RESEARCH ARTICLE

T2 mapping of lumbar intervertebral disc: quantitative evaluation of degeneration in relation to Pfirrmann grading system and a template for intervertebral disc segmentation

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Abstract

Background: To assess the feasibility of using T2 relaxation time mapping at 3 Tesla (3T) magnetic resonance imaging (MRI) for detection and classification of lumbar intervertebral disc degeneration, introducing an objective model of disc segmentation for accurate disc assessment.

Materials and Methods: The present study is a single-center prospective evaluation including 185 lumbar intervertebral discs from a cohort of 37 patients with chronic lower back pain. For the quantitative classification of disc degeneration, three regions of interest (ROIs) were drawn on T2 maps, and the Pfirrmann grading system was used for qualitative assessment. Intergroup evaluation was performed with paired t-tests. Analysis of variance (ANOVA) was used to compare the mean value of T2 mapping, and Tukey's multiple comparison test was applied to determine differences in mean values of T2 mapping among the Pfirrmann categories.

Results: The ANOVA test analysis of ROIs showed that there is a statistically significant difference ($p < 0.001$) among average T2 relaxation time mapping values in different Pfirrmann score groups, and Tukey's multiple comparison tests revealed that mean values of T2 map among the different grades of Pfirrmann differ from the rest ($p < 0.001$) except grade V. Paired t-tests revealed significant differences in mean values of T2 map between different ROIs.

Conclusion: This study showed that quantitative T2 mapping of the lumbar intervertebral discs at 3T MRI may overcome the subjective element of qualitative classification systems for degenerative intervertebral disc disease. Also, a new template of disc segmentation with more ROIs would be more sensitive for the assessment of disc degeneration. HIPPOKRATIA 2023, 27 (2):75-81.

Keywords: T2 mapping, Pfirrmann score, intervertebral disc degeneration, magnetic resonance imaging, MRI spine, intervertebral disc segmentation

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Introduction

Low back pain (LBP) is ubiquitous in the Western world. It has been suggested as one of the main ailments responsible for disability worldwide, the prevalence of which is estimated at approximately 31 % in the general population[1-3]. LBP is considered to have a multifactorial origin and is typically classified into specific and non-specific LBP[2]. In the latter category, intervertebral disc degeneration (IVDD) is acknowledged as a frequent underlying cause, while IVDD-mediated back pain is characterized as discogenic pain[4,5]. Despite the tremendous progress noted in the field of spine imaging during the last years, the diagnosis of IVDD and the delineation of the origin of discogenic pain remain to date challenging[6-9].

Spine magnetic resonance imaging (MRI) comprises an indispensable modality for the diagnosis of IVDD and discogenic pain[10]. MRI can noninvasively assess the discovertebral complex and the internal disc morphology based on conventional T2-weighted imaging (T2WI). The signal intensity on T2WI allows qualitative and semi-quantitative assessment of the disc based on the water and proteoglycan content and collagen breakdown. Thereby, T2WI allows an approximate estimation of disc aging and degeneration[11-12]. Subsequently, changes in the signal intensity can indicate IVDD, and the most widely used qualitative system for disc degeneration assessment based on sagittal T2WI is the five-grade system introduced by Pfirrmann et al, which is based on evaluation of the signal intensity, the distinction between nucleus pulposus (NP) and annulus fibrosus (AF), and the disc height[13].

Some significant limitations of the qualitative scaling systems include their moderate reliability and the low-sensitivity for early IVDD diagnosis[14-16]. With respect to the former, subjective grading of the extent of disc degen-

eration and significant inter- and intra-observer variability may confound and delay IVDD diagnosis, with consequent delays in treatment initiation. Since qualitative methods may fail to detect early IVDD stages, it is crucial to identify biochemical markers that can reliably detect IVDD at early stages[17,18]. In turn, especially in cases in which clinical symptoms are pronounced but qualitative neuroimaging remains normal, the use of quantitative T2 mapping enables prompt IVDD diagnosis and treatment initiation. Minimally-invasive approaches have been recently gaining ground for early IVDD treatment, including basivertebral nerve radiofrequency ablation, mesenchymal stem cell and platelet-rich plasma therapies[19].

