



Imaging Analysis of the High-Intensity Zone on Lumbar Spine Magnetic Resonance Images: Classification, Features and Correlation with Low Back Pain

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Aim: Early studies suggested that the high-intensity zone (HIZ) on lumbar MRI was a diagnostic sign of painful internal disc disruption (IDD). However, recent studies have questioned its diagnostic value. This study is conducted to explore imaging features of HIZ and to investigate the correlation between these characteristics and low back pain (LBP), further studying the predictive value of HIZ.

Methods: A retrospective study of 1188 cases was performed. MR images were read and analyzed by two experienced, blinded radiologists.

Results: A total of 575 (48.4%) individuals exhibited HIZ. The prevalence of posterior HIZ (32.3%) was significantly higher than that of anterior HIZ (23.6%; $P < 0.01$). Round type was the most common shape (61.0%) on sagittal view. Only 37 HIZs (4.6%) were identified on axial views. A total of 263 HIZ discs (32.5%) were found to have additional diagnostic signs of IDD, which is difficult to distinguish from the annulus fibrosus. In subjects with consecutive slides showing HIZ, the incidence of LBP was significantly higher than in single-slide HIZ individuals (58.0% vs 48.6%, $P < 0.05$).

Conclusion: MRI-visualized HIZ is a highly valuable method of screening for lumbar IDD. It is demonstrated that consecutive-slide HIZ was a more reliable indicator for discogenic LBP than single-slide HIZ.

Keywords: lumbar spine, intervertebral disc, MRI, high-intensity zone, low back pain

Introduction

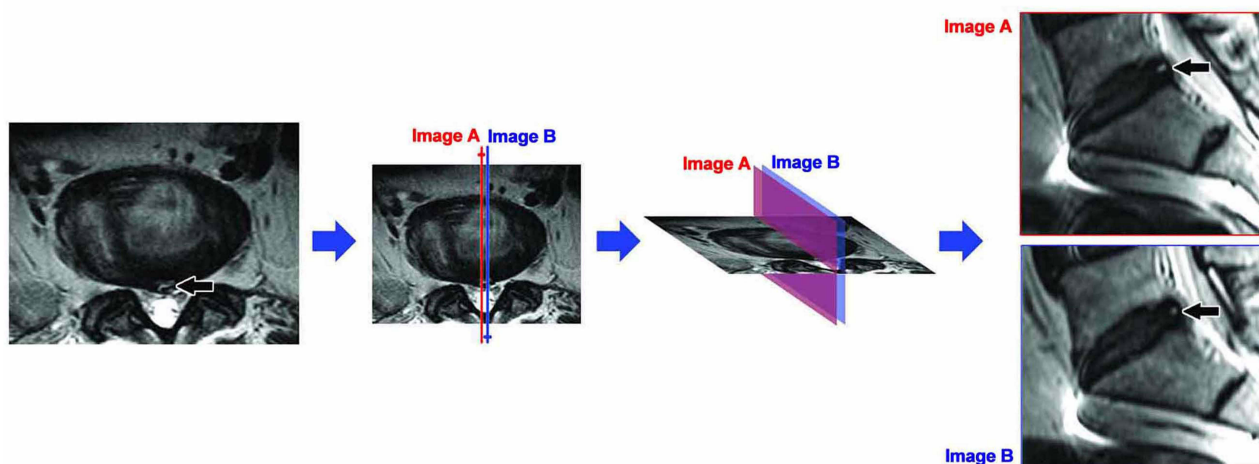
Direct videoendoscopic visualization is the only surgical method that directly shows internal disc disruption (IDD) structural changes. Computed tomography/discography (CTD), including morphologic assessment and a pain provocation test, is recognized as the best imaging modality to directly determine the presence of IDD and discogenic low back pain (LBP).¹⁻³ According to prior studies, the role of CTD is crucial in diagnosing painful discs and improves interpretation of case-specific diagnostic value of other methods, eg, high-intensity zone (HIZ) change, as a gold standard.^{3,4} However, discography is an invasive procedure, and accidental puncture of discs can lead to premature or hastened degeneration.⁵ Therefore, a noninvasive method to reliably diagnose discogenic LBP would be of enormous clinical value.

