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RESEARCH ARTICLE

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MRI-based measurement of in vivo disc mechanics in a young population due to flexion, extension, and diurnal loading

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Abstract

Background: Intervertebral disc degeneration is often implicated in low back pain; however, discs with structural degeneration often do not cause pain. It may be that disc mechanics can provide better diagnosis and identification of the pain source. In cadaveric testing, the degenerated disc has altered mechanics, but in vivo, disc mechanics remain unknown. To measure in vivo disc mechanics, noninvasive methods must be developed to apply and measure physiological deformations.

Aim: Thus, this study aimed to develop methods to measure disc mechanical function via noninvasive MRI during flexion and extension and after diurnal loading in a young population. This data will serve as baseline disc mechanics to later compare across ages and in patients.

Materials & Methods: To accomplish this, subjects were imaged in the morning in a reference supine position, in flexion, in extension, and at the end of the day in a supine position. Disc deformations and vertebral motions were used to quantify disc axial strain, changes in wedge angle, and anterior–posterior (A-P) shear displacement. T_2 weighted MRI was also used to evaluate disc degeneration via Pfirrmann grading and T_2 time. All measures were then tested for effect of sex and disc level.

Results: We found that flexion and extension caused level-dependent strains in the anterior and posterior of the disc, changes in wedge angle, and A-P shear displacements. Flexion had higher magnitude changes overall. Diurnal loading did not cause level-dependent strains but did cause small level-dependent changes in wedge angle and A-P shear displacements.

Discussion: Correlations between disc degeneration and mechanics were largest in flexion, likely due to the smaller contribution of the facet joints in this condition.

Conclusion: In summary, this study established methods to measure in vivo disc mechanical function via noninvasive MRI and established a baseline in a young population that may be compared to older subjects and clinical disorders in the future.

KEYWORDS
bending, disc mechanical function, diurnal, intervertebral disc, MRI, T_2, in vivo

1 | INTRODUCTION

Intervertebral disc degeneration is often implicated in low back pain, the leading cause of years lived with disability worldwide, however, not all degenerated discs cause pain.[1,2] Disc degeneration is currently assessed by magnetic resonance images (MRI) with qualitative and subjective grading schemes of signal intensity and structural morphology.[3] While interpretation of these grading schemes attempts to determine the source of pain in patients when multiple disc levels are degenerated, they have a low sensitivity and specificity for pain.[4–10] An alternative indicator of disc health and pain may lie in the mechanical function of the disc which cannot be assessed via static MRI. In cadaveric testing, the mechanical properties and composition are composed of degenerated spine segments and disc tissues (e.g., with degeneration, segments have lower compressive modulus, the nucleus pulposus has less water, and the annulus fibrosus has lower tensile modulus).[11–24] Despite the sensitivity of these mechanical parameters, these measurements require the disc to be excised, which is destructive and alters the prestrains, boundary conditions, and hydration compared to the in vivo condition. Discography is one of the few clinical methods to evaluate in vivo disc mechanical function, and it successfully identifies painful versus nonpainful discs based on opening pressure (a measure of nucleus pulposus pressure which is when the injection pressure causes the dye to enter the disc), while morphological assessment could not do the same.[9,10,25,26] Despite its success in identifying painful discs, discography is rarely used, as it is invasive and may injure the disc.[8,25,27] Therefore, developing in vivo assessment of disc mechanical function is critical to understanding the health of the disc and to creating a more specific and sensitive method to detect pain.

MRI provides the ability to assess disc mechanical function noninvasively with the disc under physiologic conditions. Unlike lateral radiographs, MRI acquires a 3D volume of the spine rather than a two-dimensional (2D) projection. Computed Tomography (CT) also produces three-dimensional (3D) volumes but is better suited for bone imaging, as it has very little signal in the disc. Specifically, by taking MR images in different postures or at different times of day, disc deformations can be quantified using image registration methods. We have previously applied image registration to MR images of cadaveric motion segments under compression to obtain internal strains.[28–30] Additionally, in vivo disc deformations measured from MRI have primarily focused on disc changes resulting from compressive loading.[31–36] Since low back pain can be exacerbated or abated by certain postural bending positions, measurement of in vivo disc mechanics during flexion and extension may be particularly informative in identifying painful discs by detecting aberrant disc deformations. As there is a lack of in vivo evaluation of lumbar disc mechanics in bending in the literature, one goal of this study is to quantify in vivo disc mechanics in flexion and extension.

Disc degeneration and low back pain do not affect human populations or spinal levels homogenously. For example, low back pain and disc degeneration vary between males and females in older populations.[37–40] Additionally, disc degeneration and surgical intervention are more common at lower lumbar levels.[41–44] Thus, our study will explore the effects of sex and level on disc mechanical function. As we are developing novel measurement and analysis of disc mechanical function, we will assess if we are applying a measurable change to the discs for the loading conditions used and whether that change is influenced by sex or spinal level. This should be established in a young, healthy cohort to understand the baseline function of the disc in vivo. In the future, the same methods can be applied to a larger sample set to test for aberrant function of discs due to natural aging and then in discs that are sources of pain.

Therefore, the objective of this study was (1) to establish methods and analyses to evaluate the in vivo mechanical function of the disc via noninvasive MRI in flexion and extension postures and during diurnal loading and (2) to measure baseline disc mechanics as a function of sex and level in a young, asymptomatic population. Measures of in vivo disc function included disc strain, changes in wedge angle, and disc anterior–posterior shear. These measures were compared across sexes and levels to test if these factors influence mechanics and were related to T_2 relaxation time, a compositional biomarker for disc degeneration.[7,45,46] These data established mechanical function parameters, and we hypothesized that in vivo mechanical measures would depend on disc level, but not subject sex, in our young asymptomatic population.

2 | METHODS

2.1 | Subjects

Healthy subjects with no history of back pain were recruited under IRB approved protocols ($n = 16$, 23–31 years old, 8 male and 8 female). Average subject age was 25.9 ± 2.6 years old (Female: 24.8 ± 1.6 years old, Males: 27.0 ± 3.0 years old). Subjects had a mean BMI of 23.7 ± 2.3 (Female: 23.6 ± 1.8 years old, Males: 23.8 ± 2.8 years old). The difference in BMI between males and females was <0.3, though the difference in weight was 31 pounds. Each subject filled out the Oswestry Low Back Pain Disability Questionnaire to determine their Oswestry Disability Index.[47,48] An Oswestry Disability Index under 20% indicates no to minimal disability from low back pain. All subject Oswestry Disability Indices were ≤4% (0.5% ± 1.2%).

2.2 | Loading protocol

We performed MRI to measure discs mechanics resulting from changes between the Reference (morning supine scan) and three conditions: flexion position, extension position, and diurnal loading. Five disc levels, L1–L2 through L5–S1, were imaged and included in the analysis for a total sample size of 80 discs. To minimize variation, MRI sessions were performed at the same time each day (with the morning scanning starting at 8:00 a.m. and the evening scanning at 7:00 p.m.), and subjects were asked to get at least 8 h of sleep, so that they would have been laying down for at least 8 h overnight, and to have minimal activity prior to arriving. Upon arrival, they would lie supine for 45 min to unload the spine prior to starting MRI scanning on a

