Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Effect of Natural Standing and Rest on Solute Transport Pathways in Hypermobile and Immobile Human Lumbar Intervertebral Discs. Results from Delayed Post-Contrast Upright MRI Study

J Naresh-Babu

nareshspine@yahoo.com

Mallika Spine Centre

Paishetty Vinender

Mallika Spine Centre

Kamazala Prudvi Kumar Reddy

Mallika Spine Centre

Research Article

Keywords: Intervertebral disc, Upright MRI, Contrast-agent diffusion, Segmental mobility, Physiological loading

Posted Date: November 11th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-11394721/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Additional Declarations: No competing interests reported.

Effect of Natural Standing and Rest on Solute Transport Pathways in Hypermobile and Immobile Human Lumbar Intervertebral Discs. Results from Delayed Post-Contrast Upright MRI Study.

ABSTRACT

Purpose: To examine how physiological states of resting and standing effect the nutrient transport in mobile, hypermobile and immobile lumbar intervertebral discs.

Methods: This prospective study included 15 healthy participants (10 males, 5 females; mean age, 25.2 ± 3.6 years), divided into three groups: normally mobile, hypermobile (bilateral L5 pars defects), and immobile (lumbosacral transitional vertebrae), with five participants per group. Six-hour delayed post-contrast (0.3mmol/kg) T1-weighted MR images were obtained using a 0.25-T upright positional MRI system in supine, standing, and immediate post-standing recovery positions. Three-dimensional segmentation using 3D Slicer enabled regional enhancement analysis of the central nucleus pulposus (CNP), peripheral nucleus pulposus (PNP), and superior and inferior endplate zones.

Results: *Normal* discs showed standing-associated enhancement loss (wash-out) in both CNP and PNP, followed by recovery, particularly peripherally. *Hypermobile* discs demonstrated the largest standing-associated reduction in CNP enhancement of approximately 2.8 times that of normal discs, with incomplete regain in recovery position. *Immobile* discs demonstrated the greatest peripheral enhancement loss and limited central recovery. Their superior endplate exhibited a marked, reversible enhancement increase during standing, while the inferior endplate showed comparatively little positional variation.

Conclusions: For the first time, present study documented acute effects of natural standing and rest on solute transport of human lumbar discs with different mobility patterns in vivo. Despite similar morphology, discs at hypermobile and immobile segments demonstrated different patterns of enhancement wash-out on standing as well as different recovery patterns during rest.

Keywords: Intervertebral disc; Upright MRI; Contrast-agent diffusion; Segmental mobility; Physiological loading.

ABBREVIATIONS

IVD – INTER VERTEBRAL DISCS

MRI – MAGNETIC RESONANCE IMAGING

ROI – REGION OF INTEREST

EPZ – END PLATE ZONE

NP – NUCLEUS PULPOSUS

Sup EPZ – SUPERIOR END PLATE ZONE

Inf EPZ – INFERIOR END PLATE ZONE

PNP – PERIPHERAL NUCLEUS PULPOSUS

CNP – CENTRAL NUCELUS PULPOSUS

SD – STANDARD DEVIATION

EP – ENHACEMENT PERCENTAGE

SI – SIGNAL INTENSITY

INTRODUCTION

The human intervertebral disc (IVD) relies on a delicate homeostatic balance between its load-bearing mechanical environment and the efficiency of nutrient transport pathways. As a largely avascular structure, the IVD depends predominantly on diffusion through the vertebral endplates, supplemented by transport through the peripheral annulus fibrosus, to obtain essential nutrients such as glucose and oxygen and eliminate metabolic waste products, including lactate. [1, 2] the efficiency of this transport is influenced by endplate permeability, solute characteristics, tissue composition and cellular metabolic demand. Disruption of this balance may compromise cellular viability and matrix homeostasis, potentially contributing to the initiation and progression of disc degeneration. [1, 3]

Despite extensive research, the influence of physiological loading and spinal mobility on solute redistribution within the IVD in vivo remains incompletely understood. Previous investigations have examined disc deformation, fluid-content changes and nutrient transport using cadaveric specimens, experimental models and controlled loading protocols. [4,5] Although these approaches have provided important insights into disc biomechanics, their ability to reproduce the complex loading conditions encountered during everyday activities is limited. Upright, weight-bearing magnetic resonance imaging (MRI) offers an opportunity to investigate spinal structures under physiological axial loading and to evaluate positional changes in disc morphology and segmental relationships that may not be apparent during conventional supine imaging.[6, 7] This approach is particularly relevant when studying intervertebral segments with different mobility characteristics, including hypermobile and relatively immobile segments, in which the mechanical environment may differ despite similar morphological appearances.

