Mechanical, Chemical, and In Vivo Characterization of Biphasic HA/βTCP 3-D Printed Scaffolds for Custom Bone Repair Applications

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Statement of Purpose: To examine the physical, chemical, and *in vivo* properties of biphasic hydroxyapatite (HA) / beta tri-calcium phosphate (βTCP) composite scaffolds, for custom replacement of bone structures *in vivo*. Basic ceramic structures (rods) as well as 3D-printed (direct-write) scaffolds were fabricated for mechanical/chemical testing, *in vitro* studies, and animal studies using a rabbit trephine defect model. The *in vivo* study was used to examine bone and soft tissue response to the scaffolds. The scaffolds used were either empty, filled with calcium sulfate (CS), or chitsosan (CH). The physical and chemical properties will help determine the ideal scaffold configuration for specific bone applications (ie;.craniofacial versus orthopaedic).

Methods: A 15/85% HA/βTCP mixture was used to create rods, which were fired at 1100°C. These rods were mechanically tested using a modified 3-point bend method (n=10) to determine the load to failure and load versus displacement plot. In addition to mechanical testing, *in vitro* dissolution and chemical characterization studies were performed to examine mass loss and the crystal size and consistency of the HA/βTCP material before and after firing. Direct write (DW) technology was used to 3-D print lattice scaffolds composed of the same material. These had 270µm strut elements (after firing), and regions with different strut spacings (and as well as solid barrier layers. They were also subjected to *in vitro*, physical, and chemical analysis, and were implanted into bilateral 11mm diameter trephine defects in 24 White New Zealand rabbits. There were three types of scaffolds tested: empty, CS filled, and CH filled. Most of the animal work was conducted using CS filled scaffolds evaluated at 8 and 16 weeks.

Results: 3-point bending and compression tests were used to determine the base line properties of the 15/85 HA/βTCP. These HA/βTCP rods had a maximum flexural load of 74.23±17.24 N/mm. This value was used to find the strength of cylindrical rods in three-point flexure, using the formula, $\sigma = {}^{8PL_0}\!/_{\pi D^3}$ [1]. The average strength of these rods was 27.44±6.34 MPa. The 3-D scaffolds of the same material failed in compression at 416.82±22.21N. The *in vitro* mass loss study showed significant mass loss of the empty scaffolds when compared to those of filled with either CS or CH [2]. The *in vivo* study results exhibit significant bone in-growth in the 15/85 HA/βTCP scaffolds filled with CS. Scaffold volume fractions ranged from 44 to 68% depending on scaffold strut spacing. Total volume of new bone formation ranged from 30±6 to 33±8% at 8 weeks, and 41±13 to 48±14% at 16 weeks depending on scaffold volume fraction. Bone formation as a function of available volume ranged from 51±10 to 81±7% at 8 weeks, and 70±14 to 86±13 at 16 weeks. Significant scaffold remodeling was observed at both time periods, and the largest amounts of scaffold remodeling were observed in the 44% volume fraction scaffolds. These lost ~30% of their volume at 16 weeks. Strut size was reduced from about to 267±8µm to 167±35µm (Figure 1).

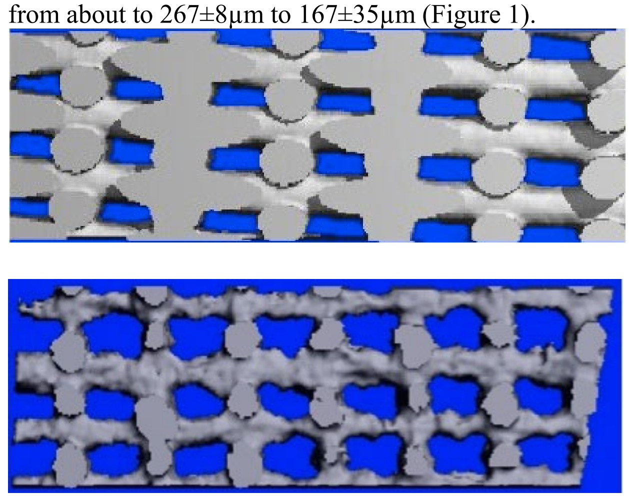

Figure 1: (top) MicroCT image of a 3D reconstructed image of a scaffold pre-implantation. (bottom) A 16-week 15:85 HA/βTCP scaffold (44% volume fraction scaffold) showing extensive osteoclastic erosion of the implanted scaffold

Conclusion: The biphasic HA/βTCP ceramic has good initial compressive strength in strut form as well as in 3-D printed form. CS filling enhances mechanical properties and does not impede bone ingrowth as the CS is soluble in vitro and in vivo. Scaffolds with smaller volume fraction (larger pores) show more bone in-growth and remodeling when compared to the smaller pore scaffolds. The smaller pore scaffolds exhibited a lamellar bone in-growth pattern while the larger pore scaffolds showed a trabecular bone pattern. The results suggest that scaffold porosity can be used to control amounts of bone ingrowth and remodeling. This suggests that scaffold design can be used to control the mechanical and bone ingrowth properties, and that scaffolds can be designed for the specific mechanical and temporal requirements needed for different craniofacial and orthopaedic bone repair applications.

References:

[1]ASTM, 2008, C 1684 – 08

[2]Cretiu-Vasiliu, C., 2008, Masters Thesis, Oklahoma State University, Stillwater, OK.