Thesis

# Analyse de la cartographie T1 et de sa variation diurne des disques intervertébraux au sein d'une population jeune et asymptomatique de 50 volontaires

GALLEY, Julien

**Abstract**

Le but de ce travail de recherche est d'évaluer le temps de relaxation T1 des disques intervertébraux au sein d'une population jeune et en bonne santé, en utilisant différents temps d'inversion-récupération, et d'y analyser la variation diurne. Deux examens par résonance magnétique de la colonne lombaire ont été réalisés le même jour matin et soir chez chacun des 50 volontaires. Les temps de relaxation T1 ont été calculés au sein des noyaux pulpeux ainsi que des anneaux fibreux. Nous avons constaté une variation diurne significative au sein des noyaux pulpeux avec une valeur moyenne de 1142 ± 12 ms le matin et de 1085 ± 13 ms le soir. Une différence significative entre les différents niveaux a également été mise en évidence, corrélant d'autres études anatomiques. La cartographie T1 des disques intervertébraux est une technique très sensible d'évaluation du contenu en eau du disque intervertébral et présente un grand potentiel dans l'analyse longitudinale des disques intervertébraux.

Reference

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# Real T1 relaxation time measurement and diurnal variation analysis of intervertebral discs in a healthy population of 50 volunteers

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ABSTRACT

*Purpose:* To measure the real T1 relaxation time of the lumbar intervertebral discs in a young and healthy population, using different inversion recovery times, and assess diurnal variation.
*Material and methods:* Intervertebral discs from D12 to S1 of 50 healthy volunteers from 18 to 25 years old were evaluated twice the same day, in the morning and in the late afternoon. Dedicated MRI sequences with different inversion recovery times (from 100 to 2500 ms) were used to calculate the real T1 relaxation time. Three regions of interest (ROIs) were defined in each disc, the middle representing the nucleus pulposus (NP) and the outer parts the annulus fibrosus (AF) anterior and posterior. Diurnal variation and differences between each disc level were analyzed.
*Results:* T1 mean values in the NP were $1142 \pm 12$ ms in the morning and $1085 \pm 13$ ms in the afternoon, showing a highly significant decrease of 57 ms ($p < 0.001$). A highly significant difference between the levels of the spine was found. The mean T1 of the *anterior* part of the AF was $577 \pm 9$ ms in the morning and $554 \pm 8$ ms in the afternoon. For the *posterior* part, the mean values were $633 \pm 8$ ms in the morning and $581 \pm 7$ ms in the evening. It shows a highly significant decrease of 23 ms for the anterior part and 51 ms for the posterior part (all $p < 0.001$).
*Conclusion:* T1 mapping is a promising method of intervertebral disc evaluation. Significant diurnal variation and difference between levels of the lumbar spine were demonstrated. A potential use for longitudinal study in post-operative follow up or sport medicine needs to be evaluated.


## 1. Introduction

Back pain is very common but challenging medical condition that often affects young individuals and has a major impact on work capacity [1]. Although its established association with intervertebral disc degeneration and the fact that the physiopathology has been thoroughly studied [2,3], the cascade of events leading to clinical manifestation are not fully understood. Besides, a significant number of people presenting disc degeneration are asymptomatic [4,5].

The intervertebral disc is composed of an outer shell known as the annulus fibrosous (AF) and an inner part, the nucleus pulposous (NP). The AF consists of 15–25 lamellae of collagen strongly attached to the endplates and reinforced by the two longitudinal ligaments. It confers the tensile and shear strength of the disc. The NP contains collagen fibers, elastic fibers and a gel-like area of proteoglycans (PGs) with hydrophilic chondroitin and keratin sulfate, which bind water molecules [2]. Alteration of these components seen during disc degeneration will impact the mechanical properties and cause a progressive loss of the disc water content.

Even though intervertebral disc components are the same, each disc of the lumbar spine can be considered as a unique entity. The intervertebral disc is part of a complex structure made of the endplates, the disc itself, numerous ligamentous structures (longitudinal anterior and posterior, flavum, interspinous, supraspinous, intertransverse), muscles and facet joints. At both ends of the lumbar spine, the dorsolumbar and lumbosacral junction will also influence the motion of the adjacent discs. All those interactions will make the discs act differently. The degrees of movement of each level has been shown to be distinct [6–8].