Advances in quantitative MRI have also enabled the investigation of disc solute transport through serial post-contrast imaging. Following intravenous administration of a gadolinium-based contrast agent, temporal changes in signal intensity within the vertebral body, endplate and disc can be used to characterize contrast-agent redistribution and provide an indirect assessment of transport pathways.[8, 9] Rajasekaran and colleagues demonstrated distinct temporal enhancement patterns in human lumbar discs and highlighted the importance of endplate integrity in determining the extent and distribution of contrast penetration.[8] Subsequent studies have further investigated post-contrast enhancement patterns across healthy, ageing and degenerated discs.[9] However,

gadolinium-based contrast agents serve as surrogate tracers; their kinetics should not be interpreted as direct measurements of glucose or oxygen transport. Moreover, the extent to which physiological loading and subsequent rest influence contrast redistribution in morphologically normal discs with different mobility characteristics remains insufficiently characterized.

Previous research has therefore established the importance of endplate-mediated transport, the utility of serial post-contrast MRI for evaluating disc diffusion, and the value of upright imaging for assessing the spine under physiological loading. [1, 6, 8, 10] Nevertheless, the interaction between segmental mobility, prolonged standing and subsequent rest in determining contrast redistribution within morphologically similar intervertebral discs remains an important knowledge gap. The present study aims to investigate the effects of standing and rest on the temporal pattern of post-contrast signal redistribution in morphologically similar intervertebral discs exhibiting different mobility phenotypes. By integrating upright MRI with serial post-contrast imaging, this study seeks to characterize differences in contrast-agent transport associated with distinct mechanical environments and to explore whether functional differences can be identified before overt morphological degeneration becomes apparent.

METHODS

Study design and participant selection: This prospective study was approved by the Institutional Ethics Committee. All participants provided written informed consent after receiving a detailed explanation of the study procedures, upright MRI acquisition and intravenous contrast administration.

Fifteen healthy volunteers (10 males and 5 females; age range, 20–30 years) were enrolled. All participants demonstrated Pfirrmann grade I morphology of the L5–S1 intervertebral disc, providing a relatively homogeneous baseline morphological assessment.

Based on segmental mobility characteristics, participants were classified into three physiologic motion phenotypes: (Table I)

1. Normally mobile group (n = 5): Individuals with normal L5–S1 segmental motion and no identifiable structural abnormalities on imaging.

2. Hypermobile group (n = 5): Individuals with bilateral L5 pars interarticularis defects and demonstrable segmental mobility on flexion–extension radiographs.

3. Immobile group (n = 5): Individuals with lumbosacral transitional vertebrae exhibiting partial or complete sacralization and no measurable L5–S1 segmental motion on flexion–extension radiographs.

Table I. Baseline demographic and radiological characteristics

Parameter	Normally mobile	Hypermobile	Immobile	Total
Number of participants	5	5	5	15
Sex (M/F)	3/2	4/1	3/2	10/5
Mean age ± SD (years)	24.8 ± 3.2	25.6 ± 3.9	25.1 ± 3.8	25.2 ± 3.6
Disc level analyzed	L5–S1	L5–S1	L5–S1	
Pfirrmann grade	I	I	I	

Contrast administration and imaging protocol: All participants underwent serial non-contrast and post-contrast MRI examinations using a standardized protocol adapted from previously published investigations of intervertebral disc contrast-agent diffusion. [8,9,11] A gadolinium-based contrast agent was administered intravenously at a dose of 0.3 mmol/kg body weight, following the protocol specified for the study.

Three imaging conditions were evaluated:

1. Baseline supine position: Reference condition for assessing intervertebral disc signal intensity before and after contrast administration.

2. Upright standing position: Used to investigate the effects of physiological axial loading on disc signal characteristics.

3. Recovery supine position: Acquired after the upright examination to evaluate changes in disc signal characteristics following the transition from standing to supine positioning.

