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Use of an Osteoinductive Biomaterial (rhOP-1) in Healing Large Segmental Bone Defects

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Objective: To assess the radiographic, histologic, and mechanical characteristics of new bone formation in large segmental bone defects treated with a new osteoconductive material, recombinant human osteogenic protein-1 (rhOP-1).
Design: In vivo animal study.
Intervention: Sixteen dogs (thirty-two limbs) with an ulna segmental defect (2.5 centimeters) were randomized to three treatment groups: rhOP-1, collagen alone, and no implant.
Main Outcome Measurements: Radiographic evidence of defect healing, mechanical testing (torsional strength) as compared with thirty-one control intact dog ulnas, and histologic analysis.
Results: At twelve weeks, complete radiographic healing was observed in twenty-five of twenty-eight defects (89 percent) treated with rhOP-1. The mechanical strength of the rhOP-1-treated defects at twelve weeks was 65 percent of that of intact ulnas. Histologic analysis revealed that defects treated with rhOP-1 were bridged with lamellar and woven bone that was in continuity with the host bone.
Conclusions: The results indicate that osteoinductive materials, which have the ability to quickly fill and heal large defects, may have advantages over osteoconductive materials, which are typically used to fill smaller non-load-bearing bone voids.
Key Words: Osteoinductive, Bone morphogenic proteins, rhOP-1, Bone graft substitutes, Segmental bone defects.

The use of osteoconductive and osteoinductive biomaterials promises to become a clinically important alternative to autogenous bone grafts and allografts. Because 6 to 20 percent of patients have complaints of pain, hypersensitivity, or anesthesia related to the harvesting of iliac crest bone grafts, and three to nine percent suffer more serious problems (3,38,54), alternatives to autogenous bone grafting are desirable. The use of autogenous bone grafting can also be limited by lack of sufficient tissue, especially in children and patients in whom a previous graft excision has been performed. Allograft bone has been useful, but its lack of osteogenicity, greater resorption rate, and potential for immunogenicity can limit its effectiveness (1,11,15). Transmission of the human immunodeficiency virus (HIV) in allograft bone has been reported (2).

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Osteoconductive materials provide a scaffold for bone ingrowth, act as a space filler, and osteointegrate with surrounding bone. Calcium phosphate ceramics, in particular, have been shown to be biocompatible, nontoxic, and capable of direct bonding with bone because of the chemical similarity to components of natural bone mineral (16,17,42). The hydroxyapatite (HA) form of calcium phosphate closely resembles the bone mineral component of natural vertebrate hard tissue (9,17,27). Examples of commercially available osteoconductive bone graft substitutes include Collograft (hydroxyapatite/tricalcium phosphate particles combined with purified fibrillar collagen; Zimmer, Inc., Warsaw, IN, U.S.A.) and ProOsteon (a porous natural form of calcium phosphate derived from marine coral; Interpore Orthopaedics, Inc., Irvine, CA, U.S.A.).

Osteoinductive materials provide growth factors such as bone morphogenic proteins (BMPs) and transforming growth factor-beta (TGF-β) which promote bone formation. Recombinant bone morphogenetic proteins have been extensively proven in animal models to effectively heal large segmental defects (4,5,7,10,37). The purpose of this study was to assess the radiographic, histologic, and mechanical characteristics of new bone formation in large segmental bone defects treated with a new osteoinductive material, recombinant human osteogenic protein-1 (rhOP-1).