HIZ is a sign on lumbar spine T2-weighted magnetic resonance (MR) images and was found a diagnostic sign of painful IDD with a positive predictive value of 86%.^{6,7}

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Graphical Abstract

Consecutive slides HIZ



Prior work has reported that the HIZ changes along the endplate margin in the region of Sharpey's fibers, enhanced on injection of gadolinium-DTPA, indicate inflammation and neovascularization.⁸ In the past few decades, there has been considerable debate over the predictive value of HIZ on lumbar MR images for LBP.^{4,9–14} However, increasing evidence suggests that HIZ, the classical sign described by Aprill and Bogduk,⁶ indicates a part of the natural history of disc degeneration,^{14,15} but is not a reliable indicator of symptomatic IDD.^{4,10,11,14} In practice, HIZ signs appear in various forms and can be characterized utilizing spatial location and analysis with lumbar MR imaging sequences.^{16,17} Generally, the diagnostic utility of HIZ imaging results is still a matter of question. A deep understanding of the cellular pathogenesis underlying these features is of critical necessity for understanding and implementing HIZ-related clinical decision-making frameworks.

In order to explore imaging features of HIZ found in lumbar MR images and investigate the correlation between these characteristics and LBP symptoms, we retrospectively reviewed lumbar MR images from 5940 discs in 1188 cases alongside their corresponding medical records.

Materials and Methods

Study Subjects

Among them, 511 subjects with LBP and 677 without were diagnosed by orthopedic surgeons with a standard clinical

evaluation including physical examination and MR imaging, etc. LBP, in this study, was defined as low back pain with or without referred pain in the lower limb, which persisted for at least 6 weeks.¹⁸ Criteria for exclusion in this study were as follows: (1) medical records were incomplete; (2) the MR image quality was poor; (3) the structure of spine was disordered; (4) evidence of the presence of diseases, such as infection, trauma, spondylolisthesis, lumbar spinal stenosis syndrome, tumor, metabolic bone disease. If there were two or more records of one patient, the most recent record was included in this study.

MR Imaging

All lumbar MR imaging examinations were performed with a spinal surface coil using a 1.5 Tesla superconducting MR system (Signa, GE Medical System, Milwaukee, Wisconsin, USA). All subjects were examined in the supine position to acquire sagittal T1-weighted spin echo (Repetition Time (TR): 450–500 msec; Echo Time (TE): 15–20 msec; 256×192 Matrix; Section Thickness 3–4 mm; Intersection Gap 0.5–1 mm), sagittal T2-weighted spin echo (TR: 2200–3500 msec; TE: 90–120 msec; 256×192 Matrix; Section Thickness 3–4 mm; Intersection Gap 0.5–1 mm) and Axial T2-weighted spin echo (TR: 2400–3500 msec; TE: 90–120 msec; 256×256 Matrix; Section Thickness 4 mm; Intersection Gap 0.5 mm) MR imaging with a fixed imaging protocol. All MR images were collected and stored in the

picture archiving and communication system (PACS; GE Centricity, GE Healthcare).

Outcome Measures

Diagnostic criteria for HIZ were adapted from the descriptions of Aprill and Bogduk,⁶ Wang et al^{16,19} and Carragee et al.¹⁰ Briefly, a high-intensity signal located in the substance of the posterior, anterior, anterolateral, or posterolateral annulus fibrosus, dissociated from the signal of the nucleus pulposus, was inspected to be approximately the same intensity as the cerebrospinal fluid signal at the same level on lumbar T2-weighted MR images. All lumbar HIZs were classified into dot type, round type, vertical type, or irregular type on the basis of shape on sagittal T2-weighted MR images (Figure 1). Dot type was defined as small dot HIZ. Round type was defined as concentric, oval, or

analogous figure Vertical type was defined as a vertical layer to the adjacent endplate, and irregular type was noted as shapes that did not fit into any of these three categories (dot, round, or vertical). The HIZs located in similar position of the same disc on two or more adjacent sagittal images were counted as the same one, ie, consecutive slides HIZ (Figure 2). The number of consecutive slides, which displayed the same HIZ was recorded. Localization method of HIZ followed the process described by Wang and Hu.¹⁶