The three positional acquisitions were performed consecutively, with only the time required for repositioning between examinations. The standing protocol was standardized across participants to minimize procedural variability. Delayed post-contrast T1-weighted imaging was performed 6 hours after contrast administration. All MRI examinations were initiated at 08:00 hours to minimize potential diurnal variation. Participants were instructed to avoid strenuous physical activity throughout the study period.

MRI acquisition parameters: MRI examinations were performed using a 0.25-T open upright MRI system (G-Scan Brio, Esaote, Genoa, Italy) equipped with a dedicated multichannel spine coil. Supine imaging was performed with the patient table in the horizontal position, while upright weight-bearing imaging was obtained by rotating the table to 90° (Fig I). Upright MRI facilitates evaluation of spinal anatomy under physiological loading and assessment of positional changes in the lumbar spine. [6, 7]

Identical imaging protocols were applied in both positions. Sagittal T2-weighted fast spin-echo sequences were acquired with a repetition time/echo time (TR/TE) of 2860/90 ms and a slice thickness of 4 mm. Sagittal T1-weighted spin-echo sequences were acquired with a TR/TE of 560/26 ms and the same slice thickness. The acquisition matrix was 224 × 208, the field of view was 320 × 320 mm, and the interslice gap was 0.5 mm. [6, 7]

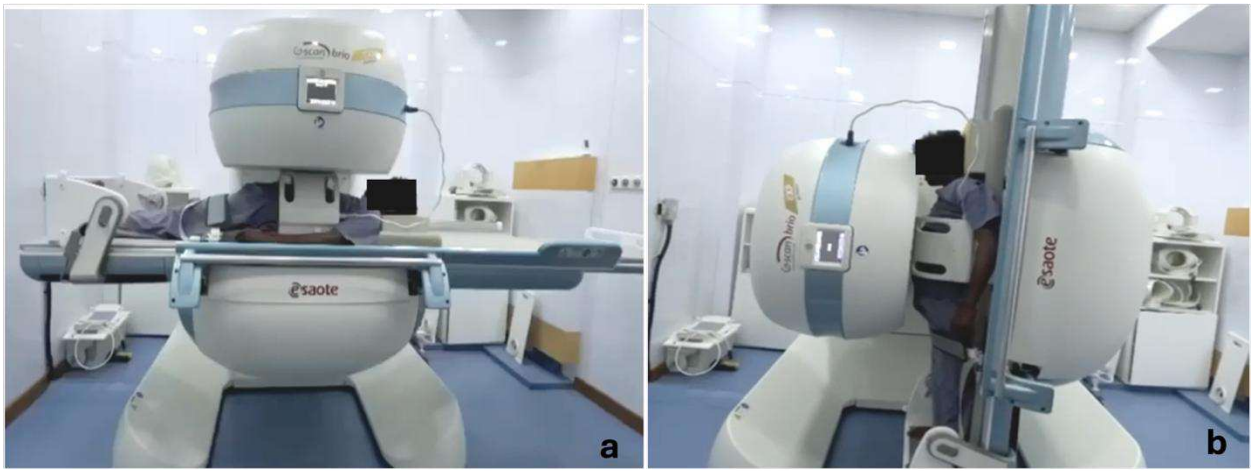


Fig I MRI acquisition using a 0.25-T upright MRI system in the supine (a) and standing (b) positions.

Image processing and segmentation: All MRI datasets were exported in Digital Imaging and Communications in Medicine (DICOM) format and processed using 3D Slicer (version 5.8.1), an open-source platform for medical image visualization and analysis.[12] Preprocessing included N4 bias-field correction to reduce low-frequency signal intensity inhomogeneity,[13] followed by resampling to isotropic voxel dimensions of 1 × 1 × 1 mm. Image intensity discretization was performed using a fixed bin width of 25, in accordance with established radiomics standardization recommendations.[14, 15] The same preprocessing parameters were applied uniformly across participants and imaging positions.

The L5–S1 intervertebral disc and adjacent endplates were manually segmented in three dimensions using the Segment Editor module in 3D Slicer (Fig II). Four anatomically defined regions of interest (ROIs) were analyzed: the superior endplate zone (Sup-EPZ), inferior endplate zone (Inf-EPZ), central nucleus pulposus (CNP) and peripheral nucleus pulposus (PNP).

