Hydrogels that Mimic the Viscoelastic Behavior of the Nucleus Pulposus Under Dynamic Torsional Loading

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Statement of Purpose: Hydrogels have been proposed as suitable biomaterials for replacement of the nucleus pulposus of degenerative intervertebral discs. Despite claims that hydrogels mimic the mechanical behavior shown by the natural tissue, loading modes other than static compression have not been evaluated. Previous studies have demonstrated that the nucleus pulposus exhibits a more "fluid like" nature under static loading and a more "solid like" nature under dynamic loading. Torsional shear testing has been shown to be an appropriate means to quantify the viscoelastic properties of biological tissues.[1] Our study aims to identify a physiologically stable hydrogel whose mechanical behavior in shear matches that of the non-degenerated nucleus pulposus.

Methods: Hydrogels were formed following known literature preparations and were allowed to equilibrate in Hank's solution for 48 hours prior to analysis. Water content was determined for comparison to the natural tissue via thermogravimetric analysis. The viscoelastic behavior of all prepared materials was compared with that of sheep nucleus pulposi. Sheep spines have been shown to be biomechanically analogous to human spines.[2] Dynamic frequency sweep experiments were performed in torsional shear over the range 0.1<f<10 Hz using a Bohlin rheometer in a parallel plate configuration. Plots of the storage modulus G' and the loss modulus G'' as a function of frequency served as the basis of comparison for all material. Upon identification of an appropriate hydrogel, physiological stability was assessed by submersion in Hank's solution. Resistance towards hydrolysis was evaluated by observing mass loss with time. In parallel, the viscoelastic behavior of the hydrogel was re-evaluated at regular intervals to ensure that no reduction in mechanical strength had occurred.

Results / Discussion: The reaction of poly(vinyl alcohol) with glycidyl methacrylate followed by photocrosslinking provided hydrogels whose storage moduli were within the range of G' values obtained from the sheep nucleus pulposi.[3] G' could be varied in a predictable manner by changing the weight percentage of photoinitiator (Fig. 1).

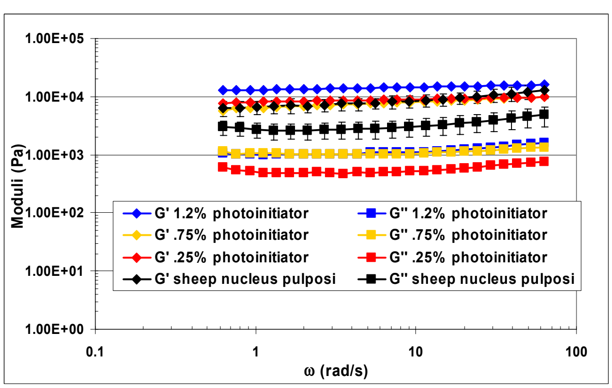

Fig. 1. G' and G'' versus frequency for hydrogels generated with different photoinitiator concentrations and for the sheep nucleus pulposi

Water content of the hydrogels was determined to be between 81 % and 86 %, comparable to known values in human nucleus pulposi and to values measured from the sheep nucleus pulposi. Physiological stability was evaluated over the course of 4 weeks. Despite a 4 % mass loss, the mechanical strength was maintained (Fig. 2).

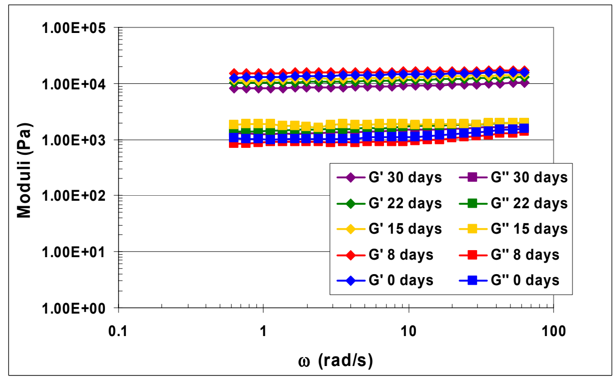

Fig. 2. Evaluation of physiological stability of photopolymerized hydrogels

Conclusions: Our research group has identified a physiologically stable hydrogel that approaches the mechanical strength of the nucleus pulposus. Further changes in the hydrogel network must be brought about such that both G' and G'' are relatively high. Presumably, variations in the conditions under which photocrosslinking is allowed to occur will affect the viscoelastic properties. Due to the lability of the ester bonds, incorporated within the hydrogel, towards hydrolysis, the material will likely undergo a slow degradation under physiological conditions. Results thus far suggest that mechanical strength is preserved despite some mass loss with time. Photocrosslinked hydrogels that biodegrade slowly may provide an appropriate scaffold for tissue engineering. Recent literature has suggested the use of mesenchymal stem cells for nucleus pulposus regeneration.[4] In addition to possessing similar mechanical strength to the natural tissue, suitable scaffolds must conform to the irregular shape of the disc cavity and allow for a homogeneous distribution of cells. The hydrogels discussed above, seeded with cells and various growth factors, may be crosslinked *in vivo* following injection into the enucleated space. Stem cells would thereby be entrapped within the matrix and all problems associated with form would be eliminated. Photocrosslinked hydrogels are ideal candidates for nucleus pulposus replacement. Similarity in mechanical strength has been demonstrated, and the method by which the hydrogel is formed suggests the potential for future work in the area of tissue engineering.

References:

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