The Effect of an Injected Chemical Crosslinker on the Stability of the Intervertebral Disc

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Introduction

Previous studies have demonstrated that collagen crosslink augmentation effectively reduced instability in intervertebral joints. Soaking discs in a genipin based crosslinking agent resulted in a 41% smaller neutral zone in bovine specimens and a 77% smaller instability score in human specimens (Hedman, 2006).

Modification of a complete motion segment using an injectable agent has yet to be demonstrated. Injecting the crosslinking reagent closely replicates how the reagent would be delivered to a patient in the clinic. Soaking relies primarily on passive diffusion of genipin into the disc, while injection provides a hydrostatic pressure that drives the treatment throughout the disc. We hypothesize that an optimized crosslinking reagent injected into the annulus fibrosis of the intervertebral disc can directly alter the mechanical stiffness and associated flexion-extension stability in a manner similar to soaking. The purpose of this study was to quantify the change in stability of the disc during flexion-extension loading after injection of the disc’s annulus with a genipin based crosslinking reagent.

Method

Twelve oxtail bone disc bone segments were prepared by stripping the paraspinal musculature and potting both ends in rigid urethane. After preparation, specimens were wrapped with moist gauze and kept overnight at 4°C while under a 45 N axial load. Our laboratory has observed that this protocol allows fluid in the disc to equilibrate after an injection.

Before baseline testing, specimens were allowed to sit at room temperature under load for at least 1 hr before placing them in the test machine. For the baseline test, a tangential load was applied at a constant displacement of 0.2 mm/sec until the target load of ±6 N was achieved, at which time the load was reversed creating a displacement controlled, triangular shaped load profile with ±6 N force limits. Measurements of the applied force and crosshead location were sampled during the test at 30 Hz. Specimens were tested with the load applied along the anatomic midline of the disc with sagittal plane (anterior–posterior) followed by frontal plane (lateral–lateral) directed loading. Gravitational tangential loading was measured in the neutral position and subtracted from applied force measurements.

Digital images of each specimen were used to determine the distance from the load to the disc center. Force and displacement data were then transformed into moment and angle data for analysis. The specimen stability was described by calculating the linear region slopes and the neutral zone slope and length as described by Yerramalli (2006). Differences in the treated and untreated distributions were tested using the Wilcoxon Rank Sum and Mann Whitney U nonparametric tests.

Result

Sham treated specimens demonstrated an overall mean decrease in neutral zone modulus of 18% and an overall mean increase in neutral zone length of 10% relative to their pretreatment values. Crosslink treated specimens demonstrated an overall mean increase in neutral zone modulus of 47% and an overall mean decrease in neutral zone length of 4% relative to their pretreatment values. The paired increase in the neutral zone modulus in the crosslink treated group was significantly different from the decrease in neutral zone modulus seen in the sham group, p=0.015, but the difference in neutral zone length due to the injection treatment was not significantly different for the treatment types, p=0.069.

Discussion

Our study data demonstrated that treatment of the disc by injection into the annulus with a genipin based crosslinking agent altered the neutral zone mechanics. Previous work has shown that chemical crosslinking affects the basic mechanical properties of tissue (Parry 1978) and reduces joint instability (Hedman 2006, Yerramalli 2006, Barbir 2008) and we expected that crosslinking of the disc annulus with an injection would increase bulk stiffness and therefore increase the specimen stability. The neutral zone modulus in the genipin crosslinked discs was increased 65% relative to the sham treated joints. It was interesting to note that the observed 47% decrease in neutral zone length after injection treatment corresponded closely with the previously reported 41% decrease in neutral zone after soaking. The injection of a crosslinking agent appears to be a viable means to influence systematic changes in the mechanics of the IVD, including joint stabilization.

References

Yerramalli; Biomech Model Mechanobiol 2006
Parry; Pr Royal Society of London 1978, pp 305-321