Imaging as a routine examination is still controversial at the onset of symptoms [9]. However, if needed, MRI is now considered as the non-invasive method of choice to analyze intervertebral disc components. It allows clear distinction between the AF and NP with high spatial resolution. Sagittal T2-weighted images have become the first line analysis to evaluate intervertebral discs hydra-

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**Table 1**
MRI parameters.

| | | | *Inversion recovery sequences* | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Sequences | Sagittal T1 | Sagittal T2 | Sag IR TI 100 | Sag IR TI 200 | Sag IR TI 400 | Sag IR TI 600 | Sag IR TI 900 | Sag IR TI 1200 | Sag IR TI 1800 | Sag IR TI 2500 |
| TE | Min Full | 102 | Min Full | Min Full | Min Full | Min Full | Min Full | Min Full | Min Full | Min Full |
| TR | 340 | 3547 | 5775 | 5775 | 5775 | 5775 | 5775 | 5775 | 5775 | 5775 |
| TI | – | – | 100 | 200 | 400 | 600 | 900 | 1200 | 1800 | 2500 |
| Echo train length | 3 | 23 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 |
| FOV | 34 | 34 | 26 | 26 | 26 | 26 | 26 | 26 | 26 | 26 |
| Matrix | 384 × 224 | 320 × 256 | 288 × 160 | 288 × 160 | 288 × 160 | 288 × 160 | 288 × 160 | 288 × 160 | 288 × 160 | 288 × 160 |
| Slice thickness | 3.5 | 3.5 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Slice spacing | 1 | 1 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
| Number of slices | 15 | 15 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
| Acquisition time | 03:08 | 02:58 | 01:38 | 01:38 | 01:38 | 01:38 | 01:38 | 01:38 | 01:38 | 01:38 |

TE = echo time, TR = repetition time, TI = inversion recovery time.

tion. A five grades classification was proposed by Pfirrmann [10] and is commonly accepted as the reference qualitative grading system. Several quantitive analyses have been evaluated using different MRI techniques. T1 rho imaging [11–16] has been proven to be a sensitive tool for early disc degeneration changes detection, showing a correlation between the T1 rho values and proteoglycan content. T1 rho differs from real T1 by the fact that it has both elements of T1 and T2 weightening [17]. Quantitative T2 approach also seems to be sensitive to early degeneration [16,18–20].

It has also been shown that diurnal changes occur in normal intervertebral discs using lumbar length measurement (height loss) and T2 mapping (decreasing T2 values) [21,22].

T1 mapping has been evaluated in different part of the body, like brain [23] and cartilage [24–26] and was demonstrated to be correlated to water content [27,28]. But in the current literature there is a lack of studies about T1 relaxation time measurement in the intervertebral discs.

The purpose of this study was to define reference values in a young and healthy population and to analyze its diurnal variation.

## 2. Materials and methods

This study was approved by the CT CER (*Communauté de travail des Commissions Suisses d'éthique pour la recherche sur l'être humain, Lausanne*)

### 2.1. Participants

Fifty healthy and asymptomatic volunteers were included in this study: mean age 21.6 ± 2.4, age range 18–25 years, 23 females and 27 males. Recruitment for the study was from medical staff or acquaintances and university students. The number of subjects was estimated using F-test based on data we measured on 20 symptomatic patients.

Each participant was asked to fill forms about their health history and medication.

Inclusion criteria were: good health, absence of any back symptom, age between 18–25 years.

Exclusion criteria were: medical history of back pain, radiculopathy or neurological deficit, back trauma, previous back surgery or infiltration, osteoarticular or connective tissue disease, body mass index of >25, contraindication to MRI.

All the participants were asked to have normal daytime activity and to avoid any heavy work (not to bear weights over 10 kg) or any sport during the day of examination.

Written informed consent was obtained from all participants.

### 2.2. MR imaging

The examinations were performed between the 23th December 2014 and 14th July 2015. All the volunteers were scanned twice the same day (once in the morning at 8 am and once in the late afternoon around 5 pm) in a relax supine position.

MR imaging was performed using a 1.5T MR unit (Optima 360 Advance, GE Healthcare, Waukesha, WI, USA).