IDD was evaluated as an intervertebral disc protrusion, extrusion, or other diagnostic signs.^{17,20–22} Disc protrusion was defined as localized or focal displacement of nucleus pulposus beyond the confines of the annulus fibrosus. Disc extrusion, as defined in this study, was considered to be when the distance between the edges of the disc material beyond the intervertebral disc space was greater than the distance

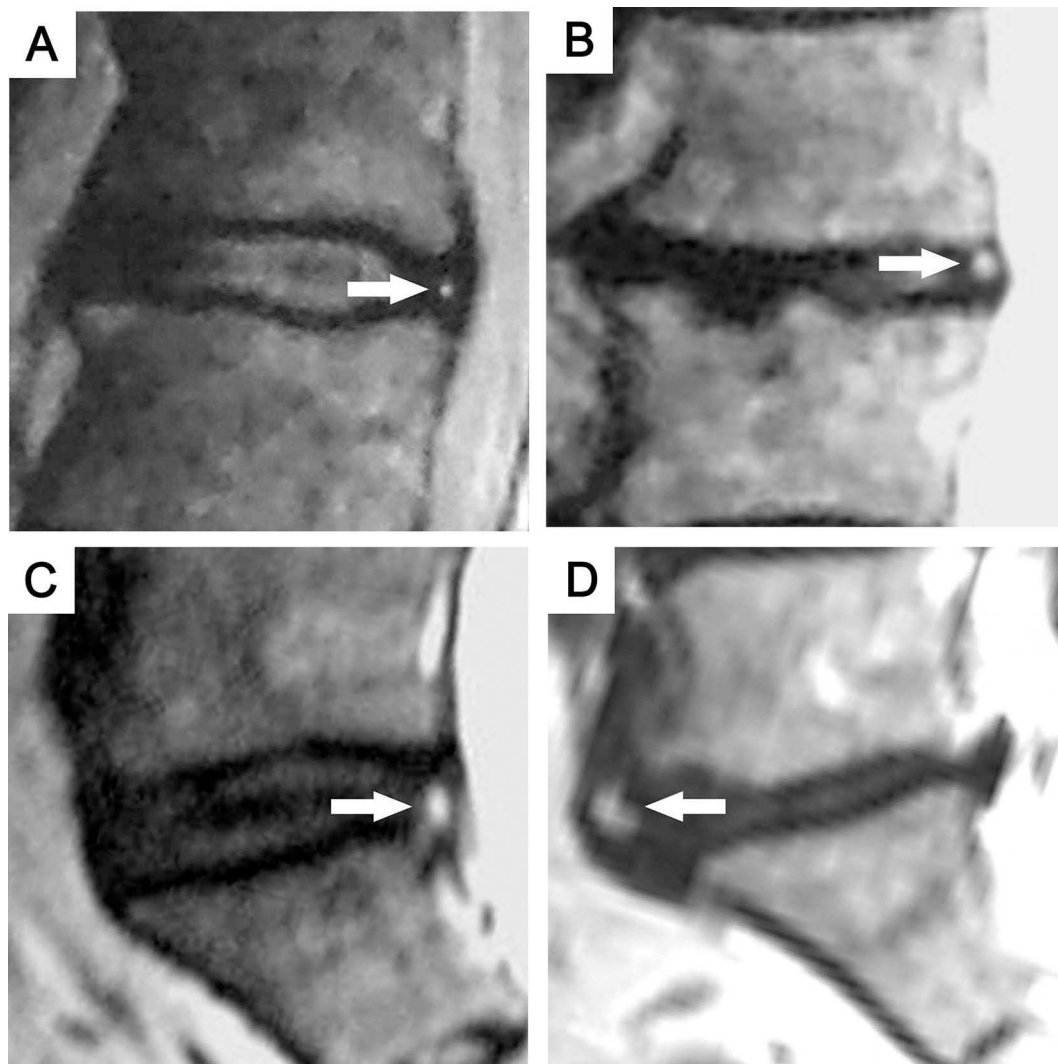


Figure 1 Morphological classification of HIZ on sagittal T2-weighted MR images. (A) Dot type; (B) round type; (C) vertical type; (D) irregularity type.

