INTRODUCTION: Degenerative disc disease affects nearly twelve million people in the United States. Conventional MR and radiographic techniques are able to detect late-stage degenerative changes (i.e., changes in disc morphology, height, hydration, bulge, and herniation), but these methods are not sensitive to early degenerative changes. In addition, the ability to distinguish between normal disc aging and degeneration has not been established. A non-invasive technique to determine changes in extracellular matrix content could advance the diagnosis of early disc degeneration. \( T_1 \) relaxation, defined as relaxation in the rotating frame after a spin-lock pulse, allows the study of slow motion physico-chemical interactions such as those between water and extracellular matrix molecules. In studies of articular cartilage, \( T_1 \) was found to be strongly correlated with proteoglycan content [1]. A relationship between \( T_1 \) and intervertebral disc degeneration has yet to be established. The objectives of this study were to measure the correlation between \( T_1 \) and disc degeneration \( \text{in vivo} \) and to investigate the relationship between \( T_1 \) and biochemical content \( \text{in vitro} \).

METHODS: Imaging was performed on a Siemens Sonata 1.5T whole body scanner under an IRB approved protocol. \( T_1 \)-weighted MR images were acquired both \( \text{in vivo} \) (\( n = 10 \) volunteers, age 40 to 60 years with no history of back pain or surgery) and \( \text{in vitro} \) (\( n = 7 \) human lumbar spines, age 15 – 81 years). A series of sagittal \( T_1 \)-weighted MR images was acquired using a self-compensating turbo spin-echo sequence [2] with parameters: FOV = 28 x 28cm, slice thickness = 4mm, acquisition matrix 512 x 512; TE/TR = 3000ms/12ms. \( \text{In vivo} \) scans were acquired using a 400 Hz pulse and spin-lock durations from (15 to 70ms). Total scan time was approximately 35 min. The cadaveric tissue was imaged with five evenly distributed spin-lock pulse durations (from 15 to 75ms) with pulse amplitude of 500 Hz. \( T_1 \) was calculated on a pixel-by-pixel basis by linear regression of intensity data to an exponential decay function of spin lock time (TSL): S(TSL) = \( S_0 \cdot e^{-\rho \cdot \frac{TSL}{T1}} \). Values were used to create spatial maps of \( T_1 \), and mean \( T_1 \) was computed from a circular region of interest taken within the center of the nucleus pulposus. Region of interest was selected independently by two investigators and average \( T_1 \) reported.

Diagnostic clinical \( T_1 \)-weighted images were acquired (\( \text{in vitro} \) and \( \text{in vivo} \)) and used for assessment of degenerative grade according to an established 1-5 classification scale [3]. Nucleus pulposus tissue was harvested from the cadaveric samples and used for analysis of water content and s-GAG content using the DMMB assay. Correlations between biochemical content, degenerative grade, and \( T_1 \) relaxation were computed with significance set at \( p<0.05 \).

RESULTS: Average \( T_1 \) was greater in younger, non-degenerate discs (Fig 1). There was a negative correlation between \( T_1 \) and degenerative grade (\( \text{in vivo} r = -0.76, \text{in vivo} r = -0.86 \)) (Fig 2). \( T_1 \) was not significantly correlated with age \( \text{in vivo} (r = -0.19) \) (Fig 2). In \( \text{in vitro} \), \( T_1 \) was strongly correlated with s-GAG/wet weight (\( r = 0.70 \)) and moderately correlated with water content (\( r = 0.58 \)) (Fig 3).

DISCUSSION: In the studied age group (40 to 60 years), we found that \( \text{in vivo} \) \( T_1 \) was significantly correlated with degenerative grade but not significantly correlated with age. This suggests that quantitative \( T_1 \)-weighted MRI may potentially distinguish between the aging and degenerative processes of the intervertebral disc. To date, aging and degeneration have proved difficult to separate, making difficult the diagnosis of degeneration, the determination of mechanisms for progression of degeneration, and the development of appropriate treatments. The potential to discriminate between degeneration and normal aging may prove to be a critical advantage of this technique.

In the clinical setting, quantitative measurements of \( T_1 \) may be advantageous over current grading schemes that are susceptible to observer bias and are limited in their ability to detect subtle changes because they are based on a 5-level ordinal scale. This lack of specificity is illustrated by the correlation between \( T_1 \) and degenerative grade. As shown in Fig 2, a single degenerative corresponded to a large range of \( T_1 \) values in this study. In contrast to current grading schemes, \( T_1 \) provides a quantitative, spatial measurement on a continuous scale. Moreover, \( T_1 \) imaging is easily performed on a clinical scanner with no hardware modifications.

We find that \( T_1 \) is correlated with proteoglycan and water content, suggesting that the parameter is sensitive to changes in the biochemical content of the extracellular matrix. Future work is planned to quantify the influence of specific matrix constituents on \( T_1 \). This imaging modality may be used to non-invasively probe disc biochemistry.

Quantitative MR imaging has been previously applied to the intervertebral disc [4,5], however a separation between aging and degeneration has not been established. Results from this preliminary study suggest the potential utility of \( T_1 \) as an \( \text{in vivo} \) diagnosis of intervertebral disc degeneration that is sensitive to the changes in extracellular matrix content that occur in early degeneration. The success and indication of new treatment strategies for disc degeneration, such as biologic treatments and nucleus pulposus replacements, will depend on accurate diagnosis of early degeneration in the disc.

REFERENCES:

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