



# Lumbar intervertebral disc diurnal deformations and T2 and T1rho relaxation times vary by spinal level and disc region

John T. Martin<sup>1</sup> · Alexander B. Oldweiler<sup>1</sup> · Andrzej S. Kosinski<sup>2,3</sup> · Charles E. Spritzer<sup>4</sup> · Brian J. Soher<sup>4</sup> · Melissa M. Erickson<sup>1</sup> · Adam P. Goode<sup>1,2,5</sup> · Louis E. DeFrate<sup>1,6,7,8</sup>

Received: 18 June 2021 / Revised: 16 November 2021 / Accepted: 18 December 2021 / Published online: 24 January 2022  
© The Author(s), under exclusive licence to Springer-Verlag GmbH Germany, part of Springer Nature 2022

## Abstract

**Purpose** Magnetic resonance imaging (MRI) is routinely used to evaluate spine pathology; however, standard imaging findings weakly correlate to low back pain. Abnormal disc mechanical function is implicated as a cause of back pain but is not assessed using standard clinical MRI. Our objective was to utilize our established MRI protocol for measuring disc function to quantify disc mechanical function in a healthy cohort.

**Methods** We recruited young, asymptomatic volunteers (6 male/6 female; age 18–30 years; BMI < 30) and used MRI to determine how diurnal deformations in disc height, volume, and perimeter were affected by spinal level, disc region, MRI biomarkers of disc health (T2, T1rho), and Pfirrmann grade.

**Results** Lumbar discs deformed by a mean of  $-6.1\%$  (95% CI:  $-7.6\%$ ,  $-4.7\%$ ) to  $-8.0\%$  (CI:  $-10.6\%$ ,  $-5.4\%$ ) in height and  $-5.4\%$  (CI:  $-7.6\%$ ,  $-3.3\%$ ) to  $-8.5\%$  (CI:  $-11.0\%$ ,  $-6.0\%$ ) in volume from AM to PM across spinal levels. Regional deformations were more uniform in cranial lumbar levels and concentrated posteriorly in the caudal levels, reaching a maximum of 13.1% at L5–S1 (CI:  $-16.1\%$ ,  $-10.2\%$ ). T2 and T1rho relaxation times were greatest in the nucleus and varied circumferentially within the annulus. T2 relaxation times were greatest at the most cranial spinal levels and decreased caudally. In this young healthy cohort, we identified a weak association between nucleus T2 and the diurnal change in the perimeter.

**Conclusions** Spinal level is a key factor in determining regional disc deformations. Interestingly, deformations were concentrated in the posterior regions of caudal discs where disc herniation is most prevalent.

**Keywords** Spine · Intervertebral disc · Biomechanics · Magnetic resonance imaging · T2 relaxation time · T1rho relaxation time

## Introduction

The lumbar intervertebral discs play a critical mechanical role in the spine, but naturally degenerate with age and are implicated in low back pain, a condition that affects 70–85% of the population [1]. Radiographic and magnetic resonance

imaging (MRI) are routinely performed to assess disc pathologies, but standard findings (e.g., reduction in disc signal on T2 MRI, disc narrowing on radiography) are only weakly correlated with low back pain [2, 3]. In the absence of effective diagnostic imaging and clinical examination findings, clinicians are left to identify pain sources by probing at-risk

✉ Louis E. DeFrate  
lou.defrate@duke.edu

<sup>1</sup> Department of Orthopaedic Surgery, Duke University School of Medicine, Durham, NC, USA

<sup>2</sup> Duke Clinical Research Institute, Duke University School of Medicine, Durham, NC, USA

<sup>3</sup> Department of Biostatistics and Bioinformatics, Duke University School of Medicine, Durham, NC, USA

<sup>4</sup> Department of Radiology, Duke University School of Medicine, Durham, NC, USA

<sup>5</sup> Department of Population Health Sciences, Duke University School of Medicine, Durham, NC, USA

<sup>6</sup> Department of Biomedical Engineering, Duke University, Durham, NC, USA

<sup>7</sup> Department of Mechanical Engineering and Materials Science, Duke University, Durham, NC, USA

<sup>8</sup> Duke University Medical Center, Medical Sciences Research Building I, 203 Research Drive, Room 375, DUMC Box 3093, Durham, NC 27710, USA

regions (e.g., epidural spinal injection, discography) to exclude potential pain generators (e.g., arthritic discs/facets, stenosed neuroforamina). This diagnosis and treatment strategy is time-consuming, costly, and often invasive. Our global hypothesis is that evaluating disc mechanical function through non-invasive imaging will empower clinicians to directly identify a primary cause of low back pain.

Because aberrant spine function is associated with low back pain [4, 5], measuring normal in vivo disc function is critical to understanding back pain. There have been several pre-clinical research efforts to evaluate disc function via imaging [6–9]. In addition to these, our lab has developed an MRI framework to measure changes in three-dimensional (3D) disc geometry that result from physical activity in human subjects [10]. To do so, pre- and post-activity MRI scans are acquired, 3D models of the discs are generated at each timepoint, and shape changes are quantified with sub-pixel precision. We have also applied quantitative MRI sequences like T2 mapping and T1rho mapping that can estimate tissue water and proteoglycan content in vivo [11, 12]. By combining these techniques, we can determine the relationships between disc composition and function in an in vivo setting.

