Herniation and Hydration Alters Quantitative MRI Parameters of the Intervertebral Disc

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INTRODUCTION: Quantitative magnetic resonance (qMR) imaging has been shown to provide a qualitative assessment of soft tissue composition, including water and glycosaminoglycan (GAG) contents. Previous studies have demonstrated a strong correlation between qMR parameters, including T2- and T1ρ-relaxation times, and degenerative changes in intervertebral disc biochemical composition [1-3]. Disc degeneration is noted by an increase in collage type I composition, an increase in collagen crosslinking, and a decrease in water content and GAG composition, making it difficult to denote whether changes in qMR parameters are due to structural or compositional changes. However, diurnal loading and disc herniation cause a change in water and GAG composition without associated compositional and structural changes noted with degeneration. Approximately 10% of the disc's water composition flows out of the disc during diurnal loading [5], and the altered hydration condition results in a decrease in disc joint stiffness [4, 5]. A herniated disc, and its treatment (discectomy), is noted by a sudden loss of nucleus pulposus (NP) material through the annulus fibrosus (AF), causing decreases in GAG composition, a decrease in tissue swelling capacity, and an increase in stress distribution from the NP to the AF [6].

It is not clear whether qMR-imaging techniques can be used to detect changes in water or GAG composition associated with changes in hydration and herniation. Moreover, there is conflicting data in the literature whether T2 or T1ρ is more sensitive to water or GAG composition, partly due to GAG's role in attracting water molecules. A systematic control of disc composition is necessary to accurately evaluate the relationship between tissue composition and qMR parameters. Therefore, the objective of this study was to evaluate the effect of hydration and NP GAG content on qMR parameters of healthy intervertebral discs.

METHODS: Bone-disc-bone motion segments were prepared from the caudal spine of skeletally mature bovines. Motion segments were divided into two studies to investigate: 1) the effect of hydration through osmotic loading (n = 7), and 2) the effect of GAG loss from discectomy (n = 6) on qMR properties. To evaluate the effect of hydration, samples were hydrated overnight in either 0.15 M phosphate buffered saline (PBS, ~300 mOsm/kg) or a hyperosmotic solution consisting of polyethelene glycol (PEG, ~3000 mOsm/kg). To evaluate the effect of NP GAG composition, GAGs were either physically removed, similar to discectomy [6], or degraded with chondroitinase ABC (200μL of 0.3 U/mL chABC) to cleave GAG molecules [7]. A vertical incision was made in the AF and surgical rongeurs were used to extract NP tissue (66.1 ± 10.8 mg or 5-10% of total NP volume) [2]. Healthy intact discs served as the control.

A custom-built birdcage coil (diameter = 4.5 mm) was used to acquire images at the mid-disc height (7T Bruker animal scanner). A series of images were acquired with a T2-weighted sequence to create T2- and T1ρ-relaxation maps (T2-mapping: multi-slice multi-echo sequence, TE times: 8.3, 24.9, 41.4, 58.0, 74.6, 91.1, 107.7, and 124.6 msec, TR of 5000 msec; T1ρ-mapping: B1 field = 40μT; turbo spin lock (TSL) durations = 25, 50, 75, 100, 125, and 175 msec; resolution = 128 x 128, FOV = 4.5 cm x 4.5 cm). To calculate relaxation times, the equations shown below were used to curve-fit pixel intensity values (S) with respect to TE or TSL for T2- and T1ρ-relaxation times, respectively (Fig. 1) [4]. The analysis was performed on a pixel-by-pixel basis, and the average relaxation time was calculated for NP and AF regions by manually selecting the boundary between the NP and AF (Matlab, Mathworks, Inc.). Curve-fits that were lower than $R^2 = 0.8$ were removed from the dataset. A paired Student's t-test was performed on the average T2- and T1ρ-relaxation times from the NP and AF. Significance was assumed at $p \leq 0.05$ and a trend was defined as $0.05 < p \leq 0.1$. Data was normalized to the intact control under 0.15 M PBS.