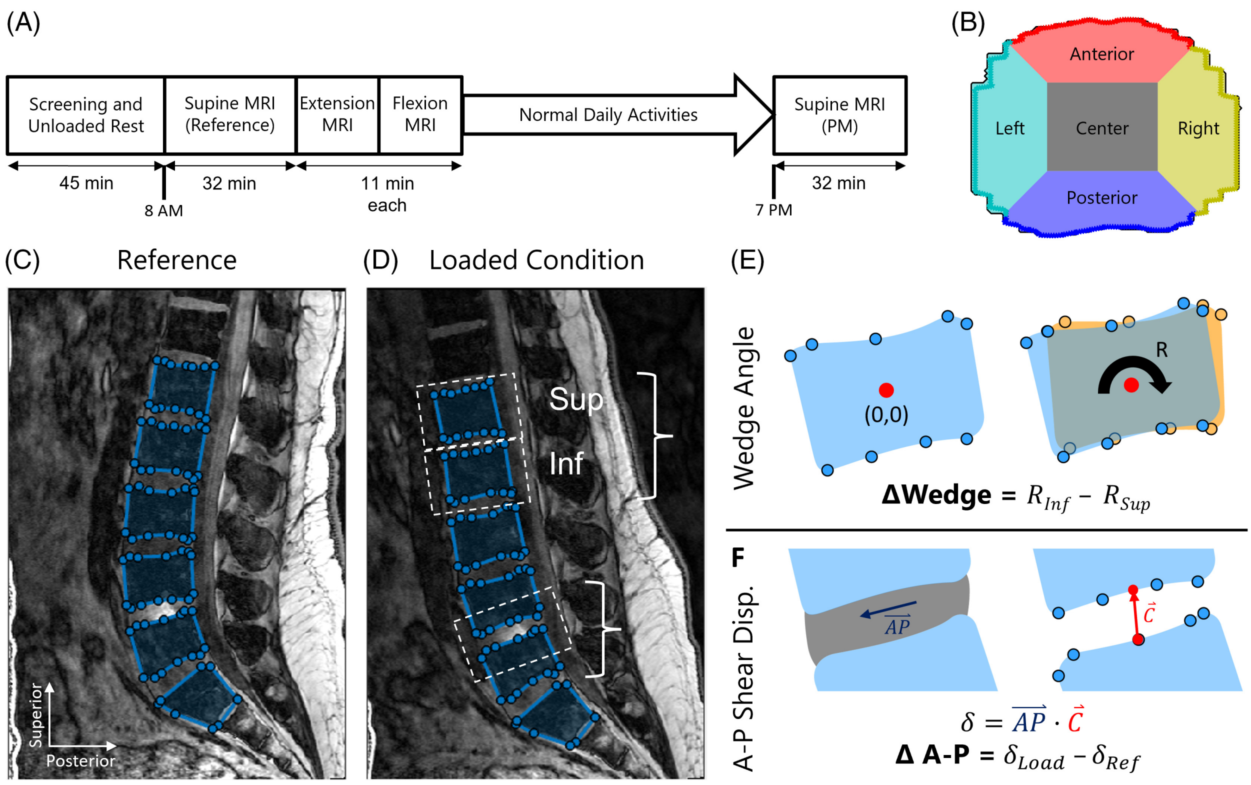

FIGURE 1 (A) Schematic of experiment timing. (B) Representative L4–L5 disc regions for in vivo strain. (C, D) Reference and Loaded MRI showing vertebral body bony landmark point sets, which are used for wedge angle and A-P shear calculation. L1 and L2 boxes represent wedge angle calculation examples, while L4–L5 box represents A-P shear example. (E) Schematic of wedge angle calculation. Red circle represents vertebra centroid. R = rotation between reference (blue) and loaded (orange) point sets. Change in wedge angle = difference in rotations of inferior and superior vertebra for each disc. (F) Schematic of A-P shear calculation. Gray = disc. AP = anterior–posterior basis vector of the disc. C = vector between inferior and superior endplate point set centroids

TABLE 1 MRI sequence parameters

Sequence	TR	TE	Resolution	Run time
T_1 FLASH	9.6 ms	3.7 ms	0.52 × 0.52 × 3.0 mm	11 min
T_2 CPMG	3000 ms	13.6, 27.2, …, 340 ms	0.6 × 0.6 × 5.0 mm	14.5 min
T_2 TSE	4540 ms	124 ms	0.49 × 0.49 × 5.0 mm	6 min

padded gurney with a pillow under their head (Figure 1A).[15,32,33] The morning MRI consisted of a Reference scan in the supine position followed by scans in Extension and Flexion postures. Bending postures were achieve using pads and pillows and each subject had as much bending as could be achieved within the constraints of their height (constrained by MRI bore diameter) and their physiological flexibility. The subject returned for a PM scan in the supine position to measure Diurnal effects. Between morning and evening scans, each subject wore an activity monitor (Pro-Fit) to track steps taken and were instructed to go about their day normally.

2.3 | Scanning protocol

Three MRI sequences were used for this study (Table 1): (1) a T_1w FLASH (Fast Low Angle Shot) sequence for disc strain and geometry, (2) a T_2 CPMG (Carr–Purcell Meiboom–Gill) for T_2 relaxation time measurement, and (3) a T_2w TSE (Turbo Spine Echo) for Pfirrmann grading. Images were taken in the sagittal plane. All three sequences were run during the Reference and PM conditions. Only the FLASH sequence was run in the Extension and Flexion positions because T_2 time, which is water-dependent, does not change with these posture conditions over the duration of the scanning time.[49]

2.4 | Data analysis

Several outcome measures were quantified as listed below and as described in detail in the following paragraphs (Table 2). Disc degeneration was evaluated using the Pfirrmann grading scale (from T_2 TSE) and T_2 relaxation time calculation (from T_2 CPMG).[3,7,45,46] Disc mechanical function was assessed from FLASH images, where axial

TABLE 2 Outcome measures, sequence utilized for measurement, and method of measurements

	Measure	Method	Sequence
Disc degeneration	Pfirrmann grade	Graders[3]	T_2 TSE
	T_2 time*	Noise corrected exponential fit[50]	T_2 CPMG
Disc mechanical function and geometry	In vivo strain*	Image registration[28–30,54]	T_1 FLASH
	Disc height	Mid-sagittal area/A-P width [New]	
	Disc volume	Manual segmentation[58]	
	ΔWedge angle*	Vertebral motion [New]	
	Cobb angle	Vertebral motion[59,60]	
	A-P shear displacement*	Vertebral motion [New]	

Note: Asterisk indicates primary measures of the study.

strain, change in disc wedge angle, and anterior–posterior (A-P) shear displacement were the primary measures. Axial strain was measured via image registration. Disc wedge angle and A-P shear were assessed in the midsagittal plane from vertebral motions. In addition, for comparison to literature, discs were segmented, the height and volume calculated, and strains quantified from these data. Cobb angle was also measured to validate change in disc wedge angles.

Pfirrmann grading was performed by three trained graders (KDM, JMP, and EJV) who reached a consensus on each disc's grade. A Pfirrmann grade of I indicates a healthy disc, while grade V indicates a completely collapsed (degenerated) disc.[3] T_2 time was calculated for a circular ROI in the center of the nucleus pulposus, as previously described, by fitting a noise-corrected exponential to the 25 echoes of the T_2 CPMG sequence.[50,51] The noise-corrected exponential fit is important because it has less bias and uncertainty when compared to traditional monoexponential fitting methods for tissues, such as the disc, that have low signal-to-noise ratio.[50] We chose T_2 time rather than T1ρ time because, while they are highly correlated and both influenced by water content, T_2 time is more widely available on MR scanners and does not require a special license.[52,53]

Axial disc strain was quantified using image registration between the 3D image volumes in the Reference MRI (supine morning scan) and the MRI acquired in the Flexion, Extension, and PM conditions. First, discs were manually segmented. Next, individual disc 3D volumes were created by cropping the region of each segmented disc plus a 5 mm margin from the full spine MRI dataset. The cropped image in each loaded condition (Flexion, Extension, and PM) was then registered to the Reference image (AM supine) using diffeomorphic deformable image registration with a $\sigma = 2$ pixels (1 mm) smoothing filter as regularization (ANTs open-source software).[28,30,54] Image registration quality was evaluated for all 240 registrations using Dice similarity coefficient (where a Dice of 0 means there was zero overlap of the objects, while 1 means perfect overlap of the objects), where the loaded image's manual disc segmentation was transformed to the Reference image via the calculated registration and then compared to the Reference image's manual disc segmentation. Dice coefficient was high for this study, indicating strong registrations (0.92 ± 0.03), comparable to the best of prior literature.[55,56]

The anatomic disc coordinate system was defined for each disc with its left–right axis the same as the left–right patient axis from the MRI scanner. Maintaining both this constraint and orthogonality, the A-P and axial (superior–inferior) axes were set to align as closely as possible with the second and third principal axes of the segmented disc volume determined via principal component analysis. The displacement of each voxel from the Reference to loaded states was obtained from the image registration in this disc coordinate system. Axial strain (i.e., strain in the disc's axial direction) was calculated for each point in the disc's axial plane. Starting at each point, rays were cast in the superior and inferior directions and the resulting intersections with the disc's superior and inferior boundaries (from the segmentation) were used as fiducial markers. Axial strain was thus calculated as (change in disc height)/(original disc height) for every point across the disc's axial plane. To analyze average axial strain by disc region, each disc was divided into five regions (anterior, posterior, central, left, and right; Figure 1B). This axial disc strain calculated using image registration is defined as "in vivo disc strain" throughout this article.

In addition to in vivo disc strain, disc height and volume from segmentations were also measured to compare to previous work. Disc height was calculated from the mid-sagittal slice of the FLASH image by dividing the area of the disc over the anterior to posterior width.[57] Volume was measured via manual segmentation of all slices of the FLASH image.[58] The Midsagittal Height Strain and Volume Strain were calculated as the percent change in the height or volume, respectively, compared to the Reference state for each loading condition.

Change in disc wedge angle was calculated for each level using a custom program (MATLAB 2021a, MathWorks, Natick, MA). A point set comprised of bony landmarks on the vertebral endplates were selected in the midsagittal slice of the FLASH image in each of the four loading conditions (Reference, Flexion, Extension, PM; Figure 1C,D). Each landmark was chosen consistently across all four conditions. The centroid of the point set was found for each vertebra in each loading condition and set to the origin (Figure 1E). Next, the rotation matrix defining the rigid rotation of each point set between the loaded condition and the Reference was calculated for each vertebrae using a least squares solution based on singular value decomposition (Figure 1E). The angular rotation (R) was then found from this rotation matrix. The change in wedge angle (ΔW) of each disc was calculated as the difference in *R* between the inferior and superior vertebrae of the disc of interest, $\Delta W = R_{\mathrm{inf}} - R_{\mathrm{sup}}$ (Figure 1E). Additionally, Cobb angle was measured in the mid-sagittal plane as the angle between a line along the inferior endplate of the L1 vertebra and the superior endplate of the S1 vertebra.[59,60] Change in Cobb angle was then calculated by subtracting the Cobb angle in the Reference condition from the loaded condition to measure the amount of bending induced. For validation, the change in Cobb angle was compared to the sum of the ΔW for all the discs in the same spine. For both measures, the apex of the angle was posterior to the disc, such that a positive change indicates extension, and a negative change indicates flexion.

