

Analysis of chronic low back pain with magnetic resonance imaging T2 mapping of lumbar intervertebral disc

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Received: 12 August 2014 / Accepted: 13 December 2014 / Published online: 5 February 2015
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Abstract

Background Magnetic resonance imaging (MRI) T2 mapping utilizes the T2 values for quantification of moisture content and collagen sequence breakdown. Recently, attempts at quantification of lumbar disc degeneration through MRI T2 mapping have been reported. We conducted an analysis of the relationship between T2 values of degenerated intervertebral discs (IVD) and chronic low back pain (CLBP).

Methods The subjects who had CLBP comprised 28 patients (15 male, 13 female; mean age 48.9 ± 9.6 years; range 22–60 years). All subjects underwent MRI and filled out the low back pain visual analog scale (VAS) and Japanese Orthopaedic Association Back Pain Evaluation Questionnaire (JOABPEQ). The disc was divided into the anterior annulus fibrosus (AF), the nucleus pulposus (NP), and the posterior AF, and each T2 value was measured. This study involved 25 asymptomatic control participants matched with the CLBP group subjects for gender and age (13 male, 12 female; mean age 43.8 ± 14.5 years; range 23–60 years). These subjects had no low back pain, and constituted the control group.

Results T2 values for IVD tended to be lower in the CLBP group than in the control group, and these values

were significantly different within the posterior AF. The correlation coefficients between the VAS scores and T2 values of anterior AF, NP and posterior AF were $r = 0.30$, -0.15 and -0.50 . The correlation coefficient between the JOABPEQ scores (low back pain) and T2 values of anterior AF, NP and posterior AF were $r = -0.0041$, 0.11 and 0.42 . Similarly, the JOABPEQ scores (lumbar function) were $r = -0.22$, -0.12 and 0.57 .

Conclusions The results indicated a correlation between posterior AF degeneration and CLBP. This study suggests that MRI T2 mapping could be used as a quantitative method for diagnosing discogenic pain.

Introduction

Low back pain (LBP) is common disease, and is one of the most serious problems worldwide. Intervertebral disc degeneration (IVDD) is considered to be the principal tissue as a source of LBP [1], although many other structures also have been suggested [2–4]. There are many reports concerning discogenic LBP from the aspect of pathology, diagnosis, and treatment; however, the mechanism and treatment still remain unclear.

Magnetic resonance imaging (MRI) is an important modality for diagnosis of degenerative intervertebral disc (IVD). Signal variation of the discs on T2-weighted images reflects age and degeneration and allows for the determination of disc degeneration. Specifically, since signal strength in the MRI is related to water and proteoglycan content, changes in MRI signal strength in the nucleus pulposus can indicate IVDD [5, 6]. IVDD has been classified by T2-weighted images using the system described by Pfirrmann et al. [7], but since this classification is based on visual evaluation, the quantification of degeneration using

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this strategy is unclear. In recent years, there have been several reported attempts using MRI T2 mapping and MRI $T_{1\rho}$ mapping to quantify lumbar disc degeneration [8–12]. MRI T2 mapping utilizes the T2 relaxation time for quantification of moisture content and collagen sequence breakdown. In the previous work of Takashima et al. [13], they used MRI T2 mapping to quantify the extent of IVDD, and reported a correlation with Pfirrmann classifications. Recently, there have been a few reports regarding the quantitative evaluation of discogenic LBP with MRI T2 mapping and MRI $T_{1\rho}$ mapping, but the number is small. In this study, we used MRI T2 mapping to quantify IVDD and investigate possible correlations between these quantified values and the low back pain visual analog scale (VAS) scores and Japanese Orthopaedic Association Back Pain Evaluation Questionnaire (JOABPEQ) [14] scores.

Materials and Methods

Ethical approval was obtained from the hospital board of ethics. All subjects were provided with written and verbal explanations of the study and provided their consent before participating.