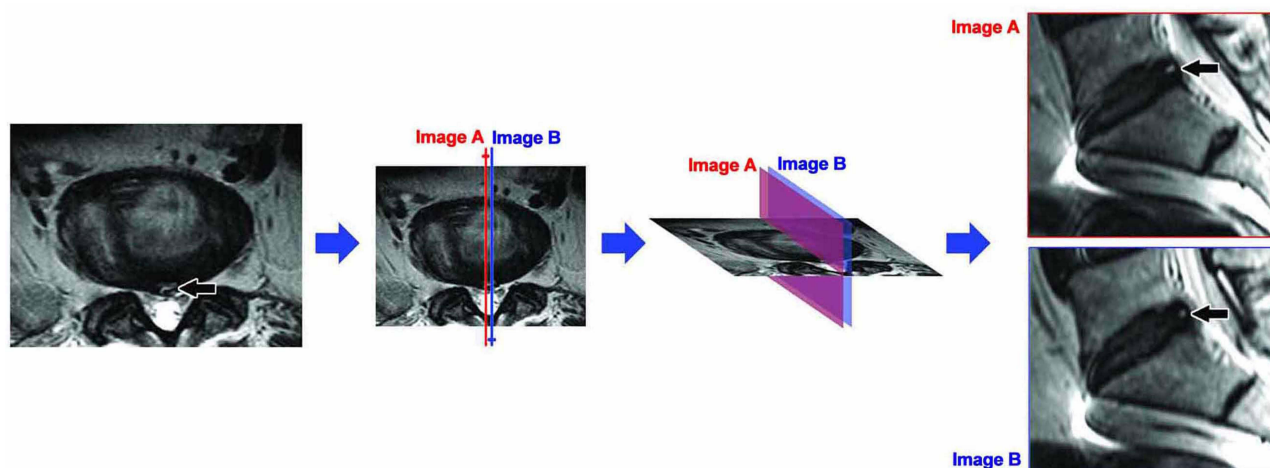


Figure 2 Consecutive slides HIZ. Axial T2-weighted MR image of the lumbar spine shows a HIZ in the posterior annulus fibrosus at L5/S1 (black arrow). Two adjacent sagittal images, slide A (red) and B (blue), show HIZs in similar position at L5/S1 (black arrow), ie Consecutive slides HIZ. It indicates the same HIZ lesion on Axial T2-weighted MR image.

between the edges of the base of the disc material beyond the intervertebral disc space. In addition to HIZ, other diagnostic signs of IDD included “rat tail,” “mallet head,” or other irregular shape signals on sagittal T2-weighted MR images extending from the nucleus pulposus forward or posterior into the signal of the annulus fibrosus (Figure 3).²²

Disc bulge was defined as a disc displacement beyond the contour of the normal disc space, usually greater than 25% (90°) of the circumference of the disc and typically less than 3 mm beyond the edges of the adjacent vertebral body apophyses.^{21,23}

Data Collection

Baseline characteristics, ie, gender and age, were obtained from medical records. LBP symptoms as diagnosed by orthopedic surgeons and physical examination reports were obtained from medical records. The diagnosis and analysis of HIZ were performed by two blinded experienced radiologists, ie, they were unaware of any demographic or clinical characteristics of the subjects. MR image readings and localizations were conducted by the two radiologists independently and separately. If the two results were different, the two radiologists discussed the image until they agreed upon an outcome. If the two radiologists still disagreed on the result, a third reader was invited to perform an independent reading. All data were collected and entered into SPSS software for analysis.

Statistical Analysis

Measurement data were described as the mean, standard deviation (SD), and range. Enumeration data were

expressed as a percentage. Differences in ratios were compared using Pearson chi-square tests for categorical variables. Odds ratio (OR), positive predictive value (PPV), negative predictive value (NPV), quotient of positive probability (QPP), quotient of negative probability (QNP), specificity (S), sensibility (E) and kappa coefficient (κ) were calculated to assess diagnostic accuracy. For all the statistical tests, P values less than 0.05 were considered statistically significant. Statistical analysis was performed using Statistical Package for the Social Sciences 22.0 software (IBM SPSS Statistics ver. 22.0 for Windows, IBM Corporation, Armonk, NY, USA).

Ethics Statement

The protocol was reviewed and approved by the clinical trial ethics committee/institutional review board (IRB) of Qingdao Municipal Hospital, Qingdao, China (2021–072). For this anonymous retrospective study, formal consent was not required according to the ethical standards. This study was conducted in accordance with the Declaration of Helsinki.