A-P shear displacement of the superior vertebra relative to the inferior vertebra for each disc was also calculated using a custom program (MATLAB R2021a, MathWorks, Natick, MA). First, principal components analysis (PCA) was applied to the disc segmentation to determine the A-P basis vector ($\overrightarrow{AP}$) of each disc in each loading condition (Figure 1F). Next, the point set of vertebral endplate points described above for wedge angle calculation were split into superior and inferior endplates, and the centroid of each endplate was found (Figure 1F). The vector ($\overrightarrow{C}$) across the disc, from the centroid of the inferior to superior endplate, was then found. Next, the A-P distance between endplate centroids (δ) was calculated as the dot product of the A-P basis vector and the vector across the disc: $\delta = \overrightarrow{AP} \cdot \overrightarrow{C}$. Finally, the A-P shear displacement (ΔA-P) was calculated as the difference in δ between the Reference and the loaded condition: $\Delta A - P = \delta_{\mathrm{Load}} - \delta_{\mathrm{Ref}}$ (Figure 1F). Anterior motion was defined as positive and posterior motion as negative.

2.5 | Statistical analysis

All outcome measures were first checked for outliers, normality, equal variance, and for means different from zero when split by level and sex (5 lumbar levels $\times$ 2 sexes $=$ 10 groups). Outliers were defined as data points outside of the first and third quartiles by more than 1.5 times the inter-quartile range and removed from further analysis (average <2 out of 80 discs removed per outcome measure). Normality was checked via Shapiro–Wilk's test, and all level and sex pairs were normal for all primary measures. The only non-normal group was the male L2–L3 in mid-sagittal height strains under Diurnal loading, but it was not removed because statistical outcomes were not altered with removal. Equal variance was checked via Levene's test. Only two measures had unequal variance. Both were then checked via Friedman's test which did not show significance. Additionally, model residuals were checked and were normally distributed, so model interpretation was accepted. To assess the detectability of measurements, the changes from Reference to loaded conditions were compared to zero via *t*-test with the null hypothesis that the mean changes equal zero (difference from zero test). We found ample detectability of our primary measures with each having multiple level and sex pairs different from zero.

Statistical analyses tested for the effect of lumbar level and sex on primary outcome measures and for associations between outcome measures. Outcome measures were evaluated using mixed-effect models with the following effects: level (fixed), sex (fixed), subject (random), level*sex, and subject*level where sex was nested in subject. When the effect of level or sex was significant, Tukey HSD test was used to assess differences between individual groups. For Diurnal loading, for in vivo strain, the effect of disc region as a fixed effect was also added to the model above. In Flexion and Extension, only the anterior and posterior regions were considered for in vivo strain for statistical analysis as the center, right, and left regions lie along the axis of bending. Associations between outcome measures and (1) disc degeneration, (2) disc functional measures, or (3) steps walked between Reference and PM sessions were explored using a linear model of the following design: Measure1 $\sim$ Measure2 $+$ Level. This allowed for associations between measures to be tested with the level of effect being controlled for. Significance level for all tests was set at $p < 0.05$. With a sample size of 16 subjects, our study is powered to detect an effect size of 0.9 with a power of 0.80.

3 | RESULTS

Disc degeneration was characterized by Pfirrmann grade and T_2 time. Of the 80 discs in the study, 26 were Pfirrmann grade I, 40 grade II, 6 grade III, and 8 grade IV. No grade V was present in this cohort. Higher Pfirrmann grades were more common at lower lumbar levels (Figure 2A). T_2 time did not vary by level (Figure 2B). T_2 and Pfirrmann grade correlated to one another ($R^2 = 0.61$, $p < 0.0001$) where higher grades had lower T_2 (Figure 2C). There were no differences in disc degeneration by sex. Additionally, only one outcome measure was significantly impacted by sex (posterior strain in extension), so only level effect will be discussed in the rest of the results (Table S1).

3.1 | Flexion loading

3.1.1 | In vivo strain

Flexion bending produced significant changes in anterior and posterior disc axial strain as described below (Figure 3A). Anterior strain was compressive and there was a significant effect of level ($p = 0.001$, Figure 4A), where strains increased at lower lumbar levels, except for L5–S1. L1–L2 (−2.2% strain) was significantly less compressive than L3–L4 (−6.2% strain) and L4–L5 (−7.5% strain). Posterior strain was tensile, trending toward significance with larger strains in lower lumbar levels ($p = 0.06$, Figure 4B); posterior tensile axial strain increased between L1–L2 (4.2% strain) and L4–L5 (7.9%) and L5–S1 (7.8%).

3.1.2 | Change in wedge angle (ΔW)

Flexion caused a decrease in wedge angle, where level has a significant effect ($p = 0.001$, Figure 4C). Lower levels had a larger decrease in wedge angle than upper levels with significant differences between the bottom two levels (L4–L5–5.7°) and each of the top three levels (L1–L2–1.9°). We compared the change in Cobb

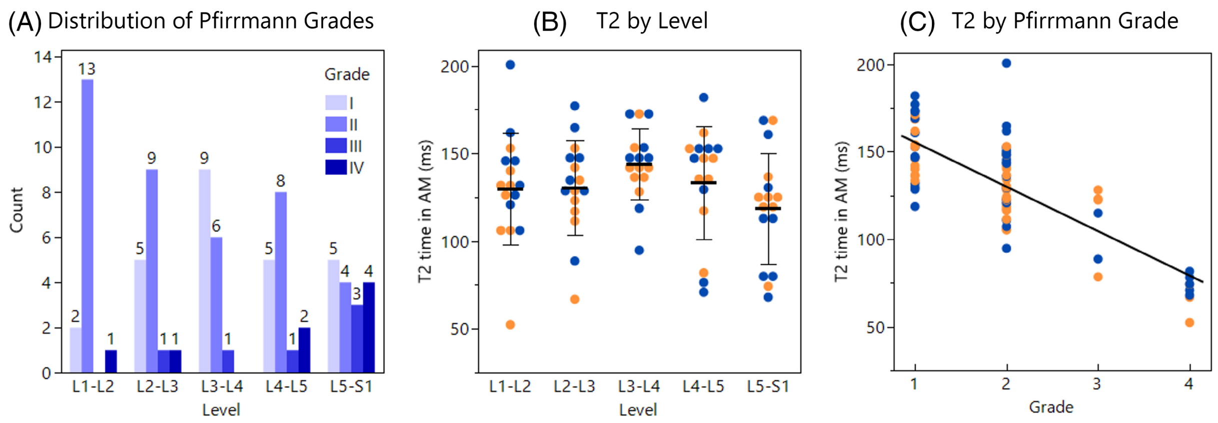

FIGURE 2 (A) Distribution of Pfirrmann grade by level. Lower levels have more degenerated discs. (B) T_2 times in the AM by level for all discs. There was no level effect on T_2 in the AM. (C) Correlation of T_2 to Pfirrmann. Higher Pfirrmann grade is related to lower T_2. Blue = male, orange = female

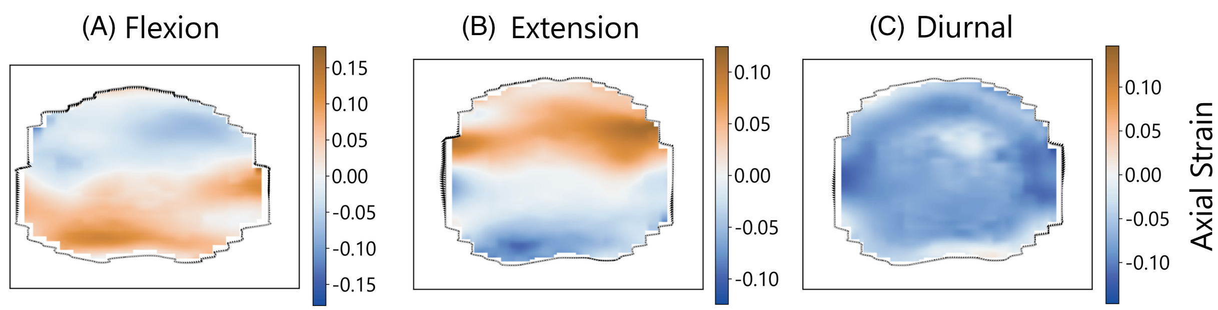

FIGURE 3 Representative axial strain maps of L4–L5 discs after (A) Flexion, (B) Extension, and (C) Diurnal loading. Flexion induces compression in the anterior of the disc and tension in the posterior. Extension induces the opposite. Diurnal loading causes compression across the full disc

angle to the sum of ΔW for each level for each spine. The average difference between Cobb angle and the sum of ΔW was only $-0.19° \pm 1.35°$ and not significantly different from each other. This agreement validates the measurement method for ΔW. Cobb angle changed $-19.58° \pm 6.74°$ due to Flexion. There was also no correlation between Reference Cobb angle and change in Cobb angle with Flexion ($p = 0.56$), indicating that the amount of flexion achieved is not related to their supine Reference curvature. Change in wedge angle normalized by the total Cobb angle change can be found in Table S5.

