Degeneration Reduces Human Intervertebral Disc Equilibrium Modulus in Stress Relaxation

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Introduction: The intervertebral disc provides flexibility and load support to the spinal column. It achieves this function by a combination of solid matrix elasticity and fluid pressurization. Since the disc is permeable, sustained loading results in fluid flow, causing a time-dependent (viscoelastic) mechanical response. Quantification of the disc’s viscoelastic properties is important because they determine the disc’s response to diurnal and activity-related cyclic loading. These properties are altered by disc degeneration, with detrimental consequences to function. In creep (fixed load) tests, degeneration was correlated with decreased stiffness, but results for the characteristic time constant were mixed [1-3]. These studies used upper lumbar and thoracic discs. Viscoelastic tests have not been performed on the degeneration-prone L4L5 disc. Moreover, viscoelastic properties may be sensitive to applied strain, which would not be apparent in single-load creep tests. Prior work also quantified degeneration using subjective integer grading scales; quantitative MRI grading has recently been proposed as an alternative [4]. The objective of this study, therefore, was to test the hypothesis that degeneration affects physiologic (hours-scale) stress relaxation in human L4L5 intervertebral discs, using 3 strain levels, with degeneration assessed by both integer and quantitative methods.

Methods: Human intervertebral discs (14; 7 M; 7 F; age 41-93 years) were collected from cadavers, sealed in plastic, and stored frozen. Disc degeneration was assessed from mid-sagittal MRI using both the Pfirrmann integer scale and quantitative MRI (mean T1ρ and T2 MRI intensity within the nucleus) [4]. By integer grade, four discs were grade 2, seven were grade 3, and two were grade 4.

Mechanical testing of each disc began with free swelling for 18 hours in 4 °C PBS, then equilibration at room temperature to 50 p < 0.1 was trending. Quantitative MRI grading has recently been proposed as an alternative [4]. None. None. −55 None. −2. −0.6 s. None. None. −2.

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−2.5 MPa + 0.039 MPa * ε * T1ρ) and T2 (E∞ = −2.5 MPa + 0.028 MPa * ε * T2). E∞ was the only parameter significantly correlated to T1ρ or T2 (p = 0.2 for E1 ~ T1ρ; others, p > 0.5).

Although the relaxation times t1 and t2 did not depend on degeneration, they were sensitive to applied strain (p < 0.001) (Fig. 1d, e). For each percent strain, the slow relaxation time t1 increased 76 ± 5 s and the fast relaxation time t2 increased 7 ± 0.6 s. The zero strain intercepts were not significantly different from zero (t1: 95% CI −55-11 s; t2: 95% CI 85-510 s).

Discussion: Severe degeneration (grade 4) was associated with a decrease in equilibrium modulus (E∞) regardless of applied strain. Compared to healthier discs (grade 2) a severely degenerate disc’s equilibrium modulus was reduced by almost half. For a given load, a degenerate disc will thus undergo about twice as much strain as a healthy disc. This excess strain could increase the degenerate disc’s vulnerability to structural damage, particularly in the context of cyclic loading. Degeneration as measured by quantitative MRI was also related to E∞, with lesser T1ρ and T2 values associated with a decrease in E∞. Although E∞ was the only rheological parameter associated with degeneration by either quantitative MRI or the integer scale, relationships with the other parameters may have gone undetected due to the small number of degenerate discs.

Although the integer and quantitative MRI degeneration measures were both significantly related to equilibrium modulus (E∞), these relationships had different causes. Discs classified as degenerate by the integer scale had reduced E∞ for all strain levels...
(Fig. 1a), but low T1ρ and T2 scores were only associated with reduced E∞ at strains > 8% (Fig. 1c). This relationship was caused by two discs with high T1ρ and T2, both grade 2, which exhibited strain-stiffening. It is plausible that this strain stiffening behavior was caused by greater glycosaminoglycan content (which is correlated with T1ρ and T2) resulting in increased equilibrium osmotic pressure. Integer grading of overall disc degeneration is not entirely equivalent to quantitative MRI of the nucleus; the choice of scale depends on the application.

Strain magnitude did not significantly affect the modulus terms (E∞, E1, and E2), but did significantly increase the relaxation time constants (τ1 and τ2). Since the disc did not recover between tests, the 17% strain and 25% tests started from a state of compaction and reduced permeability, increasing the relaxation time. This strain-sensitivity may have implications with respect to degeneration, since a degenerate disc will undergo more compressive strain than a healthy disc. This excess strain in the degenerate disc would have the secondary effect of increasing relaxation time.

**Significance:** Degeneration-related changes in the intervertebral disc’s viscoelastic properties have important implications for function. Loss of equilibrium modulus with degeneration could make the disc vulnerable to further damage and height loss, accelerating the cascade of degeneration. Additionally, the increase in stress relaxation time with applied strain indicates that matrix compaction decreases fluid flow within the disc, potentially impairing disc nutrient supply and post-loading recovery. The observation of these effects in L4L5 discs is particularly relevant, as the lower lumbar discs are most prone to height loss and degeneration. Finally, while both standard integer grading and quantitative MRI are capable of classifying mechanical properties by degeneration state, their performance characteristics differ. No single grading system can (yet) distinguish between all kinds of degeneration, and further work is required in this area.

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**References:**

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