Results

One thousand one hundred and eighty-eight cases (including 5940 discs) who accepted lumbar spine MR imaging examinations between March, 2010 and October, 2015 were reviewed and included in the study. There were 553 females (46.5%) and 635 males (53.5%) ranging from 16 to 90 years of age (Mean 48.3 years; SD 16.3). A total of 575 (48.4%) individuals out of 1188 subjects exhibited

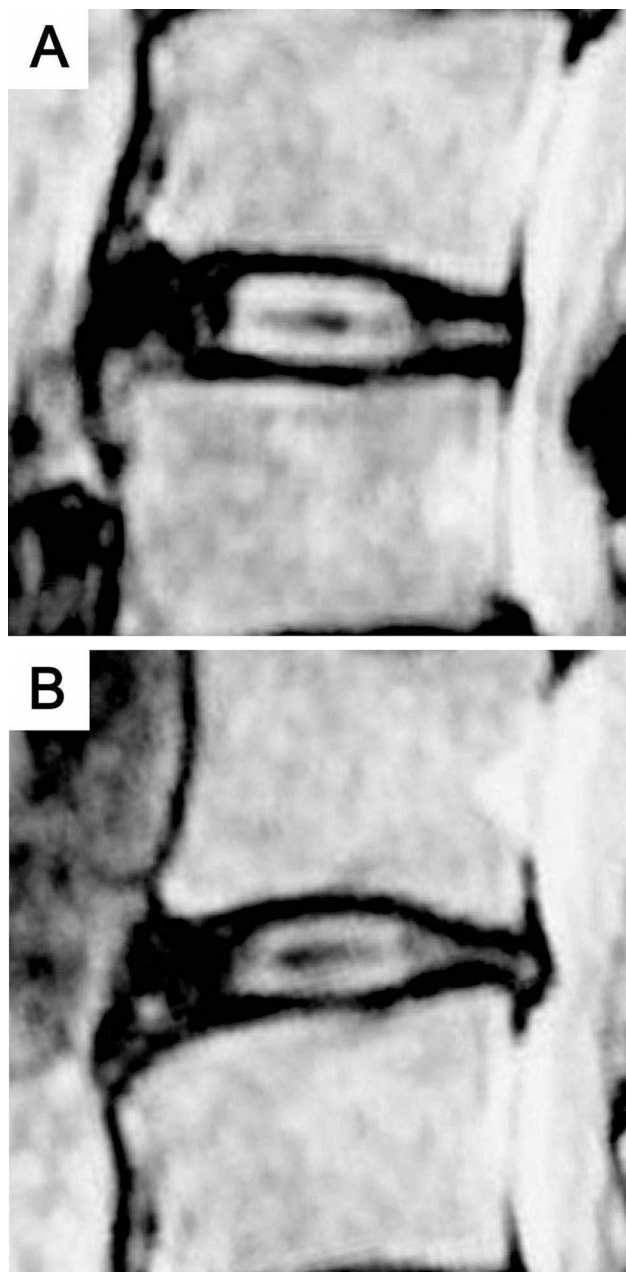


Figure 3 Abnormal signals extending from nucleus pulposus forward or posterior into the signal of the annulus fibrosus on sagittal T2-weighted MR images. (A) “Rat tail” abnormal signal; (B) “Mallet head” abnormal signal.

HIZ on T2-weighted MR images. Of the 575 HIZ individuals, 316 were males (55.0%). The mean age was 53.5 ± 13.1 years (range: 16–86 years).

Prevalence and Localization of HIZ

One hundred and eighty-three individuals were found to have multiple discs with HIZ. HIZ was noted in the posterior or anterior annulus fibrosus on MR images, and the prevalence of posterior HIZ (32.3%) was significantly

higher than that of anterior HIZ (23.6%; $\chi^2=22.607$, $P=0.000$). All HIZs were located in the outer annulus close to the outer edge of the annulus fibrosus (Figures 1 and 2). Only a part of irregularity-type HIZs extended into middle annulus. Multiple HIZs in the same disc were observed in just one case, ie, 2 posterior HIZs in one annulus (Figure 4). The prevalence and localization of HIZ are illustrated in Table 1.