3.1.3 | A-P shear displacement (ΔA-P)

Flexion caused A-P shear displacement which had a significant effect of level ($p = 0.0001$, Figure 4D). Flexion caused a gradient of anterior to posterior motion of the superior vertebra relative to the inferior vertebra. L1–L2 (2.6 mm) was greater than L3–L4 (1.0 mm), L4–L5 (−0.6 mm), L5–S1 (−1.8 mm). L2–L3 (1.8 mm) and L3–L4 were greater than L4–L5 and L5–S1. The direction of A-P shear shifted from anterior in upper levels to posterior in lower levels.

3.1.4 | Correlations with disc degeneration and within disc mechanical function

We ran correlations between the mechanical outcome measures and disc T_2, a marker of disc degeneration, in the reference position (Figure 5A). For Flexion, all primary outcome measures correlated with T_2 ($p < 0.05$ for anterior and posterior strain, Wedge angle change, A-P shear displacement). Discs with lower T_2 had more axial strain in the anterior or posterior regions. The two strongest correlations were between change in wedge angle ($R^2 = 0.38$, lower $T_2 \sim$ higher ΔW) and A-P shear displacement ($R^2 = 0.52$, lower $T_2 \sim$ posterior ΔA-P). There were significant correlations between the change in wedge angle and the strains in the anterior and posterior regions of the disc when controlled for level ($p < 0.05$, $R^2 > 0.36$). There were no significant correlations between A-P shear displacement and disc strains or change in wedge angle when controlled for level ($p > 0.33$).

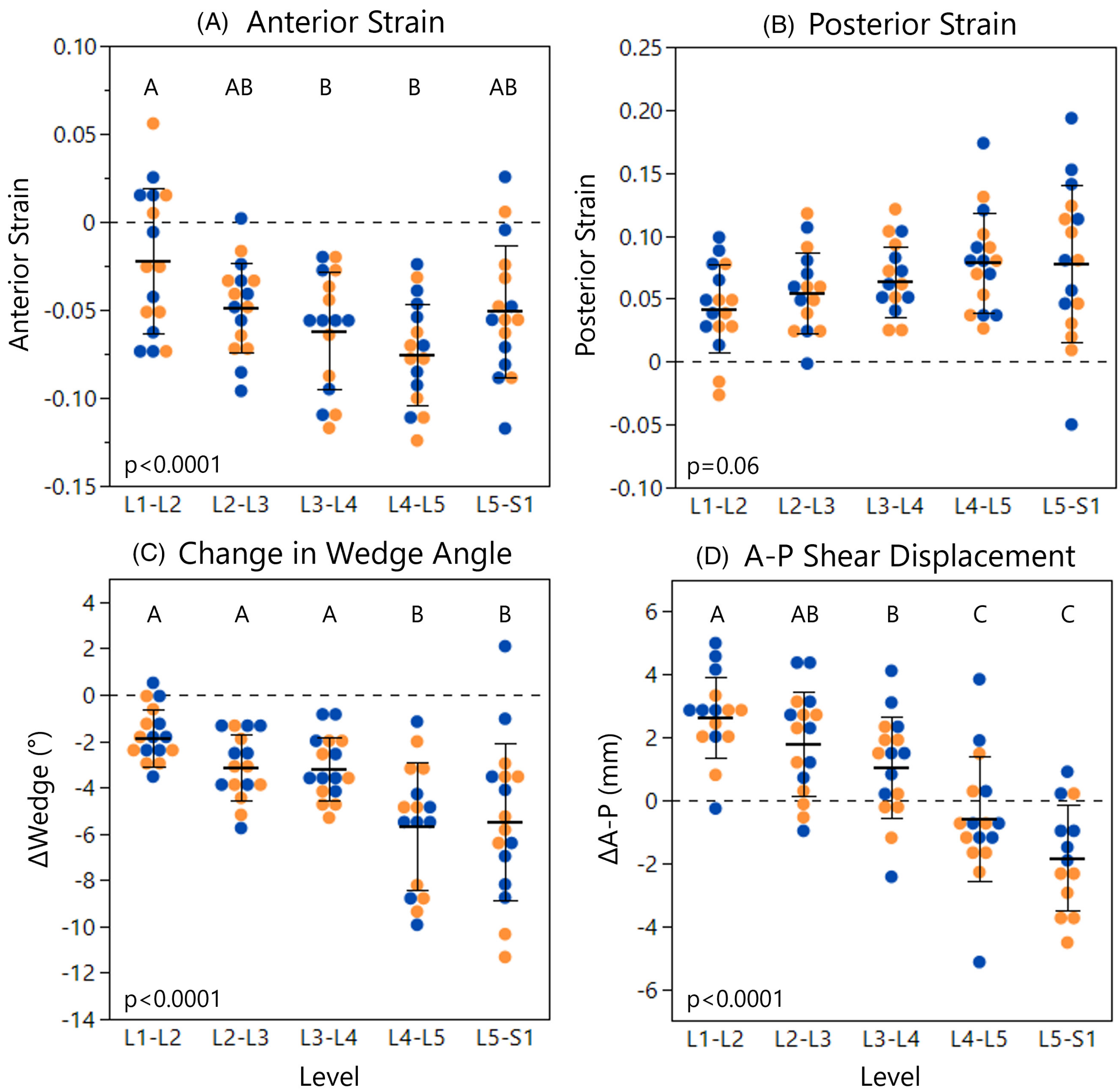

FIGURE 4 Effects of Flexion on (A) disc strain in the anterior region, (B) disc strain in the posterior region, (C) change in wedge angle, and (D) A-P shear. Mean and standard deviation shown by black lines. Outliers are removed. Blue = male, orange = female. Flexion caused compressive strain in the anterior region of the disc and tensile strain in the posterior. Wedge angle change increased with lower lumbar level. Superior vertebrae moved anteriorly at cranial levels and posteriorly at caudal levels. *p*-values indicate level effect. All outcome measures had significant effects with level, besides a trend in posterior strain. Levels not sharing a letter are significantly different from one another

3.2 | Extension loading

3.2.1 | In vivo strain

Extension caused large strains in the anterior and posterior regions of the disc (Figure 3B). Anterior strain was tensile and there was a significant effect of level, with larger strains in the upper lumbar levels ($p = 0.0001$, Figure 6A). L1–L2 (7.6% strain) and L2–L3 (7.3% strain) were significantly higher than L4–L5 (4.1% strain) and L5–S1 (2.3% strain). Posterior strain was compressive with an effect of level ($p = 0.008$, Figure 6B) though no levels were statistically different from one another in the post hoc test. There were again larger strains in upper lumbar levels. Posterior strains in extension tended to decrease from upper levels, L1–L2 and L2–L3 (−3.1% and −5.3%, respectively), to lower levels, L5–S1 (−0.8%). Posterior strain in extension was the only measure influenced by sex, where strain was higher for females (−3.7%) compared to males (−1.9%, $p = 0.04$).

3.2.2 | Change in wedge angle (ΔW)

Extension increased the wedge angle and was affected by level ($p = 0.003$, Figure 6C). The ΔW was larger at upper lumbar levels, with L1–L2 (2.6°) and L2–L3 (3.2°) different from L5–S1 (0.9°).

The average difference between Cobb angle and the sum of ΔW was only −0.59° ± 2.12°; this showed good agreement between

(A) Flexion

	T_2	Anterior Strain	Posterior Strain	ΔWedge	ΔA-P
T_2		0.28 (0.03)	0.17 (0.03)	0.38 (0.01)	0.52 (0.03)
Anterior Strain			0.45 (0.0001)	0.44 (0.0001)	0.23 (0.33)
Posterior Strain				0.36 (0.0001)	0.11 (0.40)
ΔWedge					0.3 (0.40)
ΔA-P					

(B) Extension

	T_2	Anterior Strain	Posterior Strain	ΔWedge	ΔA-P
T_2		0.35 (0.55)	0.21 (0.85)	0.21 (0.50)	0.47 (0.91)
Anterior Strain			0.39 (0.09)	0.43 (0.002)	0.36 (0.70)
Posterior Strain				0.36 (0.02)	0.07 (0.97)
ΔWedge					0.24 (0.32)
ΔA-P					

(C) Diurnal

	T_2	Strain	Change in T_2	ΔWedge	ΔA-P
T_2		0.02 (0.42)	0.19 (0.0002)	0.11 (0.91)	0.18 (0.54)
Strain			0.08 (0.04)	0.01 (0.79)	0.01 (0.86)
Change in T_2				0.14 (0.46)	0.11 (0.57)
ΔWedge					0.13 (0.90)
ΔA-P					

FIGURE 5 Correlation matrices for primary outcome measures in (A) Flexion, (B) Extension, and (C) Diurnal Loading. Top number in each cell is R^2, and bottom number in parentheses is p-value for association between measures after controlling for level effect. Green shading = $p < 0.05$. Yellow shading = $p < 0.1$. (A) Flexion showed many statistically significant associations between outcomes measures, including all mechanical function measures relating to T_2. (B) Extension showed some relations between ΔW and strain. (C) Diurnal Loading did not show any associations between mechanical function outcome measures

measures. Cobb angle changed 9.92° ± 2.71° due to extension. There was also no relationship between Reference Cobb angle and change in Cobb angle with Extension ($p = 0.24$), indicating that the amount of extension achieved is not related to their supine Reference curvature. Change in wedge angle normalized by the total Cobb angle change can be found in Supplemental Table 5.