Signal intensity (SI) measurements were obtained for each ROI across the three positional conditions using the corresponding pre-contrast and delayed post-contrast T1-weighted images. Percentage enhancement (EP) was calculated using the following formula EP = Post-contrast SI – Pre-contrast SI / Pre-contrast SI × 100.

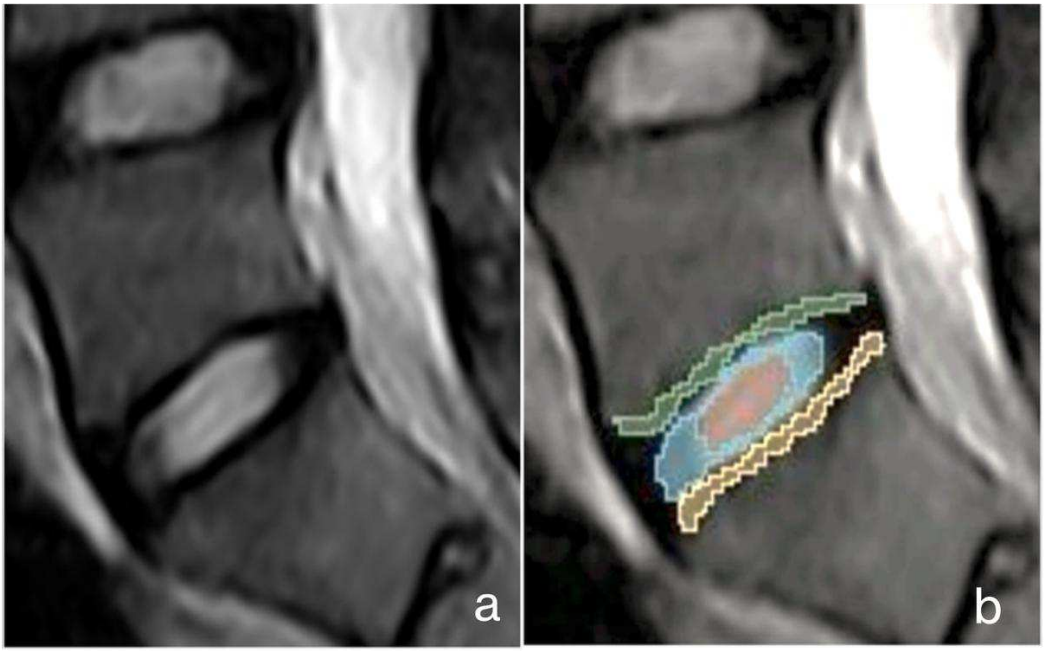


Fig II (a) Sagittal MRI Image of level of interest acquired for segmentation. (b)Three-dimensional segmentation of the L5–S1 intervertebral disc showing the superior endplate zone, inferior endplate zone, central nucleus pulposus and peripheral nucleus pulposus with color gradients.

RESULTS

Despite similar morphology and Pfirrmann grade I appearance, the three-disc phenotypes demonstrated distinct patterns of delayed post-contrast enhancement across supine, standing, and recovery conditions. (Table II)

1.Normal Discs: In normal discs, compared to pre-contrast supine, at 6 hours there was an enhancement of 14.63% at central nucleus pulposus (CNP) in supine position. But on standing, the enhancement decreased from to 7.23% representing a reduction of 7.40 percentage points. The peripheral nucleus pulposus (PNP) showed a larger reduction, from 16.60% to 3.28% (13.32 percentage points). Following return to the supine recovery position, PNP enhancement increased to 5.45%, representing a recovery-associated increase of 2.17 percentage points from the standing value.

2. Hypermobile Discs: Hypermobile discs demonstrated a substantially greater standing-associated reduction in disc region. The PNP enhancement decreased from 12.65% to -0.27%, a reduction of 12.92 percentage points. Hypermobile discs demonstrated a substantially greater standing-associated reduction in CNP enhancement than normal discs. CNP enhancement decreased from 5.79% in supine to −14.70% during standing, a change of -20.49 percentage points. This reduction was approximately 2.8 times the absolute change observed in normal CNP. The more pronounced phenotype-specific difference was therefore evident in the CNP rather than the PNP. During recovery, CNP enhancement increased from -14.70% to -6.82%, representing a rebound of 7.88 percentage points. PNP enhancement also increased, from -0.27% to 4.68%, a recovery-associated increase of 4.95 percentage points. Despite these increases, neither compartment returned to its corresponding supine enhancement value. Superior EPZ enhancement was negative in all three conditions, changing from -23.70% in supine to -30.46% during standing and −30.24% during recovery. The standing-associated change was -6.76 percentage points, followed by a minimal increase of 0.22 percentage points during recovery. In contrast to the marked changes in NP enhancement, the superior EPZ demonstrated little recovery-associated change after standing.

