Poly(ε-caprolactone) Shape Memory Polymer for Filling Critical-Sized Defects

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Statement of Purpose: Treatment of critical-sized bone defects often relies on autologous bone grafts that have inherent limitations, including second site morbidity and donor site scarcity. As an alternative to bone grafting, substantial effort has focused on developing synthetic graft substitutes, including polymeric scaffolds, which could address these limitations. Current scaffold technologies are generally limited in their ability to conform to critical-sized defects while also providing rapid load bearing. This limitation could be addressed through the use of shape memory polymer (SMP) scaffolds. SMPs are a class of active materials that have the ability to "memorize" a permanent shape, be manipulated and fixed to a temporary shape, and later recover to the permanent shape through a triggering event, such as heating. This technology has previously been successfully used for other medical applications including deployable stents [1] and aneurysm occlusion devices [2]. We recently reported the first cytocompatible topography change using an SMP substrate [3]. The programmable nature of SMP scaffolds could be harnessed to fill critical-sized defects of various geometries and sizes while enabling more rapid load-bearing than space filling hydrogels. The objective of this study was to develop a 3D SMP scaffold that can be triggered to expand under cytocompatible conditions.

Methods: SMP scaffolds were fabricated using a modified porogen leaching technique, in which a functionalized poly(ε-caprolactone) (PCL) macromer was mixed with NaCl in a 9:1 salt-to-PCL ratio by weight and subsequently crosslinked via thiol-ene chemistry. Salt particles were fused for 24 h in a humidity chamber prior to adding the macromer solution. Once the polymer was cured, salt particles were extracted with water, yielding a porous foam scaffold with high porosity and interconnectivity. Shape memory characterization of the scaffold was performed using a dynamic mechanical analyzer measuring compressive strain fixing and recovery. The resulting porous architecture before fixing, after fixing, and after recovery was investigated with scanning electron microscopy (SEM) and microtomography. Tuning of the functional recovery temperature to a cytocompatible temperature was achieved through both composition and deformation temperature adjustments. Cell studies were performed using human adipose derived stem cells to investigate cell viability and cell proliferation on the scaffolds.

Results: The porogen-leaching technique yielded polymeric scaffolds featuring porosities >80% with high interconnectivity. These scaffolds exhibited excellent shape fixing and shape recovery characteristics, with fixing and recovery ratios of 99% and 95%, respectively. Prior to deformation and fixing, pores were open and interconnected, whereas after compressive deformation pore architecture collapsed; pore structure was able to then recover to the original size and shape after recovery (Figure 1). The functional recovery of the scaffolds was easily tuned by adding a second functionalized macromer to the system. This hydrophilic macromer, once hydrated, served to decrease the recovery temperature to 37 °C. Deformation temperature also served as a viable method for controlling the recovery temperature, with lower deformation temperatures leading to lower recovery temperatures. Preliminary cell studies using Live/Dead viability assay revealed cells remained viable atop the scaffold after 2 d and 4 d (data not shown). SEM imaging revealed cells attached and spread throughout the scaffold (data not shown).

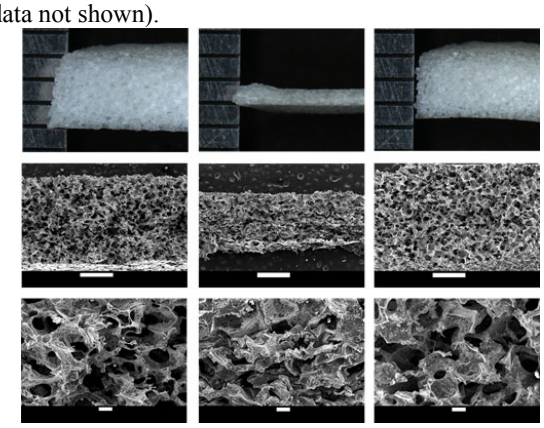

Figure 1. Compressive shape memory behavior and effect on pore morphology: Compressive shape memory (left) before compression, (middle) after compression and fixing, and (right) after recovery show that the SMP scaffold is able to recover back to the original state and restore its porous architecture. Scale bars: 1 mm (middle row) and 100 μm (bottom row)

Conclusions: This work demonstrates a shape memory scaffold for space filling of critical-sized defects. Scaffolds with tunable recovery temperatures and excellent shape fixing and recovery ratios were fabricated. The scaffolds are highly porous and cytocompatible and can serve as candidates for *in vivo* studies.

Shape memory functionality may be harnessed for treatment of critical-sized defects. They offer the possibility of minimally invasive delivery along with more rapid load-bearing than that of hydrogel-based scaffolds.

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References

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