3.2.3 | A-P shear displacement (ΔA-P)

Extension caused A-P shear displacement with a significant effect of level ($p = 0.0001$, Figure 6D). From cranial to caudal, flexion caused a gradient of posterior to anterior motion of the superior vertebra. L1–L2 (−0.7 mm) and L2–L3 (−0.4 mm) were different from L3–L4 (0.8 mm), L4–L5 (1.8 mm), L5–S1 (1.3 mm). Also, L3–L4 was different from L4–L5.

3.2.4 | Correlations with disc degeneration and within disc mechanical function

We ran correlations between the outcome measures and disc T_2 in the reference position (Figure 5B). For extension, no outcome measures correlated to T_2 ($p > 0.49$). There were significant correlations between ΔW and strains in the anterior and posterior regions ($p < 0.05$, $R^2 > 0.36$). There were no significant correlations between A-P shear displacement and disc strains or change in wedge angle ($p > 0.32$).

3.3 | Diurnal loading

There was a wide range of steps walked by the subjects between the AM and PM scanning sessions (6084 ± 2234 steps, 1290–9410 steps). There were no correlations of any outcome measures for any loading condition to steps walked. T_2 decreased from the Reference value in the morning to the evening PM value by an average of 8.5 ± 18.4 ms, which was significantly different from 0 ($p < 0.0001$). There was no effect of level ($p = 0.68$) on change in T_2 from Reference to PM (Figure 7A).

3.3.1 | In vivo strain

Diurnal loading caused a homogenous compressive strain across the disc, with no significant difference between regions ($p = 0.72$, Figure 4C, Table S3) and no significant effect of level ($p = 0.79$, Figure 7B). The mean Diurnal axial strain was −5.1% ± 1.9% ($n = 80$) across all levels and sexes.

We also measured strain based on change in height and change in volume in order to compare to previous studies (Table S2). We expect these measures to be less accurate than the in vivo strain based on image registration because the change in height is only at the midsagittal plan and the volume measurement is less accurate at the lateral boundaries where scanning resolution is larger. Like in vivo strain, there was no effect of level on either measure ($p = 0.91$ for midsagittal height strain and $p = 0.21$ for volumetric strain). Midsagittal height strain across all levels was −7.03% ± 3.36%. Volumetric strain across all levels was −7.02% ± 2.96%. In vivo strain from image registration was significantly correlated with both midsagittal height strain ($p < 0.0001$, $R^2 = 0.26$) and volumetric strain ($p = 0.037$, $R^2 = 0.13$), as expected since they are intended to represent the same effect.

3.3.2 | Change in wedge angle (ΔW) and A-P shear displacement (ΔA-P)

Change in Wedge angle and A-P Shear Displacement were both very small in Diurnal loading, with only a few level and sex pairs different

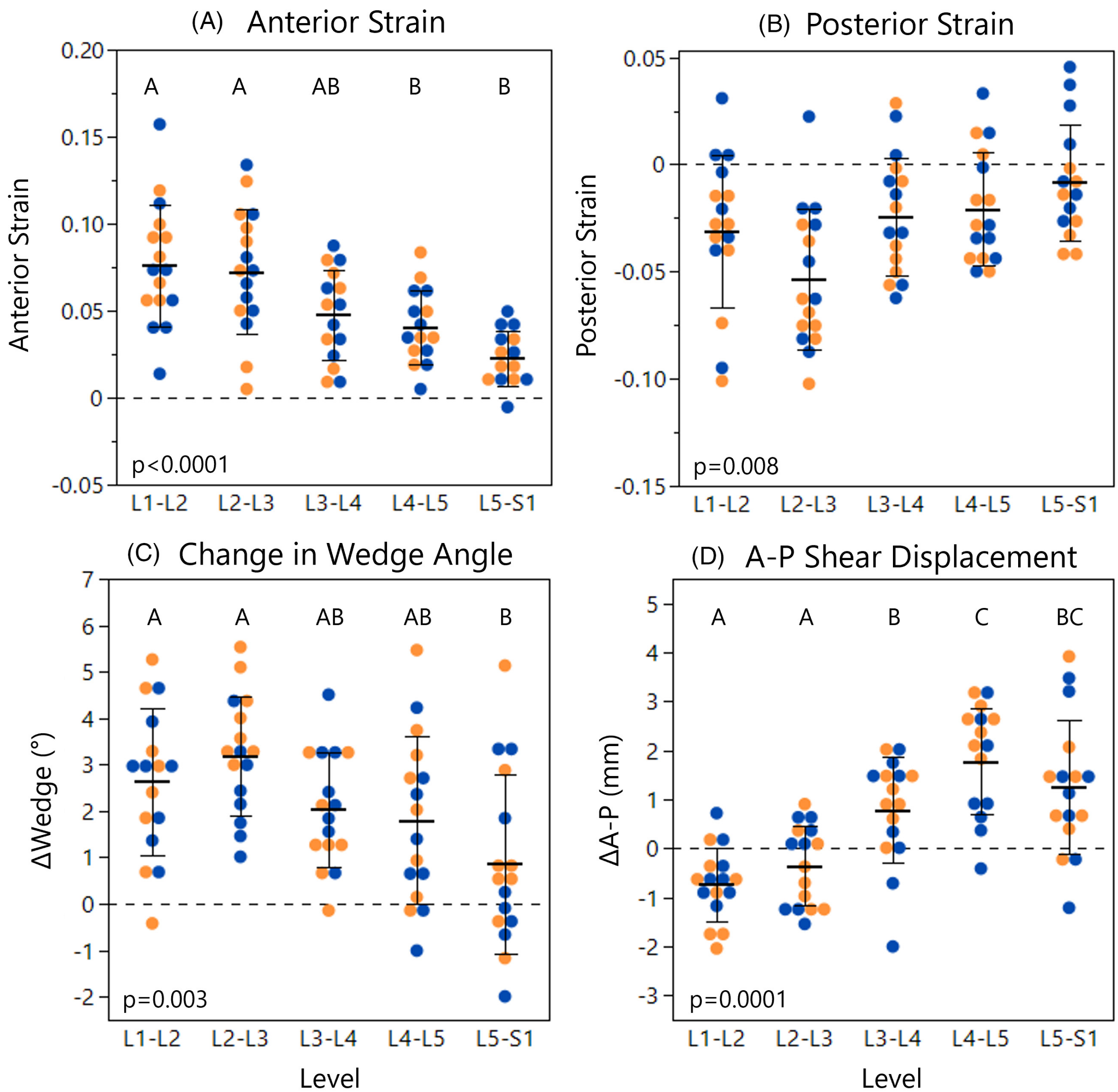

FIGURE 6 Effects of Extension on (A) disc strain in the anterior region, (B) disc strain in the posterior region, (C) change in wedge angle, and (D) A-P Shear. Mean and standard deviation shown by black lines. Outliers are removed. Blue = male, orange = female. Extension caused tensile strain in the anterior region of the disc and compressive strain in the posterior. Wedge angle change was highest at upper lumbar levels. Superior vertebrae moved posteriorly at cranial levels and anteriorly at caudal levels. *p* values indicate level effect. All outcome measures had significant effects with level. Levels not sharing a letter are significantly different from one another

from zero (ΔW: Female L1–L2 and Male L2–L3, ΔA-P: Female L1–L2). ΔW did not vary with Diurnal loading (average per level <1°). Diurnal changes in wedge angle showed a trend by level ($p = 0.06$, Figure 7C), where ΔW tended to change from L1–L2 (−0.8°) to L5–S1 (0.0°). Cobb angle changed −0.28° ± 3.11°. A-P shear displacement was small after Diurnal loading (average per level <0.5 mm). Diurnal changes in ΔA-P varied by level ($p = 0.01$, Figure 7D), but no levels were statistically different from others. More upper levels had anterior shear displacement (L1–L2 0.4 mm), while lower levels had posterior shear displacement (L5–S1–0.3 mm).

3.3.3 | Correlations with disc degeneration and within disc mechanical function

We ran correlations between the outcome measures and the Reference T_2 (Figure 5C). No outcome measures were correlated to T_2 from the Reference scan in the morning. However, there was a significant correlation between diurnal strain and diurnal change in T2 ($p = 0.04$, $R^2 = 0.08$). There were no correlations between disc mechanical measures: disc strain, change in wedge angle, and A-P shear displacement ($p > 0.05$).