$$S(TE) = S_o\, e^{(-TE/T2)} \qquad \& \qquad S(TSL) = S_o\, e^{(-TSL/T1\rho)}$$

RESULTS: Pixel-by-pixel curve fitting resulted in good fits throughout the disc ($R^2 > 0.8$; Fig. 1A & B). However, some regions in the outer AF were too dark for a reliable fit (Fig. 1 – missing pixels). The average NP qMR parameters for intact control discs were 1.8X greater than the average AF T2- and T1ρ–relaxation times (***T2*** **-** NP: 54.1 ± 12.8, AF: 29.8 ± 4.2; ***T1ρ*** **-** NP: 107.8 ± 28.3, AF: 60.0 ± 11.8, pooled average n = 13), which were comparable to measured differences in GAG composition (NP: 5.46 ± 0.16%/ww, AF: 4.04 ± 0.22%/ww). In general, the range of T1ρ values were greater than T2 values for both the NP and AF regions. There was a significant increase in NP T2 times with hyper-osmotic loading (Fig. 1 – solid, dark red bar) and a trend for an increase in NP T1ρ relaxation times with hyper-osmotic loading (i.e., 'reduced hydration'; Fig. 1 – solid, light red bar). There was a significant decrease in NP T1ρ times with discectomy (Fig. 1 – striped, dark blue bar) and a trend for a decrease in NP T2 relaxation times with discectomy (Fig. 1 – striped, light blue bar). No changes in qMR parameters were observed in the NP or AF with enzymatic digestion of GAGs with chABC ($p > 0.3$).

DISCUSSION: Quantitative MR may provide a valuable noninvasive assessment tool for patient specific treatment strategies and diagnosis. In this study, physical removal of NP tissue through the AF was used to mimic compositional and structural changes following a disc herniation injury. The damage in the AF did result in a region that could not be analyzed. However, physical removal of GAGs was more effective than enzymatic digestion, which showed no differences in qMR parameters and was likely due to cleaved GAG molecules remaining in the disc space after the digestion [8]. There were no differences in AF T2- or T1ρ-relaxation times with hydration or NP GAG removal, suggesting that our analysis was specific to changes in NP composition, which may be important for detecting early degenerative changes. Ongoing work is focused on increasing our sample size and future work will determine whether changes in qMR parameters are correlated with the amount of NP tissue removed (~10% in this study).

SIGNIFICANCE: In conclusion, these findings support the notion that T2 relaxation times are sensitive to changes in NP water composition, while NP T1ρ relaxation times are more sensitive to sudden changes in GAG composition, as experienced following disc herniation injury.

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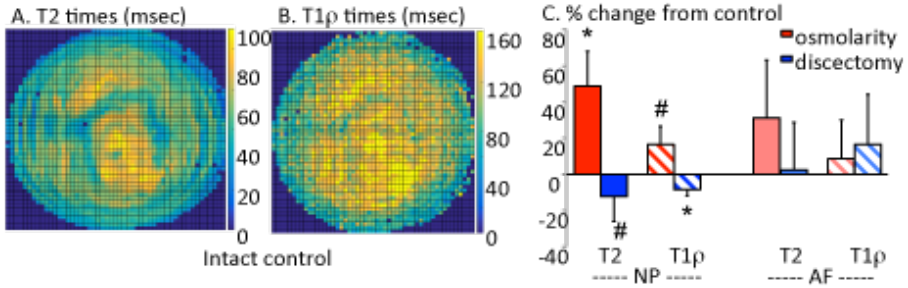

Figure. (A & B) T2 and T1ρ relaxation maps for a representative control disc. (C) Percent change in qMR parameters with changes in hydration via osmotic loading and changes in NP GAG composition via discectomy. * represents $p \leq 0.05$ and # represents a trend.