Building on our previous work in developing an MRI protocol for evaluating site-specific changes in disc height [10], the objective of this study was to quantify how disc deformations and biomarkers of disc composition varied by spinal level and disc region in young, asymptomatic volunteers. To do so, we leveraged previous work on diurnal changes in the lumbar discs [13] and measured diurnal changes in disc geometry (mean height, volume, perimeter) and regional disc height in 3D. We also evaluated regional disc composition through T2 mapping and T1rho mapping. We hypothesized that disc deformations and T2 and T1rho relaxation times vary by disc region and spinal level. Furthermore, we identified a subset of discs in this young, healthy group that was degenerated and performed a preliminary analysis of disc deformation in the context of degeneration.

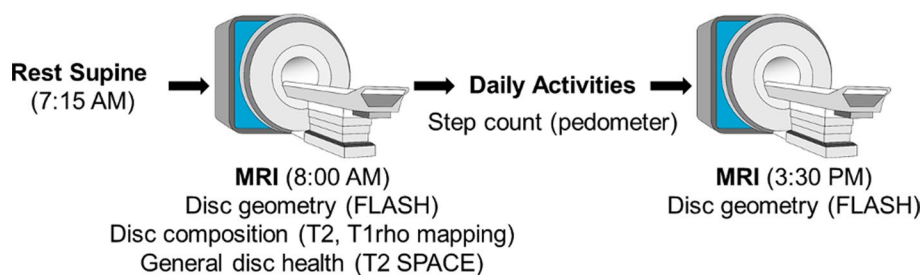
## Methods

### Subject recruitment

After approval from the Duke Health IRB, we enrolled twelve participants (6 M, 6F) between the ages of 18 and 30 and with body mass index (BMI) < 30. Participants were excluded if they had a history of spine deformity; spine surgery; low back pain; sciatica; arthritis in the knee, hip, hand, or neck; diabetes; or smoking. Participants also completed the National Institutes of Health Task Force on Research Standards for Chronic Low Back Pain (NIH RTF) questionnaire. This series of questions formally evaluates spine health and low back pain [14] and includes items on pain intensity, pain interference, physical function; scores range from 9 (healthy) to 50 (severely diseased).

### Imaging protocol

Participants were scanned at AM and PM time points to measure diurnal changes in disc geometry, and at the AM time point to quantify baseline T2 and T1rho relaxation times (Fig. 1). Participants arrived at the MRI facility at 7 AM, rested for 45 min in a supine position ( $49 \pm 4$  min) to allow for the disc tissues to equilibrate, and were subsequently imaged on a 3 T MRI system (Siemens TIM Trio, Erlangen, Germany). Participants were scanned for geometry (3D FLASH) [10], composition (T2 mapping and T1rho mapping), and to assess disc degeneration by Pfirrmann grading (T2-weighted SPACE). Scan parameters are shown in Table 1. Following the MRI scan, participants were given a pedometer (Zip; Fitbit, Inc., San Francisco, CA) to track their step count and returned to their normal workday. Participants returned to the MRI facility at 3:30 PM and were scanned a second time to measure PM disc geometry (time between scans: 7 h  $17 \pm 8$  min). Because discs recover while subjects are supine during the scan, only disc geometry (not T2 or T1rho) was measured at the PM time point.



**Fig. 1** Imaging Protocol. Participants entered the MRI facility at 7:15 AM, rested supine for 45 min, and were transferred to the MRI system for disc geometry (FLASH), disc composition (T2 mapping, T1rho), and Pfirrmann grade (T2-weighted SPACE) evaluation. Par-

ticipants were given a pedometer, went about their normal workday, and returned at 3:30 PM for a second measurement of disc geometry. *MRI* magnetic resonance imaging

**Table 1** MRI sequence parameters

Sequence	FLASH (3D)	T2w SPACE (3D)	T2	T1rho
AM time point	8:00	8:00	8:00	8:00
PM time point	3:30	–	–	–
Purpose	Geometry	Pfirrmann grading	Composition	Composition
Repetition time (ms)	9	2500	3630	4000
Echo or spin lock time(s) (ms)	3.7	223	20, 40, 60, 80, 100, 120, 140	20, 40, 60, 100 (500 Hz)
Flip angle (°)	20	100	180	15
Resolution (mm)	1×1×1	0.9×0.9×0.9	1×1×3	1×1×3
Acquisition time (min:sec)	5:54	5:00	5:31	13:44

*MRI*, magnetic resonance imaging

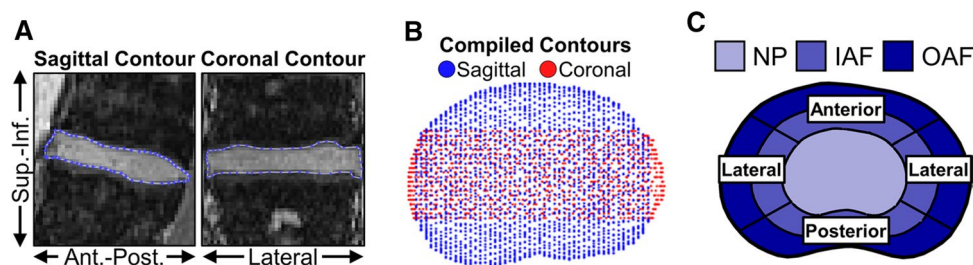
## Image analysis

AM and PM image stacks were manually segmented with custom software (MATLAB R2016b; MathWorks, Natick, MA) to generate 3D disc models. A blinded rater (ABO) manually segmented discs on the FLASH image stacks to generate 3D disc models. Mean height, volume, perimeter, and regional height were calculated as described previously [10]. Regional height was calculated in the nucleus pulposus (NP) and the outer annulus fibrosus (OAF) and inner annulus fibrosus (IAF) divided into anterior (A), lateral (L), and posterior (P) regions (Fig. 2). Diurnal variations were expressed as percent change from AM to PM. Disc contours were then transferred to T2 and T1rho image stacks and average T2 and T1rho relaxation times were calculated in each region using a one-term exponential decay. In evaluating regional height loss, T2, and T1rho, we assumed left–right symmetry. Finally, Pfirrmann grades were assigned by a postdoctoral researcher (JTM).