The subjects comprised patients (over 20 years and under 60 years old) who had non-specific chronic low back pain (CLBP) that had persisted for ≥ 3 months and whose symptoms did not improve with medication or conservative treatments such as therapeutic exercise. All subjects underwent MRI and filled out the VAS scores (0–100 mm) and JOABPEQ scores (0–100 points) after a washout period of at least 4 weeks. We marked out the patients whose VAS scores were more than 30 mm. Additionally, a clinical radiologist examined and graded as I–V the midsagittal sections of MRI T2-weighted images of the 5 lumbar discs, using the system described by Pfirrmann. Disc degeneration mainly occurs at the lower lumbar region and is commonly noted as single or contiguous multilevel involvement, particularly involving the L4–L5 disc [15]: it is probable that degeneration of the L4–5 disc is the pain generator in discogenic LBP. We screened the subjects whose disc degeneration at L4–5 level was grade III–V, but another discs were grade I–II. The exclusion criteria included neoplasm, infection, fracture or history of lumbar vertebral surgery. We also excluded patients with neurologic symptoms of the lower leg, or obvious instability, which could be identified as a pain generator that caused LBP and might be improved with surgical treatment. The subjects comprised 28 patients (15 male, 13 female; mean age, 48.9 ± 9.6 years; range 22–60 years) who were examined at our hospital and satisfied the diagnostic criteria. This study involved 25 asymptomatic control participants matched with the CLBP group subjects for gender and age (13 male, 12 female; mean age

43.8 ± 14.5 years; range 23–60 years). These subjects had no LBP, and constituted the control group.

Studies were performed using a GE Signa HDx 1.5-T scanner with a spine coil (GE Healthcare, Milwaukee, WI, USA). T2-weighted sagittal images [TR 4,000 ms, TE 102 ms, receive band width (RBW) ± 31.25 kHz, field of view (FOV) 24 cm, matrix 384×288 , slice thickness/gap 4 mm/1 mm, number of excitations (NEX) 4, total scan time 3 min and 4 s] were obtained.

Next, a T2 map was created using the T2 values in the midsagittal section from sagittal sections centered on the lumbar midline region with optimized 8 echo multi-spin echo (TR/first echo TE, last echo TE, 1,000/14.8, 118.6, RBW ± 15.63 kHz, FOV 22 cm, matrix 320×256 , slice thickness/gap 4 mm/4 mm, 5 slices, NEX 2, total scan time 8 min and 34 s) obtained with an Advantage Workstation (version 4.4, Functool; GE Healthcare, Milwaukee, WA, USA). However, the first echo from the multi-spin system was excluded to minimize the effect of the stimulated echo. The T2 map was calculated in each pixel from the signal intensity (SI) in the respective TE using the following calculating formula: $SI \frac{1}{4} e^{-TE} = T2$

For measurement, the disc was divided into five equal areas, the first covering the anterior annulus fibrosus (AF), the middle covering the nucleus pulposus (NP), and the last covering the posterior AF, as used in the report by Trattng et al. [16]. The mean values in the region of interest (ROI) were measured (Fig. 1). T2 values were measured by a PhD (H.T., with 7 years of experience in spine MR image analysis) using MedCalc (version 10.2.0.0; MedCalc Software, Mariakerke, Belgium).

We compared T2 values of the CLBP group with the control group. We also investigated possible correlations between these quantified values at the L4–5 level (a total of 28 lumbar discs) and the VAS scores and JOABPEQ scores (low back pain and lumbar function) in the CLBP group.

Differences among groups were compared using the Mann–Whitney *U* test. The relationship between T2 values of IVD and CLBP were analyzed by Spearman's rank-correlation coefficient. A *P* value of less than 0.05 was considered statistically significant.

Results

Measurements of T2 values in IVD (L4–5) in the control and CLBP groups are shown in Fig. 2. T2 values for the control and CLBP groups were 70.2 ± 14.4 ms and 63.4 ± 20.1 ms, respectively, for the anterior AF (Fig. 2a); 80.8 ± 31.3 ms and 71.7 ± 16.7 ms, respectively, for NP (Fig. 2b); and 70.3 ± 15.8 ms and 54.4 ± 9.7 ms, respectively, for the posterior AF (Fig. 2c). T2 values for IVD tended to be lower in the CLBP group than in the

