The Indications and Use of Bone Morphogenetic Proteins in Foot, Ankle, and Tibia Surgery

Saadiq F. El-Amin, MD, PhD[a,b,c], MaCalus V. Hogan, MD[d], Answorth A. Allen, MD[e,f], Jonathan Hinds, BS[g], Cato T. Laurencin, MD, PhD[h,i,*]

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TISSUE ENGINEERING IN FOOT AND ANKLE SURGERY

Orthopedic surgery has been influenced significantly by progress in tissue engineering, which over the last several years has made major strides in the creation of engineered tissue for potential clinical use. Tissue engineering is an interdisciplinary science that combines the basic principles of biology, chemistry, physics, and engineering to construct living tissues from their cellular components. Engineered tissue

[a] Division of Orthopaedic Surgery, Southern Illinois University School of Medicine, PO Box 19679, Springfield, IL 62794-9620, USA
[b] Department of Computer and Electrical Engineering/Biomedical Engineering Program, Southern Illinois University, Carbondale, IL 62901, USA
[c] Department of Medical Microbiology, Immunology and Cell Biology (MMICB), Southern Illinois University School of Medicine, Springfield, IL 62794-9620, USA
[d] Academic Orthopaedic Training Program, Department of Orthopaedic Surgery, University of Virginia, Box 800159, Charlottesville, VA 22908, USA
[e] Department of Orthopaedic Surgery, The Hospital for Special Surgery, 535 East 70th Street, New York, NY 10021, USA
[f] Weill Cornell Medical College, New York, NY, USA
[g] University Medical and Dental School of New Jersey-Robert Wood Johnson, 1 Robert Wood Johnson Place, New Brunswick, NJ 08901, USA
[h] Department of Orthopedic Surgery, The University of Connecticut School of Medicine, University of Connecticut Health Center, 263 Farmington Avenue, Farmington, CT 06030, USA
[i] Department of Chemical, Materials and Biomolecular Engineering, The University of Connecticut, Storrs, CT, USA
* Corresponding author. Department of Orthopedic Surgery, The University of Connecticut School of Medicine, University of Connecticut Health Center, 263 Farmington Avenue, Farmington, CT 06030.
E-mail address: laurencin@uchc.edu

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is hoped to make the augmentation or replacement of congenitally defective, impaired, injured, or otherwise damaged human tissue with synthetic biologic material possible.[1] To date, this kind of engineering has made significant advances in the design and development of biologic tissues such as the bladder, aorta, skin, breast, muscle, bone, cartilage, and tendon.[2–8] These engineered tissues have been studied in many aspects with regard to their close correlation and biocompatibility with natural tissue counterparts, biostability and integration into host material, and ultimate restoration of normal structural and functional characteristics.[1–8]

Tissue engineering is defined as the application of biologic, chemical, and engineering principles toward the repair, restoration, or regeneration of living tissues using biomaterials, cells, and other factors, alone and in combination.[9] In orthopedics, emerging treatment strategies are geared toward the improved repair and regeneration of musculoskeletal tissues. The construction of engineered bone substitutes incorporates many important design considerations to ensure the development of matrices that mimic the 3-dimensional properties of native tissue. The matrix serves as a template or scaffold material for the optimal growth of cells and new tissue formation. Ideally the material is chosen based on the intended function and use of the tissue-engineered matrix. The design considerations span from mechanical integrity to porosity.[10]

Advances in foot and ankle orthopedics have been imperative in the improvement of clinical outcomes that pertain to the treatment of fractures, repair of delayed unions and nonunions, and arthrodeses. Improvements in internal fixation, soft tissue handling, and biologic manipulation of fractures, such as use of growth factors, stem cell augmentation, electricity, and ultrasonography, have all contributed to this improvement.[11]

Soft tissue injuries and fractures of the lower extremity present issues when the natural healing process of the body is unable to occur or does not do so effectively. This process is important, especially in the case of fracture nonunions or significant traumatic bone loss, making surgical intervention to bridge the gap necessary. For bone formation to occur, certain types of cells must be present during several biologic events, such as the availability of mesenchymal stem cells and their ability to serve as osteogenic cells. In addition, the osteoconductive property of bone is important. Osteoconduction is the property by which a graft, when placed in an osseous site, functions as a scaffold for the attachment and proliferation of bone-forming cells, neovascular ingrowth, and deposition and calcification of the bone matrix. Osteoconductive agents include calcium ceramics and collagen. Commercially, there are a variety of crystalline calcium-based ceramics, including tricalcium phosphate granules, coralline hydroxyapatite, and calcium hydroxyapatite composites. Type I collagen alone is usually a poor graft substitute. To enhance neo-osteogenesis, collagen is often combined with growth factors (ie, bone morphogenetic proteins [BMPs]), progenitor cells, or other osteoinductive components.[12] Examples of calcium-based ceramics include Healos (DePuy Spine, Inc, Raynham, MA, USA), which is composed of cross-linked collagen coated with hydroxyapatite, and Collagraft (Zimmer and Collagen Corporation, Warsaw, IN, USA), which consists of a mixture of porous beads composed of 60% hydroxyapatite and 40% tricalcium phosphate ceramic and fibrillar collagen.[13]

Osteoinduction is equally important because it is the biologic stimulus that can direct and upregulate the formation of bone and migration of bone-forming cells. Osteoinductivity is the property by which the graft recruits mesenchymal stem cells and modulates their conversion to bone-forming cells to produce new bone even at extraskeletal implant sites. Osteoinductive agents include platelet gel concentrates,