Bioactive Shape Memory Polymer Scaffolds for Bone Defect Repairs

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Statement of Purpose: Thermoresponsive shape memory polymers (SMPs) are stimuli-sensitive materials that can be fixed in a temporarily deformed shape and subsequently return to original shape with application of heat.[1] Compared to non-porous SMP solids, porous SMPs are lightweight, highly compressible and are desirable for applications requiring diffusivity and permeability. For example, polyurethane (PU) SMP foams have been used as embolic sponges for aneurysm occlusion.[2]

We have previously reported that a refined solvent casting/salt leaching (SCSL) method can be used to develop a porous poly(ε-caprolactone) (PCL) SMP scaffold based on UV-crosslinkable diacrylated PCL macromers.[3] In this study, the PCL scaffold was submersed in an aqueous solution of dopamine which spontaneously forms polydopamine onto the surface of pore walls. Polydopamine coating has been shown to improve cell adhesion on a wide variety of materials[4] and has also been used as a universal tool for biomineralization of scaffold in tissue engineering.[5] Thus, the effects of polydopamine on the physical properties as well as bioactivity of our PCL SMP scaffolds were examined.

Methods: *Fabrication.* Diacrylated PCL macromer (M_n ~10,000 g/mol) was synthesized as previously described.[3] To fabricate one cylindrical scaffold, 1.8 g of NaCl salt (~460 μm) was placed inside a 3 mL glass vial (I.D. = ~13 mm) and 7.5 wt% of DI water was added. The mixture was then stirred and dried overnight causing the salt to fuse into a "continuous porogen template". The macromer solution (0.15 g/mL in dichloromethane) and 15 vol% photocatalyst solution (10 wt% 2,2-dimethoxy-2-phenylacetophenone in 1-vinyl-2-pyrrolidinone) were combined and added to cover the salt. The vial was then exposed to UV-light for 3 min. After salt leaching and subsequent air-drying, the scaffold was submersed in dopamine hydrochloride solution (2 mg/mL in 10 mM Tris buffer, pH = 8.5) at 150 rpm for 16 h. The scaffold was then extensively rinsed with DI water and dried *in vacuo* for 24 h. Finally, the scaffold (with or without the coating) was heat treated at 85 °C for 1 h, followed by cooling to RT.

Characterization. Porosity of the scaffold was calculated using the equation: $\%P = [\rho_{solid\ SMP} - \rho_{SMP\ scaffold}]/\rho_{solid\ SMP} \times 100$. Compressive modulus (E) was determined from compression tests using Instron 3345 tensile tester at a strain rate of 1.5 mm/min. Shape memory properties were determined via strain-controlled thermal mechanical compression tests (TA Instrument Q800) with the following protocols: (1) after equilibrating at 60 ºC for 5 min, compressing to a maximum strain (ε_m = 50%), (2) holding at ε_m for 5 min and then quickly cooling to 25 ºC to fix temporary shape, (3) removing load and immediately measuring ε_u, (4) reheating the foam to 60 ºC and measuring the recovered strain ε_p. Shape fixity (R_f) and shape recovery (R_r) were calculated using the equations $R_f = \varepsilon_u/\varepsilon_m$; $R_r = (\varepsilon_m - \varepsilon_p)/\varepsilon_m$, respectively. Bioactivity of the scaffold was evaluated by soaking the scaffold in simulated body fluid (SBF) at 36.5 °C for 7 d and examining the formation of surface hydroxyapatite using scanning electron microscopy (SEM) (JEOL 6400).

Table 1. Scaffold properties with and without coating

Sample	E (MPa)	R_f (%)	R_r (%)
Uncoated	4.3 ± 0.4	102.2 ± 0.1	94.7 ± 1.5
Coated	4.4 ± 0.2	102.5 ± 0.7	95.3 ± 0.9

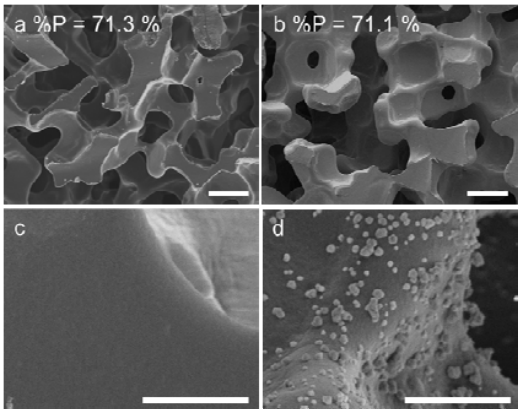

Figure 1. SEM images of (a) uncoated scaffold; (b) coated scaffold; (c) uncoated and (d) coated scaffold after soaking in SBF for 7 d. Scale bar is 200 μm for (a) and (b), and 50 μm for (c) and (d).

Results: After salt leaching, heat treatment at 85 °C caused scaffold shrinkage and a corresponding decrease in pore size due to the reorganization of PCL crystalline domains into closer proximity.[3] The larger pore size of scaffold prior to heat treatment enhanced the permeation of dopamine solution and thus the coating uniformity.

After heat treatment, the physical properties of the coated scaffold were compared with that of an unmodified PCL scaffold. Due to the low thickness,[4] the polydopamine coating did not affect the physical properties including pore features (**Figure 1a-b**) as well as compressive modulus and shape memory properties (**Table 1**). However, a significant amount of hydroxyapatite formed on the polydopamine-coated scaffold after soaking in SBF for only 7 d (**Figure 1c-d**), indicating the excellent surface bioactivity.[6]

Conclusions: Bioactive SMP scaffold was fabricated via a refined SCSL method and the subsequent application of a polydopamine coating. Potentially, this scaffold can be used as "self-fitting" scaffold for bone defect repairs.

References: **1.** Lendlein A. Angew Chem Int Ed. 2002;41:2034-2057. **2.** Ortega J. Ann Biomed Eng. 2007;35:1870-1884. **3.** Zhang D. *in revision*. **4.** Ku SH. Biomaterials. 2010;9:2535-2541. **5.** Ryu J. Adv Funct Mater. 2010;13:2132-2139. **6.** Kokubo T. Biomaterials. 2006;15:2907-2915.