Consequently, a pressing need for precise quantification of IVDD has emerged, and many strategies with various proposed measures for IVDD quantification on MRI have been introduced based on noninvasive visualization of the intervertebral disc region-specific ultrastructure and microenvironment. The basis of this quantitative approach is that, in IVDD, biochemical changes precede morphological changes. Thus, quantitative approaches can promptly evaluate biochemical changes, including depiction of proteoglycan, water and collagen loss, allowing early detection of IVDD[20,21]. Furthermore, spatial changes inside different areas of the intervertebral disc, including NP and AF, can be early detected and measured using quantitative approaches.

Prior studies with novel MRI techniques have provided preliminary evidence on the correlation of qualitative and quantitative IVDD classification systems. In particular, previous research has focused on the assessment of the microstructure of intervertebral disc using T1 rho (T1ρ), diffusion weighted imaging (DWI) with apparent diffusion coefficient (ADC) values and spectroscopy, correlating their findings with the Pfirrmann classification system[22-26]. The objectives of the present study were threefold: i) we aimed to assess T2 relaxation time as an IVDD measure, ii) we introduced a template for an appropriate segmentation for accurate calculation of the entire intervertebral disc, and iii) we examined the relationship between T2 relaxation time and Pfirrmann classification in the intervertebral discs of lumbar spine using a 3 Tesla (3T) MRI scanner.

Materials & Methods

Subjects

This single-center prospective study comprised a cohort of thirty-seven patients (17 males and 20 females) who had fully recovered from an episode of LBP within the preceding year, with LBP symptoms defined as midline spinal pain with or without accompanying leg pain or sensory deficit. The study was conducted according to the Declaration of Helsinki, and the local institutional review board approved the study (Ethics Committee of Attikon University Hospital, Protocol No. 17180219996, approval date: 16/03/2018). All recruited participants were thoroughly informed, and written informed consent was acquired before participation. Inclusion criteria comprised presence of LBP symptoms within the previous year without obvious causes i.e., fracture, tumor, extensive facet joint degeneration. Exclusion criteria included previous back surgery or pain relief therapeutic intervention and contraindications to MR scanning, including discontinuation of scanning due to claustrophobia.

MRI protocol and MRI data acquisition

The same lumbar spine imaging protocol was utilized for all participants on a 3T Achieva TX MRI scanner (Philips Healthcare, Amsterdam, The Netherlands) equipped with a fifteen-channel surface sense-spine coil. The protocol included the conventional sequences: a T2-weighted Turbo-Spin echo (TSE), a T1-weighted TSE, a T2-weighted short-tau inversion recovery (STIR) in sagittal plane, and a T2-weighted TSE and a T1-weighted TSE in axial plane parallel to the intervertebral discs. Besides the routine imaging protocol, a T2 TSE multi-echo sequence was acquired on sagittal plane to estimate the T2 relaxation times (Table 1). The protocol included eight echoes, with the first echo at 25 milliseconds (ms) and echo spacing at ΔTE =25. The MRI software Philips IntelliSpace Portal (Philips Healthcare, Amsterdam, The Netherlands) automatically calculated T2 and T2 relaxation maps.

Image analysis (Pfirrmann scores and quantitative measures of T2 mapping)

Each lumbar disc in each subject (a total of 185 intervertebral lumbar discs) was assessed by two independent, experienced musculoskeletal MRI radiologists for qualitative classification via visual inspection of midsagittal T2WI. The degenerative five-grade score was based on the proposed classification system by Pfirrmann et al, assessing the height of the disc, the signal intensity, the structural morphology, and the distinction between NP and AF[13]. In case of discordance between the raters, the two radiologists discussed the findings until an agreement was reached. For quantitative disc degeneration classification based on the T2 relaxation time map, a region of interest (ROI)(three per disc) was manually placed by a trained medical physicist using OsiriX software (OsiriX MD 10.0.2, Pixmeo SARL, Geneva, Switzerland) in order to eliminate inter-operator-related variations after thorough examination slice by slice, identifying any motion or other type of artefacts, mainly from the aorta or the nearby vertebral body. The middle ROI was drawn on the sagittal image of the T2 map at the level of the most visible part of NP at each lumbar level, taking into consideration any disturbance of the spinal alignment - kyphoscoliosis (from the anterior longitudinal ligament towards the posterior longitudinal ligament, including part of the AF and part of the NP. At the same time, the lateral ROIs (lateral 1-lateral 2) were placed on either side of the middle ROI (right and left paramedian, respectively). For every assessed lumbar intervertebral disc, each mean value of each ROI was registered; in addition, we calculated and registered the average value from the sum of the three ROIs per disc.