The standard MR protocol using sagittal T1-weighted fast spin echo and sagittal T2-weighted fast spin echo sequences was used for morphological analysis and Pfirrmann classification of each disc. Dedicated sequences were then realized for T1 relaxation time measurements. As conducted before [27], we used the inversion recovery techniques with different inversion recovery times (from 100 to 2500 ms). The detailed parameters are shown in Table 1. T1 relaxation times were obtained using software (T1 Mapping-Functool Research, Advantage Windows Workstation GE, Milwaukee) calculating the curve of the longitudinal relaxation from the signal values measured pixel by pixel on the different inversion times. The value obtained for a relaxation of 63% of its maximal value is considered as the real T1 relaxation time of the tissue [29–31] (Fig. 1). For a defined region of interest (ROI), the T1 value is defined as the average value of all the pixels contained in this defined area.

### 2.3. Image analysis

Six intervertebral discs (D12-S1) were examined for each exam of all participants. Six hundred intervertebral discs were separately analyzed. All discs were classified according to the Pfirrmann classification based on the T2-weighted images.

For T1 relaxation time measurement, we had to define different regions of interest (ROIs) throughout the disc in the sagittal plane. Different previous studies [19,20] defined 5 equal ROIs from

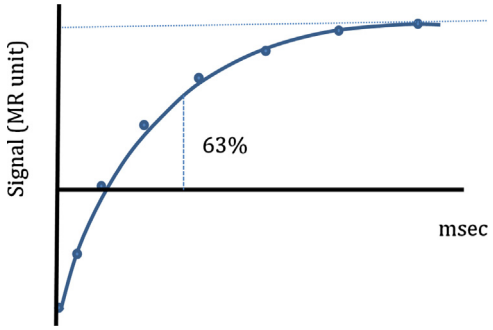


**Fig. 1.** Schematic curve drawn by the different inversion recovery times values (blue dots). T1 is defined as the time at 63% of the full recovery.

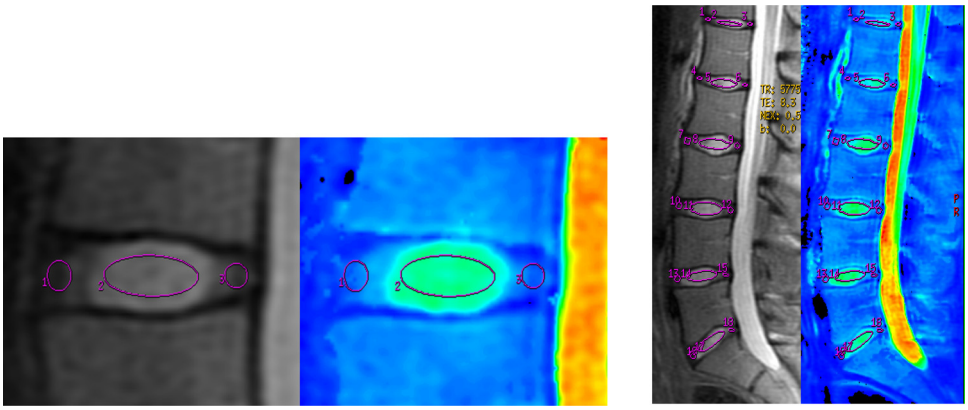

**Fig. 2.** Disc segmentation with 3 different ROIs (Region Of Interest): On the left, ROI placement: the middle one the nucleus pulposus (NP), the two outer parts representing the annulus fibrosus (AF). On the right, example of all the ROI of an exam from D12 to S1.

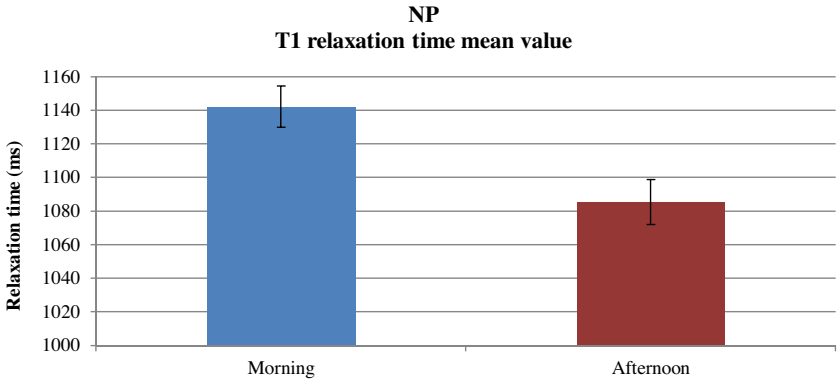


**Fig. 3.** T1 relaxation time mean values (ms) of the NP of all the discs. Error bars represent 95% confidence interval. NP = nucleus pulposus.