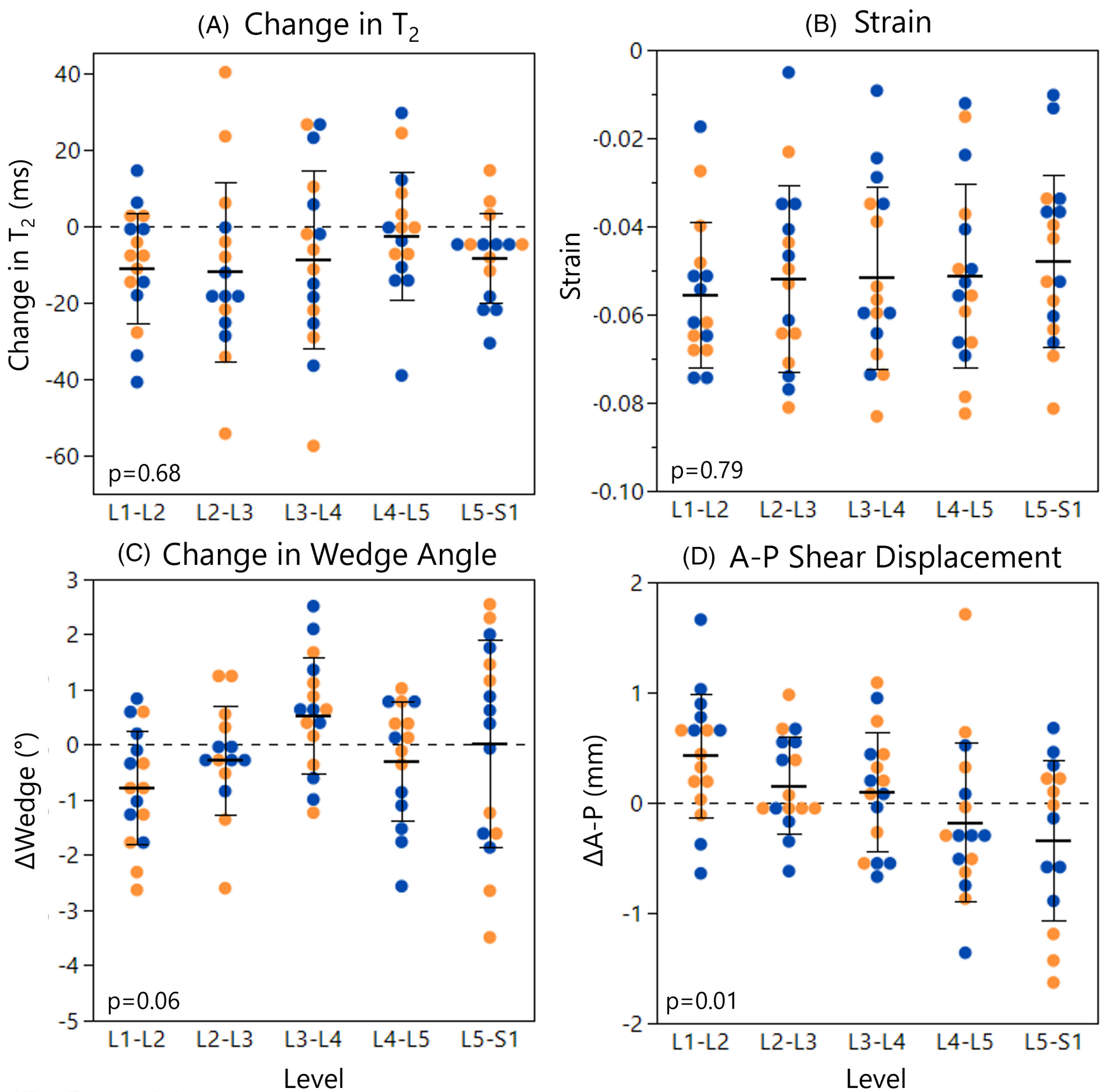

FIGURE 7 Effects of Diurnal loading on (A) change in T_2, (B) average disc strain across all regions, (C) change in wedge angle, and (D) A-P shear. Mean and standard deviation shown by black lines. Outliers are removed. Blue = male, orange = female. Diurnal loading caused compressive strain across the disc. T_2 time decreased throughout the day with loading. There were little changes in wedge angle or A-P translation with diurnal loading, but both measures were affected by level. *p* values indicate level effect. Levels not sharing a letter are significantly different from one another

4 | DISCUSSION

In this study, we measured in vivo disc axial strain, wedging, and A-P shear due to Flexion, Extension, and Diurnal loading using MRI in a young asymptomatic population. Our loading methods were sufficient to create measurable disc changes, and we are the first to report in vivo strains in bending posture in the lumbar spine. Flexion and Extension produced large anterior and posterior disc strains, changes in wedge angle, and A-P shear displacement that depended on of spinal level. It is interesting that Flexion and Extension caused a gradient across levels, where the direction of the gradients was opposite between Flexion and Extension. For example, Flexion caused higher strains in the lower lumbar levels (both tensile and compressive), while Extension caused higher strains in the upper lumbar. Additionally, Flexion caused higher magnitudes of changes in all three measures (strain, change in wedge angle, and A-P shear displacement) compared to Extension. We found that level often influenced disc mechanical function, particularly in bending, but sex almost never did. This influence of level on disc mechanics is likely due to the effects of disc geometry and the center of rotation across the levels.

Experimentally, subjects can achieve greater levels of Flexion than Extension, therefore, Flexion may be the most informative loading condition to study disc mechanics and the effect of degeneration. We observed that Flexion produced the highest magnitude of mechanical outcome measures, and there were stronger correlations between these mechanics and nucleus pulposus T_2. This larger contribution to joint mechanics of Flexion compared to Extension or Diurnal loading is likely due to the spine and disc anatomy, the relative contribution of the facet joints, and the line of action of loads relative to the disc center of rotation. Functional spinal unit motion involves the interplay of the disc and the facets. It is likely that the disc plays a more prominent role in Flexion, whereas the facets have a greater relative contribution in Extension. In Extension, the contact of the facet joints limits the range of motion that can be applied, resulting in smaller changes than in Flexion where the facets have less impact. Similarly, facet joint contact also supports axial compression in Diurnal loading, reducing potential disc strains. Moreover, in Diurnal loading, the compressive loading is along the spine center of rotation, with little off-axis loading, resulting in small changes in wedge angle and A-P shear displacement. Not only were mechanical changes largest in Flexion, T_2, a measure of disc degeneration, correlated with all mechanical measurements in Flexion but very few in Extension or Diurnal loading. Additionally, herniation and low back pain are often associated with Flexion bending, and in our study, we saw that Flexion caused very large tensile strains in the posterior of the disc where many herniations and annulus fibrosus failures occur. It should be noted that the reference condition is not "an unloaded, zero strain" condition, because, in the reference condition, the disc is under an unknown magnitude of prestrain due to muscle force, body weight, and internal pressure. Therefore, while our results report that some disc regions are in tension relative to the reference loaded condition, it is most likely that these disc regions are rather in less compression relative to the actual disc strain. Overall, these observations suggest that Flexion is the more important loading condition to study in vivo disc mechanical function. It is important to note that our bending measures were made in the AM, and it has been reported that spine flexibility, intradiscal pressure, and facet joint contact are all altered by diurnal variation.[61]

Diurnal loading caused *homogeneous* compressive strains across the disc that was not level dependent and were not correlated with the Reference T_2 time. Our strains (−4.8% to −5.5% mean strain) and lack of level-dependence generally agree with Martin et al. (−6% to −8% mean strain), although our strains were slightly smaller.[32] This strain difference is likely not a meaningful one[32] and could be related to difference in subject populations. In contrast, our strains were homogenous, with no regional difference, whereas in Martin et al., strains were higher in the posterior outer AF region.[32] There are a few possible explanations for this difference. First, since the posterior outer AF has a small disc height, a higher strain could occur due to $\delta L/L_0$, where initial L_0 is small. Alternatively, the large number of regions and therefore statistical comparisons could lead to a false positive or the large in-plane voxel size (1 × 1 mm in[32] vs. 0.5 × 0.5 mm in current study) could contribute to measurement error. Therefore, although our strain maps and statistical analyses suggest homogenous strains in Diurnal loading, it remains to be determined whether the posterior outer AF has a larger axial strain than the rest of the disc. Strain measurements based on changes in volume also agreed between studies (−6.1% to −8.1% in current study compared to −5.4% to −8.5%[32]). Overall, it is interesting to know the in vivo compressive strain due to Diurnal loading, because physiological compression strains alone are unlikely to initiate failure (e.g., herniation), and because small changes in ΔW and ΔA-P were observed, and no correlation with level or T_2 (e.g., degeneration) were observed, consistent with other studies.[31,32] We conclude that Diurnal loading is less informative to assess disc mechanical function than Flexion or Extension.

We explored the effects of sex, body mass index (BMI), and steps walked on disc mechanics. There were no sex-related differences in disc mechanics in the young population in this study, except for the posterior strain in extension. While in vivo disc mechanics in an older population remain unknown, there are sex differences in both degenerative grade and low back pain for older populations compared to younger ones, where older populations exhibit a larger difference between males and females than younger ones.[37–40] Therefore, future work will continue to explore the potential of sex differences in disc mechanics with age. BMI was not related to any outcome measures, although our subjects did not span a large range of BMIs. The difference in weight between males and females in our study was 31 pounds, but the BMI difference was <0.3, so while the males were heavier overall, the ratio of height to weight was similar. Steps walked between the morning Reference and PM scans had large variability but did not impact mechanics in Diurnal loading. This suggests, consistent with other studies,[31–33] that steps walked does not cause important disc compression above that experienced during normal activities of daily living such as sitting and standing.

