Introduction: Degenerative disc disease (DDD) is a debilitating disease characterized by the degeneration of the intervertebral disc (IVD) that results in reduced mobility and is often associated with increased pain. The IVD is an avascular tissue whose ability to resist deformation is dependent on the interactions of the matrix constituents, consisting a network of type 2 collagen and proteoglycans that work together to imbibe cationic fluids. The proper mechanical and structural function of the IVD is highly dependent on its tissue material properties. Post-translational modification of long-lived proteins through the process of nonenzymatic glycation (NEG) occurs under the presence of oxidizing sugars in the extra-cellular space and results in the increased crosslinking due to the formation of Advanced Glycation End-products (AGEs). The accumulation of AGEs has been shown to adversely affect the tissue material properties of orthopedic tissues including bone and cartilage. Due to its lack of vascularity with little turnover of proteins, the IVD is susceptible to the accumulation of AGEs, and degenerated IVDs have been shown to have increased elevated levels of AGEs.

Hypothesis: The accumulation of advanced glycation end-products may alter the ability of the IVD tissues to retain water and affect the tissue material behavior.

Methods: 40 lumbar/thoracic intervertebral discs were removed from 4 sheep lumbar-thoracic spines for a total of 80 tissue samples. Using a previously established in vitro ribosylation procedure, the tissues were matched by location to undergo a 0, 2, 4, 6, 8-day incubation period in a ribose-rich solution. After the respective incubation times, they were mechanically assessed and analyzed for water composition, and the extent of nonenzymatic glycation. One-way ANOVA was used to determine the effects of NEG incubation period on mechanical properties and water content. Multiple regression analyses were used to determine relationships between AGEs, disc tissue material properties, and water content.

Results & discussion: Water content in both tissue types decreased significantly with incubation time in both the AF (p< 0.001) and NP (p< 0.05) tissues. Regression analyses showed a significant inverse relationship between decreasing water content and increasing AGEs. Furthermore, the decrease in water content in the NP tissue is more susceptible to losses in water content due to increases in AGEs than in AF tissues. The increase of AGEs in the tissue also resulted in a stiffening of the tissue as indicated by the indentation modulus. The accumulation of AGEs in collagenous tissues has been previously shown to deteriorate its energy dissipation capability and disrupt the tissue’s structure-function relationship. We demonstrate for the first time that the loss of tissue water content can be induced in a dose-dependent manner through nonenzymatic glycation. Furthermore, the loss of water content directly modulates the tissue material properties of the IVD tissues. The resulting biochemical behavior reduced the tissue’s ability to retain its viscous component. It is possible that the accumulation of AGEs could alter the charge-density characteristics of the tissue that further contributes to the loss tissue water content. The alterations in both the elastic and viscoelastic properties at the tissue level may be directly related to the decreasing disc height observed in discs with elevated AGEs.