Morphology of HIZ

Morphological classification of HIZ in the posterior/anterior annulus fibrosus on sagittal T2-weighted MR images is illustrated in Table 2. Dot type HIZ was more likely to be missed due to its small area. We found that round type was the most common shape of HIZ in both the posterior and anterior annulus (posterior: 59.2%, anterior: 63.4%, combined: 61.0%). Some vertical type HIZs shaped like a “comma” were more common in cases of bulged disc and were frequently located in the inferior part of the outer annulus. HIZ on axial T2-weighted MR images was frequently recognized as either linear or fusiform bright signal parallel to the adjacent outer edge of disc (Figure 2). However, only 37 HIZs (4.6%) were identified on axial views in this sample.

HIZ and the Other Diagnostic Signs of IDD

Of the 810 HIZ discs, 263 (32.5%) were found with diagnostic signs of IDD other than disc herniation. One

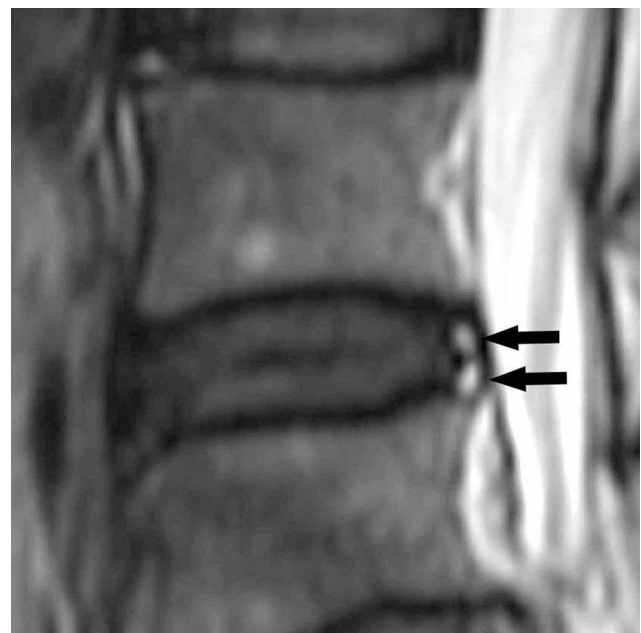


Figure 4 Sagittal T2-weighted MR image shows 2 posterior HIZs (black arrow) at L4/5.

Table 1 Prevalence and Localization of HIZ (n=1188)

Characteristics	n	Anterior	Posterior	Significance	
				χ^2	P value
HIZ	811	355	456	22.607	0.000
HIZ disc	810	355	455		
HIZ individual	575 ^a	280	384		
HIZ prevalence (%)	48.40	23.57	32.32		

Note: ^aEighty nine individuals had both anterior/ posterior HIZ.

Table 2 Morphological Classification of HIZ on Sagittal T2-Weighted MR Images (n=811)

Classification	Anterior HIZ		Posterior HIZ		Total	
	n	%	n	%	n	%
Dot type	45	12.68	71	15.57	116	14.30
Round type	225	63.38	270	59.21	495	61.04
Vertical type	54	15.21	69	15.13	123	15.17
Irregular type	31	8.73	46	10.09	77	9.49
Total	355	100	456	100	811	100

HIZ (a single HIZ in one disc) was identified in a herniated disk in the inferior part of large disc extrusion (Figure 5). The other diagnostic signs of IDD, ie, “rat tail,” “mallet head,” or other abnormally shaped signals, were relatively brighter than the annulus fibrosus signal, but lower than the signal intensity of normal nucleus pulposus (Figure 3). Indeed, it is sometimes difficult to accurately distinguish abnormal signal from the normal annulus.

Correlation Between Consecutive Slides HIZ and LBP

One hundred and seventy-five lumbar discs exhibited consecutive HIZ on 2 slides (Figure 2), and 11 discs showed consecutive HIZ on 3 slides. Of the 575 HIZ subjects, 176 (30.6%) had HIZ on consecutive slides (either 2 or 3 consecutive sagittal slides) and 296 (51.5%) experienced LBP. In patients with consecutive-slide HIZ, the incidence of LBP was significantly higher than that in individuals with single-slide HIZ (58.0% vs 48.6%, $\chi^2=4.259$, $P=0.039$). The specificity of consecutive slides HIZ in excluding LBP was 89.1%, which was higher than that of HIZ in general (combined single and consecutive specificity of 58.8%). Consecutive HIZ MRI visualization has a better odds ratio for patients to have discogenic LBP given its better profile of sensibility, specificity and negative and positive predictive values compared to single HIZ

MRI given its low specificity despite a better sensibility. These results are reported in Table 3.