3. Immobile Discs: Immobile discs exhibited a different pattern of enhancement change. Unlike normal and hypermobile discs, immobile discs showed inconsistent patterns of disc enhancement with CNP enhancement decreased from -5.17% in supine to -17.45% during standing, a reduction of 12.28 percentage points. PNP enhancement showed a larger reduction, from -0.59% to -18.65%, corresponding to 18.06 percentage points. During recovery, CNP enhancement increased only from −17.45% to −16.06%, a change of 1.39 percentage points. In contrast, PNP enhancement increased from −18.65% to −10.80%, a recovery-associated increase of 7.85 percentage points.

Table II. Regional delayed (6 hrs) post-contrast enhancement of L5–S1 discs and adjacent endplate zones across segmental mobility phenotypes and imaging positions.

	Normal (Healthy Discs)	Hypermobile (Discs at Spondylolytic Segments)	Immobile (Discs at Transitional Segments)
Central Nucleus Pulposus			
Supine	14.63	5.79	-5.17
Standing	7.23	-14.70	-17.45
Recovery	0.73	-6.82	-16.06
Peripheral Nucleus Pulposus			
Supine	16.6	12.65	-0.59
Standing	3.28	-0.27	-18.65
Recovery	5.45	4.68	-10.80
Superior Endplate Zone			
Supine	9.81	-23.70	13.16
Standing	3.30	-30.46	43.76
Recovery	1.16	-30.24	12.70
Inferior Endplate Zone			
Supine	6.59	10.26	9.57
Standing	4.71	22.01	7.99
Recovery	0.56	6.59	7.37

DISCUSSION

The results of the study documents that intervertebral discs with similar morphology and Pfirrmann grade I appearance demonstrate distinct solute transport properties in different segmental mechanical environments. Using upright MRI at six hours after contrast administration, we compared normal, hypermobile and relatively immobile L5–S1 segments in supine, standing and post-standing recovery positions. Despite similar morphological grading, the three phenotypes differed in the magnitude and regional distribution of standing-associated enhancement changes, the subsequent recovery response and the behaviour of the superior endplate zone (EPZ). The novelty lies in comparing three human biological mobility phenotypes within the same positional imaging framework. The hypermobile group comprised participants with bilateral L5 pars interarticularis defects and demonstrable segmental mobility, whereas the immobile group

comprised participants with lumbosacral transitional vertebrae and no measurable motion on flexion and extension radiographs.

Previous human studies have established that delayed post-contrast MRI can investigate time-dependent contrast distribution in lumbar discs and that mechanical loading can alter this response. Previous MRI study of 100 healthy lumbar discs from 20 volunteers, enhancement was assessed at 0, 2, 6, 12 and 24 hours in supine, standing and post-standing recovery positions.[10] That study described standing-associated reduction in NP enhancement as “wash-out” and the subsequent regain of enhancement after returning supine as “squeezing-in” phenomenon. The present study extends that work by comparing positional enhancement patterns across naturally occurring mobility phenotypes rather than examining normal discs alone. Earlier, Arun et al. [16] studied 40 normal lumbar discs in eight volunteers and found that sustained supine loading reduced the rate of contrast transport into the central disc; enhancement continued to rise during recovery after unloading. These studies support the importance of loading history and recovery when interpreting delayed enhancement, although their protocols differ from the present study. To our knowledge, this study represents a novel human in-vivo comparison of three distinct segmental mobility phenotypes using delayed post-contrast MRI under natural weight-bearing conditions.

