Influence of Age, BMI, Gender and Lumbar Level on T1ρ Magnetic Resonance Imaging of Lumbar Discs in Healthy Asymptomatic Adults

Einfluss von Alter, Geschlecht, BMI und lumbalem Level auf T1ρ-MRT-Bildgebung lumbaler Bandscheiben gesunder asymptomatischer Erwachsener

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Key words
t1ρ, spine, magnetic resonance imaging, lumbar disc, asymptomatic adults

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ZUSAMMENFASSUNG
Ziel Ermittlung der Größenordnung der T1ρ Werte der lumbalen Bandscheiben in gesunden asymptomatischen Probanden bei 1,5 T. Zusätzlich wurde der Einfluss von Alter, body mass index (BMI), Geschlecht und lumbalem Level auf die T1ρ Relaxation.


Ergebnisse Das Alter zeigte einen signifikanten Einfluss auf die T1ρ Relaxationszeit in allen lumbalen Leveln wobei zunehmendes Alter mit abnehmenden Relaxationszeiten verbunden war. Darüber hinaus zeigte sich ein signifikanter Unterschied zwischen den Altersgruppen A vs. C und B vs. C (P = 0,0008 und P = 0,0149). Kein signifikanter Unterschied bestand zwischen den T1ρ Relaxationszeiten von Männern und Frauen (P > 0,05). Der BMI zeigte eine signifikante negative Korrelation mit der T1ρ Relaxationszeit (P < 0,0001). Hinsichtlich des lumbalen Levels zeigte sich eine signifikante Abnahme der Relaxationszeiten von L1/2 zu L5/S1 (P = 0,0013).


Kernaussagen
- Steigendes Alter vermindert die T1ρ Relaxationszeit der Bandscheiben signifikant (P < 0,05)
- Geschlecht zeigt keinen signifikanten Einfluss auf die T1ρ Relaxationszeit (P > 0,05)
- BMI korreliert signifikant negativ mit der T1ρ Relaxationszeit (P < 0,01).
- Signifikant niedrigere Relaxationszeiten der unteren gegenüber oberen LWS (P < 0,01).
ABSTRACT

Purpose To assess the T1ρ range of lumbar intervertebral discs in healthy asymptomatic individuals at 1.5 T and to investigate the influence of age, body mass index (BMI), gender, and lumbar level on T1ρ relaxation.

Materials and Methods In a prospective study, a total of 81 volunteers aged 20–80 years were included in this study and divided into three age groups (A: 20–39 y; B: 40–59 y; C: 60–80 y). All of the volunteers underwent magnetic resonance imaging (MRI) at 1.5 T with acquisition of sagittal T1ρ images. The calculated T1ρ relaxation times were correlated with age, BMI, gender, and lumbar level relative to the total disc, the annulus fibrosus, and the nucleus pulposus.

Results Age had a significant influence on T1ρ relaxation times at all lumbar levels, with increasing age being associated with reduced relaxation times. There was also a significant difference between age groups A vs. C and B vs. C (P = 0.0008 and P = 0.0149, respectively). No significant differences in T1ρ relaxation time were observed between men and women (P > 0.05). BMI showed a significant negative correlation with T1ρ relaxation times (P < 0.0001). Analysis of the lumbar level revealed a significant decrease in relaxation times from L1/2 to L5/S1 (P = 0.0013).

Conclusion Increasing age correlated significantly with advanced lumbar disc degeneration in asymptomatic individuals, particularly in those aged 60 or older. Increasing BMI correlated significantly with increasing degeneration. The lower discs showed more degeneration than the upper ones.

Key Points
- Increasing age significantly reduces the T1ρ relaxation time in the intervertebral discs (P < 0.05)
- Gender does not significantly influence T1ρ relaxation times (P > 0.05)
- BMI shows a significant negative correlation with T1ρ relaxation times (P < 0.01)
- Significantly shorter relaxation times in lower lumbar spine vs. upper lumbar spine (P < 0.01)

Citation Format
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Introduction

Magnetic resonance imaging (MRI) is the gold standard for examining the lumbar discs in routine clinical practice [1]. Degenerative changes are frequently found, with growing prevalence in patients of increasingly advanced age. However, these changes do not necessarily always correlate with the patients’ clinical symptoms. Signs of degeneration may even be found in asymptomatic adults. For surgeons and physicians, it is crucial to correlate the radiographic findings with the clinical symptoms in order to develop specific treatment strategies. It is therefore important to have information about the prevalence of degenerative changes in healthy asymptomatic individuals.