anterior to posterior, the number 1 and 5 representing the annulus fibrosus and the three in the middle (number 2–4) the nucleus pulposus. We opt for three ROIs in total representing anatomic area. Two virtual horizontal lines of the outer border of each endplates were defined. An ovoid ROI between those lines, less than half of the length of the disc, center on the middle, was considered to be the nucleus pulposus area. Two round ROIs, less than fifth of the total length, were placed on the two outer part of the disc and defined as the annulus fibrosus area (Fig. 2). All the measures were done by one radiologist with 4 years of radiology and 2 years of orthopedic and spine surgery experience. The intraobserver reliability was evaluated on ten patients with a correlation coefficient of >0.9.

### 2.4. Statistical analysis

Independent samples *t*-test were performed to analyze the difference between two groups (morning vs afternoon). A P value of $\leq$0.05 was considered to be significant and a P value of $\leq$0.001 highly significant. We have considered a confidence interval reflecting a significance level of 5%. To compare the different levels of the spine against the others, ANOVA test with post-hoc Bonferroni was realized. All the test and graphs were realized using *Microsoft Excel version 14.5.5* and *SSPS statistic 23*.

## 3. Results

In total, 600 intervertebral discs were evaluated (50 participants, 6 discs from D12 to S1, 2 examinations the same day). Using the aforementioned method, 1800 ROIs were drawn.

All the discs were classified according to the 5 grades Pfirrmann classification. We found 584 discs classified grade I or II, 14 grade III and 2 grade IV. Grades I and II discs were considered representative of normal disc and used for measurements to define reference values.

### 3.1. Nucleus pulposus (NP)

The mean T1 relaxation time values of the NP are represented in Table 2.

The mean value of all discs together was 1142 ± 12 ms at the morning examination and 1085 ± 13 ms in the afternoon (Fig. 3). The decrease between these two groups is highly significant with a P value < 0.001. Each level separately showed a highly significant difference (P value < 0.001) between the morning and afternoon values.

The difference between the levels (ANOVA) was highly significant (P value < 0.001). Comparing the different levels to each other (post-hoc Bonferroni), the majority of pairs of were significantly different (Table 3).

The highest mean values (for the morning as well as the afternoon) were measured in L4-L5 (morning 1234 ± 11 ms, evening 1181 ± 23 ms). We noticed the tendency of a progressive increase of values from D12-L1 to L4-L5 before decreasing in L5-S1 (Fig. 4).

The mean delta (difference between morning and afternoon values) for all levels was −57 ms (1142-1085). And taken separately, we noticed an inverted tendency with progressive decrease from D12-L1 until the lowest level L3-L4 (40 ± 5 ms) before going up again.

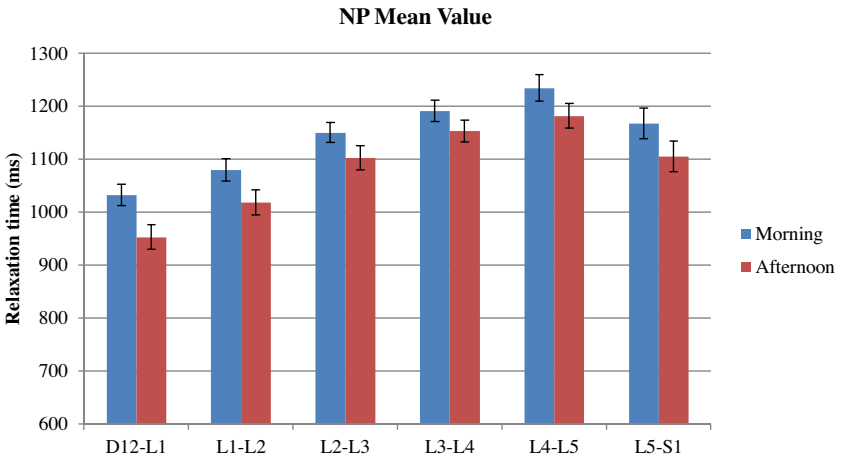


**Fig. 4.** T1 Relaxation time mean values (ms) for morning and afternoon for each level. Error bars represent 95% confidence interval. NP = nucleus pulposus.

