EXOGENOUS CROSSLINKING DECREASES NEUTRAL ZONE IN INTERVERTEBRAL DISCS

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INTRODUCTION:

The microstructure of the annulus fibrosus extracellular matrix can affect the stability of the intervertebral joint. Collagen crosslinks have recently been described as “sacrificial bonds” that function to protect the tissue and dissipate energy (1). Severely degenerated intervertebral discs have been shown to have lower quantities of both non-reducible (2) and age-related endogenous collagen crosslinks (3). Parallel testing in our laboratory has demonstrated the ability for non-toxic exogenous crosslinking of annulus fibrosus to improve the fatigue-resistance of the tissue. In this study, the effect of non-toxic exogenous crosslinking on intervertebral joint stability was investigated. Neutral zone (NZ) has been shown to be a sensitive indicator of spinal instability (4,5). The specific objective of this study was to determine if non-toxic crosslink augmentation (CA) could increase intervertebral joint stability evidenced by neutral zone reduction.

METHODS:

Three separate experimental protocols were conducted. The first study utilized ten calf lumbar intervertebral joints consisting of hemi-vertebrae, potted in polyurethane, and the intervening disc. The pedicles were cut and the posterior processes removed. The discs were randomly divided into a 0.330% genipin crosslinked group and Phosphate Buffered Saline (PBS) soaked controls. The specimens were soaked for 2 days at room temperature in their respective solutions. Five pure flexion-extension ramp cycles (± 4 Nm maximum moments at 0.1 Deg/s) were applied using an MTS 858 materials testing system with custom 4-degree of freedom fixtures while moment and rotation angle were recorded. The second study repeated the test protocol using nine moderately and severely degenerated human lumbar intervertebral joints. Similar to the calf discs, the posterior processes were removed.

The objective of the third experiment was to compare the effect of crosslinking treatment on discs with known degrees of pre-existing mechanical instability. This experiment utilized twelve moderately and severely degenerated human intervertebral discs. Flexion-extension pure moments were first applied to each intervertebral joint after two days of soaking in normal room temperature PBS. This testing was then immediately followed with two more days of room temperature soaking, this time in the 0.330% genipin treatment. The specimens were then retested in flexion-extension. It was recognized that the additional two days of room temperature exposure could produce a measurable degradation in mechanical properties that would detract from any instability reduction achieved by the crosslinking treatment.

The fifth cycle of each data set was used to assess joint instability. Instability was assessed by two calculations: conventional neutral zone quantified the size of the low stress region (± 0.5 Nm) of the sagittal plane bending curve, and an instability score that was defined as the neutral zone to total range of motion ratio divided by the slope of the curve in the low-stress region.

RESULTS:

The calf controls had a 27% larger NZ, by the conventional calculation method (Fig. 1), as compared to the crosslinked discs (P<0.010). The instability score (Fig. 2) was 37% worse for the calf controls than for the crosslinked discs. The mean control NZ and instability scores of the human discs were 3.4 and 7.8 times as large, respectively, as those for the calf discs. The human discs' standard deviations were 37 and 68 times larger than the calf’s. The human control NZs were 67% larger than the treated discs on average, with an instability score that was 392% larger than the treated discs (P=0.030). Yet there was less than a 3% difference in total range of sagittal motion. The NZs of the human controls prior to treatment were 8% larger than the same discs after crosslinking, while their corresponding instability scores were 77% worse before crosslinking. The neutral zone reduction was observed to be greater in discs that had large (NZ>1.5) initial neutral zones. The neutral zones of the large NZ controls were 30% larger than after treatment, with 120% larger instability scores compared to after crosslinking treatment. The opposite results were observed with the relatively small NZ specimens—the discs appeared more unstable after treatment than before. The small NZ controls had neutral zones that were 43% smaller than after treatment with 45% smaller instability scores.

DISCUSSION:

These results demonstrate that non-toxic crosslink augmentation can effectively reduce instability of intervertebral discs. The stabilizing effect was observed to be greater in the more mechanically unstable discs. Crosslinking did not appear to affect the total range of sagittal motion. Repeated 2-day room temperature soaking of cadaveric discs appeared to further degrade the discs thus somewhat masking the effect of crosslinking. Oxland and Panjabi (4) demonstrated that neutral zone was sensitive to the progression of instability. Consequently, by reducing the neutral zone, CA may help combat the progression of instability in degenerative disc disease.

REFERENCES: