

The Shear Modulus of the Nucleus Pulposus Measured Using MR Elastography: A Potential Biomarker for Intervertebral Disc Degeneration

Daniel H. Cortes¹, Jeremy F. Magland², Alexander C. Wright², and Dawn M. Elliott¹

¹Biomedical Engineering, University of Delaware, Newark, DE, United States, ²Radiology, University of Pennsylvania, Philadelphia, PA, United States

Target audience: This abstract presents preliminary results on the application of MR Elastography (MRE) to evaluate the mechanical integrity of the intervertebral disc. The results from this study will benefit researchers and clinicians working on new methods for the early diagnosis of intervertebral disc degeneration.

Introduction: Intervertebral disc degeneration is characterized by a progressive cascade of changes in organization and mechanical properties of the annulus fibrosus (AF), nucleus pulposus (NP), and end plates. In early degeneration, proteoglycan fragmentation in the NP leads to decreases in water content, osmotic pressure and stiffness. Advanced stages of degeneration are characterized by a transition of the nucleus from a gelatinous material to a fibrous one, as well as height loss and the presence of fissures and tears in the AF. The structural changes characteristic of advanced degeneration are considered permanent due to the slow matrix turnover of disc cells. Therefore, early diagnosis of disc degeneration is critical for the success of any molecular or biological treatment strategy. It is known that the shear modulus of the NP changes significantly even for mild degeneration [1], and therefore it has potential for the diagnosis of early changes in the degeneration cascade. However, the shear modulus of the NP has not been measured non-invasively.

Purpose: The objectives of the this study are: 1) to develop MRE methods to measure the shear modulus of the NP of intervertebral disc segments, 2) to quantify the effect of disc degeneration on the shear modulus measured using MRE, and 3) to compare the shear modulus to other MR-based biomarkers of disc degeneration.

Methods: *Specimens:* 16 cadaveric lumbar spines were obtained through an approved tissue source (NDRI, Philadelphia, PA). Spines were frozen and later dissected into disc segments (vertebra-disc-vertebra) from which 30 were chosen from levels T12 to L5 that covered the largest possible range of Pfirrmann scores. On the day of MRE testing, discs were thawed and sealed in plastic to prevent dehydration. *MRE setup:* An electromechanical actuator was constructed to apply vibrations (at 1250 Hz) to disc segments. A commercial transmit-receive RF surface coil (circular, 3-inch diameter) was used and the actuator was designed to exactly fit within the loop of the coil to provide optimal filling factor and SNR. A 3D gradient echo pulse sequence was modified to include an oscillating gradient to measure displacements in three orthogonal directions as a function of time. A previously developed inverse method was used to calculate the shear modulus of the NP [2]. *Imaging:* Prior to freezing, cadaveric spines were imaged in a 3T Siemens whole-body scanner to map T1 ρ and T2 relaxation times and to determine Pfirrmann score using previously developed protocols [3,4]. Then an axial T2 map was obtained (2D fast spin echo, TR/TE = 3000/12, 24, 48, 98, 192 ms, voxel = 1x1x2 mm³) at 7T (for higher SNR), with mean T2 in a 8x8 mm² ROI used to represent NP, and also displacements were measured at 7T in the same axial section using the above MRE sequence (TR/TE = 100/16 ms, 64x64x6 matrix, voxel = 1x1x1 mm³, 30° flip). Shear modulus of NP was calculated in a 8x8x4 mm³ volume. *Validation:* The MRE methodology was validated in agarose gels of different concentrations (1-4%) by comparing shear moduli, as measured by MRE (at 3T), to those measured by mechanical testing in torsion.

Results: Shear moduli of agarose gels measured by MRE and torsion were highly correlated ($r = 0.95$, $p = 0.0003$) (Fig. 1). The shear modulus of human NP decreased with increasing degeneration ($r = -0.496$, $p = 0.009$) (Fig. 2). There also was a correlation between MRE shear modulus and T2 ($r = 0.55$, $p = 0.007$) (Fig. 3). In addition, we found a correlation between Pfirrmann score and T2 ($r = -0.72$, $p < 0.0001$) (not shown), and, at 3T, between T1 ρ and T2 ($r = 0.908$, $p < 0.001$) and between Pfirrmann score and T2 ($r = -0.548$, $p = 0.007$). Surprisingly, however, the correlation between Pfirrmann score and T1 ρ was not significant ($r = -0.11$, $p = 0.579$). Likewise there was not a significant correlation between shear modulus and T1 ρ ($r = -0.122$, $p = 0.560$), or T2 ($r = -0.265$, $p = 0.222$) at 3T.