One of the earliest, important studies on abnormal MRI of the lumbar spine in asymptomatic individuals, published by Boden et al. in 1990, presented the MRI results for 67 adults and identified degenerative changes in approximately one-third of them [2]. The authors concluded that there is a need for strict correlation between MRI changes, patient age, and symptoms before any treatment decisions are made [2]. Other studies showed that degenerative changes can be found to some extent in asymptomatic subjects [3, 4].

The study by Boden et al. was based only on qualitative MRI data. Today, quantitative imaging techniques are available [5]. Among these, T1ρ imaging appears to be the most promising method to become available for routine use in the study of disc pathology [6]. The T1ρ relaxation time describes the spin-lattice relaxation in the rotating frame that occurs after application of a spin-lock pulse. This spin-lock technique makes it possible to observe slow-motion processes such as interactions between water and extracellular matrix molecules [7]. Early studies showed a significant correlation between the T1ρ relaxation time and the loss of proteoglycan molecules in cartilage [8]. In the spine, T1ρ relaxation times showed relevant correlations with the amount of proteoglycans in the extracellular matrix of the lumbar disc, with longer relaxation times indicating greater amounts of proteoglycans [7, 9, 10]. In addition, T1ρ relaxation times correlated significantly with the water content in the intervertebral lumbar disc [7]. In comparison with T2 mapping, earlier studies suggest that T1ρ might be more sensitive to early degenerative changes, especially in the annulus fibrosus [11, 12]. T1ρ therefore appears to be a promising noninvasive tool for detecting early disc degeneration in vivo.

The purpose of the present study was to systematically evaluate the differences in T1ρ data for the lumbar intervertebral discs in asymptomatic individuals of different ages. In addition, it was investigated whether body mass index (BMI), gender, and lumbar level influence T1ρ relaxation times. In the study, T1ρ was used as a noninvasive indicator for disc degeneration and the ability of T1ρ to quantify disc degeneration was assumed [11–13].

Materials and Methods

This prospective study was approved by the local ethics committee (ref. no. 2013–025-F-S) and supported by a research grant from the German Spine Society. All of the participating volunteers provided written informed consent prior to examination.

Volunteers

This study included healthy asymptomatic individuals between 20 and 80 years old. The exclusion criteria were: any current lumbar
back pain or pain radiating into the leg(s) at the time of examination; a medical history including any lumbar back pain or radiating pain requiring any type of medical treatment; any history of lumbar back pain or radiating pain lasting more than 24 hours; and any inability to work due to the above symptoms. Based on the fact that degeneration increases with age, three groups were defined in order to evaluate age-related effects: group A: 20–39y; group B: 40–59y; group C: 60–80y. In addition, the volunteers’ sex, height, weight, and body mass index (BMI) were recorded. Each individual underwent a standardized physical examination and structured interview by an experienced orthopedic spine surgeon before inclusion in the study. In addition, each volunteer completed a standardized questionnaire regarding medical history focusing on back pain and spine pathologies.

**Magnetic Resonance Imaging**

All of the images were acquired using a 1.5-T clinical MRI system (Achieva; Philips Healthcare, Best, Netherlands) with an eight-channel coil. Sagittal T1ρ images with 14 slices in the lumbar spine were acquired for all subjects. The spin-lock times were 0, 10, 20, 40 and 80 ms. Other imaging parameters were as follows: repetition time msec/echo time msec 14/7; flip angle 15°; field of view 200 × 200 × 42 mm; acquisition matrix 248 × 215; and specific absorption rate < 0.2 W/kg.

**Image Analysis**

The T1ρ images were analyzed using specially developed software (Fraunhofer MEVIS, Institute for Medical Image Computing, Bremen, Germany). With the help of this software program, T1ρ maps were calculated on a pixel-by-pixel basis using a monoexponential decay mode: $M(\rho) = M_0 \times \exp(-\rho SLT / T1\rho)$. $M_0$ and $M(\rho)$ denote the equilibrium magnetization, and T1ρ refers to the prepared magnetization for each slice thickness (SLT). T1ρ maps were generated from these data for each section by fitting all pixel intensity data as a function of SLT, using a Levenberg-Marquardt fitting algorithm.

T1ρ segmentation was performed on sagittal T1ρ maps for each disc from L1/2 to L5/S1 in each individual by manually outlining the total intervertebral disc and the nucleus pulposus. This made it possible to investigate the intervertebral disc in general, as well as to differentiate between the annulus fibrosus and the nucleus pulposus (an example is shown in Fig. 1). Finally, three different mean relaxation times were calculated for each disc.

To account for potential interobserver variability in outlining the whole intervertebral disc or the nucleus pulposus and annulus fibrosus, intervertebral discs in 10% of the study population were segmented by two readers and the calculated T1ρ relaxation times were compared.

