Capillary Forces and Multiscale Porosity Synergistically Enhance Osteointegration in Biphasic Calcium Phosphate Scaffolds

Amy Wagoner Johnson[1,2], Laurence Rustom[1,2], Thomas Boudou[2], Siyu Lou[2,3], Isabelle Pignot-Paintrand[2], Brett Nemke[4], Yan Lu[4], Mark Markel[4] and Catherine Picart[2]

[1]University of Illinois at Urbana-Champaign, Urbana, IL; [2]University Grenoble Alpes and CNRS UMR 5638, Grenoble, France; [3]Shanghai Jiao Tong University, Shanghai, China; [4]University of Wisconsin - Madison, WI

Statement of Purpose: The purpose of this study was to demonstrate and quantify the synergistic effects of capillary forces and multiscale porosity for osteointegration in biphasic calcium phosphate (BCP) scaffolds. Osteointegration of bone scaffolds in defects that do not spontaneously heal still presents a major challenge in bone defect repair. Previous work showed that capillary forces generated by micropores in BCP scaffolds with both micro- and macropores, draw cells and fluid from the defect into the pores when scaffolds are implanted in the defect[1]. This study aims to quantitatively compare bone regeneration in these scaffolds that have, or do not have, micropore-induced capillary forces at implantation. The scaffold system consists of layers of orthogonal BCP rods and scaffolds are fabricated by robotic deposition. The space between scaffold rods constitutes macropores. The rods can contain microporosity, with fully interconnected micropores less than 20 μm in diameter, and thus have multiscale porosity. Or, scaffold rods can be solid. These two types of scaffolds are referred to as microporous (MP) and non-microporous (NMP) scaffolds, respectively.

Methods: Scaffolds were fabricated according to established protocols[2,3]. Sacrificial polymethylmethacrylate (PMMA) microspheres added to the ink generate microporosity during sintering. Sintering at 1300°C for 2 hours burns out these and other chemical additives leaving behind fully interconnected micropores with nominally average size of 5 μm and 2 μm interconnections between pores[4]. For this study, the 8 mm diameter sintered scaffolds were divided into three groups: MP-Dry, MP-Wet and NMP. MP-Dry samples were implanted in the dry state, without hydration. MP-Wet and NMP served as two different controls for conditions without capillary forces. MP-Wet samples were submerged in PBS solution in order to fill the micropores with fluid, prior to implantation; capillary forces draw in the PBS solution when submerged. As a result, the capillary forces are not "available" to draw in cells and fluid from the defect at implantation. Thus, MP-Wet had microporosity, but no capillary forces at implantation. NMP samples do not have microporosity, by definition, and therefore cannot draw in cells and fluid via capillarity when implanted; NMP scaffolds had neither microporosity nor capillary forces. Three defects were made on each side of the mandible, resulting in six defects per pig, according to established and approved protocols[1]. Samples were implanted for 3 weeks and then analyzed quantitatively by micro-computed tomography (micro-CT).

Results: The average bone volume fraction, BVF, the bone growth front, BGF, and the BVF as a function of normalized radius, BVF(r*), were measured using micro-CT data. The average BVF was larger for both MP-Dry and MP-Wet compared to NMP (Fig. 1A). Bone distribution was assessed by measuring the depth of BGF from the edge towards the center of the scaffolds and by BVF(r*). Fig. 1A is a 2D map of the bone density and the BGF. The front was deeper into MP-Dry compared to MP-Wet and NMP (Fig. 1A). Both MP-Wet and NMP had significantly lower BVF at the center of the scaffold compared to MP-Dry. BVF(r*) varied less in MP-Dry from edge to center, again indicating a more uniform bone distribution for MP-Dry (Fig.1B).

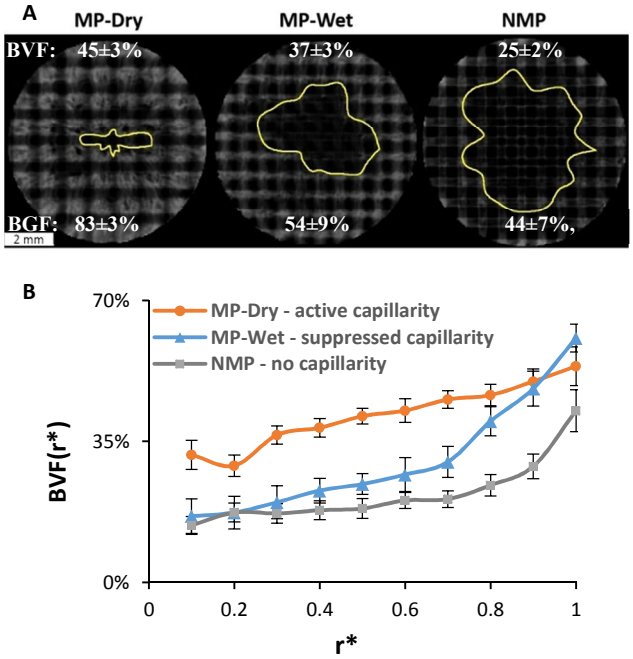

Figure 1. (A) Bone distribution showing BGF for representative samples. Values for BVF and BGF are included. **(B)** BVF(r*) for all samples. MP-Dry has more bone at the center ($p<0.05$) and a more shallow slope, indicating a more uniform bone distribution.

Conclusions: Using two controls for capillary forces, MP-Wet and NMP, micro-CT data and histology (not shown) demonstrate that capillary forces and multiscale porosity work synergistically to enhance osteointegration in BCP scaffolds. The stark contrast in bone distribution and ingrowth in the presence of capillarity highlights the synergistic utility of the capillary mechanism and multiscale porosity in enhancing osteointegration. The results have important implications in repair of large bone defects that will not heal spontaneously.

References: 1. Polak SJ. Acta Biomater 2013;9:7977–86; 2. Hoelzle DJ. Acta Biomater 2008;4:897–912; 3. Hoelzle DJ. J Biomech Eng 2011;133:10100; 4. Lan Levengood SK, Biomaterials 2010;31:3552–63.