Three-Dimensionally Printed β-Tri-Calcium Phosphate/Hydroxyapatite-Bone Morphogenic Protein Scaffolds for Long Bone Regeneration

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Statement of Purpose: Using specialized three-dimensional (3-D) printing technology, combined with fillers and bioactive molecules. Scaffolds can be designed and characterized to demonstrate the efficacy of synthetic, off-the-shelf and custom fabricated 3-D scaffolds for long bone repair. Direct-write (DW) fabrication allows for 3-D creation of off the shelf or custom parts (designed to match individual need by Computed Tomography (CT) scan data) with tailored interconnected porosity that other methods lack. Previous research suggests that Bone Morphogenic Protein (BMP) will stimulate growth and differentiation of new bone. The Beta-Tri-Calcium Phosphate (β-TCP) / Hydroxyapatite (HA) shell and strut scaffold components may provide mechanical strength, conduct bone throughout the scaffold directionally and remodel over time. We hypothesize that using a bioactive filler, such as BMP, these scaffolds may successfully regenerate bone over critical sized bone defects in an *in vivo* model.

Methods: Scaffolds (10 mm long, 4.5 mm outer diameter, 2.25 mm inner diameter) were implanted in New Zealand White Rabbits (n=12 per time point) with 10 mm full critical size radial defect for 2, 4 and 8 weeks. The scaffolds are made from 85% β-TCP : 15% HA ink and were designed using ROBOCAD-computer aided design software and fabricated using a 3-D Printing Robocast machine. Scaffolds were sintered at 1100^{o}C for 4 hours; post-sintering scaffolds consisted of approximately ~95% β-TCP : 5% HA. Micro-CT and histological analysis (Figure 1) were conducted in order to determine the degree of new bone formation and remodeling.

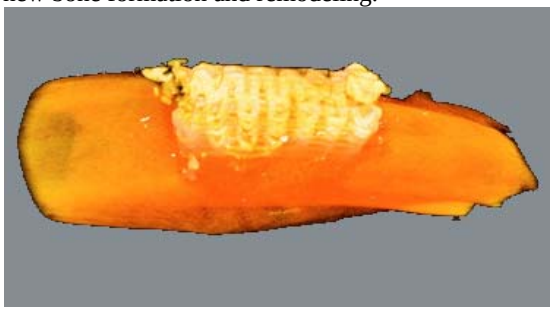

Figure 1: MicroCT of scaffold within the rabbit radius defect at 4 weeks.

Results: Scaffolds with the BMP showed bone remodeling cells and bone bridging across the scaffold's medullary canal (Figure 2). The reconstructed microCT images show more bone formation, remodeling and integration in β-TCP/HA-BMP scaffolds than in β-TCP/HA scaffolds without BMP. Histological analysis showed increased bone formation but decreased osteoconduction in β-TCP/HA-BMP scaffolds; a minimum amount of bone remodeling cells adhered to the scaffold's surface (Figure 2).

Figure 2: Scaffold with BMP at 4 week time point.

Conclusion: B-TCP/HA scaffolds are highly biocompatible and can rapidly and successfully regenerate and remodel bone in critically sized long bone defects in a rabbit model. Custom designs (micro and macro-porosity) and fabrications of β-TCP/HA scaffolds may be used in for the potential repair of critical sized defects in the long bone. Different inks can be used to fabricate different regions of the scaffold, depending on anticipated mechanical and remodeling requirements. Scaffolds may be filled with different component materials that can be released at different times. For instance, a certain portion of the long bone replacement segment might be filled with a more concentrated bone stimulating growth factor, designed to be release at a later time. Altering the outer cap, strut size and interconnectivity of the scaffold may also offer several potential advantages: continuous supply of nutrients, greater cellular and tissue ingrowth, and enhanced revascularization. Thus, making these scaffolds efficient and customizable for the specific need of the patient.

Significance: Using specialized 3D- printing technology, combined with fillers and bioactive molecules, scaffolds can be designed and characterized to demonstrate the efficacy of synthetic, off-the-shelf and custom fabricated scaffolds for the repair of long bone defects. We hypothesize that these customizable scaffolds may successfully regenerate bone over critical sized bone defects in an *in vivo* model.