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In vivo tissue responses to thermal-responsive shape memory polymer nanocomposites

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ABSTRACT

To explore the safe use of thermal-responsive shape memory polymers (SMPs) as minimally invasive tissue scaffolds, we recently developed a class of biodegradable POSS-SMP nanocomposites exhibiting stable temporary shape fixing and facile shape recovery within a narrow window of physiological temperatures. The materials were covalently crosslinked from star-branched building blocks consisting a bioinert polyhedral oligomeric silsesquioxane (POSS) core and 8 degradable poly(D,L-lactide) (PLA) arms. Here we examine the degradation profiles and immunogenicity of POSS-SMPs as a function of the PLA arm lengths using a rat subcutaneous implantation model. We show that POSS-SMPs elicited a mild foreign body type immune response upon implantation. The degradation rates of POSS-SMPs, both *in vitro* and *in vivo*, inversely correlated with the length of the PLA chains within the crosslinked amorphous network. Upon *in vivo* degradation of POSS-SMPs, a second acute inflammatory response was elicited locally, and the inflammation was able to resolve over time without medical interventions. One year after the implantation of POSS-SMPs, no pathologic abnormities were detected from the vital/scavenger organs examined. These minimally immunogenic and biodegradable SMPs are promising candidates for scaffold-assisted tissue repair where both facile surgical delivery and controlled degradation of the scaffold are desired for achieving optimal short-term and long-term clinical outcomes.

1. Introduction

Thermal-responsive shape memory polymer (SMP) can be imparted with a permanent shape above a critical transition temperature (T_{trans}) when it is cast. Such a permanent shape, formed at the material's elastic state without external stress, can be retained or "memorized" as the material cools to a temperature below its T_{trans}. The material can be subsequently deformed into any desired temporary shape by force at $T>T_{trans}$, and be fixed as it cools down to $T<T_{trans}$. When a thermal stimulus ($T>T_{trans}$) is re-applied, the SMP can revert to its less strained permanent shape. These unique properties are attractive for tissue engineering applications as the SMP may be delivered in a minimally invasive temporary shape to an area of tissue defect, and subsequently revert to a permanent shape that precisely conforms to the defect upon thermal triggering [1,2]. For safe clinical applications, a combination of stable temporary shape fixation at body temperature, a rapid and complete shape recovery at a T_{trans} slightly above physiological temperature, and suitable mechanical and biological properties of the SMP will be ideal.

Towards this end, we recently developed an amorphous SMP network crosslinked from a star-branched macromer (Fig. 1A) containing polyhedral oligomeric silsesquioxane (POSS) nanoparticle core and eight poly(DL-lactide) (PLA) arms [3]. The rigid POSS nanoparticle core facilitated maximal participation of the urethane-tethered PLA arms in the elastic deformation and recoiling process with reduced excessive chain–chain entanglement below and above T_{trans}, respectively. Consequently, the resulting POSS-SMP nanocomposites, with cortical bone-like modulus (~2 GPa) at body temperature, could stably hold their temporary shape for >1 year at room and body temperatures and achieve full shape recovery with a $T_{trans} < 50\ ^{\circ}C$ in a matter of seconds. To fully explore the potential of POSS-SMPs as self-fitting tissue scaffolds and implants, biocompatibility of this new class of thermal responsive materials needs to be investigated [4,5].

Given the bioinert nature of the POSS core [6], the established clinical use of PLA as bioresorbable sutures [7,8], and the prevalence of polyurethanes in medical implants [2], we hypothesize that