## Statistics

Whole-disc diurnal deformations ( $\Delta$  mean height,  $\Delta$  volume, and  $\Delta$  perimeter) were evaluated using mixed-effects models that accounted for correlations within subjects. Spinal level was treated as a fixed effect while the subject was treated as a random effect. Regional diurnal deformations and regional T2 and T1rho relaxation times were similarly analyzed using mixed-effects models. Each spinal level was modeled separately with the disc region treated as a fixed effect and the subject was treated as a random effect. For pairwise post-hoc comparisons, the difference of least squares means between each spinal level was calculated and a Tukey–Kramer correction was used for multiple comparisons. Discs with Pfirrmann grades I–III were included in these analyses ( $n = 5$  discs removed).

We evaluated associations between whole-disc diurnal deformations and other factors (BMI, step count, NP T2, NP T1rho). Mixed modeling was performed to evaluate the relationship between a diurnal disc deformation as a dependent variable and each factor as an independent fixed variable. Subject was considered a random effect.



**Fig. 2** MRI Segmentation Protocol. **a** FLASH MR images were manually segmented in the sagittal and coronal planes to develop the 3D geometry of the disc. **b** Sagittal and coronal contours were compiled to develop a point cloud that represented the disc volume. **c** Discs were divided into anatomical regions representing the anterior, lat-

eral, and posterior portions of the NP, IAF, and OAF. This figure is adapted from [19] with permission from *Journal of Biomechanics*. IAF inner annulus fibrosus, MRI magnetic resonance imaging, NP nucleus pulposus, OAF outer annulus fibrosus

A subset of discs were degenerated based on Pfirrmann grading (Grade I: 18%; Grade II: 64%; Grade III: 11%; Grade IV: 7%, Grade V: 0%) and we preliminarily analyzed the associations between Pfirrmann grade and disc parameters using mixed effects models. Pfirrmann grade was included as a fixed effect while subject was treated as a random effect. Post-hoc comparisons are performed as described above.

The residual diagnostics of each model were inspected visually to confirm normality and  $p < 0.05$  was used to indicate statistical significance. Analyses were performed with SAS (SAS 9.4; SAS Institute Inc., Cary, NC). Throughout

the text and figures, data are described with means and 95% confidence interval limits.

## Results

### Participant characteristics

All participants were pain-free and had excellent spine health with no NIH RTF scores greater than 10 (Table 2). In addition, the mean step count of all participants (5840) was similar to the daily average for adults in the United States (5117) [15]. One participant did not complete T2 and T1rho imaging for logistical reasons.

**Table 2** Participant demographics

N	12
Age (years; mean, range)	25 (19–30)
BMI (kg/m <sup>2</sup> ; mean, range)	22.6 (19.4–27.0)
Step count (steps; mean, range)	5840 (2187–10,697)
NIH RTF score (mean, range)	9.3 (9–10)
Gender, female <i>n</i> (%)	6 (50)
Employment status, <i>n</i> (%)	
Student	11 (92)
Working now	1 (8)
Education level, <i>n</i> (%)	
Bachelor's degree	9 (75)
Some college, no degree	2 (17)
Professional school degree	1 (8)
Race, <i>n</i> (%)	
White	6 (50)
Black or African American	4 (33)
Asian	2 (17)
Ethnicity, <i>n</i> (%)	
Not Hispanic or Latino	11 (92)
Hispanic or Latino	1 (8)
Current smoker, <i>n</i> (%)	0 (100)
Low-back operation, <i>n</i> (%)	0 (100)

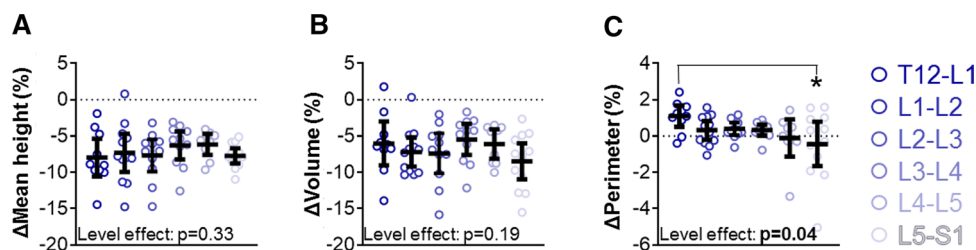
BMI body mass index, NIH RTF National Institutes of Health Task Force on Research Standards for Chronic Low Back Pain

### Diurnal changes in whole-disc geometry by spinal level

Disc height and volume decreased from AM to PM with no statistical differences between spinal level, while disc perimeter increased at the cranial levels and decreased at the caudal levels, which was statistically different (Fig. 3). The change in mean disc height ranged from  $-6.1\%$  ( $-7.6\%$ ,  $-4.7\%$ ) to  $-8.0\%$  ( $-10.6\%$ ,  $-5.4\%$ ) (Fig. 3a) The diurnal change in disc volume ranged from  $-5.4\%$  ( $-7.6\%$ ,  $-3.3\%$ ) to  $-8.5\%$  ( $-11.0\%$ ,  $-6.0\%$ ) (Fig. 3b). Neither the change in disc height nor volume was affected by spinal level. Disc perimeter increased  $1.1\%$  ( $0.5\%$ ,  $1.7\%$ ) at T12–L1 and decreased  $-0.4\%$  ( $-1.7\%$ ,  $0.8\%$ ) at L5–S1, illustrating a gradual decrease in disc bulging from cranial to caudal that was statistically significant (Fig. 3c).

