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Altered helical axis patterns of the lumbar spine indicate increased instability with disc degeneration

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ABSTRACT

Although the causes of low back pain are poorly defined and indistinct, degeneration of the intervertebral disc is most often implicated as the origin of pain. The biochemical and mechanical changes associated with degeneration result in the discs' inability to maintain structure and function, leading to spinal instability and ultimately pain. Traditionally, a clinical exam assessing functional range-of-motion coupled with T2-weighted MRI revealing disc morphology are used to evaluate spinal health; however, these subjective measures fail to correlate well with pain or provide useful patient stratification. Therefore, improved quantification of spinal motion and objective MRI measures of disc health are necessary. An instantaneous helical axis (IHA) approach provides rich temporal three-dimensional data describing the pathway of motion, which is easily visualized. Eighteen cadaveric osteoligamentous lumbar spines (L4–5) from throughout the degenerative spectrum were tested in a pure moment fashion. IHA were calculated for flexion–extension and lateral bending. A correlational study design was used to determine the relationship between disc measurements from quantitative T2* MRI and IHA metrics. Increased instability and out-of-plane rotation with diminished disc health was observed during lateral bending, but not flexion–extension. This new analysis strategy examines the entire pathway of motion, rather than simplifying spinal kinematics to its terminal ends of motion and provides a more sensitive kinematic measurement of disc health. Ultimately, through the use of 3D dynamic fluoroscopy or similar methods, a patient's functional IHA in lateral bending may be measured and used to assess their disc health for diagnosis, progression tracking, and treatment evaluation.

1. Introduction

Low back pain is one of the most prevalent health complaints in the US, with an estimated 70–85% of the population developing back pain at some point in their life, creating a significant financial burden (Andersson, 1999). Although many causes of low back pain are poorly defined and indistinct, intervertebral disc (IVD) degeneration remains the primary cause for such symptoms. Throughout the degenerative process the proteoglycans in the nucleus pulposus are cleaved, resulting in decreased water content, hydrostatic pressure, and disc height (Urban and Roberts, 2003). These changes in the biochemical composition diminish the mechanical competency of the disc, thus altering the interaction between the nucleus and annulus during loading (Adams et al., 1996). The discs' inability to maintain structure and function may cause spinal instability leading to discogenic pain, nerve root pinching, or cord occlusion (Adams, 2004). The traditional definition of clinical spinal instability, as defined by Panjabi, is "the loss of normal pattern of spinal motion" (Panjabi, 2003).

Routine clinical exams for back pain include a functional exam, assessing the patient's spine motion and the presentation of pain, as well as diagnostic imaging of the intervertebral disc. Degeneration is traditionally evaluated using conventional T2 weighted sagittal magnetic resonance imaging (MRI) using a qualitative grading system assessing hydration levels and disc height, such the technique described by Pfirrmann et al. (2001). It has been shown that these categorical grading systems are not sensitive enough to detect early signs of degeneration, likely due to their subjectivity, and rarely provide clinically useful insights (Arana et al., 2010; Raininko et al., 1995). Therefore, emerging quantitative MRI techniques have recently been published, which avoid the pitfalls associated with qualitative measures by probing the biochemical content and structural integrity of the tissue (Ellingson et al., 2013a; Johannessen et al., 2006; Lotz et al., 2012; Mwale et al., 2008). These techniques may have a

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profound impact on the treatment of disc degeneration, especially with their ability to detect and quantify the subtle changes occurring at the early stages in the degeneration process.

