



The relevance of high-intensity zones in degenerative disc disease

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Abstract

Purpose The purpose of this study was to review the current understanding of high-intensity zones (HIZ) in the lumbar spine with particular attention to its imaging phenotype and clinical relevance.

Methods A review was conducted of studies related to HIZ. Particular attention was made to imaging phenotypes and classification, and its relationship with discogenic low back pain (LBP).

Results The most current classification system of HIZ is based on location (anterior and posterior), morphology (round, fissure, vertical, rim, or giant types), and its appearance on both T1- and T2-weighted magnetic resonance imaging (MRI). HIZ are commonly manifested with disc degeneration. Hence, both conditions share similar risk factors such as the effect of frequent and prolonged disc loading. The clinical significance of HIZ however is not conclusive. Provocative discography is not sensitive (~70%) for eliciting a concordant pain response. Population-based studies have conflicting results regarding the prevalence (14–63%) of HIZ and its correlation with LBP.

Conclusions HIZ are likely a risk factor for discogenic LBP. However, its etiology and pathophysiology are not well understood. Some clinical studies suggest a link between its occurrence and LBP. However, the results are not consistent as a result of studies which are underpowered and based on heterogeneous study populations, lacking control groups, and without standardized imaging phenotypes. HIZ may be an important pain biomarker that should be further studied. With more modern MRI technology and a detailed classification system, future large-scale population studies will improve our knowledge on its role in the disc degeneration cascade and development of LBP.

Keywords High-intensity zones · HIZ · Lumbar spine · Back pain · Phenotype · Disc degeneration · MRI

Introduction

Low back pain (LBP) is a leading cause of disability around the world and is a significant health and economical burden [1–3]. Due to its heterogeneous nature, treatment should be individualized and target particular pain generators to achieve good outcomes. Nevertheless, the culprit is not easily identified with conventional diagnostic tools [4, 5].

Discogenic LBP is one of the most common manifestations caused by intervertebral disc disruptions in up to 39% of patients [6]. Diagnosis is often difficult for discogenic LBP. Clinical symptoms of pain in the flexed posture are crude

and imaging lacks pathognomonic signs. Traditionally, discography is used with dual purpose as diagnosis and pain relief. Contrast injection into a potentially diseased disc may provide morphological information due to the contrast flow while a provoked pain response similar to the usual pain character may help identify the source of discogenic LBP [7, 8]. However, there are drawbacks to using discography as it is an invasive procedure with risk of infection and nerve injury [7, 8]. In addition, it may cause accelerated disc degeneration as a result of trauma by the injection needle [8]. As such, there is reduced interest for using discography to diagnose disc disruptions.

Since magnetic resonance imaging (MRI) has become readily available to clinicians, it has become the gold standard for assessing the disc structure [9, 10]. Hence, it has mostly replaced discography for identifying disc disruptions. Yet, due to the common findings of disc herniation or intensity changes on MRI in asymptomatic individuals [11], there is increased interest in describing a clinically significant and easily recognizable disc phenotype for discogenic LBP.

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High-intensity zones (HIZ), first described by Aprill and Bogduk in 1992, can be regarded as visible annular tears on MRI [9]. Classically, it only refers to the posterior annulus fibrosus and is only seen on T2-weighted MRIs. Similar occurrence of these disc phenotypes was observed on lumbar computerized tomography (CT) discography, and was found to have clinical correlation with LBP [9]. Hence, HIZ may be an imaging marker for discogenic LBP. Given the non-invasive nature of MRI, the detection of HIZ as an indicator of annular tears revolutionized our diagnostic toolset and significantly reduced the utility of discography for this purpose.