There are some limitations to this study. First, wedge angle and A-P shear displacement were calculated in the mid-sagittal plane and not using the full vertebral volume. Since the vertebrae are rigid and healthy discs are expected to have lateral symmetry in geometry and mechanics, we expect midsagittal plane measurements to capture the overall behavior of the spine, however, if a disc were asymmetric, then the midsagittal measurement would not account for this. Second, the amount of Flexion and Extension bending was variable and limited by the individual's flexibility and limited space inside the MRI bore. It was found, however, that there was no correlation between the change in Cobb angle (in Flexion or Extension) and subject height or BMI, suggesting that an individual's ability to fit inside the MRI bore was not the defining factor in the amount of induced Flexion or Extension. This study focuses on static loading and does not explore changes with cyclic loading. Finally, although we did not calculate accuracy of the measures, similar methods in prior work have shown that the accuracy is approximately 10% of voxel size.[33]

In conclusion, this study established novel methods to measure disc strains and deformations resulting from Flexion, Extension, and Diurnal loading using noninvasive MRI of a young, healthy population. We recommend Flexion as the more important loading condition, as disc mechanics measured during Flexion were larger and more strongly related to degeneration than measures from Extension or Diurnal loading. Importantly, spinal level had a significant effect on many mechanical measures, but sex and number of steps walked did not. These results provide critical baseline data to compare in future work with disc mechanical function in older populations and low back pain patients.

AUTHOR CONTRIBUTIONS

Kyle D. Meadows and Harrah R. Newman contributed to experiments for the study. Kyle D. Meadows, John M. Peloquin, Peter Cauchy, and Harrah R. Newman contributed to analysis of the study. Kyle D. Meadows, John M. Peloquin, Edward J. Vresilovic, and Dawn M. Elliott contributed to study design and to results interpretation. All authors contributed to writing the manuscript and have read and approved submission.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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REFERENCES

1. Wu A, March L, Zheng X, et al. Global low back pain prevalence and years lived with disability from 1990 to 2017: estimates from the global burden of disease study 2017. *Ann Transl Med*. 2020;*8*(6):299. doi:10.21037/atm.2020.02.175
2. Murray CJL, Atkinson C, Bhalla K, et al. The state of US health, 1990–2010: burden of diseases, injuries, and risk factors. *JAMA*. 2013;*310*(6):591-608. doi:10.1001/jama.2013.13805
3. Pfirrmann CWA, Metzdorf A, Zanetti M, Hodler J, Boos N. Magnetic resonance classification of lumbar intervertebral disc degeneration. *Spine (Phila, PA 1976)*. 2001;*26*(17):1873-1878. doi:10.1097/00007632-200109010-00011
4. Davies BM, Atkinson RA, Ludwinski F, Freemont AJ, Hoyland JA, Gnanalingham KK. Qualitative grading of disc degeneration by magnetic resonance in the lumbar and cervical spine: lack of correlation with histology in surgical cases. *Br J Neurosurg*. 2016;*30*(4):414-421. doi:10.3109/02688697.2016.1161174
5. Luoma K, Vehmas T, Riihimäki H, Raininko R. Disc height and signal intensity of the nucleus pulposus on magnetic resonance imaging as indicators of lumbar disc degeneration. *Spine*. 2001;*26*(6):680-686.
6. Kettler A, Wilke HJ. Review of existing grading systems for cervical or lumbar disc and facet joint degeneration. *Eur Spine J*. 2006;*15*(6):705-718. doi:10.1007/s00586-005-0954-y
7. Marinelli NL, Haughton VM, Anderson PA. T2 relaxation times correlated with stage of lumbar intervertebral disk degeneration and patient age. *Am J Neuroradiol*. 2010;*31*(7):1278-1282. doi:10.3174/ajnr.A2080
8. Bogduk N, Aprill C, Derby R. Lumbar discogenic pain: state-of-the-art review. *Pain Med*. 2013;*14*(6):813-836. doi:10.1111/pme.12082
9. Scuderi GJ, Brusovanik G v, Golish SR, et al. A critical evaluation of discography in patients with lumbar intervertebral disc disease. *Spine J*. 2008;*8*(4):624-629. doi:10.1016/j.spinee.2006.10.005
10. Massie WK, Stevens DB. A critical evaluation of discography. *J Bone Joint Surg Am*. 1967;*49*:1243-1244.
11. O'Connell GD, Sen S, Elliott DM. Human annulus fibrosus material properties from biaxial testing and constitutive modeling are altered with degeneration. *Biomech Model Mechanobiol*. 2012;*11*(3–4):493-503. doi:10.1007/s10237-011-0328-9
12. Johannessen W, Elliott DM. Effects of degeneration on the biphasic material properties of human nucleus pulposus in confined compression. *Spine (Phila Pa 1976)*. 2005;*30*(24):E724-E729. doi:10.1097/01.brs.0000192236.92867.15
13. Mimura M, Panjabi MM, Oxland TR, Crisco JJ, Yamamoto I, Vasavada a. Disc degeneration affects the multidirectional flexibility of the lumbar spine. *Spine*. 1994;*19*:1371-1380. doi:10.1097/00007632-199406000-00011
14. Farfan H, Cossette J, Robertson G. The effects of torsion on the lumbar intervertebral joints: the role of torsion in the production of disc degeneration. *J Bone Joint Surg*. 1970;*52*(3):468-497.
15. O'Connell GD, Jacobs NT, Sen S, Vresilovic EJ, Elliott DM. Axial creep loading and unloaded recovery of the human intervertebral disc and the effect of degeneration. *J Mech Behav Biomed Mater*. 2011;*4*(7):933-942. doi:10.1016/j.jmbbm.2011.02.002
16. DeLucca JF, Cortes DH, Jacobs NT, Vresilovic EJ, Duncan RL, Elliott DM. Human cartilage endplate permeability varies with degeneration and intervertebral disc site. *J Biomech*. 2016;*49*(4):550-557. doi:10.1016/j.jbiomech.2016.01.007
17. Cortes DH, Han WM, Smith LJ, Elliott DM. Mechanical properties of the extra-fibrillar matrix of human annulus fibrosus are location and age dependent. *J Orthop Res*. 2013;*31*(11):1725-1732. doi:10.1002/jor.22430
18. Cortes DH, Jacobs NT, DeLucca JF, et al. Elastic, permeability, and swelling properties of human intervertebral disc tissues: a benchmark for tissue engineering. *J Biomech*. 2014;*47*(9):2088-2094. doi:10.1016/j.jbiomech.2013.12.021
19. Iatridis JC, Setton LA, Foster RJ, et al. Degeneration affects the anisotropic and non-linear behaviors of human anulus fibrosus in compression. *J Biomech*. 1998;*31*(6):535-544. doi:10.1016/S0021-9290(98)00046-3
20. Acaroglu ER, Iatridis JC, Setton LA, et al. Degeneration and aging affect the tensile behavior of human lumbar anulus fibrosus. *Spine*. 1995;*20*(24):2690-2701. doi:10.1097/00007632-199512150-00010
21. Fujita Y, Duncan NA, Lotz JC. Radial tensile properties of the lumbar annulus fibrosus are site and degeneration dependent. *J Orthop Res*. 1997;*15*(6):814-819. doi:10.1002/jor.1100150605
22. Keller TS, Spengler DM, Hansson TH. Mechanical behavior of the human lumbar spine. I. Creep analysis during static compressive loading. *J Orthop Res*. 1987;*5*(4):467-478. doi:10.1002/jor.1100050402
23. Brown MD, Holmes DC, Heiner AD. Measurement of cadaver lumbar spine motion segment stiffness. *Spine (Phila Pa 1976)*. 2002;*27*(9):918-922. doi:10.1097/00007632-200205010-00006
24. Cortes DH, Magland JF, Wright AC, Elliott DM. The shear modulus of the nucleus pulposus measured using magnetic resonance elastography: a potential biomarker for intervertebral disc degeneration. *Magn Reson Med*. 2014;*72*(1):211-219. doi:10.1002/mrm.24895
25. Borthakur A, Maurer PM, Fenty M, et al. T1ρ magnetic resonance imaging and discography pressure as novel biomarkers for disc