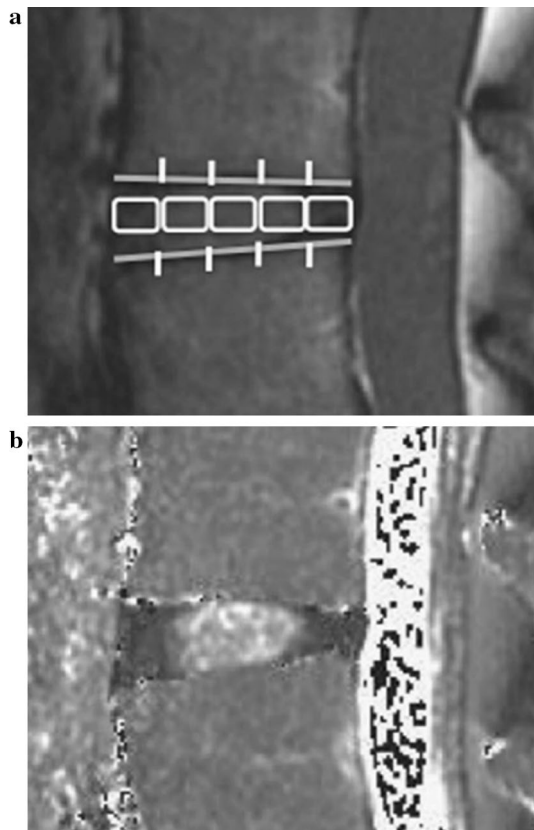


Fig. 1 In second echo image, disc was divided into five areas, designating the front of the anterior annulus fibrosus (AF), the middle of the nucleus pulposus (NP), and the last of the posterior AF (a). In the same region, we measured the mean values (b)

control group, and these values were significantly different ($p < 0.01$) within the posterior AF.

The correlation coefficients between the VAS scores and anterior AF T2 values and NP T2 values were $r = 0.30$ ($p = 0.13$) and $r = -0.15$ ($p = 0.43$), respectively, which indicated non-significant correlations (Fig. 3a, b). The correlation coefficient between the VAS scores and posterior AF T2 values was $r = -0.50$ ($p < 0.01$), which indicated a significant negative correlation (Fig. 3c). The correlation coefficient between the JOABPEQ scores (low back pain) and anterior AF T2 values and NP T2 values were $r = -0.0041$ ($p = 0.81$) and $r = 0.11$ ($p = 0.51$), respectively, which indicated non-significant correlations (Fig. 4a, b). The correlation coefficient between the JOABPEQ scores (low back pain) and posterior AF T2 values was $r = 0.42$ ($p < 0.05$), which indicated a significant positive correlation (Fig. 4c). The correlation coefficient between the JOABPEQ scores (lumbar function) and anterior AF T2 values and NP T2 values were $r = -0.22$ ($p = 0.15$) and $r = -0.12$ ($p = 0.39$), respectively, which indicated non-significant correlations (Fig. 5a, b). The correlation coefficient between the JOABPEQ scores (lumbar function) and

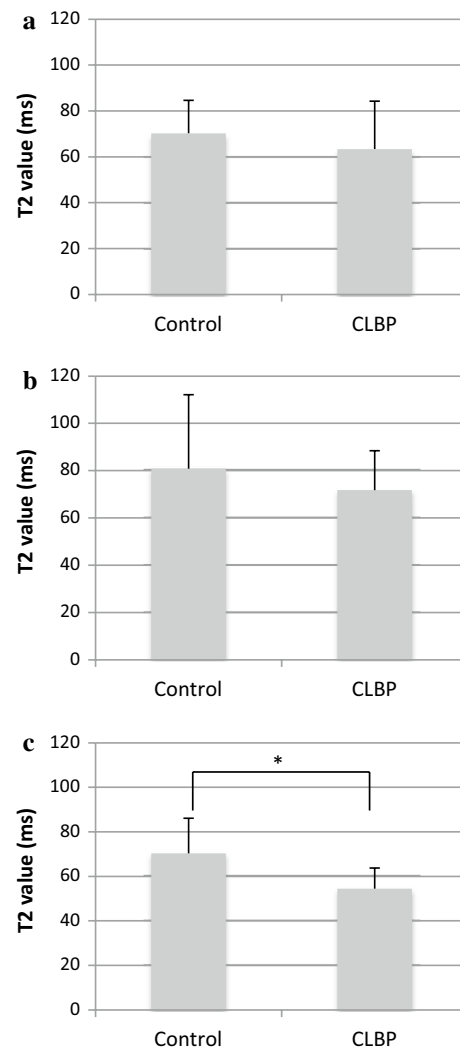


Fig. 2 Comparisons of T2 values in the control and chronic low back pain (CLBP) groups, as anterior AF (a), NP (b) and posterior AF (c). T2 values were lower in the CLBP group, and significantly different within the posterior AF. * $p < 0.01$

posterior AF T2 values was $r = 0.57$ ($p < 0.01$), which indicated a significant positive correlation (Fig. 5c).