Table 1: Lumbar spine imaging protocol and sequences' acquisition parameters used in this prospective evaluation of lumbar intervertebral discs of patients with chronic lower back pain.

	Sag T2 TSE	Sag T1 TSE	Sag T2 STIR	Ax T2 TSE	Ax T1 TSE	Sag T2 mTSE
TR (ms)	3200	548	3400	3700	647	2164
TE (ms)	100	8	60	75	8	n*25 (n =8)
ST (mm)	4	4	4	4	4	4
Voxel size (mm)	0.48 x 0.48	0.48 x 0.48	0.62 x 0.62	0.47 x 0.47	0.47 x 0.47	1.3 x 1.3
NSA	1	1	1	1	1	1
Flip angle (^{0})	90	90	90	90	90	90
TI						
Time of acquisition (seconds)	-	-	210	-	-	-

TSE: turbo spin echo, mTSE: multi-echo turbo spin echo, TR: repetition time, TE: time echo, ms: milliseconds, ST: slice thickness, NSA: number of signal averages, TI: inversion time, n: number of echoes.

Statistical Analysis

We present descriptive statistics as number (n), percentage for qualitative, and mean ± standard deviation for quantitative variables. Analysis of variance (ANOVA) was used to compare the mean of T2 map value in the several categories defined by the Pfirrmann classification system. In order to assess whether the patients classified in one of the five Pfirrmann categories have the same mean T2 map value, the variation among the means of these categories was compared with the variation within the other categories. Tukey's multiple comparison test was also applied to determine which means of T2 map value among each category based on the Pfirrmann grading system differ from the rest. The mean values within the same patient (average, lateral 1, middle, lateral 2) were also compared with paired t-tests. A p value less than 0.001 was considered statistically significant.

Results

In total, thirty-seven patients (17 males and 20 females; mean age 52.8 ± 14.2 years) who had fully recovered from an episode of LBP within the preceding year were included in the study. All participants underwent a lumbar spine MRI (as per the summarized protocol in Table 1).

Per patient, each of the five lumbar intervertebral discs was classified into the Pfirrmann grading system (I-V grade) (185 lumbar intervertebral discs were evaluated from a total of 37 included patients), with the majority classified as grade III (38.4 %; n =71), followed by grade II (28.6 %; n =53), and grade IV (27.6 %; n= 51). Table 2 summarizes the number of discs classified in each Pfirrmann grade, the corresponding lumbar level, and the mean value of T2 map in each placed ROI for each Pfirrmann grade.

Figure 1 shows a representative midsagittal T2WI of a symptomatic patient complaining of LBP for visual evaluation and Pfirrmann grading for each lumbar intervertebral disc (Figure 1A). Exemplary ROI placement in the T2 map in the right paramedian (lateral 1) (Figure 1B), midsagittal (Figure 1C), and left paramedian (lateral 2) (Figure 1D) plane at the L3-L4 level.

Figure 2 shows the boxplot with the mean value of the T2 map (ms) for each Pfirrmann grade. The overall mean T2 value was observed to be higher in intervertebral discs classified with lower degeneration grade in the Pfirrmann classification system.

From the ANOVA, the null hypothesis, which states that the mean value of the T2 map is equal among the different grades of Pfirrmann, was rejected (p <0.001),

Table 2: The number of patients in each Pfirrmann category and the corresponding disc level with T2 mapping means values (average, lateral 1, middle, lateral 2) for each Pfirrmann category.