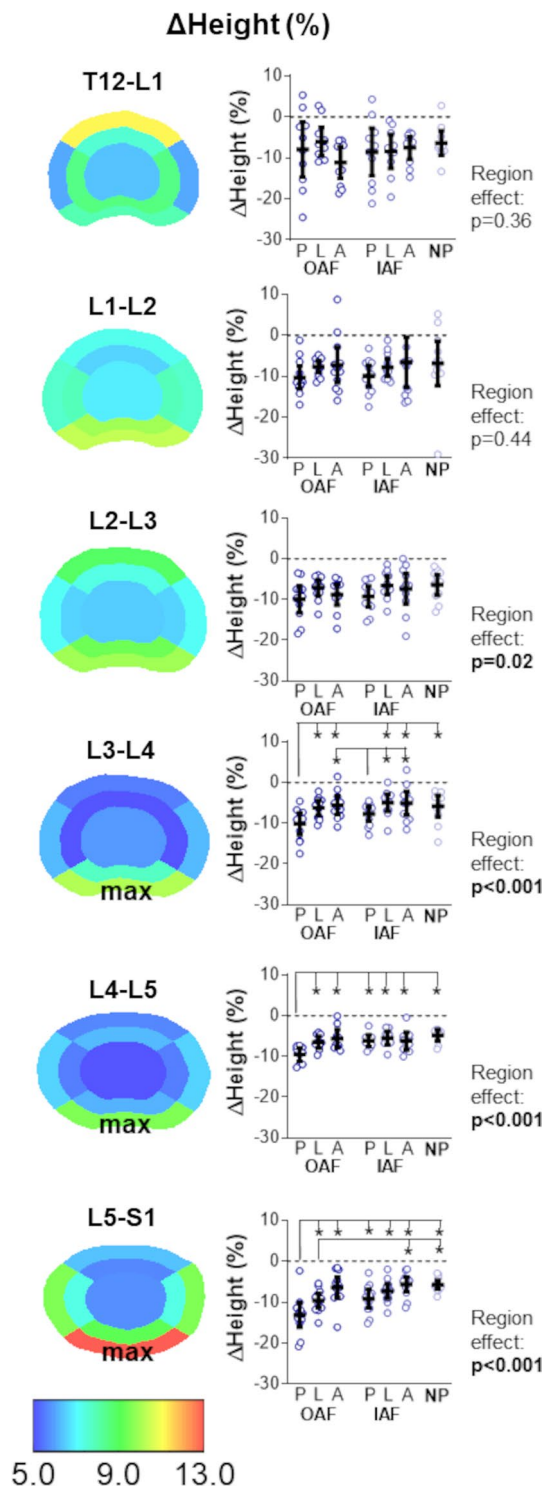
### Diurnal changes in regional disc height by spinal level

The diurnal change in disc height was greatest in the posterior regions of the most caudal discs and evenly distributed in the most cranial discs (Fig. 4). Region was significantly associated with the diurnal change in height at L2–L3,



**Fig. 3** Diurnal Changes in Whole-Disc Geometry. **a** Discs uniformly lost 6–8% height with no significant differences by level. Data are displayed as observed values with mean  $\pm$  95% CI (\*,  $p < 0.05$ , post-hoc differences of least squares means). “Level effect” is the result of an omnibus test of fixed effects. **b** Discs lost 5–9% volume over

the course of the day, with no significant differences by level. **c** Disc perimeter increased in the most cranial levels and decreased in the most caudal levels. There was a significant difference in the change in disc perimeter between T12–L1 and L5–S1 discs. CI confidence interval



**Fig. 4** Diurnal Changes in Disc Height, Baseline (AM) T2 Relaxation Time, and Baseline T1rho Relaxation Time by Disc Region. The pattern of height loss varied by level. At L3–L4, L4–L5, and L5–S1, disc deformation was concentrated in the posterior regions of the disc, while at T12–L1 and L1–L2 there were no significant differences by region. Data are displayed as observed values with mean  $\pm$  95% CI (\*,  $p < 0.05$ , post-hoc differences of least squares means). “Max” represents the location of the maximum compressive deformation. “Region effect” is the result of an omnibus test of fixed effects. A anterior, CI confidence interval, IAF inner annulus fibrosus, L lateral, NP nucleus pulposus, OAF outer annulus fibrosus, P posterior

L3–L4, L4–L5, and L5–S1. There were no statistically significant pairwise differences in the regional change in disc height at T12–L1, L1–L2, or L2–L3. However, at L3–L4, L4–L5, and L5–S1, changes in disc height were of significantly greater magnitude in the posterior region of the AF (OAF-P) than in the anterior region of the AF (OAF-A), with the greatest change in regional height occurring at L5–S1.