**Table 2**
Nucleus pulposus mean values.

| Level | Mean | CI | P value |
|---|---|---|---|
| All discs | | | |
| Morning | 1142,0 | 12,2 | <0,001* |
| Afternoon | 1085,4 | 13,4 | |
| D12-L1 | | | |
| Morning | 1032,0 | 20,3 | <0,001* |
| Afternoon | 952,8 | 23,5 | |
| L1-L2 | | | |
| Morning | 1079,5 | 20,9 | <0,001* |
| Afternoon | 1018,2 | 23,7 | |
| L2-L3 | | | |
| Morning | 1050,0 | 18,9 | <0,001* |
| Afternoon | 1102,4 | 22,6 | |
| L3-L4 | | | |
| Morning | 1191,1 | 19,9 | <0,001* |
| Afternoon | 1153,1 | 20,8 | |
| L4-L5 | | | |
| Morning | 1234,3 | 25,0 | <0,001* |
| Afternoon | 1181,4 | 23,3 | |
| L5-S1 | | | |
| Morning | 1167,4 | 29.2 | <0,001* |
| Afternoon | 1105,0 | 28,6 | |

CI: confidence interval.
* P value ≤ 0.001.

**Table 3**
Nucleus pulposus levels comparison (Post-hoc Bonferonni).

| (I) Group | (J) Group | Average difference (I-J) | Significance |
|---|---|---|---|
| D12-L1 | L1-L2 | −47.5 | 0.066 |
| | L2-L3 | −118.08 | <0,001* |
| | L3-L4 | −159.1224 | <0,001* |
| | L4-L5 | −202.2917 | <0,001* |
| | L5-S1 | −135.3902 | <0,001* |
| L1-L2 | D12-L1 | 47.5 | 0.066 |
| | L2-L3 | −70.58 | <0,001* |
| | L3-L4 | −111.6224 | <0,001* |
| | L4-L5 | −154.7917 | <0,001* |
| | L5-S1 | −87.8902 | <0,001* |
| L2-L3 | D12-L1 | 118.08 | <0,001* |
| | L1-L2 | 70.58 | <0,001* |
| | L3-L4 | −41.0424 | 0.185 |
| | L4-L5 | −84.2117 | <0,001* |
| | L5-S1 | −17.3102 | 1 |
| L3-L4 | D12-L1 | 159.1224 | <0,001* |
| | L1-L2 | 111.6224 | <0,001* |
| | L2-L3 | 41.0424 | 0.185 |
| | L4-L5 | −43.1692 | 0.138 |
| | L5-S1 | 23.7322 | 1 |
| L4-L5 | D12-L1 | 202.2917 | <0,001* |
| | L1-L2 | 154.7917 | <0,001* |
| | L2-L3 | 84.2117 | <0,001* |
| | L3-L4 | 43.1692 | 0.138 |
| | L5-S1 | 66.9014 | 0.002* |
| L5-S1 | D12-L1 | 135.3902 | <0,001* |
| | L1-L2 | 87.8902 | <0,001* |
| | L2-L3 | 17.3102 | 1 |
| | L3-L4 | −23.7322 | 1 |
| | L4-L5 | −66.9014 | 0.002** |

* P value ≤ 0.001.
** P value ≤ 0.05.

### 3.2. *Annulus fibrosus (AF)*

The mean T1 relaxation time values of the AF are represented in Table 4.

The mean value for the *anterior* part of the AF for all the discs was 577 ± 9 ms in the morning and 554 ± 8 ms in the afternoon. For the *posterior* part, the mean values were 633 ± 8 ms in the morning and 581 ± 7 ms in the evening (Fig. 5). That shows a highly significant difference (P value < 0.001) between the anterior and posterior part of the annulus fibrosus, the highest values concerning the posterior part. It also demonstrates a highly significant difference (P value < 0.001) between morning and afternoon for the anterior (−23 ms) as well as the posterior part (−51 ms) of the AF. Taken separately, each level also showed a significant difference between morning and afternoon for the anterior and posterior part. As for the NP values, we noticed a tendency of increasing values from D12 to L4/L5 and then decreasing for the anterior part of the annulus but not for posterior part (Figs. 6 and 7). The mean delta (absolute difference between morning and afternoon) didn't show an increasing of decreasing curve.