In *normally mobile discs*, standing was associated with a reduction in enhancement in both the central and peripheral nucleus pulposus (CNP and PNP) followed by regain of enhancement especially at PNP during post-standing recovery. Whereas the *hypermobile* phenotype demonstrated the largest standing-associated reduction in CNP enhancement than observed in normal discs. The subsequent recovery response provides an additional distinction with neither compartment returned to its initial supine enhancement value. In particular, the hypermobile phenotype does not demonstrate an absence of recovery. Rather, it demonstrates a substantial rebound that does not restore the initial enhancement state within the observed interval. The *immobile phenotype* was characterized by a pronounced peripheral NP enhancement reduction, limited recovery in the CNP, a more substantial PNP rebound, and a marked reversible change in superior EPZ enhancement. These findings suggest that restricted segmental mobility is associated with a different spatial pattern of delayed enhancement behavior rather than simply a uniformly attenuated response to loading.

Previous work has documented *wash-out* and *squeezing-in* phenomena of solute transport during standing and post-standing recovery in normal discs. Wash-out describes the reduction in enhancement associated with standing, while squeezing-in describes regain of lost enhancement following return to the supine position. Differences in segmental mobility may modify these processes. In hypermobile discs, standing produced a pronounced wash-out pattern in the central nucleus pulposus (NP), followed by partial squeezing-in after return to supine; however, enhancement did not return to baseline.

Regarding behavior of endplate zones, compared with normal discs, the inferior endplate in hypermobile discs showed a broadly similar directional response. In contrast, the superior endplate remained markedly negative across all positions, with minimal change between standing and recovery. In immobile discs, the inferior endplate showed comparatively little positional variation, whereas the superior endplate demonstrated a pronounced increase in enhancement during standing (13.16% to 43.76%), followed by a return towards its initial value during recovery (12.70%).

The potential clinical significance of these findings lies in the distinction between morphological appearance and functional response. All three groups demonstrated Pfirrmann grade I discs at L5–S1, yet their enhancement responses differed according to mobility phenotype. This observation raises the possibility that conventional morphological grading may not fully characterize the response of an apparently preserved disc to physiological loading. It may help identify whether apparently normal discs in hypermobile or relatively immobile segments demonstrate different responses to loading and recovery.

The findings may also inform future investigations of disc homeostasis in conditions involving altered segmental mechanics, including spondylolytic hypermobility and lumbosacral transitional anatomy. However, this study does not establish that the observed enhancement patterns predict subsequent degeneration, pain, disability or treatment outcomes. Nor does it establish a diagnostic threshold for abnormal transport behavior. The immediate clinical value is therefore conceptual.

Several limitations should be considered when interpreting these findings. The study included only 15 participants, with five in each mobility phenotype. Only the L5–S1 level was evaluated to have

comparable groups of normal, hypermobile and immobile segments. Although this provides a consistent anatomical level for comparison, the findings may not apply to other lumbar levels, where loading conditions, disc geometry and segmental mobility differ. Delayed post-contrast enhancement is an indirect marker of contrast distribution rather than a direct measurement of nutrient transport. Gadolinium-based contrast does not reproduce the transport kinetics of every physiological nutrient, and signal enhancement may be influenced by tissue characteristics, contrast kinetics, acquisition conditions and partial-volume effects. Negative enhancement values indicate a post-contrast signal below the pre-contrast reference under the stated calculation; they do not represent negative solute concentrations. The positional acquisitions were obtained consecutively at the six-hour post-contrast time point, with the time required for repositioning. The design therefore characterizes enhancement differences across positions and the immediate recovery response, rather than continuously measuring transport during standing or over a prolonged recovery period. Finally, the study used a 0.25-T upright MRI system and a signal-intensity-based enhancement calculation.

In conclusion, morphologically similar Pfirrmann grade I L5–S1 discs demonstrated distinct delayed post-contrast enhancement patterns across normal, hypermobile and relatively immobile segmental phenotypes. Hypermobile discs showed the largest standing-associated reduction in central NP enhancement, followed by partial recovery. Immobile discs showed the largest reduction in peripheral NP enhancement, limited recovery in the central NP and a pronounced reversible change in superior EPZ enhancement. These findings support further investigation of the relationship between segmental mechanical environment and regional disc–endplate enhancement behavior.

REFERENCES:

1. Urban JPG, Smith S, Fairbank JCT. Nutrition of the intervertebral disc. Spine (Phila Pa 1976). 2004;29(23):2700-9. doi: 10.1097/01.brs.0000146499.97948.52.

2. Urban JP, Holm S, Maroudas A, Nachemson A. Nutrition of the intervertebral disk. An in vivo study of solute transport. Clin Orthop Relat Res. 1977;(129):101-14.