**Baseline (AM) T2 and T1rho relaxation times by spinal level and disc region**

T2 relaxation time was greatest in the most cranial discs, maximum in the NP region at each spinal level, and varied circumferentially in the outer AF regions of discs L1–L2 through L4–L5 (Fig. 5a). For all levels, T2 was significantly greater in the NP region than all regions of the outer AF; this difference was maximum at the most cranial levels and minimum at the most caudal levels. T2 varied throughout the AF as well, significantly decreasing from the anterior AF region to the posterior AF region at levels L1–L2 through L4–L5.

Similarly, T1rho relaxation time was greatest in the NP region at each spinal level and varied circumferentially in the outer AF (Fig. 5b). T1rho values were highest in the NP with significant differences between the NP and regions of the outer and inner AF at each level. T1rho significantly varied throughout the AF, as well; T1rho was lowest in the lateral region of outer AF (OAF-L) with significant differences between the OAF-L and all other AF regions at T12–L1 through L4–L5.

**Associations between variables of interest**

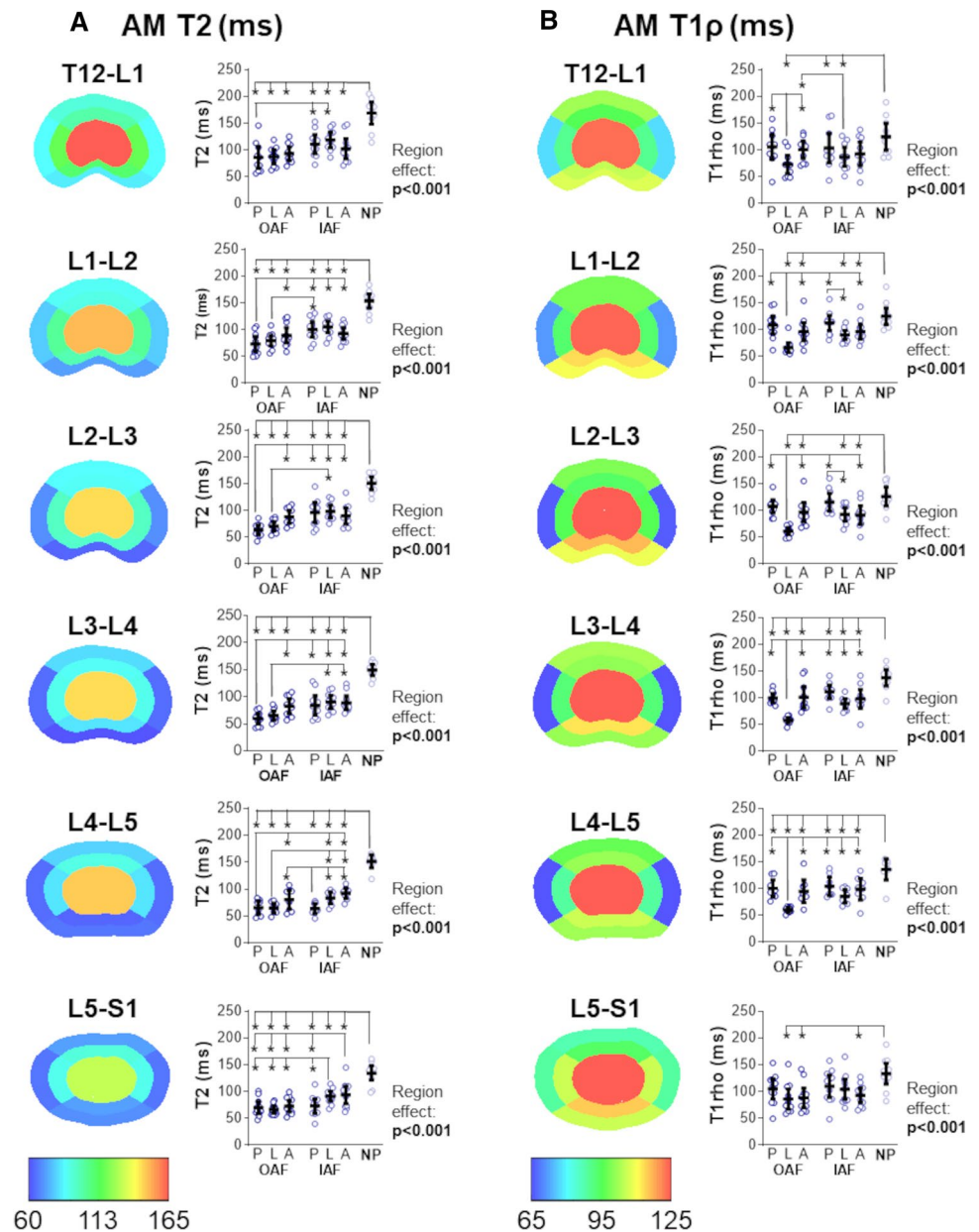
Associations between whole-disc deformations ( $\Delta$  mean height,  $\Delta$  volume,  $\Delta$  perimeter) and BMI, step count, NP T2, and T1rho relaxation times were evaluated. There were no associations between any deformations and BMI, step count, and NP T1rho. NP T2 was significantly associated with the diurnal change in perimeter ( $\beta = 0.012\%/ms$  [0.001, 0.024]), but not with the diurnal change in mean height or volume.

Pfirrmann grade (Fig. 6a) was significantly associated with NP T2 and NP T1rho; in both cases, the Grade IV group was significantly different than the Grade I group, the Grade II group, and the Grade III group (Fig. 6b). Pfirrmann grade was not associated with the change in mean disc height, disc volume, or disc perimeter (Fig. 6c).

