Structure-Function Relationships of Degenerative Annulus Fibrosus

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INTRODUCTION: Intervertebral discs (IVD) serve as the principal connection between the vertebral bones of the spine. IVD degeneration (degen) is an age-related progressive structural failure of the disc which can lead to instability and potentially leading to hypermobility of the motion segment (1). The resultant condition can be debilitating and painful through bony pain, or subsequent spinal stenosis. In some patients, coronal imbalance (degenerative scoliosis (dScoli)) causes further pain. The anisotropic lamellar structure of the annulus fibrosus (AF)is remodeled during degeneration (2). Furthermore, as degeneration occurs, some patients develop further deformities in the form of degenerative scoliosis (dScoli) (coronal translation) and degenerative spondylolisthesis (dSpondy) (sagittal translation). The aim of the present study was to measure elastic and viscoelastic shear properties and compare structural histological differences between normal, degenerative, and deformity patient samples of the AF.

METHODS: AF samples were collected from patients undergoing anterior and lateral approach surgeries, limited to the L4-5 and L5-S1 segments (UofCalgary Ethics ID REB18-1308). Normal AF samples were collected from organ donors, with lumbar radiographs to ensure normal morphology. Fifty seven patients were recruited, with standing X-rays to confirm degenerative and deformity diagnosis and definition of modified Pfirrmann grade from T2-weighted MRI images (Table 1). Mechanical shear testing of 5mm^3 AF tissue cubes was performed in circumferential and radial shear loading. Four strain intervals of 2.5% with 20-minutes of relaxation were applied, totaling 10% strain. Shear modulus was calculated using a line of best fit between each of the most relaxed points of the four strain intervals. Shear modulus was calculated using MATLAB and non-parametric Kruskal-Wallis with post-hoc Dunn's of pairwise tests were performed to compare the shear modulus amongst various diagnoses.

A subset of the mechanically tested samples was subsequently imaged with optical coherence tomography (OCT) for lamellar structure (n = 20) and was scored for degeneration through histology (n = 42). Immediately after the mechanical tests, a section of the AF cube was scanned, providing a 5mm x 5mm field of view of the transverse lamellar structure. A 2D slice was analyzed using random-forest generated segmentation (3), marking lamellar borders. The average of ~250 measurements was used to quantify lamellar thickness. These same cubes were then embedded and sectioned for hemoxylin and eosin (H&E) staining and histology scoring. Degeneration was scored followed the ORS Spine standardized scoring technique, using only the AF section (4). AF cellularity, lesions, and extracellular matrix were scored between 0-3, with higher scores noting increased degenerative changes. Lamellar thickness and degenerative scores were correlated to the shear modulus of the same AF tissue using Spearman's rank correlation coefficients.

RESULTS SECTION: Sample sizes, demographics, and results are summarized in Table 1. Shear modulus was significantly increased in normal samples ($p < 0.01$) but was not significantly different between surgical diagnosis by post-hoc tests. Radial shear modulus followed similar, but reduced trends.

Significant correlations were found between shear modulus and structural measures. (Figure 2) Increases in histological degenerative scores correlated with reductions in the shear modulus of the same AF section ($r_s = -0.64$, $p < 0.01$). Radial shear modulus and histology scores were not significantly correlated ($p = 0.15$). OCT-acquired lamellar thickness increased correlated with decreases in the shear modulus of the same AF section ($r_s = -0.77$, $p < 0.01$), with similar trends in the radial orientation ($r_s = -0.73$, $p < 0.01$)

DISCUSSION: Results from the current study suggest that the AF in surgical degenerative IVD is much less stiff in shear than normal AF. These reductions in shear modulus were correlated to the structural degeneration of the AF as determined by histology and mean lamellar thickness. No significant structural differences between degen and deformity samples were detected. Decreased shear modulus in AF may be the result of the etiology of dScoli and spinal instability and is an important target for further characterization.

SIGNIFICANCE/CLINICAL RELEVANCE: Changes in the shear modulus of AF have not been well characterized, despite it potentially contributing to spinal degeneration and acquired deformities. Reductions in shear modulus and the correlating structural changes presented here will be explored further with biochemical investigations to better understand the relationship between tissue mechanics and structure as acquired deformities develop.

REFERENCES: (1) Adams & Roughley (2006). (2) Zeldin et al. (2020). (3) Lo Versio et al. (2016). (4) Le Maitre et al. (2021)

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Figure 1

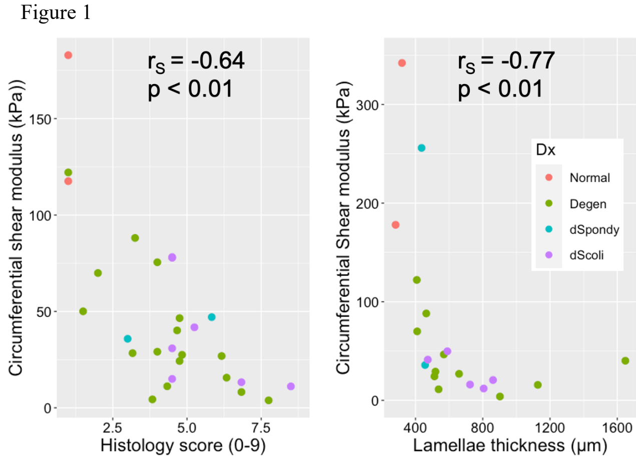

Table 1

	Normal	Degen	dSpondy	dScoli
Participants	7	29	7	14
Age	37 ± 7	47 ± 12	65 ± 6*	64 ± 8*
Sex (Female/Male)	3 / 4	18 / 13	6 / 1	6 / 8
Pfirrmann grade (1-8)		6.2 ± 1.7	6.0 ± 1.3	6.4 ± 1.8
Circumferential shear modulus (kPa)	231 ± 73	57 ± 43	36 ± 27	33 ± 21
Lamellae count	11.0 ± 1.0	4.4 ± 2.8	7.0 ± 0.0	3.2 ± 0.4
Lamellae thickness (μm)	301 ± 26	733 ± 388	446 ± 15	690 ± 159
Histology score (0-9)	1.0 ± 0.6	4.4 ± 1.9	4.3 ± 1.5	5.0 ± 1.8