3. Adams MA, Roughley PJ. What is intervertebral disc degeneration, and what causes it? Spine (Phila Pa 1976). 2006;31(18):2151-61. doi: 10.1097/01.brs.0000231761.73859.2c.

4. Malko JA, Hutton WC, Fajman WA. An in vivo magnetic resonance imaging study of changes in the volume (and fluid content) of the lumbar intervertebral discs during a simulated diurnal load cycle. Spine (Phila Pa 1976). 1999;24(10):1015-22. doi: 10.1097/00007632-199905150-00016.

5.Gullbrand SE, Peterson J, Mastropolo R, Roberts TT, Lawrence JP, Glennon JC, DiRisio DJ, Ledet EH. Low-rate loading-induced convection enhances net transport into the intervertebral disc in vivo. Spine J. 2015 May 1;15(5):1028-33. doi: 10.1016/j.spinee.2014.12.003. Epub 2014 Dec 9. PMID: 25500262.

6. Weishaupt D, Boxheimer L. Magnetic resonance imaging of the weight-bearing spine. Semin Musculoskelet Radiol. 2003;7(4):277-86. doi: 10.1055/s-2004-815675.

7. Alyas F, Connell D, Saifuddin A. Upright positional MRI of the lumbar spine. Clin Radiol. 2008;63(9):1035-48.

8. Rajasekaran S, Naresh Babu J, Arun R, Armstrong BRW, Shetty AP, Murugan S. ISSLS prize winner: a study of diffusion in human lumbar discs: a serial magnetic resonance imaging study documenting the influence of the endplate on diffusion in normal and degenerate discs. Spine (Phila Pa 1976). 2004;29(23):2654-67. doi: 10.1097/01.brs.0000148014.15210.64.

9. Rajasekaran S, Naresh-Babu J, Murugan S. Review of postcontrast MRI studies on diffusion of human lumbar discs. J Magn Reson Imaging. 2007;25(2):410-8. doi: 10.1002/jmri.20853.

10. Naresh-Babu J, Gajendra, Prajwal GS. ISSLS prize in clinical/bioengineering science 2024: How standing and supine positions influence nutrient transport in human lumbar discs? -A serial

post-contrast MRI study evaluating interplay between convection and diffusion. Eur Spine J. 2024 May;33(5):1728-1736. doi: 10.1007/s00586-024-08243-4. Epub 2024 Apr 25. PMID: 38662214.

11. Akansel G, Haughton VM, Papke RA, Censky S. Diffusion into human intervertebral disks studied with MR and gadoteridol. AJNR Am J Neuroradiol. 1997;18(3):443-5.

12. Fedorov A, Beichel R, Kalpathy-Cramer J, Finet J, Fillion-Robin JC, Pujol S, et al. 3D Slicer as an image computing platform for the Quantitative Imaging Network. Magn Reson Imaging. 2012;30(9):1323-41. doi: 10.1016/j.mri.2012.05.001.

13. Tustison NJ, Avants BB, Cook PA, Zheng Y, Egan A, Yushkevich PA, et al. N4ITK: improved N3 bias correction. IEEE Trans Med Imaging. 2010;29(6):1310-20. doi: 10.1109/TMI.2010.2046908.

14. Zwanenburg A, Vallières M, Abdalah MA, Aerts HJWL, Andrearczyk V, Apte A, et al. The Image Biomarker Standardisation Initiative: standardized quantitative radiomics for high-throughput image-based phenotyping. Radiology. 2020;295(2):328-38. doi: 10.1148/radiol.2020191145.

15. van Griethuysen JJM, Fedorov A, Parmar C, Hosny A, Aucoin N, Narayan V, et al. Computational radiomics system to decode the radiographic phenotype. Cancer Res. 2017;77(21): e104-7. doi: 10.1158/0008-5472.CAN-17-0339.

16. Arun R, Freeman BJ, Scammell BE, McNally DS, Cox E, Gowland P. 2009 ISSLS Prize Winner: What influence does sustained mechanical load have on diffusion in the human intervertebral disc? An in vivo study using serial postcontrast magnetic resonance imaging. Spine (Phila Pa 1976). 2009;34(21):2324–2337. doi:10.1097/BRS.0b013e3181b4df92.