The MRI phenotype

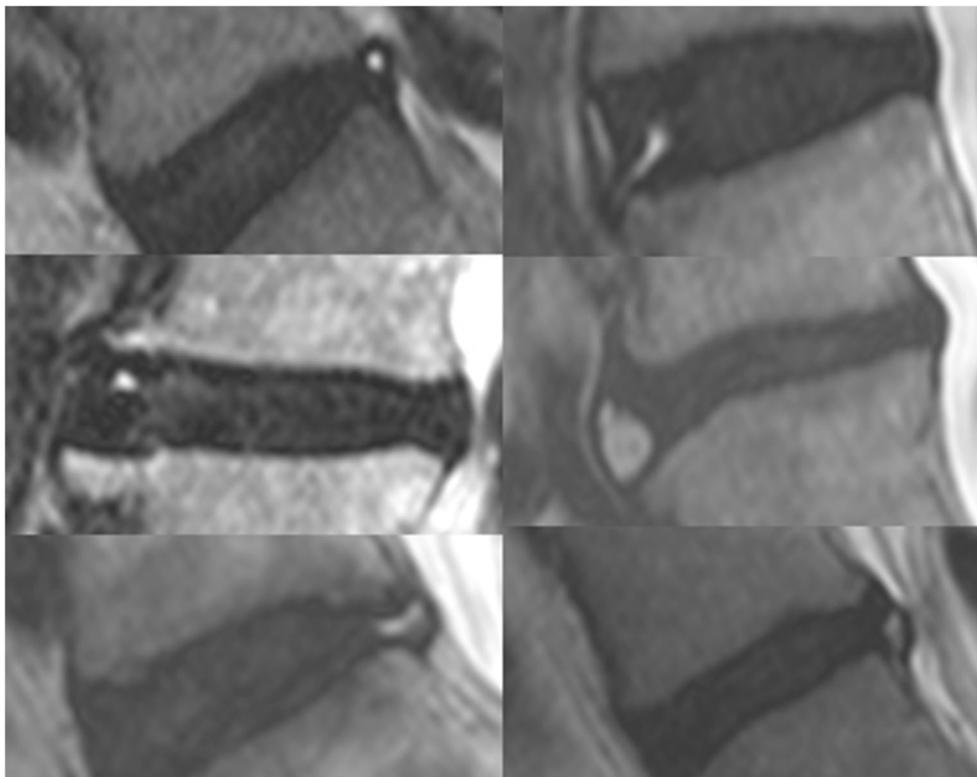
The original description of HIZ is a high-intensity focus at the posterior disc annulus on T2-weighted MRIs as described by Aprill and Bogduk [9]. It is also described as a fluid signal intensity that is brighter than the nucleus pulposus. It should also be surrounded by the annulus fibrosus completely and be present in the midline MR images. Other studies have since observed variations such as the presence in any part of the annulus including more lateral images [12, 13]. The presence of multiple HIZ at the same posterior region of the annulus has also been suggested [12]. Due to the lack of consensus for its appearance and difficulties in appreciating anterior aspects

of the disc due to older MRI technology, Tsuji H et al. [14] reported the MRI sensitivity to detect these annular tears as only 67% [12]. As such, the lack of a consistent and standard phenotype made determining the pathogenesis of HIZ impossible. Its reported prevalence had been widely variable and its clinical implications were hence doubtful [9, 12, 13, 15].

There is a need to improve phenotyping of MRI pathological features to better assess patient profiles, identify pain generators, and introduce individualized and target treatments. The drawback to the original phenotype is its simplicity, reliance on location at the annulus fibrosus, and its signal intensity. With modern MRI technology, sequences are more refined and provide better resolution for morphological classifications anywhere in the annulus even at the anterior annulus [1]. Teraguchi et al [15] proposed a new classification for HIZ based on location and morphology (Fig. 1). These types included a round type (found anteriorly and posteriorly), fissure type (found posteriorly), vertical type (found posteriorly), rim type (found anteriorly), and a giant type (found anteriorly). The location is probably related to loading as the posterior HIZ were more common in the caudal levels (i.e., L4–5 and L5–S1), while the anterior HIZ were more commonly found in the cranial levels (i.e., L2–3 and L3–4). Overall, the round type was more common.

