Porous calcium phosphate (CaP) scaffolds with a core/shell structure using indirect solid freeform fabrication (ISFF)

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Introduction: Porous calcium phosphate (CaP) scaffolds have been extensively used as the bone substitute, since their 3-dimensionally interconnected pores can stimulate the attachment, proliferation and differentiation of cells, when implanted [1-2]. However, these materials often suffer from relatively low mechanical properties because of their high porosity. Therefore, it is still a challenge to develop new ways of improving the mechanical properties of porous CaP scaffolds without sacrificing their high porosity for favorable bone ingrowth. For this goal, we herein demonstrate the utility of the indirect solid freeform fabrication (ISFF) technique using a CaP/camphene slurry to produce porous CaP scaffolds with a core/shell structure, which can mimic the architecture of natural bone having surprisingly high mechanical properties. The fabricated CaP scaffolds were characterized using various analysis tools. The compressive strength and *in vitro* tests were also carried out to evaluate the potential applications as the bone scaffold.

Method: A calcium phosphate (CaP)/camphene slurry with a ceramic content of 40vol% was prepared at 60^{0}C for 24 hours using ball-milling. In a separate preparation, negative molds with a predetermined CAD design were produced using a commercial ISFF machine (μ-Print). The prepared CaP/camphene slurry was then cast into the mold and kept at room temperature for 1h to allow the complete infiltration of the slurry into the mold, followed by freeze-drying for 48 h to remove the frozen camphene. Thereafter, the green samples were heat-treated at 500^{o}C for 10 h to remove the negative mold according to a carefully designed schedule for binder burnout and 1300^{o}C for 3 h to density the CaP walls. The porous structure of the fabricated samples was characterized by scanning electron microscopy (SEM) and micro-computed tomography (micro-CT). The porosity of the sample was calculated by measuring its dimensions and mass. The compressive strength was measured using a screw driven load frame. In addition, *in vitro* cell tests of the samples were performed using a pre-osteoblast cell line (MC3T3-E1).

Results and Discussion: The fabricated sample showed good shape tolerance without any noticeable defects, such as cracking and distortion, as shown in Fig. 1 (A), which resembled the original porous structure of the negative mold. In addition, the tightly controlled 3-D periodic pores were formed well in the core, as shown in Fig. 1 (B), indicating the complete infiltration of the CaP/camphene slurry with a high ceramic content of 40 vol% into the mold. The sample showed a linear shrinkage of ~ 20 %

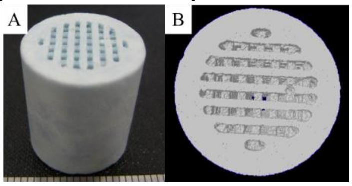

Fig. 1. (A) Optical image and (B) micro-CT image of the fabricated CaP scaffold

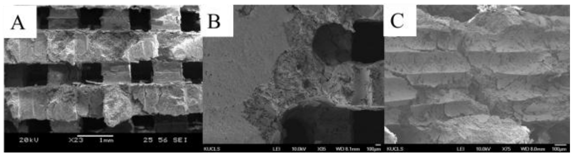

Fig. 2. SEM images of the fabricated CaP scaffold, showing (A) the 3-D periodic pores, (B) the interface between the core and shell, and (C) the densification of the CaP walls.

after sintering at 1300^{o}C for 3 h and a porosity of ~ 25 vol% that was calculated by measuring its dimensions and mass.The pore structure and densification of the CaP walls were more closely examined by SEM, as shown in Figs. 2 (A)-(C). The construction of the 3-D periodic pores in the core is clearly shown in Fig. 2 (A). The distance between the CaP walls was ~ 700 μm, which would be expected to provide a favorable environment for bone ingrowth, when implanted. Furthermore, good bonding between the core and shell was observed without any noticeable delamination (Fig. 2 (B)) due to the use of a carefully designed schedule for binder burnout. The CaP walls were densified well without large voids and cracks (Fig. 2 (C)). It should be noted that the compressive strength can be tailored simply by adjusting the porosity of the negative mold produced using a SFF machine. In addition, the *in vitro* cell test using a pre-osteoblast cell line revealed the samples to have good biocompatibility, where the cells appeared to grow and spread actively on the surfaces of the CaP walls (data not shown here).

Conclusions: Porous calcium phosphate (CaP) scaffolds with a tailored core/shell structure were produced by casting a CaP/camphene slurry into a negative mold prepared using a commercial SFF machine. The fabricated sample showed a tightly controlled pore structure, where a core had a 3-dimensional (3-D) periodic pore network formed by the removal of the negative mold, surrounded by a relatively dense shell. In addition, the sample showed good biocompatibility, as assessed by the *in vitro* cell tests.

References:

1. suA Park et al. J Mater Sci 2009; 20; 229-2342.
2.Eun-Jung Lee et al. Acta Biomaterialia. 2010; 6; 3557-3565