Discussion

Non-specific LBP is estimated to account for >85 % of all LBP cases [17]. IVDD was previously considered to be a cause of pain onset for non-specific LBP. Schwarzer et al. [18] mentioned the possibility that in 39 % of CLBP patients, the pain had a discogenic origin. Since LBP is characterized by pain aggravation in a flexure posture and pain improvement with orthosis, this gave us some help in diagnosis. However, diagnosis using this information is not very objective, nor specific. Discography has been used to

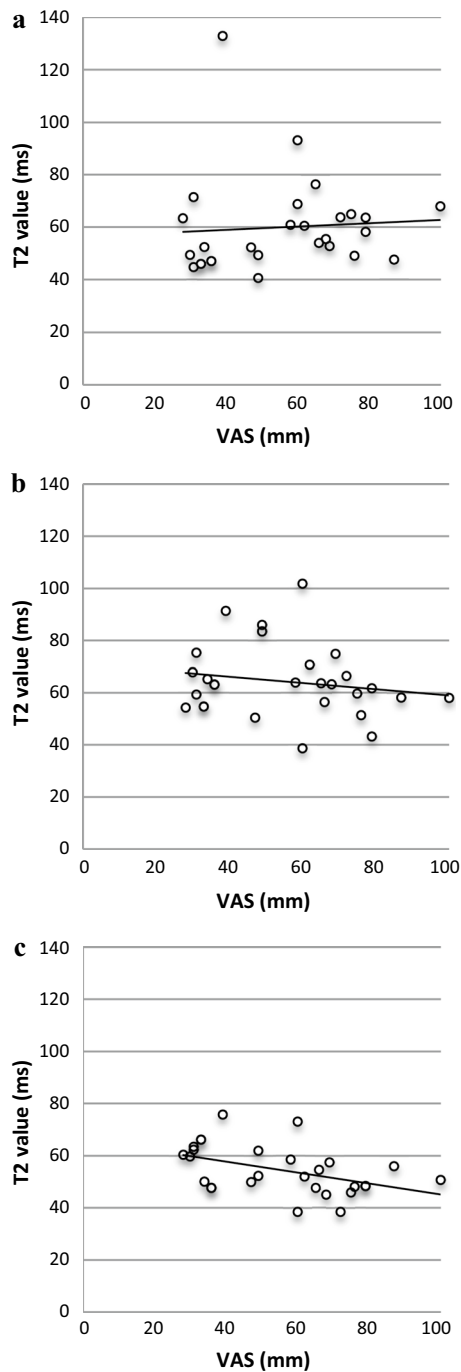


Fig. 3 The correlation coefficient between the low back pain VAS scores and T2 values of anterior AF (a) and NP (b) indicated non-significant correlation. The correlation coefficient between the low back pain VAS scores and posterior AF T2 values (c) indicated significant negative correlation

support the diagnosis of discogenic pain, but it has a high false positive rate [19] and a risk of accelerating disc degeneration [20], so we did not conduct discography. Thus, no specific diagnostic method has been established; therefore, diagnosing and treating this condition remains difficult.