## 4. Discussion

This study provides quantitative T1 relaxation time values for lumbar intervertebral discs in a young and healthy population. As expected, the results show significant difference between the AF and the NP, explained by their different components. The diurnal T1 variation between morning and afternoon (decreasing values) was significantly demonstrated for the NP and the AF of all levels. It correlates the results of previous studies showing diurnal variation with decreasing T2 values [20,22]. This daily evolving status can be explained by the loss of water content and collagen fibers orienta-

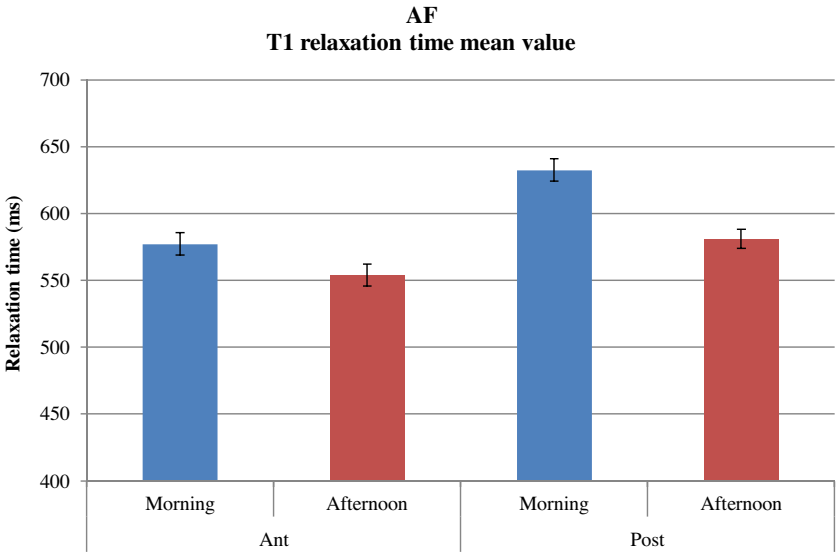


**Fig. 5.** T1 relaxation time mean values (ms) for the anterior and posterior part of the AF. Error bars represent 95% confidence interval. AF = annulus fibrosus.

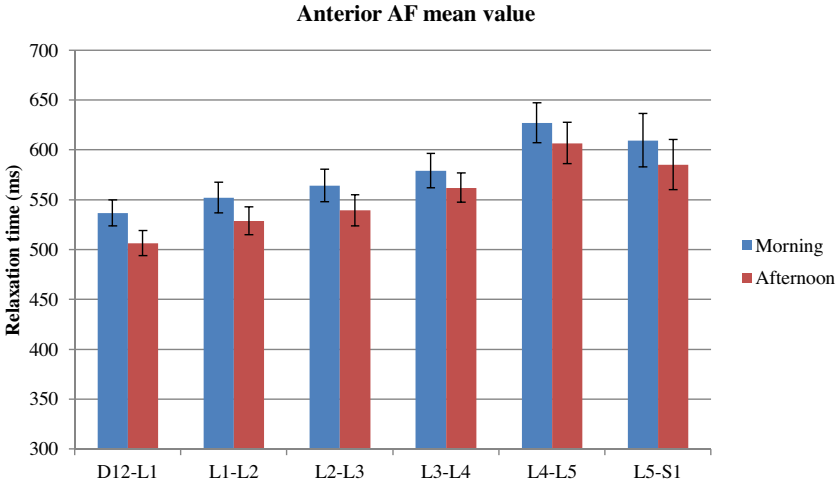


**Fig. 6.** T1 relaxation time mean values (ms) for the anterior part of the AF of each level. Error bars represent 95% confidence interval. AF = annulus fibrosus.