It is of equal importance to understand the effects of diminished disc health on the functional mechanics and stability of the lumbar spine. In fact, this topic has been the focus of several studies including *in vivo*, *in vitro*, and *in silico* experiments (Ellingson et al., 2013a; Mimura et al., 1994; Natarajan et al., 2006; Passias et al., 2011). The conventional Kirkaldy–Willis model of spinal stability throughout degeneration describes a progressive increase in range of motion (RoM), until re-stabilization and a drop in RoM (Kirkaldy-Willis and Farfan, 1982). However, there still remains a lack of congruence in published literature, especially in the RoM exhibited. There is conflicting evidence supporting RoM either increases or decreases with worsening degeneration (Ellingson et al., 2013a; Fujiwara et al., 2000; Kettler et al., 2011; Tanaka et al., 2001). These contradicting results suggest RoM is not an adequate measure of spinal health due to its lack of sensitivity. The ratio of neutral zone to range of motion (NZR), a measure of joint instability or laxity, holds greater consensus in the literature. The NZR has been shown to increase with worsening degeneration (Ellingson et al., 2013a; Mimura et al., 1994; Panjabi, 1992; Zhao et al., 2005). RoM and NZR are scalar metrics that define kinematic endpoints, however the spine can move in infinite pathways of motion to reach those endpoints, and therefore are not sufficient in describing the quality of spinal motion. Also, NZR is a kinetic measure, which is unable to be measured *in vivo*. The center of rotation (COR) offers a more in-depth description of spinal motion (Gertzbein et al., 1985; Pearcy and Bogduk, 1988). The increased migration of the COR has been shown to be a biomarker in moderately degenerative discs and Spondylolisthesis, but even this metric simplifies the complex coupled motion of the spine into only two-dimensions (Schneider et al., 2005; Seligman et al., 1984). However, this analysis strategy is not adequate for complex motions in three-dimensions. Extending the COR to show the three-dimensional axis of rotation, rather than just a pivot point, can be obtained by computing the instantaneous helical axis (IHA). An IHA analysis approach provides rich temporal three-dimensional data describing the pathway of motion, which is easily visualized. IHA patterns have been used as a metric of stability in other joints and been employed to qualitatively describe the kinematics of the spine and the efficacy of implant devices (Duck et al., 2003; Grip and Häger, 2013; Kettler et al., 2004; Schmidt et al., 2008). The quantification of spinal instability or the off of the spine's ability to maintain its patterns of displacement under physiologic loads, is of high clinical importance, and previous analysis strategies have fallen short. It is paramount, therefore, to understand normal spinal motion to assess dysfunction in those motion patterns.

The aim of this study was to investigate the potential for IHA patterns to be used as a biomarker for spinal health and stability. It is hypothesized that the IHA vectors will display greater off-axis, or out-of-plane, rotation and a larger variability in their orientation with in worsening degeneration. It is also hypothesized that the center of rotation will exhibit greater migration and a larger variability in the migration with worsening degeneration.

2. Methods

Eighteen fresh-frozen osteoligamentous lumbar spines (L3–S1) were acquired from the University of Minnesota Bequest Program (age: 53.2 ± 15.5 years; range: 21–71 years). Specimens were first examined using magnetic resonance imaging protocols to evaluate intervertebral disc health, and then biomechanically exercised in flexion, extension, and lateral bending in a pure moment fashion. A correlational study design was used to examine the relationship between instantaneous helical axis patterns of the lumbar spine and intervertebral disc degeneration, based on MR imaging.

2.1. Assessment of spinal health

All MR imaging was performed on a Siemens 3T scanner (Magnetom Trio; Siemens Healthcare). Quantitative T2* (T2 star) relaxation maps [TR(ms): 500; TE(ms): 4.18, 11.32, 18.46, 25.60, 32.74, 39.88; Voxel Size(mm): 0.5 × 0.5 × 3.0, Slices: 33] were obtained. T2* relaxation times have been shown to be strongly correlated to the proteoglycan content and biomechanical properties, including the residual stress and strain, of the intervertebral disc (Ellingson et al., 2014). The nucleus pulposus relaxation time, T2* Intensity Area, and the Transition Zone Slope were measured in accordance with our previously published work, where the average T2* relaxation time of the central ROI (ROI 3) was evaluated through all sagittal slices across the coronal plane. These metrics are displayed in Fig. 1 (Ellingson et al., 2013a). The slope of the transition zone (ms/mm) between the AF and NP on each side was linearly regressed and then averaged. Landmarks for transition zone were from 12% to 35% of the disc width from the lateral margin, as it is approximately symmetrical about the border between the AF and NP (O'Connell et al., 2007). All regressions resulted in an R^2 value of greater than 0.90. This metric quantified the distinction between the NP and AF. This quantitative analysis strategy removes the bias and subjectivity inherent in classical grading schemes and has been shown to correlate better with classical biomechanics measurements of the spine than traditional Pfirrmann grading (Ellingson et al., 2013a). Specifically, the Transition Zone Slope was shown to be the strongest predictor of disc health, and therefore will be used as the primary metric for disc health for this study.