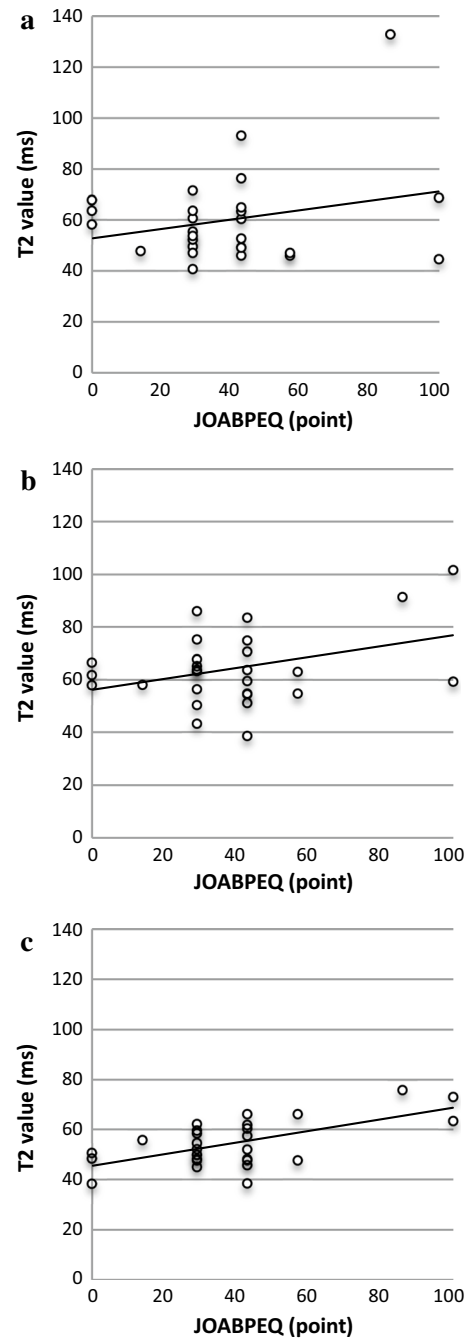


Fig. 4 The correlation coefficient between the JOABPEQ scores (low back pain) and T2 values of anterior AF (a) and NP (b) indicated non-significant correlation. The correlation coefficient between the JOABPEQ scores and posterior AF T2 values (c) indicated significant positive correlation

MRI is an important imaging technique for diagnosing structural changes in the spinal column. Conventionally, IVDD has been characterized by MRI findings according to the classifications reported by Pfirrmann [7]. However, there are problems with this technique, such as difficulty with assessments of early degeneration and the AF, as well

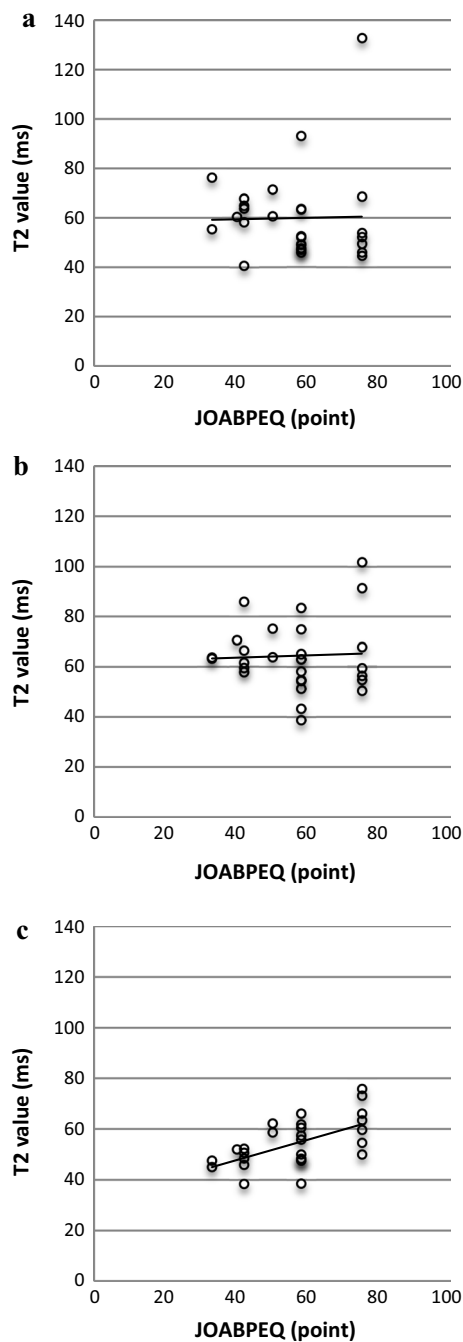


Fig. 5 The correlation coefficient between the JOABPEQ scores (lumbar function) and T2 values of anterior AF (a) and NP (b) indicated non-significant correlation. The correlation coefficient between the JOABPEQ scores and posterior AF T2 values (c) indicated a significant positive correlation

as poor reproducibility and objectivity because the classifications are visually performed.

In recent years, attempts at quantitative assessments of IVD through MRI have been reported [8–13, 21]. Borthakur et al. [21] used MRI T_{1p} mapping and reported that T_{1p} values decreased as the Pfirrmann grade advanced

