Improved Damage Resistance of Hydrogel Coatings Based on Interpenetrating Networks

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Statement of Purpose: It remains challenging to design materials for cardiovascular devices that can match the complex mechanical properties of native tissues and support long-term thromboresistance. Our lab has developed a multilayer strategy to decouple these two properties so that each one can be optimized independently. Namely, we have developed a bioactive hydrogel coating that can be applied to cardiovascular devices (e.g. vascular grafts) that provides immediate resistance of platelet attachment and promotes endothelialization for sustained thromboresistance.[1] Previously, the coating has been limited in conformability and susceptible to damage upon surgical implantation.[2,3] To improve the torqueing damage of this coating, we developed a new hydrogel interpenetrating network (IPN) chemistry with additional hydrogen bonding motifs. In this study, we demonstrate that these PEG-based IPN networks improve damage resistance and can be applied to devices using our conformable coating methodology.

Methods: Samples were fabricated from biostable polyether urethane diacrylamide (PEUDAm) 20 kDa and *N*-acryloyl glycinamide (NAGA). Single network bulk gels used for mechanical testing were fabricated with conventional photoinitiation reactions. IPNs were fabricated by swelling NAGA (20wt%), bisacrylamide (0.1mol%), and a photoinitiator molecule into the dried PEUDAm 20 kDa 10wt% first network, allowing the network to reach equilibrium swelling, then crosslinking on a UV plate. To represent historic data, polyethylene glycol (PEGDA) 3.4 kDa 10 wt% hydrogels were also fabricated and tested. Uniaxial tensile tests were performed on hydrogels with and without notches to characterize tensile properties and fracture energy, respectively. Redox hydrogel coatings of this new formulation were then formed in a two-step process. The first network PEUDAm 20 kDa was fabricated with the established diffusion mediated crosslinking method on polyurethane mesh substrates.[2] The composites were dried then swollen in a monomer solution with a photoinitiator and cured. Successful formation of the IPN was characterized by the presence of NAGA peaks in IR spectra. Thickness of the composites was measured for the first network and final network in the swollen state.

Results: As expected, the IPN hydrogel properties were intermediate of the two individual networks, **Figure 1**. The ultimate elongation of the IPN network was similar to that of the single-network PEUDAm (20 kDa, 10wt%) first network hydrogel, 248 ± 92% vs. 160 ± 34%. In contrast, the stiffness was markedly different, increasing to 145 ± 20 kPa from 20 ± 2 kPa. The fracture energy of the IPN also increased from 0.016 ± 0.001 N/m to 0.255 ± 0.098 N/m, indicating that the presence of the pNAGA network successfully dissipates fracture energy within the IPN. As compared to our previous hydrogel coating, the IPN

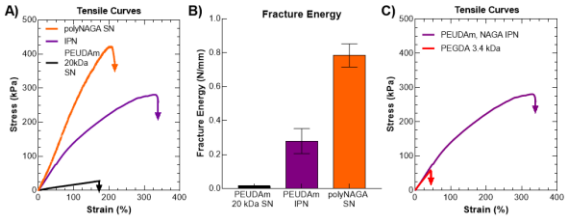

Figure 1: Mechanical properties of IPN hydrogels. (**A**) Tensile and (**B**) fracture energy characterization of IPNs vs. single networks. (**C**) Tensile testing of IPNs compared to previous network.[1,3]

hydrogel successfully matched the stiffness of PEGDA 3.4 kDa hydrogels (149 ± 20 kPa vs. 113 ± 38 kPa) with much higher ultimate elongations (38 ± 13% vs. 248 ± 92%) and fracture energy (0.014 ± 0.005 N/m 0.255 ± 0.098 N/m). Based on our previous studies, we hypothesize that this increased stiffness will enhance endothelial cell attachment and migration.[1] We have previously established high fracture energies correlate with increased resistance to suture damage.[3] Recently, resistance to damage from twisting and torqueing motions during surgery were attributed to high ultimate elongations. Indeed, we observed that the IPN coating resist torqueing damage.

Conformable coatings of the IPN networks were successfully fabricated using a modified two-step process. First, a PEUDAm hydrogel was applied with our redox-initiated, conformable coating method to set the coating thickness, tunable with time. The pNAGA second network was introduced by swelling the initial PEUDAm hydrogel coating with the monomer and photocrosslinking. This second network was confirmed by FTIR. There was a small but significant thickness decrease of the IPN as compared to the first network that was attributed to a decrease in swelling ratio with the incorporation of strong hydrogen bonding interactions.

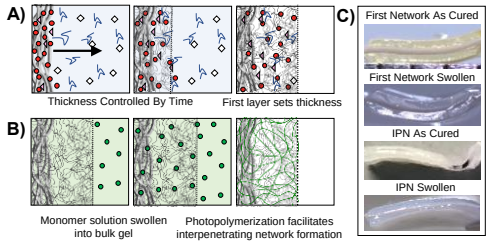

Figure 2: Conformable crosslinking methodology with IPNs (**A**) Redox diffusion-mediated crosslinking. (**B**) IPN incorporation (**C**) Hydrogel cross-sections from first network crosslinked to final swollen network.

Conclusions: These results demonstrate the improved network properties of PEUDAm-NAGA IPN hydrogel coatings. This new hydrogel coating meets requisite stiffness for endothelial cell attachment and spreading with improved damage resistance. Conformal hydrogel coatings that resist surgically associated damages will enable the fabrication of thromboresistant biomaterials.

References:(**1**) Browning, M. B., et al. *Acta Biomaterialia* **2012**, *8* (3), 1010-21; (**2**) Wancura, M., et al. *J. Mater. Chem. B* **2020**, *8* (19), 4289-4298. (**3**) Post, A., et al. *Acta Biomaterialia* **2018**, *69*, 313-322;