Discussion: In this study the shear modulus of the nucleus pulposus was measured non-invasively by MRE. The methodology was validated using agarose gels of different concentrations, which showed that the shear modulus obtained by MRE is proportional to that obtained by torsion tests, similar to the results of other studies [3,4]. Here, MRE measurements on disc segments could non-invasively measure the shear modulus of the NP in healthy, mildly and moderately degenerated intact disc segments. It was not possible to measure shear modulus for highly degenerated discs with Pfirrmann scores above 4, as expected since SNR usually decreases in degenerated discs due to lower T2 and water content. However, MRE could be readily applied to discs with Pfirrmann scores 1, 2 or 3, which characterize healthy to moderately degenerated discs. Furthermore, the significant decrease of the shear modulus of the NP with Pfirrmann score, greater than 200 kPa per unit of Pfirrmann score, indicates that the shear modulus of the NP is a sensitive biomarker that has potential for the early diagnosis of disc degeneration. T2 relaxation times at 3T and 7T decreased with increasing Pfirrmann score: T2 decreased 15% (7 ms) at 7T and 30% (45 ms) at 3T from a score of 2 to 4, while no significant correlation between T1 ρ and Pfirrmann score was observed (possibly due to the absence of samples with score 5 and the fewer samples with score 4). Other studies have shown a decrease in both T2 and T1 ρ with degeneration at 3T [5,6]. Nevertheless, using MRE we observed an 86% reduction of shear modulus versus Pfirrmann score for the same discs, which implies that the shear modulus may have a higher sensitivity.

Although the pulse sequence used in this study was designed and optimized using disc segments, it satisfies safety standards regarding RF power deposition (SAR) and nerve stimulation (dB/dt) for whole-body applications. The only component of the current MRE setup that would require modification for *in vivo* application is the electromechanical actuator, and it is feasible to design an actuator that applies motion to the lumbar spine through skin contact with the posterior elements of the vertebrae. Furthermore, we note that although a 7T whole-body scanner was used in this study, the same MRE setup can also be used in 3T or 1.5T clinical scanners.

Conclusion: This study shows that the shear modulus of the NP measured using MRE is sensitive to disc degeneration and has the potential of being used as a clinical tool to diagnose and monitor disc degeneration. The advantages of using the shear modulus of the NP as a biomarker of disc degeneration are that mechanical parameters are sensitive to both compositional and structural changes and that mechanical properties do not depend on B₀ field strength.

References: [1] Iatridis+ (1997) J Orthop Res 15:318-322. [2] Cortes+ (2012) SBC, Fajardo, PR. [3] Okamoto+ (2011) Phys Med Biol 56:6379-6400. [4] Muthupillai+ (1995) Science 269:1854-1857. [5] O'Connell (2011) J Orthop Res 29(4):547-55. [6] Johannessen+ (2006) Spine 31(11):1253-7.

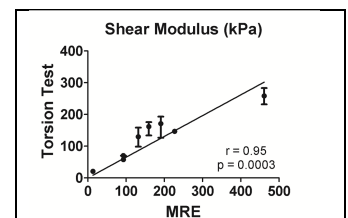


Fig. 1. Comparison of shear modulus of agarose gels measured using both torsion and MRE tests.

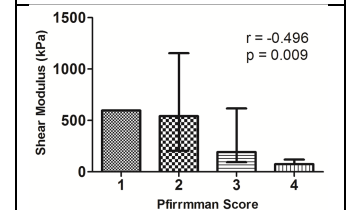


Fig. 2. Shear modulus of the NP as measured by MRE vs. degeneration of the intervertebral disc.

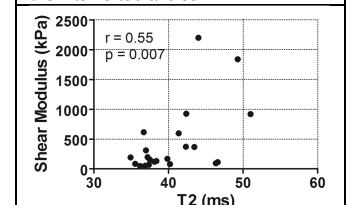


Fig. 3. Shear modulus measured by MRE vs. T2 relaxation time of the NP.