Quantitative MRI of Ovine Intervertebral Disc Health Across the Lifespan

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Disclosures: AME(5-Medtronic), EWB (5-Medtronic; 8-JBMR, BMC MSKD), CPJ (5-Medtronic), All others (N)

INTRODUCTION: Chronic low back pain is a major societal health problem with limited effective treatment options for discogenic pain. As intervertebral disc regenerative approaches are showing promise, there is a need to establish noninvasive approaches to assess treatment progress. Quantitative MRI is a leading approach to noninvasively assess disc health in humans; however, there has been limited investigation of quantitative MRI techniques in large animal models of disc degeneration. Therefore, the purpose of this study was to: 1) characterize 3T MRI measures of disc health across the *ovine* lifespan and 2) establish correlative biochemical, biomechanical, and histological measures.

METHODS: Eleven *ovine* thoracolumbar vertebral columns, with mean age 71.9 months (range: 13 to 144 months), were excised and frozen until testing. Specimens were thawed and imaged using a 3T MRI system. Conventional T2-weighted images were acquired, along with quantitative maps for each lumbar disc: (i) T2 and T2* relaxation time mapping using product multi-slice, multi-echo (MSME) spin echo and gradient echo (GRE) sequences; (ii) T2, T1ρ, adiabatic T1ρ, and adiabatic T2ρ relaxation time mapping using a custom magnetization-prepared (MP) turbo spin echo (TSE) sequence; and (iii) apparent diffusion coefficient (ADC) mapping using a product diffusion-weighted readout-segmented echo planar imaging (RESOLVE) sequence. Each disc was segmented to isolate the nucleus pulposus (NP) from the annulus fibrosus (AF) and median relaxation times were computed. After imaging, biomechanical, histologic, and biochemical analyses were conducted. Stress-relaxation tests were performed on body-disc-body constructs (posterior elements removed) of the L4-L5 and lumbosacral discs – peak and equilibrium force were measured. The frozen vertebral columns were bisected (sagittal midline) using a bandsaw, half was used for biochemical assays ([GAG] and [water]) and the other for histology (H&E and alcian blue/picrosirius red (AB/PSR), scored using Lee et al. 2021). Analyses were conducted to 1) stratify disc health by disc level and age, 2) determine the relationship between relaxation times of different sequences in the NP and AF, and 3) correlate MRI values to biomechanical, biochemical, and histological findings.

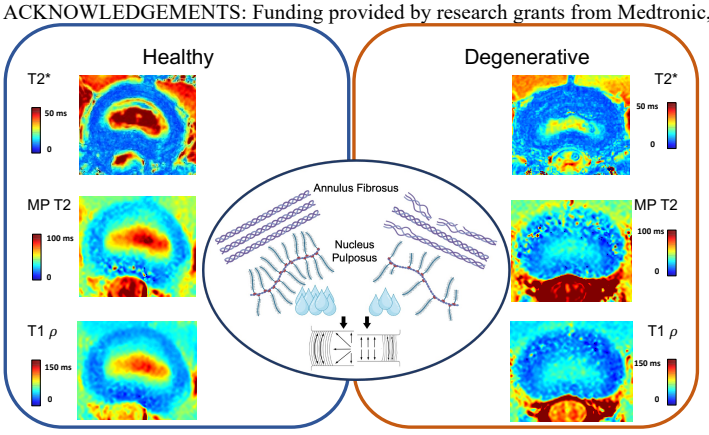
RESULTS SECTION: Quantitative MRI measures within the NP decreased as a function of age and Pfirrmann grade, whereas the MRI measures within the AF (except for ADC) increased. Discs within the lumbar region appear to be vastly different than the lumbosacral disc, based on morphology and relaxation times. T2 values in the AF were negatively (strongly) correlated with both peak and equilibrium force ($r = -0.71$; $p<0.001$ | $r = -0.74$; $p<0.001$). T2* values in the NP were positively (moderately) correlated with both peak and equilibrium force ($r = 0.62$; $p<0.01$ | $r = 0.63$; $p<0.01$). NP T2 and T2* values were (weakly) positively correlated with [water] ($r > 0.25$; $p < 0.04$) and [GAG] ($r > 0.26$; $p < 0.03$). Significant correlations were observed between MRI measures and the following key histological scores: NP Cell and Necrosis, AF Morphology, and Tears/Clefts Formation – these relationships did not consistently persist when assessing the total histological score.

DISCUSSION: Clear relationships were observed between peak and equilibrium forces with measurements of T2* and aT1ρ in the NP and T2 and T1ρ in the AF. The mechanical testing setup was designed to evaluate the integrity of the entire disc by utilizing a body-disc-body configuration with the removal of posterior elements. Through this configuration, the mechanical properties of both the NP and AF were examined, along with their interactions. Our findings indicate that T2* and aT1ρ measurements in the NP offer valuable insights into the GAG and water content, which contribute to the NP's incompressibility. During compression, the NP protrudes against the AF, subjecting the AF's fibers to tension. T2 and T1ρ measurements potentially provide information about the structural integrity of the collagen-rich AF. *Note: the study did not quantify the extent of structural degradation in the collagen fibers.

SIGNIFICANCE/CLINICAL RELEVANCE: The ovine discs included in this study showed similar characteristics across level (sans lumbosacral) and age (up to 96 months all discs ≤ 2 Pfirrmann grade) – highlighting the stability of the ovine lumbar spine as an animal model for disc health.

REFERENCES: Lee NN et al. 2022. JOR Spine. 2021

ACKNOWLEDGEMENTS: Funding provided by research grants from Medtronic, Inc. REA was supported by NIH NCATS TL1R002493 / UL1TR002494.



Theoretical Framework. The disc is comprised of two structures: NP (gelatinous material with high concentrations of proteoglycan and water) and the surrounding AF (highly organized lamellae of primarily Type I collagen). The system works synergistically to pressurize the NP and place the AF in tension. During degeneration, the proteoglycans fragment and dehydration ensues. In conjunction, the collagen fibers of the AF denature and fissures and malalignment of the AF lamellae result – disrupting the mechanical environment. T2* and aT1ρ were sensitive to changes in the NP (decrease in relaxation times with advanced degeneration) and T2 and T1ρ were sensitive to the changes in the AF (increase in relaxation times with advanced degeneration). **Top Right:** Correlation matrix between NP and AF relaxation times between each sequence – suggesting different MRI measures may provide unique disc health information. **Bottom Left:** NP T2* MRI values were consistent across lumbar levels but diminished at the lumbosacral joint. **Bottom Right:** NP T2* values decreased with age, except for the 144-month sheep.