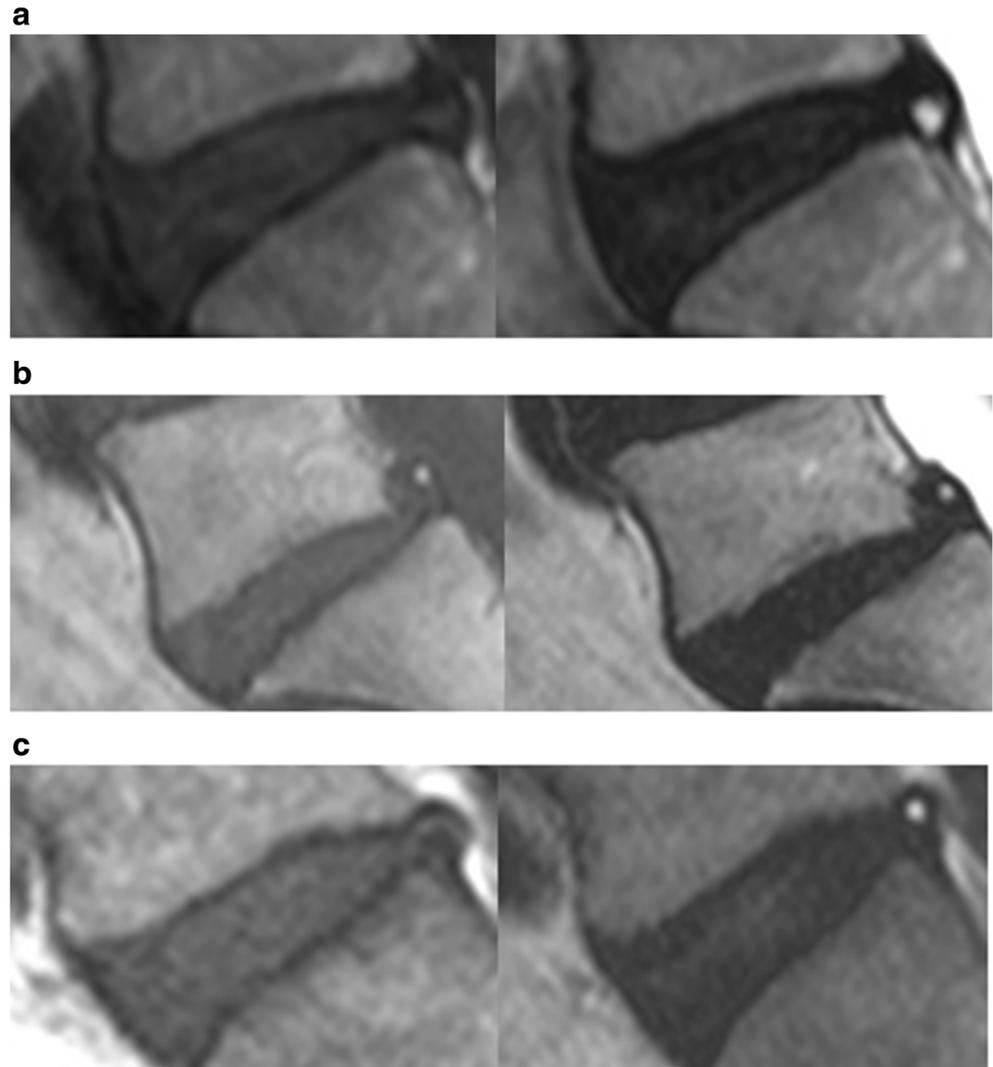
Bogduk previously suggested that asymptomatic annular tears may present as low-intensity areas on T2-

