Bone Graft Expanders: Filling the Void

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Approximately 500,000 bone graft procedures are performed each year in the United States. The surge in the demand for graft material is largely the result of an increase in the number of spinal fusion procedures being performed. In 2001, only 22,000 bone donors existed worldwide, suggesting a shortage of available allograft in the future. This has led to the growing demand for bone graft substitutes.1

BONE GRAFT MATERIALS

Skeletal regeneration requires a stable structure for bone in-growth, a source of osteoprogenitor cells, and growth factors, which signal and regulate the repair process. Autologous cancellous bone graft assists repair by providing these three elements. Autologous bone is, therefore, deemed osteoconductive, osteoinductive, and osteogenic. Cortical bone graft can be used for structural support. Bone graft harvested from the iliac crest is considered the gold standard bone graft material, but morbidity of the harvest procedure and the limited supply of bone has resulted in a demand for bone graft substitutes.

Bone graft substitute materials are available from a variety of sources. Allograft bone can be prepared as cortical struts or corticocancellous chips. Fresh frozen allograft provides the best material for structural purposes but freeze drying helps eliminate disease transmission and immune rejection. Fresh frozen or freeze-dried allograft bone is osteoconductive but cannot be considered osteoinductive or osteogenic.

The first artificial materials used as graft substitutes were calcium phosphate ceramics. Initially, sea corals were converted to hydroxyapatite products with a three-dimensional structure similar to cancellous bone.2 More recently, calcium phosphate composites and materials composed of calcium sulfate have been introduced. These different chemical compositions result in materials with varying bioabsorbability. The hydroxyapatites are purely crystalline and insoluble and are not remodeled by osteoclastic cells. Impure calcium phosphates have varying solubility and are subject to osteoclastic remodeling, allowing them to be resorbed and replaced by host bone. Calcium sulfate materials are highly soluble and disappear rapidly from skeletal sites.

The materials are available as granules, blocks, and now, cements. They are osteoconductive due to their porosity and chemical structure and are incorporated by creeping substitution. The resorption of these materials by osteoclasts leads to new bone formation within implantation sites. The materials provide structural support but each type of material has different support potential. Calcium sulfate disappears rapidly providing brief support. Tricalcium phosphate is less soluble remodeling over a longer period providing more long-term support. Hydroxyapatite is insoluble and relatively permanent, providing the greatest long-term support material. Tricalcium phosphate and calcium sulfate are prepared as cements that can be injected into skeletal defects where they harden and cure.
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These cements provide compressive support with compressive strengths as high as 55 MPa, which is similar to that of cancellous bone. Type I collagen can be added to ceramics to enhance their performance. Collagen is osteoconductive and the ideal substrate to support mineralization. It also binds various circulating growth factors, which makes collagen-containing composites weakly osteoinductive. Collagen enhances many of the mineral composites and may be the best carrier for recombinant osteoinductive proteins.

Demineralized bone matrix (DBM) is allograft bone that has been de-calcified in weak acid. The resultant DBM is 90% type I collagen and 10% noncollagenous proteins including many growth factors. Marshall Urist isolated bone morphogenetic proteins from this decalcified material. Demineralized bone matrix is osteoconductive and osteoinductive and is extremely successful in healing critical defects in animal models.

Because allograft materials are not regulated by the Food and Drug Administration, many DBM products have reached the market. These products often vary in their preparation, bone content, osteoinductivity, and handling properties. Disappointingly, little clinical evidence indicates that they provide consistent delivery of active inductive factors. Initial experience with most DBM products supports their use in treating acute fractures and filling viable bone defects. Demineralized bone matrix products cannot provide structural support and demonstrate little usefulness alone in atrophic nonunions or sites with poor vascularity or few multi-potential mesenchymal cells.

APPLICATION

One useful application for any of the bone graft substitutes is the role of autograft volume expander. Demineralized bone matrix or calcium ceramics can be added to autograft, increasing the amount of osteoconductive and inductive material in large defects. The artificial material excludes fibrous or muscle interposition and provides an excellent carrier for the viable, osteogenic cells of the autograft. This composite remains the material of choice for atrophic nonunions and spinal fusion (Figure 2).

REFERENCES


Figure 2: Radiograph shows nonunion of a distal femur fracture with failed internal fixation. Clinical photograph of the femur after debridement of the nonunion and double plating (B). Note the significant area of bone loss. Photograph after filling the defect with Opteform demineralized bone matrix (Exactech Inc, Gainesville, Fla) and Collagraft (Zimmer, Warsaw, Ind), an osteoconductive matrix of bovine collagen and hydroxyapatite/tricalcium phosphate beads (C). Radiograph at 1-year follow-up demonstrates healing of the nonunion (D).