Changes in MRI Parameters of Porcine Intervertebral Discs under Compressive Loading

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Intervertebral disc (IVD) is a major source of Low Back Pain (LBP). The health and functions of the IVD are determined by the inherent biomechanical properties and their interaction with external loading. Recent advances in quantitative Magnetic Resonance Imaging (MRI) techniques have the potential in detecting loading-induced changes in the biomechanical properties of the IVD. Twenty functional spinal units (FSU) from porcine cervical spines were imaged with a 7T scanner to obtain $T_{1\rho}$, T_2 and Apparent Diffusion Coefficient (ADC) before and after experiencing compressive loading of 263.27N for 60 minutes. Compressive loading was found to significantly decrease $T_{1\rho}$ and T_2 but not ADC, which indicated that $T_{1\rho}$ and T_2 had the potential to detect changes in the biomechanical properties of the IVD due to external loading. These parameters may provide more sensitivity and specificity to understand the injury mechanism of the IVD and contribute to early diagnosis of IVD degeneration.

INTRODUCTION

Musculoskeletal LBP remains a major socioeconomic problem, and one of the leading sources is the IVD (Fourney et al., 2011). Injuries to the disc itself can cause discogenic back pain (Brisby, 2006). Also, since the IVD interacts with other tissues to provide spinal function, compromise in IVD biomechanics may impair neuromuscular control of postural stability and make other spinal tissues more vulnerable to injury, and thus may cause LBP (Panjabi, 2006; Ning et al., 2014; Zhou et al., 2016).

The biomechanical properties of the IVD are largely determined by the concentration of the proteoglycan (PG) in the nucleus pulposus (NP) of the IVD (Adams and Roughley, 2006). When subjected to compressive load, water is expelled out from the NP, which increases the concentration of PG and the associated osmotic pressure, such that the compressive load can be balanced by such pressure and an equilibrium state can be restored. When the load is removed, water re-imbibes into the NP, which reduces osmotic pressure corresponding to the magnitude of the current load, hence, achieving a new equilibrium state (Urban and Winlove, 2007) (Figure 1).

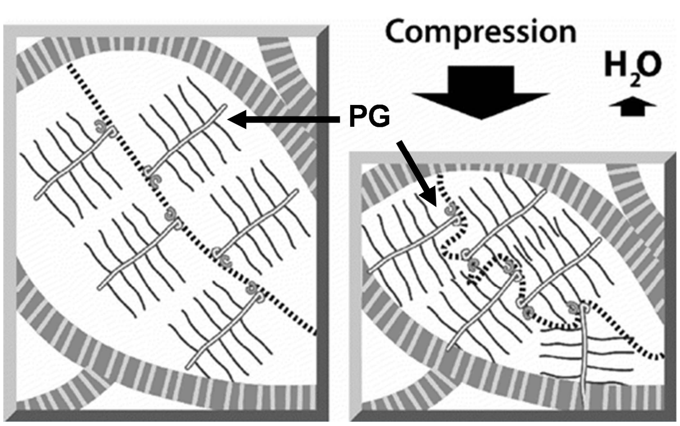

Figure 1. The expulsion of water from the IVD

The expulsion and re-imbibition of water from and to the IVD determine the time-dependent viscoelastic property of the IVD (Urban and Winlove, 2007). Therefore, the health and functions of the IVD are determined by both the inherent tissue properties (e.g. PG content, osmotic pressure and hydration) and their interaction with the magnitude and time-distribution of loading. The inherent properties of IVD are not directly determinable in-vivo; whereas, quantitative MRI parameters, such as spin–lattice relaxation in the rotating frame ($T_{1\rho}$), spin–spin relaxation (T_2) and Apparent Diffusion Coefficient (ADC) may extract pertinent information about biomechanical properties of the IVD tissue, which is useful for understanding the effects of loading on the health and functions of the IVD (Urban and Winlove, 2007). Therefore, the objective of the current study is to investigate how compressive loading changes $T_{1\rho}$, T_2 and ADC in the NP of the IVD.

METHOD

Specimens

Due to the similarity in morphometry, geometry, and curvature to the human lumbar spine, porcine cervical spines were harvested from young pigs freshly-slaughtered and used as the specimens (Noguchi et al., 2016). They were then wrapped in phosphate buffered saline (PBS) soaked gauze, sealed in plastic bags, and frozen at −20 °C until testing. Prior to testing, the cervical spines were thawed for approximately 12 hours and each cervical spine was dissected to obtain 2 functional spinal units (FSU) (C3-C4 and C5-C6) (Nikkhoo et al., 2015). Each FSU consists of 2 adjacent vertebral bodies, the IVD and all connecting ligamentous tissues between them. The posterior ligaments were removed to isolate loading to the IVD (Figure 2). A total of 20 FSUs were harvested from 10 pigs, the average (standard deviation) of the weight and age of the 10 pigs were 10.92 kg (1.49 kg) and 45.4 days (3.58 days), respectively.

