Orthobiologics in the Foot and Ankle

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KEYWORDS

• Cartilage particulate • Micronized bone • Osteoprogenitor stem cells • Amnion

KEY POINTS

- Many allogeneic biologic materials, by themselves or in combination with cells or cell products, may be transformative in healing or regeneration of musculoskeletal bone and soft tissues.
- By reconfiguring the size, shape, and methods of tissue preparation to improve deliverability and storage, unique iterations of traditional tissue scaffolds have emerged.
- This improvement, combined with new cell technologies, has shaped an exciting platform of regenerative products that are effective and provide a bridge to newer and better methods of providing care for orthopedic foot and ankle patients.

INTRODUCTION

Biologic materials play an important and increasing role in musculoskeletal repair and regeneration in general; this is especially true in the foot and ankle. Advances in stem cell recovery, isolation, and processing combined with autogeneic, allogeneic, and synthetic scaffolds present new and exciting opportunities to address challenging clinical problems like full-thickness cartilage defects, segmental bone loss, pseudoarthroses, and delayed wound healing.

This review focuses on select cartilage, bone and soft tissue repair, and regeneration strategies. Many recent developments and commercial products, although encouraging, lack sufficient basic scientific foundation and adequate clinical outcome data. The strengths and limitations of the techniques and products are discussed, and representative commercial products are compared.

CARTILAGE

A significant number of techniques are coupled with biologic materials for full-thickness cartilage defects.[1] Successful outcomes are reported with microfracture

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alone, but many of the defects, on reinspection, are incompletely healed,[2] and the resulting fibrocartilage lacks the biomechanical properties to satisfy the demands of joint function.[3,4] Although some, using T2 mapping to assess repair cartilage after microfracture, report good results along with improved functional scores,[5] short and intermediate magnetic resonance studies by others observe the resulting cartilage to be inferior to the adjacent normal cartilage.[6] Other biologic techniques include autogeneic cartilage transfer (mosaicplasty), allogeneic cartilage transfer (fresh and cryopreserved), and autologous chondrocyte transplantation.

Cartilage Graft

Mosaicplasty is a consideration for small and intermediate-size defects but is limited and complicated by donor site availability. The reconstruction is hardly congruent but remodels over time resulting in good short-term and intermediate-term results.

Structural cartilage allografts for intermediate and large defects involve both fresh and cryopreserved tissues. Cryopreserved grafts heal well and in the short and intermediate term produce acceptable functional results. Ultimately, however, they fail because the chondrocytes do not survive. Chondrocyte damage is thought to occur during the slow rate freezing process. The theory behind slow rate freezing with a cryopreservative is to limit the amount of heat released from the cell that ultimately results in crystallization and cell damage. Although techniques exist to reduce the rate of cell freezing down to $-150^{\circ}C$ in an attempt to limit the rate of cellular heat release, they do not eliminate the phenomenon and subsequent crystallization. Most isolated cells treated in this fashion survive thawing and appear to grow normally in culture. These chondrocytes in tissue, however, do not sustain normal cell function over time, and arthrosis supervenes.[7] Other factors may contribute to cell demise, such as selection of cryopreservation alternatives, surgical technique, joint congruity, the relative health of the seemingly normal adjacent cartilage, and the underlying subchondral bone.

Alternatively, fresh grafts represent the gold standard of cartilage repair and can produce excellent long-term results in select individuals. The primary limitation of this technique is graft availability and variability in processing techniques, principally, the time interval between recovery and transplantation. Chondrocyte viability decreases significantly after 21 days in primary culture based on ex vivo and reimplantation studies.[8]

Recent investigations using particulate cartilage as a structural and potentially inductive matrix after microfracture show promising results in preclinical and early clinical studies.

Cellular Therapy for Cartilage Regeneration

Cellular therapies for cartilage regeneration are not new. Autologous cartilage cell therapy (Carticel) is a long-standing commercial product. This technique requires recovery of cells from the joint, ex vivo growth and expansion, and reintroduction into the cartilage defect. Some investigators advocate this technique for patients who do not respond to microfracture for osteochondral defects in the talus.[9] Early results were encouraging, but the fundamental lack of an associated matrix on which the cells grow in vivo may be a limitation to this strategy. Stem cell therapies with or without a matrix have not been adequately studied to comment on their efficacy.

Particulate Cartilage Allografts

In the foot and ankle, particulate cartilage allografts are attractive for small and intermediate-size osteochondral defects. These allografts can be introduced arthroscopically, produce hyalinelike cartilage matrix, appear to remodel over time, and