Stem Cells in Bone Grafting: Trinity Allograft with Stem Cells and Collagen/ Beta-Tricalcium Phosphate with Concentrated Bone Marrow Aspirate

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KEYWORDS

• Bone graft • Trinity allograft • Beta-tricalcium phosphate
• Mesenchymal stem cells

The orthopedic foot and ankle surgeon needs bone grafts in the clinical situation of fracture healing and in bone-fusion procedures. Although the need for graft remains controversial for some procedures such as triple arthrodesis, many surgeons prefer to augment bone-on-bone healing with biology as well as to fill the gaps or "dead space" left after some procedures. The need for some sort of graft with traumatic cavitation or fracture comminution warrants even further merit. Frank nonunions or resection of bone, such as for avascular necrosis, infection, or tumor, provide uncontroversial need for bone graft filling. This article briefly outlines thought processes and techniques for 2 recent options for the surgeon. The Trinity product is a unique combination of allograft bone and allograft stem cells. The beta-tricalcium phosphate and collagen materials provide an excellent scaffold for bone growth; when combined with concentrated bone marrow aspirate they also offer osteoconductive and osteoinductive as well as osteogenerative sources for new bone formation.

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PART I. TRINITY EVOLUTION AS AN ALLOGRAFT AUGMENTATION

Trinity Evolution (Orthofix International NV, Boston, MA, USA) is a proprietary allograft formulation specifically created to contain 3 separate elements to induce bone healing. These include:

1. Living osteogenic cells (both mature osteoblasts and osteoprogenitor cells)
2. An osteoconductive matrix
3. Osteoinductive cytokines.

The material is essentially a mixture of a consistent and very high concentration of mesenchymal stem cells, a fine cancellous bone matrix, and an admixture of demineralized cortical bone. In concept, osteogenesis, osteoconductivity, and osteoinduction are supplied by the 3 components respectively.[1]

GRAFT HANDLING

The graft itself is processed sterilely from the donor and the mesenchymal stem cell component is concentrated by a proprietary process. It can be stored on site after shipping at –70°C to –80°C for up to 3 months and must be used immediately once thawed. Thawing is accomplished in the operating room at a temperature no greater than 39°C to avoid cellular necrosis. A fluid component is present in the preparation including dimethyl sulfoxide (DMSO) cryoprotectant and the mesenchymal stem cell–specific basal medium. This is decanted after thawing immediately before implantation (**Fig. 1**). The thawing protocol must be followed precisely, as loss of stem cell viability may otherwise result.

MESENCHYMAL STEM CELLS IN HUMAN USE

Mesenchymal stem cells (MSCs) are a population of adult mesenchymal cells that can initiate a differentiation pathway into multiple different connective and bony tissues. Multiple roles for MSCs in vivo have been described, including serving as progenitor cells for bone remodeling and repair,[2] cartilage formation,[3] vascular support,[4] hematopoietic support,[5] and as progenitors for adipocytes.[3] MSCs have been proposed for a role in a variety of human tissue engineering applications, including the treatment of nonunions or supporting healing in high-risk fusion procedures.

Recent data suggest that MSCs naturally occur as perivascular cells (formerly called “pericytes”) that are released at zones of injury. Activated MSCs then secrete large amounts of trophic and immunomodulatory cytokines. The trophic characteristics stimulate the tissue angiogenesis critical for healing as well as simulator local tissue progenitor cells. The resultant healing tissue, then, is primarily the result of the activation of the healing process of the surrounding tissue rather than directly derived from the MSCs themselves.[6]

MSCS AS AN ALLOGRAFT

The immunomodulatory cytokines are particularly important. They inhibit host lymphocyte surveillance of the injured tissues and prevent a large-scale autoimmune response.[1] The immunomodulatory characteristics of MSCs allows for the use of cells of allogeneic origin. Even the use of xenograft-sourced MSCs has been explored. Culture-expanded MSCs do not appear to elicit a significant host immune response even when directly infused intravenously.[7]