The Role of Water in Elastic Recovery of Injectable PNIPAAm-based Hydrogels

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Introduction: Solutions of Poly(N-isopropylacrylamide) (PNIPAAm) / Poly(ethylene glycol) (PEG) copolymers have been identified as candidate injectable materials for the replacement of the nucleus pulposus[1]. They undergo phase transformations from liquid to solid when the temperature is raised above the lower critical solution temperature (LCST), between 32-34°C.

Simple compression testing to determine the modulus of these materials is insufficient in evaluating their ability to serve in orthopaedic applications. The hydrogels must be able to withstand repetitive loads without permanent changes to their dimensions or water content. For this study, the effects of repeated compression and unloading cycles on the properties of hydrogels made from three formulations were studied with focus on the behavior of water in the recovery mechanism after loading.

Methods: Three polymers were synthesized for this study by a previously reported method[1]: PNIPAAm with 7% PEG grafts, PNIPAAm with 7% PEG branches, and a control PNIPAAm with no PEG. Cylindrical hydrogel samples were created from 25% solutions of each polymer. Mechanical tests were performed with an Instron (Model 3362 with 100N load cell) in 37°C PBS (pH=7.4). From a 0.1N compressive preload, each cylindrical sample was compressed to 7 kPa at a strain rate of 100% min^{-1} and then unloaded to the preload condition at the same rate. This compression/unloading cycle was repeated 4 more times for each sample (n=6 for each polymer). The cylindrical samples' height and water content were determined immediately after (n=6) and 30 minutes after (n=6) the 5th unloading period was completed for each polymer formulation. Sample height was determined by measuring the crosshead displacement needed to reach the preload load condition of 0.1N. Water content was determined for a control group of samples (n=6) representative of the water content prior to mechanical testing.

Results/Discussion: Stress-strain responses for the hydrogels made from PNIPAAm and PEG grafted PNIPAAm were similar. A higher level of strain was required with each cycle to reach the same common stress level (7 kPa). For hydrogels made from PEG branched PNIPAAm differences between the maximum strain levels achieved with the 1st and 2nd cycle were less than those observed for hydrogels made from PNIPAAm and PNIPAAm with 7% PEG grafts. Unlike PNIPAAm and PEG grafted PNIPAAm, the stress-strain responses of PEG branched PNIPAAm hydrogels only showed minimal differences after 2 cycles (Figure 1).

Recovery of sample height, normalized to the maximum deformation achieved during the 5th loading cycle, was highest for the PEG branched hydrogels (Figure 2). They exhibited only a 3.4% change in sample height while significant deformations were observed for PNIPAAm and PEG grafted hydrogels after 30 minutes of recovery. Dimensional recovery in the PEG branched hydrogels was due to a higher water content.

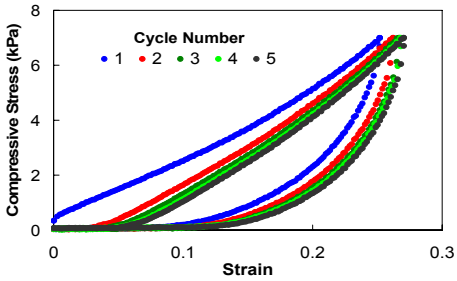

Figure 1. Representative stress-strain curves for five compression and unloading cycles on a hydrogel prepared from PNIPAAm with 7% PEG branches

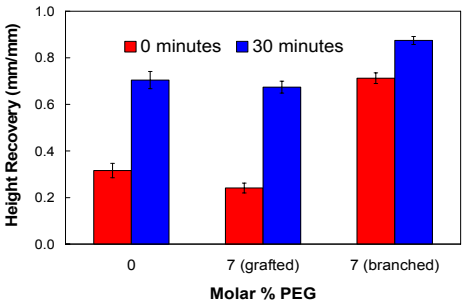

Figure 2. Recovery of sample height was normalized to the maximum deformation achieved during 5th loading cycle for the 3 polymers immediately after and 30 minutes mechanical testing.

PEG grafts and PEG branches resulted in the hydrogels maintaining their water content throughout the test. The water content of the pure PNIPAAm hydrogels significantly ($p<0.05$) decreased from 38.3% prior to the mechanical test (control sample) to 32.8% immediately after the test, but was restored after 30 minutes of recovery.

Conclusions: While PEG grafts were effective in preventing the water loss during the cyclic tests, they did not enhance the dimensional recovery of the PNIPAAm hydrogels. PEG branches form covalent linkages between PNIPAAm chains while the pure PNIPAAm and PEG grafted hydrogels only have physical interactions linking PNIPAAm chains. The networks formed by PEG branches elastically deform, allowing samples to almost recover their original shapes and sizes. Though samples in the current study were only subjected to 5 cycles, the dimensional recovery and maintenance of water content of the branched hydrogels are promising.

References: [1]JD Thomas, M Marcolongo, GW Fussell, AM Lowman, Proc SFB Ann Meet., 434, 2006.

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