In Vitro Degradation of 3D Printed Poly(Propylene Fumarate) Scaffolds

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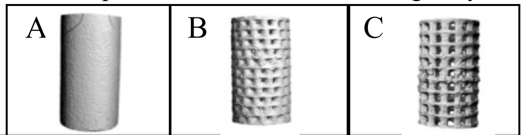
Statement of Purpose: Predicting the mechanical properties of scaffolds during degradation is integral for successful treatment of bone defect sites. In this study, porous, degradable polymer sleeve scaffolds were 3D printed using poly(propylene fumarate) (PPF), a well characterized polymer for bone tissue engineering[1]. Three different designs were investigated: aligned pore structure architecture (aligned), unaligned pore structure architecture (unaligned) and solid wall (solid). The two porous structures were designed using a modular repeating unit of a base ring with posts. A 16 week study was used to evaluate the changes in scaffold mechanical properties such as compressive modulus, mass loss, and water absorption.

Materials, Methods and Analytical Procedures Used: PPF was synthesized as previously described[2]. Scaffold designs were implemented in SolidWorks (Dassault Systèmes SolidWorks Corp., Waltham, MA) and then fabricated using an envisionTEC Perfactory® P4 additive manufacturing device. The polymer resin used for fabrication contained PPF, diethyl fumarate, bis(2,4,6-trimethylbenzoyl) phenylphosphine oxide (Ciba Specialty Chemicals, Tarrytown, NY) (BAPO), 2-Hydroxy-4-methoxyphenyl) - (phenyl) - methanone and α-tocopherol. Scaffolds were then placed in 0.01M, pH 7.4 phosphate buffered saline (PBS) in 20mL glass scintillation vials. Vials were stored at 37°C on a shaker table (75rpm) to simulate *in vivo* conditions. At each time point (days 0, 1, 7, 14, 28, 56) samples were evaluated for compressive modulus, changes in porosity, pore size and wall thickness using micro computed tomography (µCT), water absorption and changes in mass. Compressive properties were measured on an Instron mechanical testing system (5560) at a displacement rate of 10mm/min (n=5). µCT imaging was performed using a SCANCO Medical (Brüttisellen, Switzerland) µCT 100 to nondestructively image and quantify scaffold parameters (n=3). The resulting 3-D data sets were segmented using thresholds to separate pores and void spaces from polymer. Images were compiled and evaluated using Image Processing Language (IPL). The mean and standard deviation are reported.

Results: PPF scaffolds were fabricated using the envisionTEC Perfactory® P4 device. Aligned and unaligned scaffolds were designed with pore sizes of 800µm and porosities of 50%. µCT evaluation showed that the porous fabricated scaffolds had pore sizes, porosities and wall thickness similar to the theoretical values (Figure 1) after manufacture. Mass loss increased with time and reached maximum values at day 56 (Figure 2). Interestingly, the solid PPF scaffolds showed a significant increase ($p>0.05$) in the compressive modulus through day 56 compared to the moduli at day 0 and day 1 (Figure 3). This increase in compressive modulus may be due to spontaneous crosslinking[3], or possibly due to loss of amorphous regions in the polymers rather than crystalline chains. The aligned and unaligned scaffolds maintained compressive modulus levels through day 56.



	A Theoretical	A Effective	B Theoretical	B Effective	C Theoretical	C Effective
Porosity (%)	n/a	n/a	50%	47% ± 3%	50%	53% ± 9%
Pore Size (µm)	n/a	n/a	800	605 ± 22	800	585 ± 50
Wall Thickness (µm)	500	837 ± 28	500	523 ± 18	500	552 ± 79

Figure 1: µCT 3D Rendering and Characterization: 3D rendering and scaffold parameter theoretical values compared to parameters of 3D printed designs for: **(A)** solid wall scaffold, **(B)** unaligned pore structure architecture, **(C)** aligned pore structure architecture.

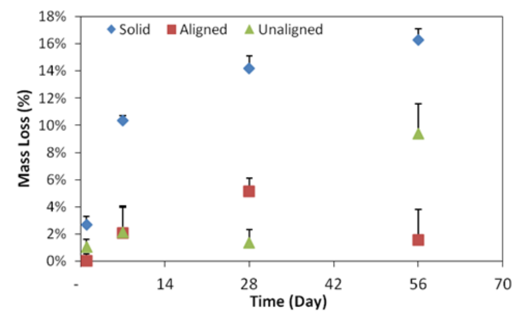


Figure 2: Mass loss of solid, aligned and unaligned pore scaffolds. Mean and standard deviation are reported (n=5)

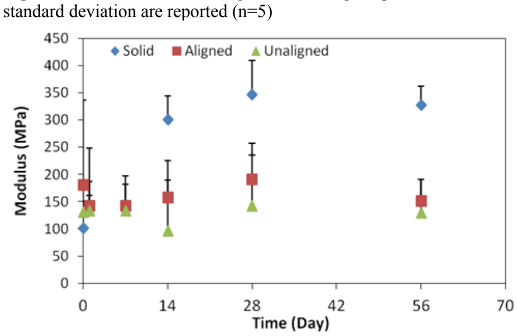


Figure 3: Compressive modulus of solid, aligned and unaligned pore scaffolds. Mean and standard deviation are reported (n=5)

Conclusion: *In vitro* degradation of 3D printed PPF scaffolds was characterized using mechanical testing and µCT. Compressive modulus of the solid wall PPF scaffold increased and reached peak values at day 28. For all scaffolds through day 56, the moduli remained greater than average trabecular bone compressive elastic moduli (50-100MPa)[3]. Therefore we conclude that 3D printed PPF scaffolds will be acceptable for the treatment of bone defects.

References: 1) Cooke, M.N., *J. Biomed. Matl. Res. B* (2002) 65-69., **2)** Kasper, F.K., *Nat. Protoc.* (2009) 4, 518-525; 2 **3)** Fisher, J.P., *Biomacromolecules, (2003)* 59 1335–1342.