Pfirrmann	n	Level					T2 mapping		
		L1-L2	L2-L3	L3-L4	L4-L5	L5-S1	Overall	Lateral 1	Middle	Lateral 2
1	2	0	1	1	0	0	127.635	129.596	134.464	118.842
2	53	18	13	7	8	7	82.856	83.196	85.231	80.136
3	71	14	15	15	13	14	65.629	65.424	66.478	64.986
4	51	4	8	12	13	14	55.849	55.650	56.869	55.026
5	8	1	0	2	3	2	-	-	-	-

n: number, L: lumbar vertebrae, L-L: lumbar intervertebral disc.

Table 3: Analysis of variance assessing the mean value of T2 map in different grades of Pfirrmann.

	DF	Sum Squares	Mean squares	F value	p value
Pfirrmann	4	26857	6714	38.57	<0.001
Residuals	173	30113	174		

DF: degrees of freedom.

Table 4: Tukey's multiple comparison test assessing the differences in mean values of the T2 map among the different grades of Pfirrmann.

Comparisons of Pfirrmann categories	Mean difference	95 % Confidence level	p value
2 vs 1	-44.780	[-70.979, -18.582]	<0.001
3 vs 1	-62.006	[-88.083, -35.928]	<0.001
4 vs 1	-71.786	[-98.004, -45.569]	<0.001
5 vs 1	-44.795	[-89.340, -0.250]	0.048
3 vs 2	-17.225	[-23.828, -10.623]	<0.001
4 vs 2	-27.006	[-34.140, -19.871]	<0.001
5 vs 2	-0.015	[-36.727, 36.698]	1.000
4 vs 3	-9.780	[-16.457, -3.104]	<0.001
5 vs 3	17.211	[-19.415, 53.837]	0.694
5 vs 4	26.991	[-9.734, 63.717]	0.258

Table 5: Paired t-tests assessing the mean values of the T2 map at different regions of interest (lateral 1, middle, lateral 2) and compared them to the T2 average value.

Comparison	DF	Mean of the differences	95 % confidence interval	t	p value
Lateral 1 vs middle	177	-1.395	[-2.552, -0.238]	-2.379	0.018
Lateral 1 vs lateral 2	177	1.824	[-0.126, 3.191]	1.824	0.070
Lateral 2 vs middle	177	-2.928	[-4.241, -1.615]	-4.401	<0.001
T2_average vs middle	177	-1.441	[-2.053, -0.828]	-4.642	<0.001

DF: degrees of freedom.

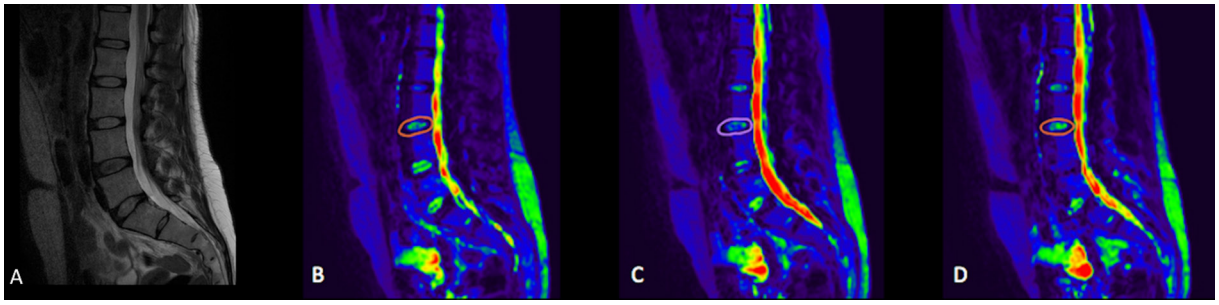

Figure 1: A representative midsagittal T2-weighted imaging (T2WI) of a symptomatic patient complaining of low back pain is shown for visual evaluation and Pfirrmann grading of each lumbar intervertebral disc (A). Exemplary region of interest placement in the T2 map in the right paramedian (lateral 1) (B), midsagittal (C), and left paramedian (lateral 2) (D) plane at the L3-L4 level.