Discussion

Pathophysiology of HIZ

Since its initial description by Aprill and Bogduk in 1992,⁶ the prevalence of HIZ in the posterior annulus has been reported in a wide range of symptomatic and asymptomatic subjects.^{6,7,9,10,14,24–26} In order to avoid the bias caused by sample size in former studies, we examined a relatively large sample of 1188 cases. In this sample, we found a 32.3% prevalence of posterior HIZ. In addition, we found a 23.6% prevalence of anterior annulus HIZ, an extended definition of HIZ sign first analyzed by Wang and Hu in 2009.¹⁹ Thus, we found that the prevalence of posterior HIZ was significantly higher than that of anterior HIZ. Prior studies have suggested that the adult lumbar disc is mainly avascular, although tiny collateral

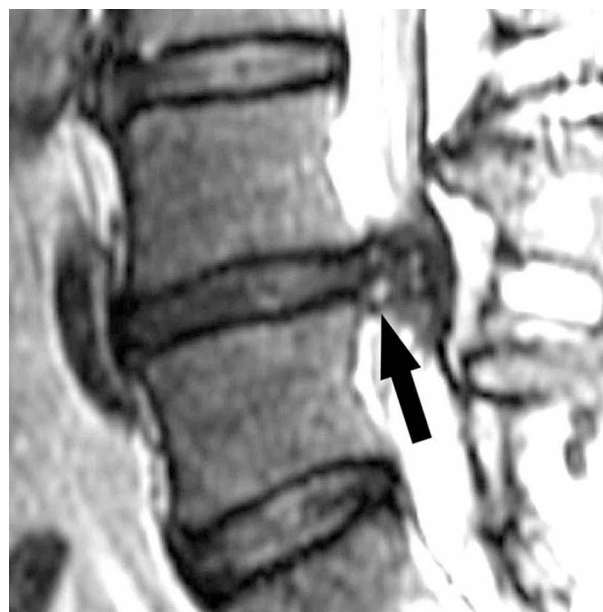


Figure 5 Sagittal T2-weighted MR image shows a HIZ (black arrow) in the inferior part of large disc extrusion at L4/5.

Table 3 Correlation Between Consecutive Slides HIZ and LBP (n=1188)

Characteristics	n	No HIZ	HIZ			Significance	
			Single Slide	Consecutive Slides	Total	χ^2	P value
Individual (n)	1188	613	399	176	575		
LBP individual	511	215	194	102	296		
LBP prevalence (%)	43.01	35.07	48.62	57.95	51.48	4.259	0.039

Notes: LBP correlation to consecutive HIZ images: OR= 2.55, PPV=0.58, NPV=0.65, QPP=2.05, QNP=0.80, S= 0.32, E=0.84, κ =0.178. LBP correlation to Single HIZ images: OR= 1.75, PPV=0.49, NPV=0.65, QPP=1.40, QNP=0.80, S= 0.47, E=0.66, κ =0.135.

Abbreviations: OR, odds ratio; PPV, positive predictive value; NPV, negative predictive value; QPP, quotient of positive probability; QNP, quotient of negative probability; S, specificity; E, sensibility; κ , Kappa coefficient.

vessels were observed in some outer annular lamellae of degenerated discs.²⁷ Peng et al harvested 11 specimens of HIZ discs from LBP patients for histologic examination, and found that the newly formed blood vessels were seen around the tears, suggesting that the HIZ lesion was primarily made up of disorganized, vascularized granulation tissue, possibly formed as a result of the healing response to annular tears.⁹ Goel et al demonstrated that high inter-laminar shear stress, caused by asymmetry in disc structure, was an important contributor to disc degeneration, especially laminae separation.²⁸ Structurally, the weak posterior part of annulus fibrosus is more susceptible to injury,²⁹ thereby increasing the probability of tear and subsequent HIZ formation. In good agreement with these data, we found that posterior HIZ was more common than anterior HIZ in our sample. Moreover, from our observation, all HIZs were located in the outer annulus near the outer edge of the annulus fibrosus. We believe that the HIZ might originate from adjacent outer annular lamellae or tissue outside the annulus fibrosus.