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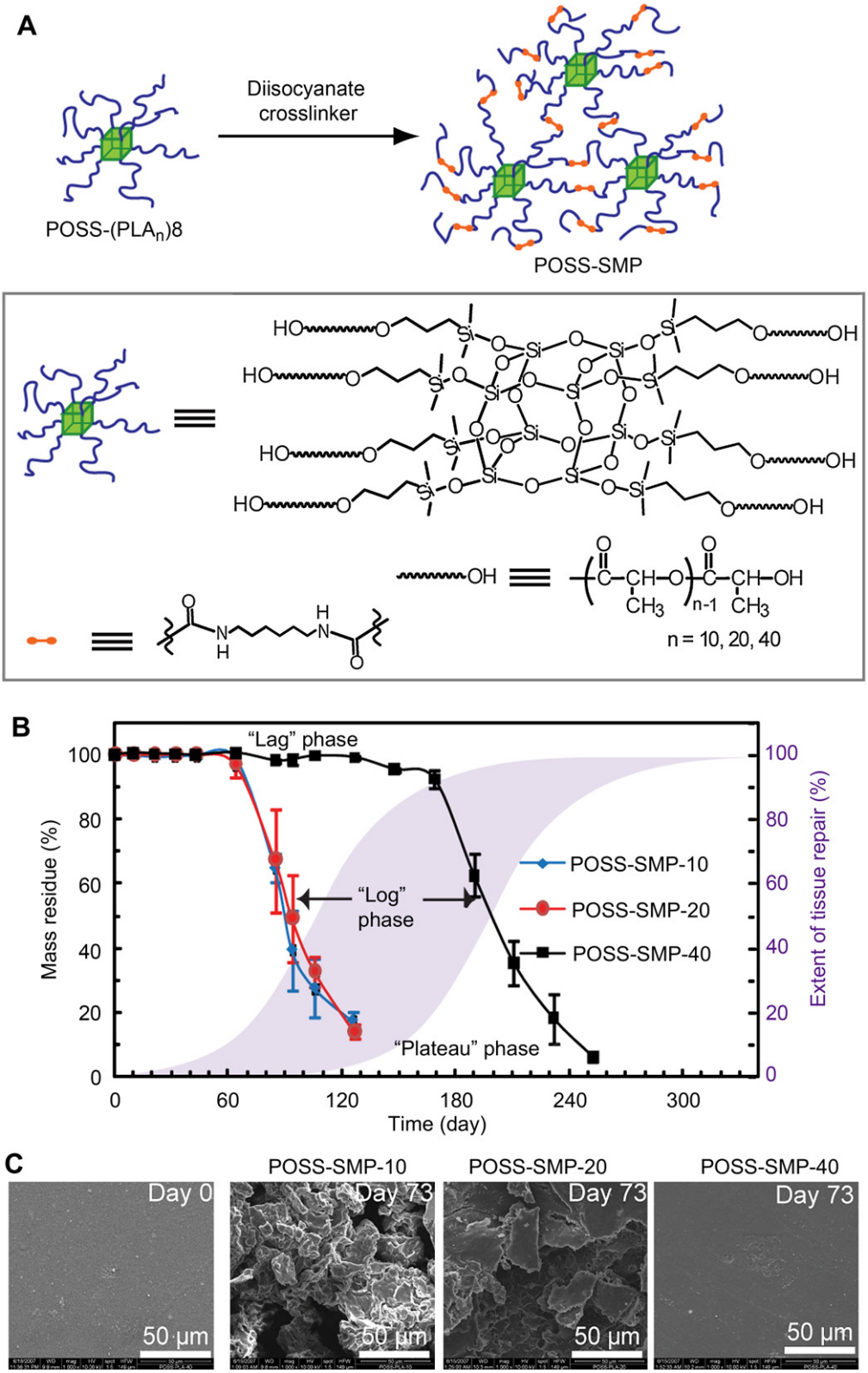

Fig. 1. Chemical composition and *in vitro* hydrolytic degradation of POSS-SMPs. (A) Star-branched macromer building blocks of POSS-SMP; (B) %Mass residue of POSS-SMPs as a function of PLA arm length upon incubation in PBS (pH 7.4) at 37 °C. A qualitative illustration of the tissue repair kinetics is shown in purple. A sample size of 3 was applied; (C) SEM micrographs of POSS-SMPs before and after 73-day incubation in PBS at 37 °C.