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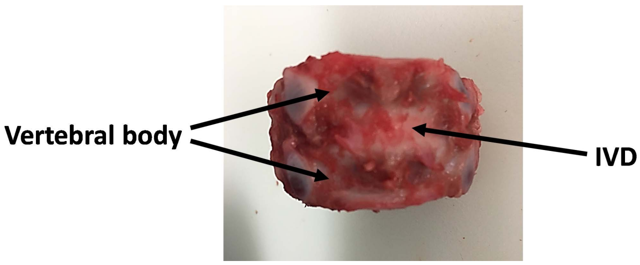

Figure 2. The structure of Functional Spinal Unit (FSU)

Experimental design

A repeated-measures experimental design was performed. $T_{1\rho}$, T_2 and ADC were obtained from the sagittal plane of the NP of the IVD before and after receiving compressive load of 263.27 N for 60 minutes. The IVD was kept compressed during imaging to maintain a constant loading condition. This load magnitude corresponds to 1500N on human lumbar IVD according to the scaling factor in IVD areas between the porcine cervical and human lumbar discs (Beckstein et al., 2008). The 3D-SSPP software (University of Michigan, Ann Arbor, Michigan) was used to determine such 1500N compressive load when simulating a 50th percentile male worker holding a 23kg load. The 23kg has been suggested as the maximum recommended weight limit by NIOSH lifting equation (Waters et al., 1993).

Experimental procedure

A computer controlled load-displacement apparatus was developed to apply compressive load inside the MRI scanner (Figure 3). FSUs were casted and drilled, then secured into the sample holder with pin insertion. PBS soaked gauze was used to wrap the FSU to maintain the hydration of the IVD (Figure 4a), sample holder was assembled into the tube (Figure 4b), and the whole apparatus was installed onto the opening of the MRI bore with the machined aluminum flange plate (Figure 4c). And the electrical components (e.g. pressure transducers and DAQ), pneumatic system (e.g. pneumatic actuator, proportional pneumatic control valve and compressed air supply) and LabView software were set up to achieve force-displacement control and monitor (Figure 4d).