**Discussion**

We measured diurnal disc deformations in young, healthy volunteers and identified changes in mean height, perimeter, and volume across the lumbar spine. From AM to PM, discs uniformly lost 6–8% in mean height and 5–9% in volume,

**Fig. 5** Diurnal Changes in Baseline (AM) T2 Relaxation Time and Baseline T1rho Relaxation Time by Disc Region. **a** T2 relaxation time was higher in the NP region than the OAF regions at each level. At L1–L2, L2–L3, L3–L4, and L4–L5, the lowest T2 values occurred in the posterior regions of the OAF. **b** T1rho was greatest in the NP region discs at each level. At L1–L2 to L4–L5, T1rho of the lateral regions was significantly lower than the anterior and/or posterior regions. Data are displayed as observed values with mean  $\pm$  95% CI (\*,  $p < 0.05$ , post-hoc differences of least squares means). “Region effect” is the result of an omnibus test of fixed effects. A anterior, CI confidence interval, IAF inner annulus fibrosus, L lateral, NP nucleus pulposus, OAF outer annulus fibrosus, P posterior



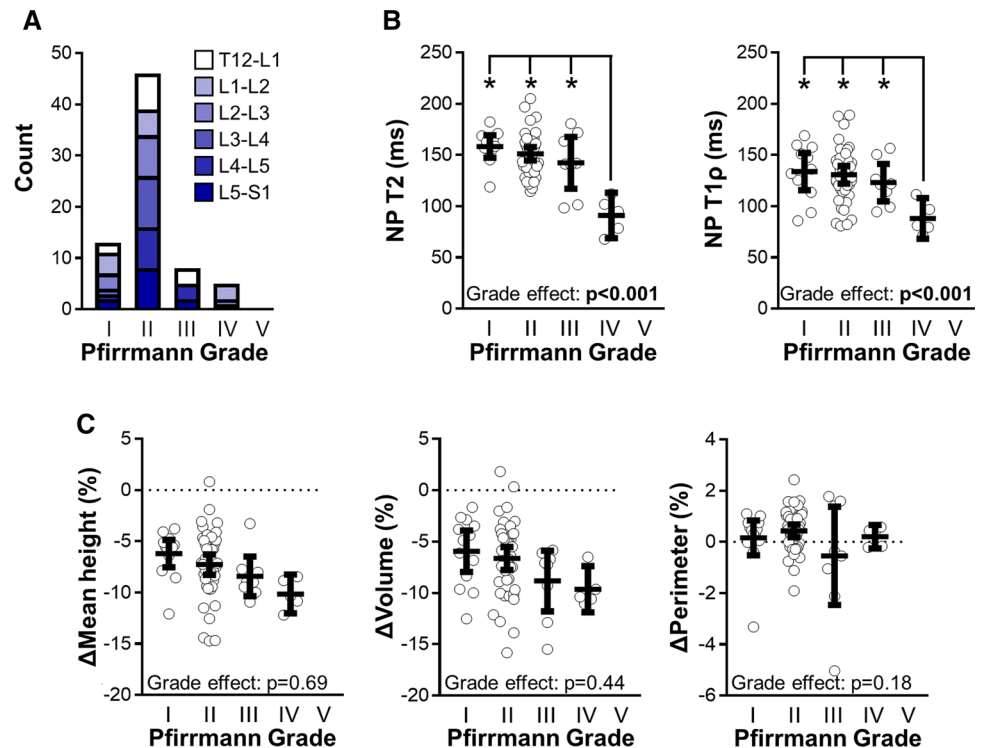
while there was an increase in perimeter in the most cranial discs (1.1%) and a decrease in the most caudal discs (−0.4%). Spinal level influenced regional disc compression patterns. Regional deformations in the most cranial discs (T12–L1, L1–L2) were more uniform, while regional deformations in the most caudal discs (L3–L4, L4–L5, L5–S1) were posteriorly concentrated with the largest posterior deformation at L5–S1 (−13%).

Our findings indicate that disc deformations vary by spinal level and disc region. At the *caudal lumbar levels*, disc compression was concentrated in posterior disc regions. Consistent with these findings, posterior AF tears are more prevalent than anterior AF tears at the lower lumbar levels [16], and posterior herniation is also more prevalent at the

lower lumbar levels [17]. Conversely, at the *cranial lumbar levels*, disc compression was more uniformly distributed. Consistent with these findings, posterior AF tears are less prevalent at the upper lumbar levels, while lateral herniation and endplate defects are more prevalent [16, 18]. It is not yet clear what level-dependent anatomical or mechanical factors influence disc deformation patterns; this is an area for future work.

We identified that T2 and T1rho relaxation times were significantly affected by spinal level, disc region, and degeneration grade. In degenerated discs, NP T2 and T1rho relaxation times were decreased, confirming that these quantitative biomarkers reflect disc health when measured in 3D. We also found that T2 and T1rho relaxation times decreased with

**Fig. 6** Associations between Pfirrmann Grade and Diurnal Deformations, NP T2 Relaxation Time, NP T1rho Relaxation Time. **a** We imaged 72 discs in 12 subjects. Of these discs, 18% were Pfirrmann grade I, 64% were grade II, 11% were grade III, and 7% were grade IV. There were no grade V discs. **b** Pfirrmann grade was a significant predictor of NP T2 and NP T1rho. Data are displayed as observed values with mean  $\pm$  95% CI (\*,  $p < 0.05$ , post-hoc differences of least squares means). “Grade effect” is the result of an omnibus test of fixed effects. **c** There were no associations between Pfirrmann grade and the diurnal changes in mean disc height, volume, or perimeter. CI confidence interval



increasing distance from the NP, matching the general pattern of water and glycosaminoglycan distribution measured in cadaver discs [19]. T2 and T1rho relaxation times varied circumferentially in the AF, which may indicate local variations in the extracellular matrix in these young participants. NP T2 relaxation times were greater in the cranial lumbar discs when compared to the caudal discs. This may indicate decreased transport/nutrient availability at the caudal levels; future work should track how altered hydration impacts the progression of disc degeneration.