and that a strong correlation was observed between T_{1p} values and the initial infusion pressure measured by discography. Takashima et al. [13] previously used MRI T2 mapping to demonstrate that the Pfirrmann grade reflected T2 values of NP and reported the quantitative evaluation of lumbar disc degeneration. Wang et al. [22] showed that T_{1p} - and T2-quantified values of NP followed the same trend with their correlations, and MRI T_{1p} mapping did not seem to offer any additional advantage over MRI T2 mapping in differentiating different severities of disc degeneration. In the present study, we used MRI T2 mapping to quantitatively investigate a possible correlation between the degree of IVDD and CLBP. The results indicated a correlation between posterior AF degeneration and CLBP. Sinuvertebral nerves, which originate from spinal nerve roots, are distributed around the posterior AF region; therefore, this area is richly innervated. IVD with myelomeres are controlled through sinuvertebral nerves and those without myelomeres are controlled through paravertebral sympathetic nerves [23, 24]. Kojima et al. [25, 26] reported that sinuvertebral nerves are divided into shallow and deep layers around the posterior longitudinal ligament area; deep-layer fibers are segmentally located in intervertebral areas of the posterior longitudinal ligament, and these fibers control posterior fiber rings. Takebayashi et al. [27] applied electrical and mechanical stimuli to L5–L6 discs of rats after inducing inflammation, and found that no reaction to stimulation was normally observed, but a reaction could be observed in the presence of inflammation. In addition, these authors reported that this stimulation was mediated by the sympathetic nerve trunk and reached the L2 nerve root. Nakamura et al. [28] reported that when sympathetic nerve trunks were removed from rats, the intervertebral posterior nerve decreased, which suggested that intervertebral posterior nerve fibers may pass through the sympathetic nerve trunk. Ohtori et al. [29, 30] inserted needles with nerve tracers anteriorly to rat intervertebral discs and reported that the posterior AF was controlled by sinus spinal and sympathetic nerves. Inoue et al. [31] reported that exposure of the nucleus pulposus to the outside of the anulus fibrosus induces nerve damage of afferent fibers of the disc in which the nucleus pulposus was exposed, with both chemical and structural factors appearing to induce sensory nerve ingrowth in small-sized neurons, with associated development of pain. We think that these changes, in which rich afferent fibers around the posterior AF grow into the disc, provide an explanation for the induction of discogenic LBP in patients with IVDD. In addition, sensory nerve endings have different sensitivities against noxious stimuli. The mechanical threshold of the front part of the IVD was 241 g (164–279 g) [32], in contrast to the back side part (longitudinal ligament), which was 80.3 g (20.9–164 g) [33]. Perhaps CLBP did not show correlations with

T2 values in the anterior AF or NP, but did in the posterior AF, because of low sensitivity against noxious stimuli in the front part of the IVD.

Invasive discography has been conventionally used to examine discogenic LBP. This technique, which can cause pain due to the injection of contrast fluid between intervertebral discs, has a high false-positive rate; therefore, it has been reported to be not entirely suitable as an index for identifying the source of pain [19, 34, 35]. Moreover, discography has been reported to cause progression of intervertebral disc degeneration [20]. However, in recent years, a number of reports have quantified the degree of lumbar disc degeneration and investigated its relationship with CLBP [21, 36]. Blumenkrantz et al. [36] reported a correlation between IVD T_{1p} values and Medical Outcomes Study 36-Item Short-Form Health Survey and Oswestry Disability Index scores and stated that T_{1p} values may become an important index for LBP evaluation. Furthermore, Borthakur et al. [21] reported that IVD T_{1p} values were significantly lower in patients with LBP than in control subjects. Moreover, discography results of patients with LBP revealed that T_{1p} values for subjects with discogenic pain were lower compared with those for subjects without discogenic pain. In addition, the authors reported that instead of invasive discographic findings, T_{1p} values could be used to diagnose the source of discogenic pain.

It seems that MRI T2 mapping is a noninvasive quantitative evaluation method that offers high reproducibility in contrast to discography. The results of the present study suggest that MRI T2 mapping could be used instead of invasive discography as a quantitative method for diagnosing discogenic pain.

This study has several limitations. Firstly, we investigated only midsagittal slices, without axial imaging analysis. Secondly, distinguishing between the AF and the NP in the setting of advanced degeneration is difficult, which complicates the setting of the ROI. Although we divided the intervertebral discs into five areas with an anterior and posterior AF in order to decrease variance between the measurements, the validity of this measuring method has not been evaluated. Thirdly, there is no evidence that the cause of non-specific LBP in our subjects originated from degeneration of the L4-5 disc.

Conclusions

The results indicated a correlation between posterior AF degeneration and CLBP. This study suggests that MRI T2 mapping could be used instead of invasive discography as a quantitative method for diagnosing discogenic pain.

Conflict of interest No funds were received in support of this work. No benefits in any form have been or will be received from commercial party related directly or indirectly to the subject of this manuscript.

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