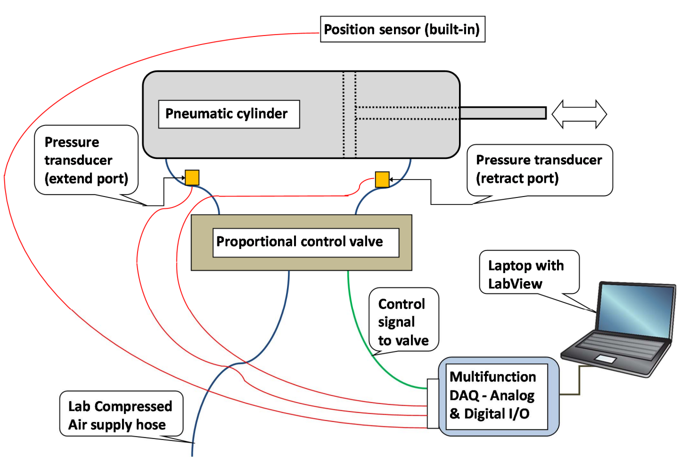

Figure 3. The diagram of the apparatus

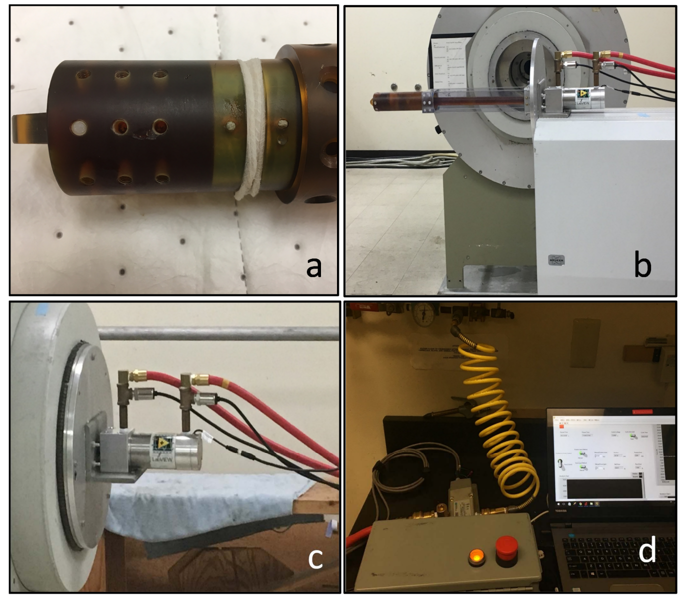

Figure 4. The computer controlled pneumatic load-displacement apparatus

The 7T Bruker Biospec imaging instrument (Bruker Inc., Billerica, MA) in the NMR facility of UC Davis was used for imaging. During MRI imaging, a series of T_2-weighted images were first performed with a series of different spin echo times (TE ranged from 15 to 75 ms, with 15 ms increments), while repetition time (TR) was kept constant at 2000 ms. A series of diffusion-weighted images (DWI) with b values range from 200 to 1000 s/mm^2 (with 200 s/mm^2 increments) were then performed, TE and TR were kept constant at 24 ms and 1000 ms, respectively. At last, five $T_{1\rho}$-weighted images were performed with spin lock time (TSL) ranging from 15 to 75 ms (15 ms increments), TE and TR were kept constant at 20 ms and 1000 ms, respectively (Figure 5). And the spin lock frequency (FSL) was kept at 500 Hz. All images were obtained from the sagittal plane of the specimen, the slice thickness was set at 1 mm for T_2 and $T_{1\rho}$ imaging, and 2.26 mm for DWI.

Figure 5. The individual $T_{1\rho}$ images with each of the five TSL

The Bruker built-in ParaVision software was used to analyze the acquired images to obtain the MRI parameters. At first, the region of interest (ROI) was defined to cover only the NP of the IVD, and the signal intensity in the ROI of the series of images was calculated. The signal intensity of these images was then fitted with the exponential decay equation of each MRI parameter, thus the desired MRI parameters (i.e. $T_{1\rho}$, T_2 and ADC) can be calculated.

Statistical analysis

Paired-t tests were performed to test the effects of the compressive load on $T_{1\rho}$, T_2 and ADC. The α value of 0.05

was set as the significance criteria. Minitab software (Minitab Inc., State College, Pennsylvania) was used to conduct all the statistical analyses.

RESULTS

The effects of compressive loading on MRI parameters were demonstrated in Table 1. After experiencing the compressive load, significantly decreased $T_{1\rho}$ was observed (from 112.43 to 93.47 ms). T_2 was also significantly decreased from 50.78 ms in the baseline condition to 33.51 ms in the compressed condition. However, ADC was not significant affected by the compressive load (P=0.353).

	$T_{1\rho}$ (ms)	T_2 (ms)	ADC (mm^2/s)
Baseline	**112.43 (6.22)**	**50.78 (4.70)**	0.002887 (0.000054)
Compressed	**93.47 (5.12)**	**33.51 (3.45)**	0.002790 (0.000084)

Table 1. Measured MRI parameters (and standard errors) with and without load. Bold fonts indicate significant differences.

DISCUSSION

The relaxation time of a tissue can be estimated as the weighted relaxation times of all the chemical components that made up of the tissue (Levine and Slade, 2013). Therefore, $T_{1\rho}$ relaxation time in the NP of the IVD is sensitive to the change in the composition of the NP. NP primarily constitutes of water (80%) and PG (15%) (Raj 2008), change in either composition can influence the $T_{1\rho}$ relaxation time. In the current study, it is believed that the applied compressive loading expelled sufficient amount of water out from the NP of the IVD, which can be detected by $T_{1\rho}$ relaxation time. Also, the decrease in $T_{1\rho}$ relaxation time in the NP indicates a reduced water content in it, which is consistent with the finding from previous studies (Johannessen et al., 2006; Souza et al., 2014).

T_2-weighted image has long been used to scan the IVD, in order to grade the IVD degeneration according to its morphology (Griffith et al., 2007). Therefore, it is not surprising that T_2 relaxation time decreases with greater IVD degeneration grades (Takashima et al., 2012). Furthermore, loss of water content is one of the most immediate and apparent changes, which occur at early stage of IVD degeneration (Stokes and Iatridis, 2004). Therefore, in the current study, T_2 relaxation time is also significantly reduced by the applied compressive loading, since such loading can expel water out from the NP of the IVD and induce early degenerative changes (Urban and Winlove, 2007). And T_2 relaxation time decreased from 50.78 to 33.51 ms in the NP of the IVD after receiving compressive load of 263.27 N for 60 minutes.

According to the previous literature, ADC is affected by the compositional variation of the IVD and the matrix integrity (Antoniou et al., 2004). In the current study, even though the water content in the NP of the IVD was reduced, ADC was not significantly affected by the applied compressive load, presumably due to the expelled water was not sufficient enough to alter ADC.