While the soft tissues of the spine may be conditioned by physical loading [20], we did not detect a relationship between BMI or step count and disc deformations. Step count may not be an effective measure of spine loading as it does not account for gravitational loading or activity timing, intensity, and duration. The disc deformations imposed by specific activities is an area for future work. Additionally, this study evaluated individuals within a narrow, healthy range of BMI. Since obesity has been linked to spine disease and back pain [21], future work should evaluate disc function over a wider BMI range.

There are conflicting reports of increased compliance [22] and decreased compliance [23] in degenerated cadaver discs. In this study, we identified a weak association between NP T2 (a marker of disc health) and the diurnal change in the perimeter. However, we could not detect an association between NP T2 and the diurnal changes in mean height or volume, nor did we detect an association between Pfirrmann grade and any diurnal changes in disc geometry. Clinical

imaging findings of degeneration alone are weakly associated with low back pain [2, 3]. We propose that imaging findings of degeneration and measurements of in vivo mechanical function provide complementary information about spine health and, when assessed in combination, could improve the diagnosis of the underlying causes of low back pain. Further, studies evaluating disc mechanical function across the spectrum of degeneration and in the context of low back pain are required.

## Conclusion

We measured diurnal deformations across the lumbar spine, identifying that lumbar discs decrease in height 6–8% on average over the course of the workday. While mean disc height loss at each level was similar, there were level-dependent patterns of regional disc height loss. Specifically, there was a more uniform pattern of deformation in the cranial discs but a posterior concentration of height loss in the most caudal discs (maximum 13%). This pattern corresponds to the typical locations of AF tears and disc herniations, and highlights the importance of measuring site-specific differences in disc compression. Taken together, our findings suggest that spinal level and disc region are key factors that determine in vivo disc deformations.

**Acknowledgements** The authors would like to thank Jean Shaffer and Raven Boykin from the Duke Center for Advanced Magnetic Resonance Development.

**Authors' contributions** JTM: conception and design, collection and assembly of data, analysis and interpretation of data, drafting of the article, critical revision of the article for important intellectual content; ABO: collection and assembly of data, analysis and interpretation of data, critical revision of the article for important intellectual content; ASK: statistical expertise, analysis and interpretation of data, technical support, critical revision of the article for important intellectual content; CES: conception and design, collection and assembly of data, analysis and interpretation of data, technical and logistic support, critical revision of the article for important intellectual content; BJS: conception and design, analysis and interpretation of data, technical support, critical revision of the article for important intellectual content; APG: conception and design, analysis and interpretation of data, critical revision of the article for important intellectual content, final approval of the article; LED: conception and design, analysis and interpretation of data, critical revision of the article for important intellectual content, final approval of the article.

**Funding** This study was funded by the National Institutes of Health (F32 AR071223, AR075399, and AR071440) and a pilot Grant from the Duke University Orthopaedic Surgery Department.

**Data availability** The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Declarations

**Conflict of interests** JTM is a consultant for DiscGenics, Inc. The other authors have no relevant financial or non-financial interests to disclose.

**Ethics approval** All experimental procedures were approved by the Duke Health Institutional Review Board (Protocol # 00073132).