**Statistics**

The influence of age, BMI, gender, and lumbar level on T1ρ relaxation was investigated, with differentiation between the total disc, the annulus fibrosus, and the nucleus pulposus. Pearson’s correlation coefficients were calculated and Student’s t-tests were carried out where appropriate. A multivariate linear mixed model was established, with the outcome variable of T1ρ relaxation time and explanatory variables of age group, BMI, lumbar segment (L1/2–L5/S1) and the three anatomic structures (total disc, nucleus pulposus, annulus fibrosus). Correlations between individual measurements taken from the same individual were accounted for by means of a subject-specific random intercept. Heterogeneous variances in measurements at the three different anatomic structures were taken into account by appropriately partitioning the variance–covariance matrix of the error term. The linear mixed model was fitted using the restricted maximum likelihood method. $P$ values were regarded as significant at $P \leq 0.05$. No adjustment for multiple testing was performed. An overall significance level was not determined and cannot be calculated.

Power analysis showed that with a sample size of at least 24–30 individuals per group, differences in the mean T1ρ relaxation times ≥ 10 ms could be detected with 80% power in a (two-sided) Student’s t-test at alpha = 5%, assuming a standard deviation of 10–20 ms.

Interobserver variability in the calculated T1ρ relaxation times from the two readers was investigated by calculating the mean relative difference as well as the intraclass correlation coefficient (ICC).

Descriptive and inferential statistical analyses were carried out using IBM SPSS Statistics for Windows, version 22 (IBM Corporation, Armonk, New York, USA) and SAS 9.4 for Windows (SAS Institute Inc., Cary, North Carolina, USA).

**Results**

A total of 81 volunteers were included (41 women and 40 men): group A (age 20–39y), n = 24 (13 women, 11 men); group B (age 40–59y), n = 30 (15 women, 15 men); group C (age 60–80y), n = 27 (13 women, 14 men). The baseline data for all of the volunteers are presented in Table 1. They all underwent the MRI examinations successfully, with no complications, and all of the data proved to be of sufficiently high quality to provide robust T1ρ results.
The pre-test revealed a mean difference in the calculated T1ρ relaxation times between the two readers of 2% for the total disc (max. difference 5%), 6% for the annulus fibrosus (max. difference 11%), and 1% for the nucleus pulposus (max. difference 7%). The intraclass correlation coefficients (ICCs) were 0.989 for the total disc, 0.937 for the annulus fibrosus, and 0.980 for the nucleus pulposus. The interobserver variability was thus very low.

The results for T1ρ relaxation times are listed in Table 2, Fig. 2–4, with differentiation between groups A–C, the various lumbar segments (L1/2–L5/S1), and the three anatomic structures (total disc, nucleus pulposus, and annulus fibrosus). Student’s t-test did not show any significant differences with regard to T1ρ relaxation times between women and men for each group, segment, or anatomic region.

Analysis of the lumbar level showed a significant decrease in the T1ρ relaxation times between L1/2 and L5/S1 (P = 0.0013). With regard to the different parts of the intervertebral disc, there were significant differences between the total disc, the nucleus pulposus, and the annulus fibrosus (P < 0.001 for all combinations). All in all, the T1ρ relaxation time was 9.6 ms lower on average in the annulus fibrosus than in the total disc and 25.2 ms lower than in the nucleus pulposus. In addition, the T1ρ relaxation time in the nucleus pulposus was a mean of 15.6 ms higher than in the total disc.

Table 3 shows the influence of age as a continuous variable (in years) on T1ρ relaxation times, using a Pearson correlation test. In relation to the three age groups (A–C), significant differences were detected between groups A and C (P = 0.0008) and between groups B and C (P = 0.0149) using a linear mixed model with inclusion of lumbar level, age group, and disc part. Additionally including BMI in the model still led to a significant difference between groups A and C (P = 0.037), while the difference between groups B and C became borderline significant (P = 0.0651).

With regard to BMI, the linear mixed model showed a significant negative correlation between BMI and T1ρ relaxation time (P < 0.0001). Table 4 presents correlations between BMI and T1ρ relaxation times relative to the different age groups, lumbar levels, and parts of the intervertebral discs. A significant impact, with high Pearson correlation coefficients of BMI on T1ρ relaxation times, was found here for several combinations of segment and age group.

**Discussion**

The aims of this study were to establish T1ρ data for the intervertebral discs in asymptomatic individuals and to evaluate the influence of age, BMI, gender, and lumbar level on T1ρ relaxation times.

