Evaluation of Novel Injectable Hydrogels

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Introduction. Researchers have begun to realize the potential benefits of treating intervertebral disc degeneration by replacing the nucleus pulposus alone. One of the material classes being studied for nucleus replacement is the hydrogel, a three-dimensional, hydrated polymer network. The development of an injectable hydrogel nucleus replacement would have important clinical consequences because it could be injected non-invasively using a needle. Aqueous solutions of poly(N-isopropylacrylamide), or PNIPAAm, have a lower critical solution temperature (LCST) between room and body temperature, making it suitable for an injectable implant material. Aqueous polymer solutions could be injected as a free flowing liquid at 25ºC and solidify to a gel within the body at 37ºC [1].

At physiological temperatures, PNIPAAm homopolymer gels hold little water and show poor elastic recovery. This work focuses on tailoring the swelling and mechanical properties of PNIPAAm gels by polymerizing NIPAAm in the presence of poly(ethylene) glycol dimethacrylate (PEGDM), thereby creating PNIPAAm-PEGDM branched copolymers. This study reports the effect that PEGDM molecular weight and NIPAAm/PEGDM molar ratio have on the water content and stiffness of the hydrogels.

Materials and Methods. PEGDM (4600 and 8,000 g/mol), was synthesized from PEG according to the procedure outlined by Bryant et al [2]. PEGDM (1000 g/mol) was purchased from Polysciences. The PNIPAAm-PEGDM copolymers were synthesized by free radical polymerization in methanol at 65°C for 48 hours, initiated with 2,2'-Azobisisobutyronitrile, 98% (Sigma-Adlrich). 15 wt% polymer-water solutions were prepared from the dry polymer.

Small volumes of solution were heated to 37°C within a closed vial for 3 hours. The precipitated gels were then immersed in phosphate buffered saline (PBS) at 37°C. A set of gels were pulled at 0, 7, 14, 30, 60 and 90 days, weighed, and subsequently dried under vacuum. Time 0 refers to a set of gels that were weighed immediately after precipitation and were never immersed in PBS. A mass swelling coefficient, *q(t)* was calculated by dividing the wet gel mass by its dry mass.

Unconfined uniaxial compression tests were also performed on gel samples after 2, 7, 14, and 30 day immersion in PBS. The hydrogel samples were loaded in an Instron mechanical testing system. Samples were compressed at a strain rate of 100% min^{-1} while submerged in a 37°C PBS bath. Data was collected as stress and strain values. The instantaneous compressive modulus was calculated as the slope of the tangent to the stress-strain curve at 10, 15, and 20% strain.

Results and Discussion. Figure 1 illustrates how *q(t)* varies with PEG branch molecular weight. The NIPAAm/PEGDM molar ratio was held constant in this experiment at 700/1. The copolymers with PEG branch molecular weights above 1000 g/mol had significantly higher water contents than the PNIPAAm homopolymer. These results confirm that the addition of PEG to the PNIPAAm polymer network increases the water content of the precipitated phase, due to the hydrophilicity of PEG.

It has been determined that a polymeric hydrogel implant should have an unconfined compressive modulus of at least 0.05 MPa for restoration of denucleated intervertebral disc stiffness [3]. The mechanical results in Figure 2 suggest that copolymers with PEG branches between 2000 and 4600 g/mol may serve as a suitable nucleus pulposus replacement. Trends in the compressive moduli of the copolymers also indicate that there is an optimum PEG branch molecular weight at 4600 g/mol that results in highest stiffness. The compressive modulus of this copolymer is comparable to that of the PNIPAAm homopolymer, which was shown to have significantly lower water content. Future studies will focus on using PEG branches to enhance the elasticity of PNIPAAm.

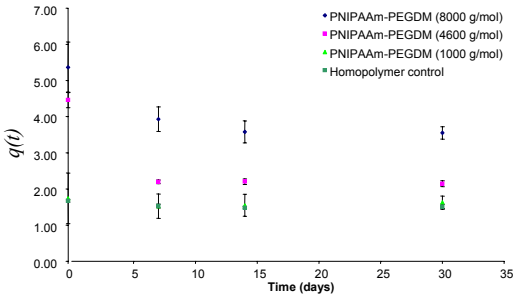

Figure 1. The mass swelling ratio q(t) of PNIPAAm/PEGDM copolymers over 30 days immersion in PBS (n=6).

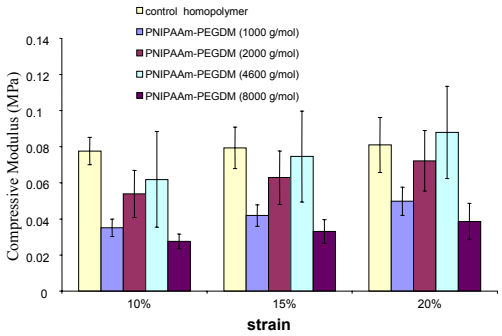

Figure 2. Compressive moduli of PNIPAAm/PEGDM branched copolymers after 48 hour immersion in PBS (n=6).

References.

[1] Costa, O. R., R. Freitas. Polymer, 2002. **43**: p. 5879 5885.

[2] Bryant, S. J., T.T. Chowdhury, D.A. Lee, D.L. Bader, K.S. Anseth. Annals of Biomedical Engineering, 2003. **32**(3): p. 407-417.

[3] Joshi, A. B. *Mechanical Behavior of the Human Lumbar Intervertebral Disc with Polymeric Hydrogel Nucleus Implant: An Experimental and Finite Element Study*. PhD Thesis, February 2004.