Fig. 1 HIZ classification by Teraguchi et al. [15] Counterclockwise from top left: posterior round type, anterior round type, posterior fissure type, posterior vertical type, anterior giant type, and anterior rim type



weighted MRI and only painful “activated” HIZ appear as high-intensity areas [16]. As such, Teraguchi et al [15] further classified HIZ into three types based on signal intensity (Fig. 2). The first type involves a low-intensity signal on T1-weighted MRI and high-intensity signal on T2-weighted MRI; the second type involves a high-intensity signal on T1-weighted MRI and high-intensity signal on T2-weighted MRI; and the third type involves an iso-intense signal on T1-weighted MRI and high-intensity signal on T2-weighted MRI. Similar to Modic changes which may progress through the types based on progressive disc degeneration [17], signal changes for HIZ may also reflect the natural course of disease. Changes that occur may represent pathological processes such as neovascularization of the annulus fibrosus, healing of a previous annular tear, and fluid collection at the site of the annular tear. Hence, both T1- and T2-weighted MRI sequences provide more information regarding the stage of inflammation and recovery.

Fig. 2 Types of HIZ on T1- and T2-weighted MRI. **a** Iso-intensity on T1 (left) and high-intensity on T2 (right). **b** High-intensity on T1 (left) and T2 (right). **c** Low-intensity on T1 (left) and high-intensity on T2 (right)



Relationship with other MRI phenotypes

Disc degeneration

Most investigators agree that HIZ are a manifestation of disc degeneration [15, 18–22]. It is commonly found with other changes such as loss of signal in the nucleus pulposus and a faster rate of disc height loss [23]. However, HIZ are not ubiquitous with late disc degeneration [19, 23, 24], and may associate more with bulging discs [13]. This is consistent with a Japanese population study [15]. HIZ that occur at the disc periphery suggest an integrity problem and thus disc prolapses are more common [18].

Modic change

Modic changes have been a focus of studying LBP [25, 26] due to its strong correlation with disc degeneration [27]. These pathological bone marrow signal changes found adjacent to

the vertebral endplates are easily detectable by MRI [28]. There are significant clinical implications of developing pain biomarkers or targeted treatment given the strong associations between Modic changes and LBP, and with HIZ [28]. However, this relationship is still inconclusive. Teraguchi et al [15] observed a strong correlation between type 2 Modic changes with HIZ, and especially posterior types. Mok et al [29], on the other hand, could not reproduce such associations in a Chinese cohort. Altered biomechanics may be the cause for both HIZ and Modic changes to co-exist. HIZ and related accelerated disc degeneration cause reduced stress dissipation across a spinal segment leading to concentrated stress areas at the disc-endplate junction manifesting as Modic changes. Hence, both may be potential markers for patients at risk of adjacent segment degeneration and accelerated disc degeneration disease.

Histological findings and relationship with MRI features

Several pathological studies have identified collections of mucoid fluid within an annular tear [9, 20, 22]. These tissues correlated with MRI findings of bright signals within an annular tear [13, 21]. Based on these findings, Yu et al [13] developed a cadaveric classification system of annular tears (Fig. 3) listed as concentric, radial, or transverse. Concentric tears are described as oval cavities with a rupture of the transverse fibres in the annulus fibrosus; radial tears are described as fissures that extend from the annulus fibrosus into the nucleus pulposus in an oblique orientation to the endplate; and transverse tears are described as tears of the outer layer of the annulus fibrosus parallel to the endplate. Fluid-filled cavities within the Sharpey's fibers are also observed in transverse tears. Concentric tears cannot be visualized on MRI as they are in the same orientation as annulus fibers. Transverse and radial tears are visualized as fluid signals whose signal intensity is higher than the nucleus material [30].

Epidemiology of HIZ

Prevalence

The prevalence of HIZ is highly variable (14–63%) in the literature and may not always be related to back pain symptoms [9, 12, 20, 22, 31–34]. However, these studies lack comparative groups and may be simply a report of a single cohort of LBP patients or heterogeneous population. Some studies suggest that LBP patients have more HIZ than asymptomatic individuals [19, 35]. Elderly patients are also more likely to have HIZ [15, 36]. This is likely related to reduced proteoglycan content with aging whereby the annulus fibrosus becomes

stiffer and weaker, leading to annular tears. Some other studies suggested similar age predispositions [24, 32, 37]. Nevertheless, these findings have yet to be validated in different ethnic groups.