To the best of the authors’ knowledge, this is the first study that has systematically investigated T1ρ imaging at 1.5 T in asymptomatic individuals between the ages of 20 and 80. According to Boden et al., three age groups were defined: A: 20–39y; B: 40–59y; and C: 60–80y [2]. Means and standard deviations showed a homogeneous distribution of ages across the groups in the study. Half of the individuals examined were women and half were men, to allow gender effects to be studied.
Age

Increasing age was associated with lower T1ρ relaxation times, with a highly significant and uniform impact (Table 3). The results in the annulus fibrosus show the shortest relaxation times and those in the nucleus pulposus the longest. The values for the total discs are in between, as mixtures of the two anatomical structures. Published T1ρ studies of the spine have reported similar results, with decreasing relaxation times with increasing age [7, 11, 13–15].

Johanessen et al. studied T1ρ relaxation times at 1.5 T in the nucleus pulposus of seven fresh frozen cadaveric human lumbar spine sections, with a mean age of 51.6 years [7]. They found decreasing T1ρ relaxation times with increasing age and degeneration, and also observed a strong linear correlation between T1ρ and the proteoglycan content.

In a study including 11 healthy volunteers at 3 T, Blumenkrantz et al. found a significant correlation between the individuals’ age and the T1ρ relaxation times measured [14]. The volunteers’ mean age was 31.3 years, with a range of 23–60 years. The significant influence of age was evident for the T1ρ relaxation time in the nucleus pulposus as well as the annulus fibrosus, but the correlation in the annulus was lower than that in the nucleus.

Another study on the influence of age on T1ρ relaxation time was carried out by Filippi et al. at 3 T using parallel-transmission MRI [15]. They studied 34 individuals (mean age: 38.4 for men and 36.5 years for women) with no history of back pain, who were further divided into four age groups (20–29, 30–39, 40–49, 50–59). A significant moderate negative correlation was observed between T1ρ and age in all of the age groups. There was also a statistically significant difference in T1ρ relaxation

<table>
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<th>Table 2</th>
<th>T1ρ Relaxation Times (in ms) for All Lumbar Segments (L1/2 to L5/S1) for the Total Disc, Annulus Fibrosus, and Nucleus Pulposus.</th>
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<td>total disc T1ρ relaxation times (ms)</td>
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<td>group a</td>
<td>66.51</td>
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<td>group b</td>
<td>58.32</td>
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<tr>
<td>group c</td>
<td>46.51</td>
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<td>annulus fibrosus T1ρ relaxation times (ms)</td>
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<td>group a</td>
<td>53.24</td>
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<tr>
<td>group b</td>
<td>48.51</td>
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<tr>
<td>group c</td>
<td>42.00</td>
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<tr>
<td>nucleus pulposus T1ρ relaxation times (ms)</td>
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<tr>
<td>group a</td>
<td>90.38</td>
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<td>group b</td>
<td>74.30</td>
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<td>group c</td>
<td>54.00</td>
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</table>

Fig. 2 T1ρ relaxation times (in ms with standard deviation) in all five lumbar discs for the three age groups (group A: blue; group B: red; group C: green) for the total disc.

Fig. 3 T1ρ relaxation times (in ms with standard deviation) in all five lumbar discs for the three age groups (group A: blue; group B: red; group C: green) for the annulus fibrosus.
times between all of the studied age groups, a finding that is also consistent with the present results.

The influence of age on T1p relaxation times in the lumbar intervertebral discs in individuals with disc degeneration and clinical symptoms was evaluated in a study by Blumenkrantz et al. [11]. Sixteen individuals with a mean age of 40.2 years were studied with imaging at 3T. There was a significant negative correlation between T1p relaxation times and age and a significant positive correlation between age and Pfirrmann grade.

In a mixed group of asymptomatic individuals and patients with low back pain, Wang et al. also found a significant reduction in T1p relaxation times along with increasing age [13]. With regard to the different parts of the intervertebral disc, the reduction was more pronounced in the nucleus pulposus than in the annulus fibrosus.

In contrast to the above studies as well as the present results, Zhou et al. did not find a significant influence of age on the T1p relaxation time [16]. They examined 80 patients with low back pain at 1.5T. While there was a significant negative correlation between Pfirrmann grade and T1p relaxation time, age was not found to have a significant influence on T1p times. One reason for the divergent results between the findings published by Zhou et al. and the present study might be the fact that Zhou et al. only studied patients with low back pain and corresponding degeneration. Their cohort also only comprised patients between 20 and 43 years old, with a mean age of 31.6 years, potentially diminishing the observed effect of age on T1p relaxation times.