2.2. Biomechanical testing

Subsequent biomechanical tests were performed on each specimen, embedded in polymethylmethacrylate and exercised in a six-axis Spine Kinetic Simulator (8821 Biopuls, Instron, Norwood, MA) (Wheeler et al., 2011). Pure moments of ±7 Nm with no axial preload (0 N) were applied with the spine. The testing apparatus allowed for unconstrained displacement inferiorly to minimize shear forces utilizing a passive *X*–*Y* table (resistance less than 0.1 N). After three cycles of preconditioning, four cycles of bending in flexion/extension and lateral bending was performed sinusoidally (0.015 Hz). The last full cycle of each bending direction, fully unloaded to fully loaded, was used for analysis. Load and moment data were collected on two six-axis load cells (AMTI M4380, Watertown, MA), one positioned superiorly and one inferiorly. A four ball infrared reflecting marker set was attached to each vertebral body and relative motion of each functional unit was recorded at 100 Hz using a 3D visual motion analysis 5-camera system (Vicon MX-F40NIR, Vicon Motion Systems, Centennial, CO). The anterior, left-lateral, and right-lateral most points along the superior ridge of the L5 vertebrae were digitized to establish the local coordinate system.

2.3. Helical axis computation

The helical axes were computed over a 0.05° increment for flexion, extension, and lateral bending (Spoor and Veldpaus, 1980; Woltring et al., 1985). Due to the potential noise inherent in such a small step size, a sensitivity analysis for the calculation of the IHA was first conducted on a healthy L4–L5 intervertebral disc during lateral bending (Fig. 2). The axes were assessed based on the low-pass cutoff frequency used in a fourth order forward-backward Butterworth filter. The low-pass cutoff frequencies presented herein are 3.2, 0.8, 0.4, and 0.2 Hz. The root mean square of the error (RMSE) was measured between the angular displacement with and without filtering. Following this analysis the kinematic data was filtered using a fourth order low-pass Butterworth filter with a cutoff frequency of 0.4 Hz, which is similar to other published values (Anderst et al., 2013; Duck et al., 2003; Woltring et al., 1994). In order to assess the accuracy of the HA orientation and COR position, a goniometer with reflective markers was dynamically rotated approximately 90° (Fig. 3). HA were calculated using the filtering parameters and step size determined above and compared to the marker placement at the center of rotation of the goniometer. The measured COR distance error was 1.04 ± 0.33 mm and orientation error was less than 0.1%.

The current study focused on only the L4–L5 level to avoid the possibility of boundary condition errors caused by the testing apparatus being attached to the superior and inferior most vertebral body. Each axis was computed at every 0.05° increments in the primary plane of bending. This was smallest step size for which stable helical axes could be calculated. The COR was defined where the IHA crosses the mid-sagittal plane (*x*, *z* plane) for flexion/extension and the coronal plane at the anterior margin of the L5 vertebral body (*y*, *z* plane) for lateral bending. Only the migration in the medial-lateral direction and anterior-posterior direction were analyzed for lateral bending and flexion/extension, respectively.

The computed IHA were used for visualization purposes, but for statistical hypothesis testing, the IHA orientation and COR location were averaged over 1 Nm windows from −6.5 Nm to 6.5 Nm and 6.5 Nm to −6.5 Nm to evaluate both loading and unloading of the spine. This analysis resulted in 7 − 1 Nm total windows, each with