degeneration and low back pain. *Spine (Phila, PA 1976)*. 2011;*36*(25):2190-2196. doi:10.1097/BRS.0b013e31820287bf
26. Derby R, Kim BJ, Lee SH, Chen Y, Seo KS, Aprill C. Comparison of discographic findings in asymptomatic subject discs and the negative discs of chronic LBP patients: can discography distinguish asymptomatic discs among morphologically abnormal discs? *Spine J*. 2005;*5*(4):389-394. doi:10.1016/J.SPINEE.2005.01.007
27. Derby R, Kim BJ, Chen Y, Seo KS, Lee SH. The relation between annular disruption on computed tomography scan and pressure-controlled diskography. *Arch Phys Med Rehabil*. 2005;*86*(8):1534-1538. doi:10.1016/j.apmr.2005.02.012
28. Showalter BL, DeLucca JF, Peloquin JM, et al. Novel human intervertebral disc strain template to quantify regional three-dimensional strains in a population and compare to internal strains predicted by a finite element model. *J Orthop Res*. 2016;*34*(7):1264-1273. doi:10.1002/jor.23137
29. Yoder JH, Peloquin JM, Song G, et al. Internal three-dimensional strains in human intervertebral discs under axial compression quantified non-invasively by magnetic resonance imaging and image registration. *J Biomech Eng*. 2014;*136*(11):111008. doi:10.1115/1.4028250
30. Claeson AA, Vresilovic EJ, Showalter BL, et al. Human disc nucleotomy alters annulus fibrosus mechanics at both reference and compressed loads. *J Biomech Eng*. 2019;*141*(11):1110011-11100112. doi:10.1115/1.4043874
31. Oldweiler AB, Martin JT. In vivo relationships between lumbar facet joint and intervertebral disc composition and diurnal deformation. *Clin Biomech*. 2021;*88*:105425. doi:10.1016/j.clinbiomech.2021.105425
32. Martin JT, Oldweiler AB, Kosinski AS, et al. Lumbar intervertebral disc diurnal deformations and T2 and T1rho relaxation times vary by spinal level and disc region. *Eur Spine J*. 2022;*31*(3):746-754. doi:10.1007/s00586-021-07097-4
33. Martin JT, Oldweiler AB, Spritzer CE, et al. A magnetic resonance imaging framework for quantifying intervertebral disc deformation in vivo: reliability and application to diurnal variations in lumbar disc shape. *J Biomech*. 2018;*71*:291-295. doi:10.1016/j.jbiomech.2018.01.045
34. Chan DD, Neu CP. Intervertebral disc internal deformation measured by displacements under applied loading with MRI at 3T. *Magn Reson Med*. 2014;*71*(3):1231-1237. doi:10.1002/mrm.24757
35. Menon RG, Zibetti MVW, Pendola M, Regatte RR. Measurement of three-dimensional internal dynamic strains in the intervertebral disc of the lumbar spine with mechanical loading and Golden-angle radial sparse parallel-magnetic resonance imaging. *J Magn Reson Imaging*. 2021;*54*(2):486-496. doi:10.1002/jmri.27591
36. Wilson RL, Bowen L, Kim W, et al. In vivo intervertebral disc deformation: intratissue strain patterns within adjacent discs during flexion–extension. *Sci Rep*. 2021;*11*(1):729. doi:10.1038/s41598-020-77577-y
37. Wang YXJ, Wang JQ, Kaplar Z. Increased low back pain prevalence in females than in males after menopause age: evidences based on synthetic literature review. *Quant Imaging Med Surg*. 2016;*6*(2):199-206. doi:10.21037/qims.2016.04.06
38. Bento TPF, dos Genebra CVS, Maciel NM, Cornelio GP, Simeão SFAP, de Vitta A. Low back pain and some associated factors: is there any difference between genders? *J Phys Ther*. 2020;*24*(1):79-87. doi:10.1016/j.bjpt.2019.01.012
39. Hüllemann P, Keller T, Kabelitz M, et al. Clinical manifestation of acute, subacute and chronic low back pain in different age groups. *Pain Pract*. 2018;*18*:1011-1023. doi:10.1111/papr.12704
40. Oh CH, Yoon SH. Whole spine disc degeneration survey according to the ages and sex using Pfirrmann disc degeneration grades. *Korean J Spine*. 2017;*14*(4):148-154. doi:10.14245/kjs.2017.14.4.148
41. Adams MA, Lama P, Zehra U, Dolan P. Why do some intervertebral discs degenerate, when others (in the same spine) do not? *Clin Anat*. 2015;*28*(2):195-204. doi:10.1002/ca.22404
42. Adams MA, Roughley PJ. What is intervertebral disc degeneration, and what causes it? *Spine*. 2006;*31*(18):2151-2161.
43. Videman T, Battié MC, Gill K, Manninen H, Gibbons LE, Fisher LD. Magnetic resonance imaging findings and their relationships in the thoracic and lumbar spine. *Spine (Phila Pa 1976)*. 1995;*20*(8):928-935. doi:10.1097/00007632-199504150-00009
44. Hirsch C, Schajowicz F. Studies on structural changes in the lumbar annulus fibrosus. *Acta Orthop*. 1952;*22*(1–4):184-231. doi:10.3109/17453675208989006
45. Welsch GH, Trattnig S, Paternostro-Sluga T, et al. Parametric T2 and T2* mapping techniques to visualize intervertebral disc degeneration in patients with low back pain: initial results on the clinical use of 3.0 tesla MRI. *Skeletal Radiol*. 2011;*40*(5):543-551. doi:10.1007/s00256-010-1036-8
46. Stelzeneder D, Welsch GH, Kovács BK, et al. Quantitative T2 evaluation at 3.0 T compared to morphological grading of the lumbar intervertebral disc: a standardized evaluation approach in patients with low back pain. *Eur J Radiol*. 2012;*81*(2):324-330. doi:10.1016/j.ejrad.2010.12.093
47. Fairbank JCT, Pynsent PB. The Oswestry disability index. *Spine (Phila Pa 1976)*. 2000;*25*(22):2940-2952. doi:10.1097/00007632-200011150-00017
48. Davidson M, Keating JL. A comparison of five low Back disability questionnaires: reliability and responsiveness. *Phys Ther*. 2002;*82*(1):8-24. doi:10.1093/ptj/82.1.8
49. Costi JJ, a Stokes I, Gardner-Morse MG, Iatridis JC. Frequency-dependent behavior of the intervertebral disc in response to each of six degree of freedom dynamic loading: solid phase and fluid phase contributions. *Spine (Phila Pa 1976)*. 2008;*33*(16):1731-1738. doi:10.1097/BRS.0b013e31817bb116
50. Meadows KD, Johnson CL, Peloquin JM, Spencer RG, Vresilovic EJ, Elliott DM. Impact of pulse sequence, analysis method, and signal to noise ratio on the accuracy of intervertebral disc T 2 measurement. *JOR Spine*. 2020;*3*(3):1-12. doi:10.1002/jsp2.1102
51. Raya JG, Dietrich O, Horng A, Weber J, Reiser MF, Glaser C. T2 measurement in articular cartilage: impact of the fitting method on accuracy and precision at low SNR. *Magn Reson Med*. 2010;*63*(1):181-193. doi:10.1002/mrm.22178
52. Wang YXJ, Zhao F, Griffith JF, et al. T1rho and T2 relaxation times for lumbar disc degeneration: an in vivo comparative study at 3.0-tesla MRI. *Eur Radiol*. 2013;*23*(1):228-234. doi:10.1007/s00330-012-2591-2
53. Blumenkrantz G, Zuo J, Li X, Kornak J, Link TM, Majumdar S. In vivo 3.0-tesla magnetic resonance T1rho and T2 relaxation mapping in subjects with intervertebral disc degeneration and clinical symptoms. *Magn Reson Med*. 2010;*63*(5):1193-1200. doi:10.1002/mrm.22362
54. Avants BB, Epstein CL, Grossman M, Gee JC. Symmetric diffeomorphic image registration with cross-correlation: evaluating automated labeling of elderly and neurodegenerative brain. *Med Image Anal*. 2008;*12*(1):26-41. doi:10.1016/J.MEDIA.2007.06.004
55. Hess M, Allaire B, Gao KT, et al. Deep learning for multi-tissue segmentation and fully automatic personalized biomechanical models from BACPAC clinical lumbar spine MRI. *Pain Med*. 2022;pnac142. doi:10.1093/pm/pnac142/6782967
56. Silvoster L, Kumar RMS. Efficient segmentation of lumbar intervertebral disc from MR images. *IET Image Process*. 2020;*14*(13):3243-3253. doi:10.1049/iet-ipr.2019.0971
57. O'Connell GDB, Vresilovic EJ, Elliott DM. Comparison of animals used in disc research to human lumbar disc geometry. [miscellaneous article]. *Spine (Phila Pa 1976)*. 2007;*32*(3):328-333. doi:10.1097/01.brs.0000253961.40910.c1

58. Yushkevich PA, Piven J, Hazlett HC, et al. User-guided 3D active contour segmentation of anatomical structures: significantly improved efficiency and reliability. *Neuroimage*. 2006;*31*(3):1116-1128. doi:10.1016/j.neuroimage.2006.01.015
59. Cobb JR. Outline for the study of scoliosis. *Instr Course Lect AAOS*. 1948;*5*:261-275.
60. Been E, Kalichman L. Lumbar lordosis. *Spine J*. 2014;*14*(1):87-97. doi:10.1016/j.spinee.2013.07.464
61. Zander T, Krishnakanth P, Bergmann G, Rohlmann A. Diurnal variations in intervertebral disc height affect spine flexibility, intradiscal pressure and contact compressive forces in the facet joints. *Comput Methods Biomech Biomed Engin*. 2010;*13*(5):551-557. doi:10.1080/10255840903337855

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