### BMI

When the effect of BMI was investigated, a significant negative correlation was found between BMI and T1p relaxation time. Further analyses relative to different age groups, lumbar levels, and the parts of the intervertebral disc showed that this correlation was particularly strong in participants in age group C (60–80y).

The only published study to date on the effect of BMI on T1p relaxation times is that of Zobel et al., which did not find any significant correlations between BMI and T1p values [17], in contrast to the results of the present study. However, it is important to note that Zobel et al. conducted their study in 63 healthy young individuals with a mean age of 22.95 years. As the most prominent correlation between BMI and T1p relaxation times was found in age group C in the present study, it might be possible that the young age of the population included in the study by Zobel et al. led to the lack of any significant influence of BMI.

With regard to studies using standard clinical MRI to assess intervertebral disc degeneration, there are no clear results in the literature on the influence of BMI. Some studies have not identified any significant influence of BMI on disc degeneration [18, 19], but the majority of studies have reported a correlation between BMI and disc degeneration [20–22].

### Gender

The results of the present study did not show any significant effect of gender on relaxation times. This finding corresponds with the results published by Filippi et al., who also did not identify any statistically significant differences in T1p values between men and women in a study at 3 T including 34 healthy volunteers [15]. In contrast, in a T1p study including healthy young adults, Zobel et al. found significantly lower relaxation times in women in the L3/4 and L4/5 discs [17]. A trend toward more severe disc degeneration in women was also reported in the study by Wang et al., who used a modified Pfirrmann grading system to assess disc degeneration [23]. They also found significant differences between men and women at the L3/4 and L4/5 levels.

Consistent with the findings of the present study, other reports on intervertebral disc degeneration have not identified a signifi-
cant influence of gender on the degenerative process using either clinical MRI [18] or MRI evaluation of fresh cadaveric spines [24].

**Lumbar level**

A significant but small decrease in the T1ρ relaxation times from levels L1/2 to L5/S1 was observed in the present study. This finding corresponds to the results reported by Vadalá et al., who noted a significant decrease in T1ρ values in the nucleus pulposus from the upper to the lower lumbar levels when evaluating asymptomatic weightlifters for early intervertebral disc degeneration [25]. This trend toward lower T1ρ relaxation times in the caudal segments of the spine was also described by Blumenkrantz et al. in a study including 16 patients suffering from intervertebral disc degeneration with clinical symptoms [11].

Studies using standard MRI techniques have also provided evidence for increased disc degeneration in the lower parts of the lumbar spine, supporting the findings of the present study [26–28]. The different loading environment of the discs in the different levels is one the well-known major reasons [29].

**Limitations**

Limitations of this study include the fact that only a single radiologist evaluated all of the T1ρ images. This is justified, however, as the described preliminary test showed a very low level of interobserver variability. In addition, studies in the literature have shown excellent reproducibility results and high levels of interobserver reliability [6, 16, 30]. It would not have been possible to control for the minimal bias in light of the fact that none of the included individuals had ever suffered from low back pain, even though each individual was examined and interviewed by an orthopedic spine surgeon. T1ρ imaging was not compared with any other imaging modalities. The main reason for this decision was to keep the total examination time for the volunteers (who underwent a standardized physical examination, structured interview and a standardized questionnaire in addition to MRI) as short as possible to ensure their willingness to take part in the study. The lack of a morphologic parameter such as the Pfirrmann Grade is justified as studies in the past have shown high correlations between T1ρ and degeneration status in symptomatic patients [6, 11, 12]. Finally, the ability of T1ρ to quantify disc degeneration was assumed [11–13].

**Conclusion**

The results of the present study, which is one of the largest studies on T1ρ imaging of the spine and includes volunteers up to the age of 80 years, confirm those of earlier investigations indicating that some degree of disc degeneration may be regarded as “normal” in asymptomatic individuals. Age showed a significant and uniform impact on T1ρ relaxation times. Furthermore, increasing

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<th>Table 4 Correlations between BMI and T1ρ relaxation times relative to age group, lumbar level, and disc part.</th>
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<td><strong>L1/2</strong></td>
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<td><strong>annulus fibrosus</strong></td>
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BMI and a more distal location of the affected discs also proved to influence disc degeneration, whereas gender showed no significant impact. The results of the study underline the possible application of T1ρ imaging in the evaluation process in patients with intervertebral disc degeneration as it is a quantitative method that isn’t susceptible to the radiologist’s experience as in the case of qualitative or semi-qualitative evaluation. Still, a close clinical correlation between symptoms and imaging findings is strongly required. Although the acquired data are not entirely transferable to other MRI systems, the results may still serve as baseline data for further studies or as comparative values for other populations.

Conflict of Interest

The authors declare that they have no conflict of interest.

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