Shear Modulus Of The Human Nucleus Pulposus Measured Using Mr Elastography Correlates With Directly Measured Mechanical Properties

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Disclosures:

Introduction: Early diagnosis of disc degeneration is critical for the success of treatment strategies. Several MR parameters, including T2 and T1-rho maps, have been proposed as markers to quantitatively evaluate the progression of disc degeneration [1, 2]. Although MR parameters are correlated with degeneration grade and the decrease of glycosaminoglycan content, they represent the dynamics of water and/or proteoglycan molecules and may not be directly related to the function of the intervertebral disc. Since the function of the disc is to transmit forces through the spine, mechanical properties may be more sensitive markers for degeneration. Therefore, non-invasive measurements of changes mechanical properties of soft tissues are needed. Recently, our group demonstrated the feasibility of using the shear modulus of the nucleus pulposus (NP) as a marker for disc degeneration [3]. The shear modulus was selected because it is sensitive to degeneration and it can be non-invasively measured using Magnetic Resonance Elastography (MRE). Our MRE experiments on cadaveric human disc segments showed that the NP shear modulus decreased with degeneration and had good specificity and sensitivity for distinguishing between normal, mild, and severe degeneration [3]. Importantly, the shear modulus for degenerated discs was similar for MRE (47 kPa) and for torsion tests (60 kPa) [3]. However, the MRE measures had a decrease in shear modulus with degeneration, which was opposite to the increase of the NP shear modulus measured using torsion [4]. A possible explanation for these differences was that the intradiscal pressure may have a contribution to the MRE shear modulus (and to the in situ disc mechanics) that are not present in unconfined excised samples. Thus, while previous comparisons were promising, to date, quantitative verification of MRE shear modulus with direct mechanical property measurements have not been confirmed. The objectives of the current study were to validate MRE measurements by comparing the shear modulus to that of excised NP samples using confined compression, and to quantify the contribution of the intradiscal pressure and glycosaminoglycan (GAG) content to the MRE shear modulus.

Methods: The NP shear modulus was measured non-invasively in 23 intact human bone-disc-bone segments from levels T12-L5 having degeneration grades from 1 to 4. An average shear modulus was calculated in a volume of 8 mm x 8 mm x 4 mm in the center of the NP. After MRE measurements, the discs were dissected and frozen at -20 °C until the day of mechanical testing. Confined compression was chosen to measure mechanical properties of excised NP samples since it preserves the intradiscal pressure. Special care was taken to maintain the hydration level of the dissected discs. Therefore, it can be assumed that tissue volume of the samples in the confined compression chamber (dia. 4 mm x 1.5 mm thickness) is the same as in-situ. The confined compression protocol consisted of an isometric swelling period until equilibrium, after which the swelling pressure was calculated. Incremental compression-relaxation ramps of 5, 10, and 15% were applied in a period of 300 sec (strain rate of 0.016%/s). Compression ramps were followed by relaxation periods of 4000, 6000 and 8000 sec, respectively for each strain increment. The shear modulus was calculated by curve fitting a neo-Hookean model to the equilibrium stress-strain response. The GAG content was measured using a DMMB assay in the tested samples and adjacent tissue. Correlations between MRE shear modulus and confined compression shear modulus, GAG content, and isometric swelling pressure were evaluated using a Spearman’s test.

Results: There was a correlation between the shear modulus measured non-invasively using MRE and directly confined compression experiments (r = 0.57, p < 0.05) (Figure 1). There was also a correlation between MRE shear modulus and the isometric swelling pressure (r = 0.51, p < 0.05) (Figure 2). This suggests that the intradiscal pressure may contribute to the MRE shear modulus. However, no correlation was observed between the MRE shear modulus and the GAG content of either the tested sample or adjacent tissue.

Discussion: This study validated the MRE measurements by comparing the NP shear modulus to those directly measured in confined compression experiments. An advantage of the protocol used was that the containing chamber maintained the intradiscal pressure during isometric swelling and compression testing, which is important because NP pressurization is an important component of its load support mechanism [5]. A moderate, but significant, correlation was obtained between MRE and confined compression shear modulus (Figure 1). The moderate value of the Spearman correlation coefficient may be caused by differences in the volume of tissue used to calculate the MRE shear modulus (250 mm^3) and the size of the samples used for confined compression (20 mm^3). The smaller volume of the confined compression samples may result in more localized values compared to MRE.

The correlation between isometric swelling pressure and the MRE shear modulus suggests a moderate contribution of the
intradiscal pressure to the MRE shear modulus (Figure 2). Due to the non-linearity of the NP, the intradiscal pressure causes a volumetric deformation resulting in an overall increase of NP mechanical properties, including the shear modulus. This effect has been recently reported in experiments in articular cartilage where the shear modulus increased for higher osmotic pressures [6]. The lack of correlation between the MRE shear modulus and GAG content suggests the change of shear modulus is related to changes in the solid matrix rather than a direct contribution of the GAGs.

The shear modulus measured using MRE is a potential biomarker for disc degeneration to directly evaluate the mechanical integrity of the disc tissues. Current MR parameters used to quantify disc degeneration, such as T2 and T1-rho, are based on changes in the dynamics at the molecular scale. Since MRE uses wave propagation to measure the shear modulus, this technique is able to evaluate the mechanical integrity of disc tissues at a larger (macro) scale. Therefore, MRE shear modulus may be more sensitive to the overall tissue function and the degeneration process. Additionally, since the shear modulus is a parameter that directly affects the mechanical behavior of disc tissues, it is possible to use numerical methods, such as finite elements, to relate variations in MRE shear modulus to changes in the overall function of the disc.

**Significance:** Early diagnosis of disc degeneration is critical for the success of any biological treatment. MRE shear modulus is a potential biomarker for evaluating changes in the mechanical integrity of disc tissues. Therefore, this parameter may facilitate the diagnosis of disc degeneration and evaluation of the effectiveness of biological treatments.

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Figure 1. MRE shear modulus measured in intact human disc segments is correlated to the shear modulus measured using confined compression of excised samples of nucleus pulposus ($r = 0.57$, $p < 0.05$).

Figure 2. MRE shear modulus is correlated to the isometric swelling pressure suggesting a moderate contribution of intradiscal pressure to shear modulus ($r = 0.51$, $p < 0.05$).