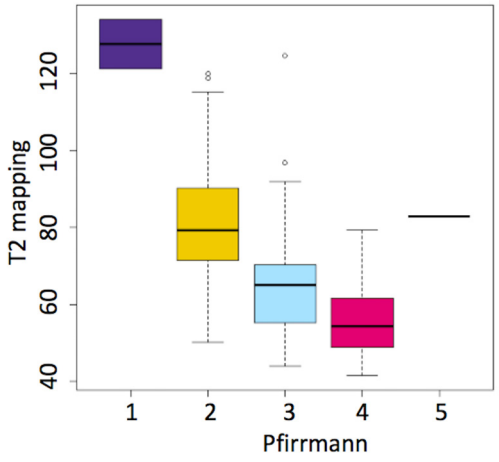

Figure 2: Boxplot with average T2 map values in milliseconds (ms) of each Pfirrmann grade.

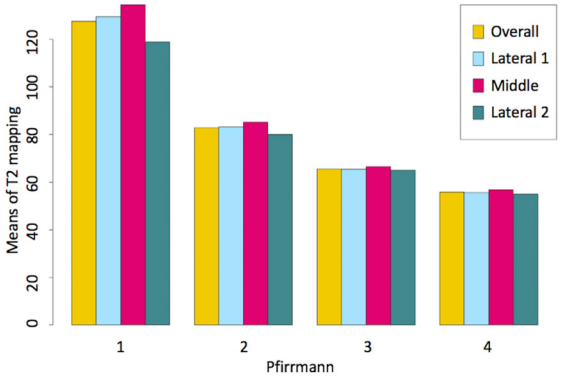

Figure 3: Bar plot for the means of T2 mapping of regions of interest for each Pfirrmann category.

as shown in Table 3. Tukey's multiple comparison tests revealed that mean values of the T2 map among the different grades of Pfirrmann differ from the rest ($p < 0.001$) except the grade V (Table 4) because the sample was limited and the disc area due to the loss of height and dehydration, was not sufficient for the ROI placement.

Furthermore, by t-test, the null hypothesis that the mean difference between each group of means compared each time is zero was rejected for lateral 1 and middle ROI, for lateral 2 and middle ROI, and for T2 average value versus middle ROI (Table 5, Figure 3).

Discussion

In this prospective cohort of symptomatic adult patients with IVDD, we assessed the role of T2 mapping in IVDD assessment by correlating to the Pfirrmann grading system. In addition, we examined a template of intervertebral disc segmentation for finer evaluation of intervertebral discs. We found that i) mean values of T2 mapping among the different grades of Pfirrmann differ from the rest ($p < 0.001$) and ii) the T2 relaxation time for the sum of three ROIs (T2 average) differs from the T2 relaxation time from the sagittal image of T2 map at the level of the most visible part of NP (T2 midline), $p < 0.001$. These results support the feasibility of using T2 relaxation time to quantify lumbar disc degeneration and IVDD diagnosis. In addition, our findings indicate an improved performance of the segmentation protocol used herein, which uses the sagittal slice with the most visible part of NP and the two adjacent lateral slices, as opposed to segmentation techniques using only the midsagittal slice.

In the literature, many novel MRI techniques have been reported analysing the microenvironment of the intervertebral disc ushering a new era in the clinical practice for the differential diagnosis of nonspecific LBP[25,26]. Some anatomical evidence should be considered to put these techniques and imaging findings into context. The intervertebral disc is the most massive avascular tissue in the adult human body, as the artery responsible for the arterial disk supply becomes atrophic in adulthood. After this stage, the main nutrient supply is dependent on metabolic pathways from the vertebral endplate, which entail both anabolic and catabolic pathways. With time, the prolonged imbalance between anabolic and catabolic sequences in discs results in the degradation of proteoglycans and water loss with this cascade of events leading to IVDD[27].