Aetiology

It remains unclear what risk factors lead to HIZ. Some suggest male gender, body mass index, smoking, and frequent axial loading to the spine as the main risks [38, 39]. However, this link may simply be an indirect link to HIZ since disc degeneration shares the same risk factors. Traumatic disc disruption is also suggested as a possible risk factor. However, the evidence is thin. In a cohort of 99 patients with HIZ, only 17 patients had experienced high-energy trauma that may cause disc disruptions [32].

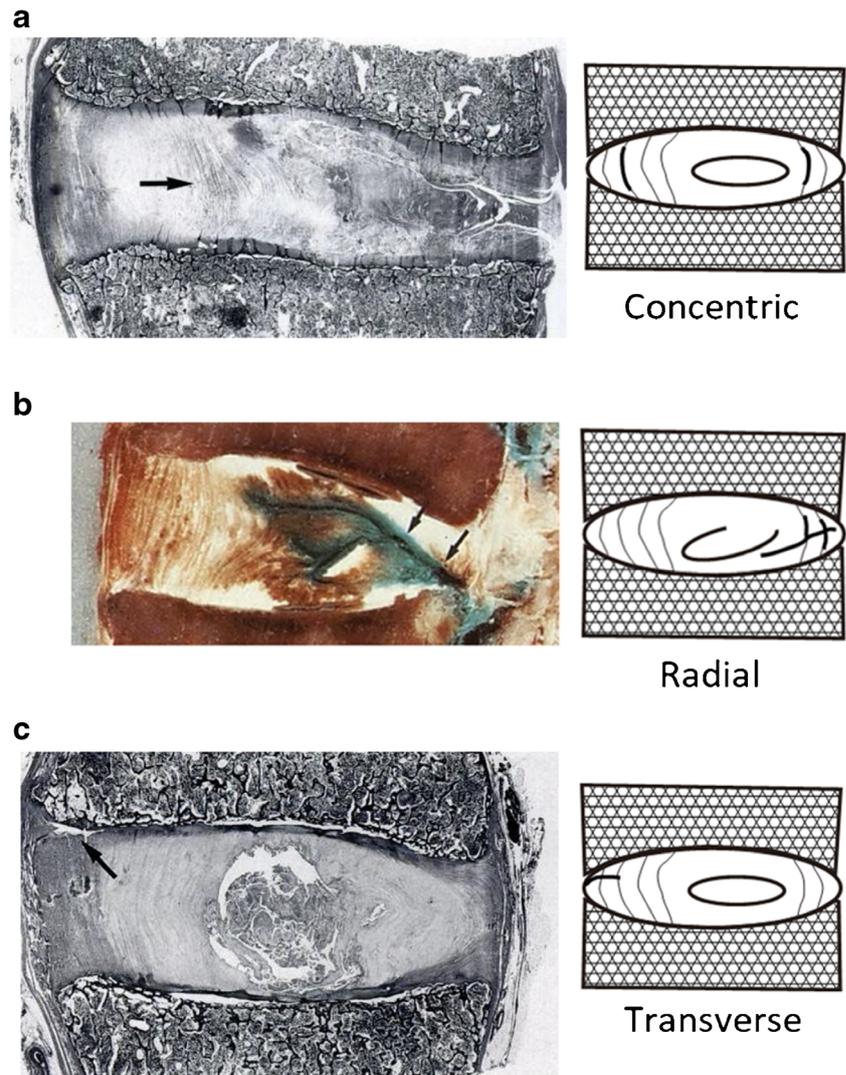
The effects of disc loading may be most supported in the literature. There are postulations correlating the position of the loading force with the type of HIZ. In one study, spinal alignment changes influenced HIZ development with extension and upright alignments as higher-risk postures compared to neutral alignment [38]. Another study by Saifuddin et al [39] demonstrated that loading the lumbar spine with 50% of a patient's body weight for five minutes was sufficient to produce HIZ. However, this was not reproduced in another study with 41 patients undergoing MRIs under loading [40]. Canvay et al [41] also studied the effects of loading on HIZ by comparing patients undergoing posterior spinal fusion surgery with those treated conservatively. At one year follow-up, the HIZ in patients who were fused disappeared on follow-up MRI while those conservatively treated had no change. Hence, the disappearance of HIZ is likely related to the absence of lumbar motion. Nevertheless, its pathophysiology still requires further study.

