites heal uneventfully and the inclusion of foreign material is questionable. One disadvantage of the calcium-based ceramics is the low mechanical strength of these porous materials.

Finally, bioactive glasses have been shown to bind to soft tissue and bone. These bioactive glasses contain different ratios of Na2O-CaO-P2O5-SiO2. There are currently two commercially available glasses advertised for applications in bone sites.

C. Native polymers

Native polymers, or extracellular matrix proteins, are commonly exploited as bone graft materials. Collagens, which comprise a majority of proteins in connective tissue such as skin, bone, cartilage and tendons, are popular candidates for such circumstances, and various collagen -based products are currently under development. The organic phase of bone is principally type I collagen. When bone is demineralized with hydrochloric acid, the method used by most commercial venders, the bone derivative is largely type I collagen and a minimal per cent mixture of cell debris, a soup of soluble signaling molecules that are resistant to acidic demineralization, and residue ECM components. The format for the demineralized bone (DBM) can be either a range of particulate matter, blocks, or strips.

Some clinicians voice laudatory praise for DBM products, while others have abandoned the notion that DBM is worthwhile. The variables influencing clinical outcome from DBM therapy include non-standardized procurement and preparation techniques, donor age and gender, reagents and quality control, and sterilization (e.g., gamma irradiate, ethylene oxide sterilize).

Clinical reports on combinations of DBM and autograft favor this composition over DBM alone and underscore DBM as an autograft expander. Due to the strength limitations of collagen-based products like these, defect dimensions are limited and must be complemented by skeletal fixation. Gainfully, osteoinductive properties are imparted to these matrices when combined with bone marrow aspirates, thus greatly enhancing the repair process.

The polysaccharide hyaluronic acid (Hy) appears to be a promising matrix material for bone tissue engineering, and is a glycosaminoglycan found in synovial fluid and cartilage. Hy has been experimentally determined to induce chondrogenesis and angiogenesis during remodeling and is being studied both individually and in combination with collagen as a matrix for bone repair. Finally, chondroitin sulfate is another glycosaminoglycan found in cartilage with potential applications as a bone tissue-engineered scaffold.

D. Composites

Composites of ceramics and polymers are also widely studied. Composites can result in substitutes with properties between each of the respective materials. For example, bovine collagen has been manufactured with HA. Collagraft is HA and bovine type I dermal collagen (95%) and type III collagen (5%). Collagraft is used for orthopedic, non-load bearing sites. A craniofacial product known as Bio-Oss collagen is being marketed. It is a combination of bovine collagen and de-organified bovine bone. Preclinical and clinical data with Collagraft has revealed mixed outcome; the Bio-Oss collagen product has not received sufficient attention in the literature. Healos® (CE Mark) is sponge-like material comprised of HA-coated collagen fibers, also used as an osteoconductive matrix. It is generally accepted that the combination of collagen and calcium-based ceramics provides a bone-like matrix that supports the adhesion, migration, growth, and differentiation of bone-forming cells.