In IVDD, as one of the leading causes of nonspecific LBP, the proteoglycan and the water content decreases translate into a signal reduction on T2WI (i.e., low signal intensity is related to loss of metabolites). The MRI T2 mapping (a T2 TSE multi-echo sequence) allows the quantitative evaluation of metabolites' concentration at each part of the disc and encompasses the calculation of relaxation time (T2 values). Thereby, T2 mapping offers significant benefits over qualitative assessment of T2WI, with respect to reproducibility and objectivity compared to visual evaluation. In detail, the concentration of water and proteoglycans, as well as the cascade of collagen breakdown involved in the pathogenesis of IVDD inside the NP and the AF are digitized, and a T2 map is acquired[28]. It should be noted, that until recently, provocative discography was the gold standard technique supporting the diagnosis of discogenic pain as the etiology of nonspecific LBP. Nevertheless, the limitations of this method, including the pain at the time of contrast injection, the high false positive rate, and the hypothesis of accelerated disc degeneration and herniation, have limited its use as a diagnostic procedure[29,30]. Therefore, more precise and accurate noninvasive diagnostic techniques for IVDD and disc aging detection are needed to guide therapeutic approaches, including advanced neuroimaging.

Diagnosing intervertebral disc degeneration at its early stages is crucial as it allows for timely implementation of preventive measures or minimally-invasive treatments to halt IVDD progression and preserve spinal function[19]. In addition, early IVDD detection is essential to reduce the risk of complications such as nerve compression or spinal instability, ultimately improving patient outcomes and reducing the need for more invasive interventions. Although the benefits of quantitative T2 mapping are evident at early disease stages, T2 mapping is also indicated in cases of moderate disc degeneration (Pfirrmann grades III and IV). In such cases, complementary to morphological changes, T2 quantification may be utilized for IVDD severity assessment and prognostication, along with monitoring of treatment responses[31].

The present study evaluated the role of relaxation time (T2 values) in IVDD of lumbar spine and correlated the findings of quantitative assessment to the classical Pfirrmann classification system. Each intervertebral disc was segmented into three slices, including the sagittal slice with the most visible part of NP and the two adjacent lateral slices (T2 average), after manually drawing an ROI from the anterior part of AF to the posterior part of AF. Our results, in line with the previously published studies, indicate that T2 mapping accurately and noninvasively quantifies the IVDD. Takashima et al and Ogon et al agreed that T2 values of NP reflect the IVDD, but they studied the intervertebral disc subdividing it into different regions and only in the midsagittal slice[32,33]. Thus, the refined segmentation of the AF used herein renders the results of the present study more precise for IVDD diagnosis.

This study expands the existing literature, as our results suggest that the average T2 relaxation time value is more indicative of IVDD than the mean value from the midsagittal slice ($p < 0.001$). A key aspect of our study is that the inclusion of AF in the ROI for the mean T2 value was based on three hypotheses: i) the AF consists of concentrically oriented collagen fibers and the cascade of breakdown in degeneration can be reflected in the quantified measure of T2 value, ii) the ability to detect degeneration in the AF may contribute to the investigation

of the pathogenesis of LBP, as the sinuvertebral nerve (nerve of Luschka) re-enters the spinal canal through the intervertebral foramen innervating the posterior part of AF among others and subsequently convey discogenic pain[34], and iii) the AF was included for the measurement of T2 values because in the setting of advanced degeneration, the distinction between NP and AF is difficult, complicating the manual ROI positioning for accurate and representative measurements for IVDD.

Some limitations should be acknowledged in the current prospective study. First, it was a single-center study with a limited number of symptomatic patients, lacking asymptomatic participants as a control group. The main reason that healthy participants were not included in our study was the advanced mean age of the cohort since degenerative changes are believed to begin in the second decade of life[35]. Second, none of the participants underwent discography, thus no discography findings were available for correlation analyses with the findings of T2 relaxation time. Third, no histological samples were acquired as no participant underwent spinal surgery.

In conclusion, we support that the MRI T2 map and T2 relaxation time can be used as diagnostic tools for quantitative assessment of IVDD and discogenic pain with the appropriate segmentation of the interval disc, including part of NP and AF (anterior AF and posterior AF) in three sagittal slices, to calculate the average T2 value as more representative value for the degree of IVDD.

Conflict of interest

The authors declare no conflict of interest.

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