In summary, in the current study, $T_{1\rho}$ and T_2 relaxation times were found sensitive to the applied compressive load, which indicates that they have the potential to detect the biomechanical changes in the NP of the IVD induced by the external loading. Therefore, they may provide more sensitivity and specificity to understand the injury mechanism of the IVD and contribute to early diagnosis of IVD degeneration, thus help reduce the prevalence of LBP.

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REFERENCE

Adams, M. A., & Roughley, P. J. (2006). What is intervertebral disc degeneration, and what causes it. Spine, 31(18), 2151-2161.

Antoniou, J., Demers, C. N., Beaudoin, G., Goswami, T., Mwale, F., Aebi, M., & Alini, M. (2004). Apparent diffusion coefficient of intervertebral discs related to matrix composition and integrity. Magnetic resonance imaging, 22(7), 963-972.

Beckstein, J. C., Sen, S., Schaer, T. P., Vresilovic, E. J., & Elliott, D. M. (2008). Comparison of animal discs used in disc research to human lumbar disc: axial compression mechanics and glycosaminoglycan content. Spine, 33(6), E166-E173.

Brisby, H. (2006). Pathology and possible mechanisms of nervous system response to disc degeneration. The Journal of Bone & Joint Surgery, 88(suppl 2), 68-71.

Fourney, D. R., Andersson, G., Arnold, P. M., Dettori, J., Cahana, A., Fehlings, M. G., ... & Chapman, J. R. (2011). Chronic low back pain: a heterogeneous condition with challenges for an evidence-based approach. Spine, 36, S1-S9.

Griffith, J. F., Wang, Y. X. J., Antonio, G. E., Choi, K. C., Yu, A., Ahuja, A. T., & Leung, P. C. (2007). Modified Pfirrmann grading system for lumbar intervertebral disc degeneration. Spine, 32(24), E708-E712.

Johannessen, W., Auerbach, J. D., Wheaton, A. J., Kurji, A., Borthakur, A., Reddy, R., & Elliott, D. M. (2006). Assessment of human disc degeneration and proteoglycan content using T1ρ-weighted magnetic resonance imaging. Spine, 31(11), 1253.

Levine, H., & Slade, L. (Eds.). (2013). Water Relationships in Foods: Advances in the 1980s and Trends for the 1990s (Vol. 302). Springer Science & Business Media.

Nikkhoo, M., Kuo, Y., Hsu, Y., Khalaf, K., Haghpanahi, M., Parnianpour, M., & Wang, J. (2015). Time-dependent response of intact intervertebral disc–In Vitro and In-Silico study on the effect of loading mode and rate. Engineering Solid Mechanics, 3(1), 51-58.

Ning, X., Zhou, J., Dai, B., & Jaridi, M. (2014). The assessment of material handling strategies in dealing with sudden loading: The effects of load handling position on trunk biomechanics. Applied ergonomics, 45(6), 1399-1405.

Noguchi, M., Gooyers, C. E., Karakolis, T., Noguchi, K., & Callaghan, J. P. (2016). Is intervertebral disc pressure linked to herniation?: An in-vitro study using a porcine model. Journal of biomechanics, 49(9), 1824-1830.

Panjabi, M. M. (2006). A hypothesis of chronic back pain: ligament subfailure injuries lead to muscle control dysfunction. European Spine Journal, 15(5), 668-676.

Raj, P. P. (2008). Intervertebral disc: anatomy - physiology - pathophysiology - treatment. Pain Practice, 8(1), 18-44.

Souza, R. B., Kumar, D., Calixto, N., Singh, J., Schooler, J., Subburaj, K., ... & Majumdar, S. (2014). Response of knee cartilage T1rho and T2 relaxation times to in vivo mechanical loading in individuals with and without knee osteoarthritis. Osteoarthritis and cartilage, 22(10), 1367-1376.

Stokes, I. A., & Iatridis, J. C. (2004). Mechanical conditions that accelerate intervertebral disc degeneration: overload versus immobilization. Spine, 29(23), 2724-2732.

Takashima, H., Takebayashi, T., Yoshimoto, M., Terashima, Y., Tsuda, H., Ida, K., & Yamashita, T. (2012). Correlation between T2 relaxation time and intervertebral disk degeneration. Skeletal radiology, 41(2), 163-167.

Urban, J. P., & Winlove, C. P. (2007). Pathophysiology of the intervertebral disc and the challenges for MRI. Journal of magnetic resonance imaging, 25(2), 419-432.

Waters, T. R., Putz-Anderson, V., Garg, A., & Fine, L. J. (1993). Revised NIOSH equation for the design and evaluation of manual lifting tasks. Ergonomics, 36(7), 749-776.

Zhou, J., Ning, X., & Fathallah, F. (2016). Differences in lumbopelvic rhythm between trunk flexion and extension. Clinical Biomechanics, 32, 274-279.