Morphology of HIZ

As the use of advanced MR equipment has gained widespread clinical use, increasing amounts and types of HIZ lesions and shapes have been identified. The classification of HIZ was based on shape, including size and angle between long axis and endplate, etc., in this study. Dot type HIZ is small and difficult to be classified by shape. "Comma" shape, commonly associated with bulged discs, may be related to the folding of annular fibers²² and mechanical effects of surrounding tissue. The shape of HIZ on axial MR images was similar to that of concentric tears in the annulus fibrosus on axial CTD images, confirming the findings of Peng et al,⁹ ie, HIZ potentially represented the vascularized granulation tissue extending along the tear. During regular axial MR scanning, sections are 3–4 mm in thickness. Therefore, it is crucial to note that

many HIZs may not appear on axial T2-weighted MR images if the size of the vascularized granulation tissue is small. We found that only 37 HIZs (4.6%) were identified on axial views in this sample, in stark contrast with our finding of HIZs on sagittal images.

HIZ and Disc Prolapsed/IDD

Clinical studies have suggested that CTD is the most reliable method for direct diagnosis of IDD. However, spinal surgeons and radiologists believe that non-invasive detection methods are more suitable for IDD screening than CTD due to associated risks.⁵ MR examination is currently considered to be the best imaging instrument for identification of ruptured discs with several features including herniated disc material, HIZ sign, and other abnormal signals in the annulus fibrosus.^{22,30} Intervertebral disc protrusion and extrusion are defined as displacement of the nucleus pulposus beyond the annulus fibrosus and indicate that the nucleus pulposus has extruded out of a ruptured disc along the annular fissure. This usually occurs within serious IDD and is easily distinguishable in medical imaging. The HIZ sign, to our knowledge, can be an indicator of IDD prior to disc herniation. Hence, we believe that HIZ and disc herniation indicate two different stages of lumbar disc disruption. In this study, only 32.5% of HIZ discs showed "rat tail," "mallet head," or other abnormal signals in the annulus fibrosus. In addition, it is difficult to distinguish abnormal signal from the annulus because of the relatively lower signal intensity. Therefore, with the exception of HIZ, we do not believe that abnormal signals in the annulus fibrosus are likely to be a valuable indicator for IDD.

Consecutive-Slide HIZ and Annular Pathologies

The HIZ sign, an imaging result, corresponds to the histologic feature of vascularized granulation tissue in the annular tears of intervertebral discs.⁹ Therefore, as a solid shape, the HIZ

lesion could theoretically be described in any plane. However, in clinical practice, sagittal MR images have been routinely utilized for assessment of HIZ since the first report by Aprill and Bogduk.⁶ Consecutive-slide HIZ on sagittal MR imaging indicates a slender HIZ parallel to the outer edge of the disc and corresponds to a relatively longer concentric tear. Several former studies have suggested that HIZ associated with pain correlated significantly with Dallas Grade 4 annular disruption,^{6,11} ie, radial fissure extending to the outer third of the annulus and involving >30 degrees of the disc circumference. We also found that there was a statistically significant association between consecutive-slide HIZ and LBP, and the clinical value of consecutive-slide HIZ was greater than that of single-slide HIZ for diagnosing discogenic LBP.

There were several limitations to this study. First, the study sample biased toward those data which were readily available in hospital records. Indeed, many individuals who may have not accepted MR examinations were excluded. It is likely that these adults would have been different in some characteristics from these study subjects. Another limitation of our study was the potential bias associated with the clinical diagnosis of LBP; provocation discography was not utilized for assessment of LBP. Finally, we found several unexpected results that have still not been explained. For example, we do not know what factors might lead to such a high prevalence of anterior HIZ, or what causes the formation of HIZ in the inferior part of the large disc extrusion.

Conclusion

MRI-visualized HIZ is a highly valuable method of screening for lumbar IDD. It is demonstrated that consecutive-slide HIZ was a more reliable indicator for LBP than single-slide HIZ.

Disclosure

The authors report no conflicts of interest in this work.

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