An Injectable Bone/Polymer Composite Void Filler for Healing of Craniofacial Bone Defects

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Statement of Purpose: This paper considers the efficacy of injectable, biodegradable polyurethane (PUR) foams with allograft mineralized bone particles (MBP) or surface-demineralized MBP (SDBP) as fillers for the treatment of bone voids and fractures. These biocompatible foams act as scaffolds, due to the foams' porosity promoting cellular infiltration and proliferation. The allograft bone component enhances the osteoconductive properties of the materials. The three-component system consists of a polyol resin, a polyisocyanate prepolymer, and allograft bone particles. With the multi-component system, the material can be injected as a liquid, which subsequently foams and cures *in situ*, minimizing the invasiveness of the procedure and allowing the porous scaffolds to fill the contours of the fracture site. The materials were injected into bilateral femoral plug defects in NZW rabbits. After 6 weeks, the femurs were extracted, imaged by Faxitron, and processed for histology to characterize new bone formation. Femurs treated with MBP/PUR and SDBP/PUR foam scaffolds were compared to determine the effect of the particle surface treatment on bone regeneration.

Methods: The trifunctional polyol of 900-Da molecular weight, T6C3G1L900, was prepared by reacting a glycerol starter with ε-caprolactone (Sigma-Aldrich, Saint Louis, MO), glycolide (Polysciences, Inc., Warrington, PA) , and D,L-lactide (Polysciences). The polyol resin was produced by mixing the polyol, water, a blowing catalyst bis (2-dimethylaminoethyl) ether (DMAEE, Sigma-Aldrich), and a tertiary amine catalyst (TEGOAMIN33, Goldschimidt, Hopewell, VA), in a Hauschild SpeedMixer™ DAC 150 FVZ-K vortex mixer (FlackTek, Inc., Landrum, SC). The lysine triisocyanate-poly (ethylene glycol) (LTI-PEG) prepolymer was prepared by reacting LTI (Kyowa Hakko USA) with 200-Da molecular weight PEG (Sigma-Aldrich). MBP were obtained from Osteotech, Inc. (Eatontown, NJ). SDBP were produced by sonicating MBP with 0.1M HCL. The polyol resin, LTI-PEG, and MBP or SDBP were sterilized by gamma irradiation at a dosage of 12.2 kGy. The three components were then hand-mixed and injected into a 5 mm diameter defect drilled into the femurs of NZW rabbits. The femurs were extracted from the euthanized rabbits after 6 weeks.

Results: The scaffolds exhibit elastomeric behavior up to 50% compressive strain, as shown in the stress-strain plots in Figure 1. The compression modulus of the SDBP/PUR foams, as determined by the stress-strain curves, was 173.37±33.05 MPa. The yield strain was ~4% and the yield stress 4 MPa. Significantly, the materials did not fail under compressive strains up to 50% and recovered >95% of their initial height after the compressive load was removed.

The foams were injected into the femurs of NZW rabbits to study the foams' ability to treat fractures and voids. X-ray images (Figure 2) suggest that after 6 weeks, femoral plugs undergo substantial remodeling and integration with host tissue, such that the boundary between the biomaterial and the host bone is not well defined. The extent of polymer degradation and new bone formation will be evaluated by histomorphometry.

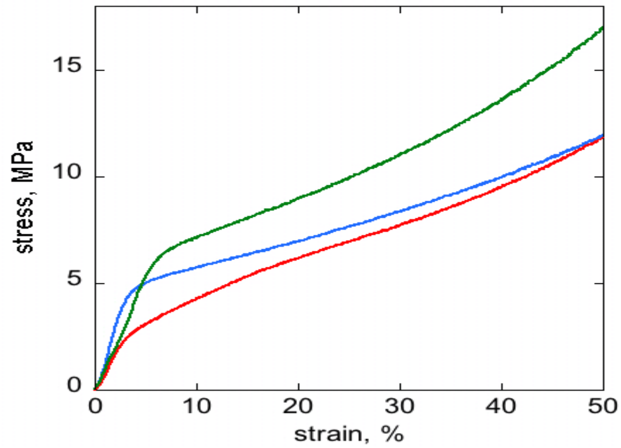

Figure 1. Compression testing of three SDBP/PUR foams

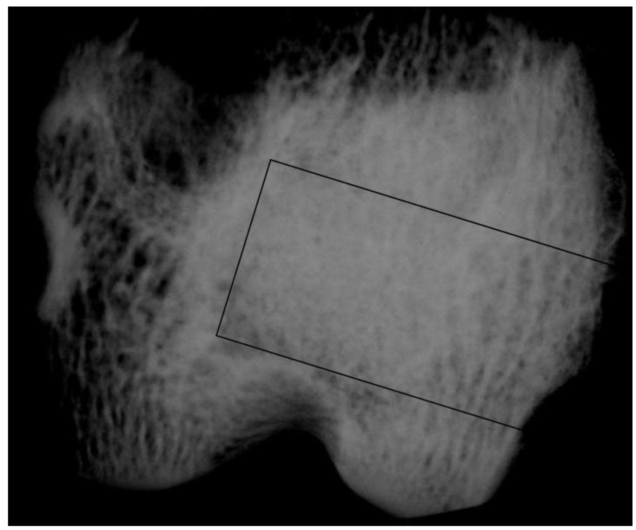

Figure 2. X-ray image of a New Zealand White rabbit femur treated with a SDBP/PUR foam. The outlined area is the original injection site.

Conclusions: Polyurethane-bone composite foams are effective as an injectable, biocompatible treatment for bone fractures and voids. *In vivo* studies suggest that the scaffolds are resorbed by the body, while supporting new bone growth. Histological studies will be performed to further evaluate the scaffolds' ability to support bone growth.

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