**Consent to participate** All involved persons gave their informed consent prior to study inclusion.

**Consent for publication** All authors have read and approved the contents of this manuscript.

## References

- Andersson GB (1999) Epidemiological features of chronic low-back pain. *Lancet* 354:581–585. [https://doi.org/10.1016/S0140-6736\(99\)01312-4](https://doi.org/10.1016/S0140-6736(99)01312-4)
- van Tulder MW, Assendelft WJ, Koes BW, Bouter LM (1997) Spinal radiographic findings and nonspecific low back pain. A systematic review of observational studies. *Spine (Phila Pa 1976)* 22:427–434
- Raastad J, Reiman M, Coeytaux R, Ledbetter L, Goode AP (2015) The association between lumbar spine radiographic features and low back pain: a systematic review and meta-analysis. *Semin Arthritis Rheum* 44:571–585. <https://doi.org/10.1016/j.semarthrit.2014.10.006>
- Mellor FE, Thomas PW, Thompson P, Breen AC (2014) Proportional lumbar spine inter-vertebral motion patterns: a comparison of patients with chronic, non-specific low back pain and healthy controls. *Eur Spine J* 23:2059–2067. <https://doi.org/10.1007/s00586-014-3273-3>
- Viggiani D, Gallagher KM, Sehl M, Callaghan JP (2017) The distribution of lumbar intervertebral angles in upright standing and extension is related to low back pain developed during standing. *Clin Biomech (Bristol, Avon)* 49:85–90. <https://doi.org/10.1016/j.clinbiomech.2017.09.003>
- O'Connell GD, Vresilovic EJ, Elliott DM (2011) Human intervertebral disc internal strain in compression: the effect of disc region, loading position, and degeneration. *J Orthop Res* 29:547–555. <https://doi.org/10.1002/jor.1232>
- Chan DD, Neu CP (2014) Intervertebral disc internal deformation measured by displacements under applied loading with MRI at 3T. *Magn Reson Med* 71:1231–1237. <https://doi.org/10.1002/mrm.24757>
- Walter BA, Mageswaran P, Mo X, Boulter DJ, Mashaly H, Nguyen XV, Prevedello LM, Thoman W, Raterman BD, Kalra P, Mendel E, Marras WS, Kolipaka A (2017) MR elastography-derived stiffness: a biomarker for intervertebral disc degeneration. *Radiology* 285:167–175. <https://doi.org/10.1148/radiol.2017162287>
- Weber CI, Hwang CT, van Dillen LR, Tang SY (2019) Effects of standing on lumbar spine alignment and intervertebral disc geometry in young, healthy individuals determined by positional magnetic resonance imaging. *Clin Biomech (Bristol, Avon)* 65:128–134. <https://doi.org/10.1016/j.clinbiomech.2019.04.010>
- Martin JT, Oldweiler AB, Spritzer CE, Soher BJ, Erickson MM, Goode AP, DeFrate LE (2018) A magnetic resonance imaging framework for quantifying intervertebral disc deformation in vivo: reliability and application to diurnal variations in lumbar disc shape. *J Biomech* 71:291–295. <https://doi.org/10.1016/j.jbiomech.2018.01.045>
- Martin JT, Collins CM, Ikuta K, Mauck RL, Elliott DM, Zhang Y, Anderson DG, Vaccaro AR, Albert TJ, Arlet V, Smith HE (2015) Population average T2 MRI maps reveal quantitative regional transformations in the degenerating rabbit intervertebral disc that vary by lumbar level. *J Orthop Res* 33:140–148. <https://doi.org/10.1002/jor.22737>
- Gullbrand SE, Ashinsky BG, Martin JT, Pickup S, Smith LJ, Mauck RL, Smith HE (2016) Correlations between quantitative T2 and T1rho MRI, mechanical properties and biochemical composition in a rabbit lumbar intervertebral disc degeneration model. *J Orthop Res* 34:1382–1388. <https://doi.org/10.1002/jor.23269>
- Boos N, Wallin A, Gbedegbegnon T, Aebi M, Boesch C (1993) Quantitative MR imaging of lumbar intervertebral disks and vertebral bodies: influence of diurnal water content variations. *Radiology* 188:351–354. <https://doi.org/10.1148/radiology.188.2.8327677>
- Deyo RA, Dworkin SF, Amtmann D, Andersson G, Borenstein D, Carragee E, Carrino JA, Chou R, Cook K, DeLitto A, Goertz C, Khalsa P, Loeser J, Mackey S, Panagis J, Rainville J, Tosteson T, Turk D, Von Korff M, Weiner DK (2014) Report of the NIH task force on research standards for chronic low back pain. *Spine J* 14:1375–1391. <https://doi.org/10.1016/j.spinee.2014.05.002>
- Bassett DR Jr, Wyatt HR, Thompson H, Peters JC, Hill JO (2010) Pedometer-measured physical activity and health behaviors in U.S. adults. *Med Sci Sports Exerc* 42:1819–1825. <https://doi.org/10.1249/MSS.0b013e3181dc2e54>
- Osti OL, Vernon-Roberts B, Moore R, Fraser RD (1992) Annular tears and disc degeneration in the lumbar spine. A post-mortem study of 135 discs. *J Bone Joint Surg Br* 74:678–682

17. Ebeling U, Reulen HJ (1992) Are there typical localisations of lumbar disc herniations? A prospective study. *Acta Neurochir (Wien)* 117:143–148
18. Samartzis D, Mok FPS, Karppinen J, Fong DYT, Luk KDK, Cheung KMC (2016) Classification of Schmorl's nodes of the lumbar spine and association with disc degeneration: a large-scale population-based MRI study. *Osteoarthritis Cartilage* 24:1753–1760. <https://doi.org/10.1016/j.joca.2016.04.020>
19. Iatridis JC, MacLean JJ, O'Brien M, Stokes IA (2007) Measurements of proteoglycan and water content distribution in human lumbar intervertebral discs. *Spine (Phila Pa 1976)* 32:1493–1497. <https://doi.org/10.1097/BRS.0b013e318067dd3f>
20. Bowden JA, Bowden AE, Wang H, Hager RL, LeCheminant JD, Mitchell UH (2018) In vivo correlates between daily physical activity and intervertebral disc health. *J Orthop Res* 36:1313–1323. <https://doi.org/10.1002/jor.23765>
21. Samartzis D, Karppinen J, Mok F, Fong DY, Luk KD, Cheung KM (2011) A population-based study of juvenile disc degeneration and its association with overweight and obesity, low back pain, and diminished functional status. *J Bone Joint Surg Am* 93:662–670. <https://doi.org/10.2106/JBJS.I.01568>
22. Mimura M, Panjabi MM, Oxland TR, Crisco JJ, Yamamoto I, Vasavada A (1994) Disc degeneration affects the multidirectional flexibility of the lumbar spine. *Spine (Phila Pa 1976)* 19:1371–1380
23. Kettler A, Rohlmann F, Ring C, Mack C, Wilke HJ (2011) Do early stages of lumbar intervertebral disc degeneration really cause instability? Evaluation of an in vitro database. *Eur Spine J* 20:578–584. <https://doi.org/10.1007/s00586-010-1635-z>

**Publisher's Note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.