Clinical significance

The clinical significance of HIZ is under constant debate. There is no consensus on whether these features are symptomatic or not and this is a result of conflicting and poor evidence. Most clinical studies describing HIZ are generally underpowered, lacking control groups, based on heterogeneous populations, and without standardization of imaging phenotypes [9, 12, 19, 20, 22, 32, 34, 36, 42].

Earlier studies utilized provocative discography to determine whether HIZ can become a biomarker for discogenic LBP [9, 12, 32]. These studies however failed to produce consistent and convincing evidence [9, 12, 19, 20, 22, 32, 34, 36, 42]. Some studies did not find any significant correlations between HIZ and any pain concordant response from discography [22, 35]. Carragee et al [19] also questioned the sensitivity of discograms as he

Fig. 3 Types of annular tears as observed on histology specimens. **a** Concentric tears. **b** Radial tears. **c** Transverse/rim tears



showed the injections may provoke pain irrespective of having LBP or not in 70% of patients.

Similar controversies exist in population-based longitudinal studies [36, 43]. In one clinical series of 623 patients, Wang et al [44] reported up to 32.1% with HIZ in at least one disc level. There was a significantly higher percentage of patients with LBP who had HIZ (57.5%) as compared to those without ($p = 0.023$). This relationship was particularly higher for more caudal disc levels (L4–5 and L5–S1) and for multiple HIZ (5.3%). Similar findings were observed by Yang et al [45] on 57 patients with disc protrusions undergoing discectomy. Up to 61% of patients with HIZ also had LBP as compared to only 32% without. Liu et al [46] also observed in their series that 45.8% of patients with HIZ had LBP as compared to only 20.2% in those without. This study also suggested the signal intensity of HIZ was more significant in those who were symptomatic (comparing cerebrospinal fluid signal intensity, $57.6 \pm 14.0\%$ vs. $45.6 \pm 7.2\%$, $p < 0.001$). Carragee et al [19] also found a predilection for patients with

HIZ to have LBP (59 vs. 24%). Symptomatic patients also had more levels with HIZ as compared with asymptomatic individuals (30.2 vs. 9.1%).

Conversely, Takatalo et al [36] did not observe any associations between HIZ and LBP in a Finnish cohort of 554 young individuals. Hancock et al [47] reported that HIZ only occurred in 30% of patients with LBP which was not significantly different from the 22% of controls in their series. In another cohort, Mitra et al [43] found no obvious differences in the appearance of HIZ with longitudinal follow-up (18.8% of HIZ were larger and 14% regressed) nor any correlation with symptomatology. Annular tears were also observed in healthy volunteers without back pain [9]. These tears may present as low-intensity fissures on imaging and only become painful when the signal becomes brighter [16]. Nevertheless, these studies are flawed due to various limitations such as the lack of a standardized classification method for HIZ and heterogeneous study populations. Future study must

adopt a standardized classification and adjustment of confounding lifestyle/environmental factors, and control for other imaging phenotypes that may influence LBP.

Conclusions

There is considerable amount of interest regarding HIZ in diagnosis and management of LBP. This is an easily identifiable phenotype on MRI and is likely a key component of the disc degeneration cascade and possible pain biomarker. However, due to the limitations of previous studies, this relationship is still not well defined. With the development of more detailed and structured classification methods, with modern MRI technology, we can improve our knowledge of its underlying pathophysiology and clinical significance. By utilizing a more standardized study approach with homogeneous populations and control groups, the role of HIZ as a pain biomarker can be expanded by correlating HIZ with LBP and validating the findings with cross-ethnic and cross-cohort studies.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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