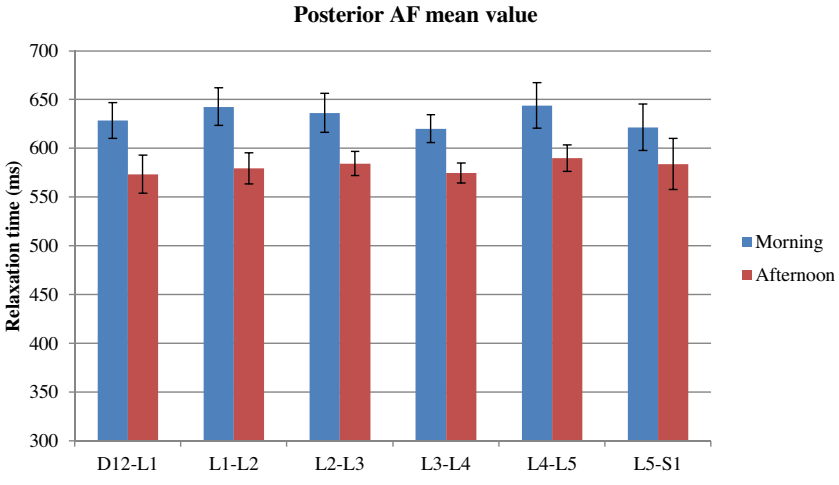


**Fig. 7.** T1 relaxation time mean values (ms) for the posterior part of the AF of each level. Error bars represent 95% confidence interval. AF = annulus fibrosus.

**Table 4**
Annulus fibrosus mean values.

| Level | | Mean | CI | P value |
|---|---|---|---|---|
| All discs | | | | |
| Anterior | Morning | 577,3 | 8,5 | <0,001* |
| | Afternoon | 554,0 | 8,3 | |
| Posterior | Morning | 632,6 | 8,4 | <0,001* |
| | Afternoon | 581,0 | 7,0 | |
| D12-L1 | | | | |
| Anterior | Morning | 536,8 | 13,0 | <0,001* |
| | Afternoon | 506,7 | 12,6 | |
| Posterior | Morning | 628,6 | 18,2 | <0,001* |
| | Afternoon | 573,5 | 19,6 | |
| L1-L2 | | | | |
| Anterior | Morning | 552,1 | 15,4 | <0,001* |
| | Afternoon | 528,8 | 14,0 | |
| Posterior | Morning | 642,8 | 19,4 | <0,001* |
| | Afternoon | 579,5 | 16,2 | |
| L2-L3 | | | | |
| Anterior | Morning | 564,3 | 16,2 | <0,001* |
| | Afternoon | 539,4 | 15,6 | |
| Posterior | Morning | 636,5 | 20,0 | <0,001* |
| | Afternoon | 584,5 | 12,2 | |
| L3-L4 | | | | |
| Anterior | Morning | 579,4 | 17,2 | 0,012** |
| | Afternoon | 562,0 | 14,7 | |
| Posterior | Morning | 620,4 | 14,4 | <0,001* |
| | Afternoon | 574,8 | 10,1 | |
| L4-L5 | | | | |
| Anterior | Morning | 627,1 | 20,1 | 0,041** |
| | Afternoon | 606,8 | 20,9 | |
| Posterior | Morning | 644,0 | 23,5 | <0,001* |
| | Afternoon | 590,0 | 13,7 | |
| L5-S1 | | | | |
| Anterior | Morning | 609,7 | 26,9 | 0,048** |
| | Afternoon | 585,2 | 25,0 | |
| Posterior | Morning | 621,6 | 23,9 | <0,001* |
| | Afternoon | 584,1 | 26,3 | |

CI: confidence interval.
* P value ≤ 0.001.
** P value ≤ 0.05.

tion variation in the disc due to the diurnal axial load [20,32]. All those structural changes will influence the T1.

As aboved-mentioned, T1 is correlated to the hydration state of the tissue and therefore its components. An interesting point supported by this study is the difference between the levels of the spine. Different T1 values show that each level is a proper entity with slightly different disc hydration state (and therefore components). Blumenkrantz et al. [12] as well as Zobel et al. [13] already mentioned a difference between levels using the T1 rho mapping. We managed to prove this difference with significant values, due to the larger number of subjects.

As proven by Cook et al. [8], the lumbar spine shows a significant different range of motion between each level. They analyzed three different range of motion: flexion extension (FE), lateral bending (LB) and axial torsion (AT). FE range of motion tended to increase from L1 to S1. On the other hand, LB and AT range of motion tended to be greater in center of the segment with the highest values in L4-L5. Our values also show this tendency, growing from D12-L1 to L4-L5 before going down in L5-S1. As discussed earlier, the T1 is correlated to the hydration state of the disc. So, comparing our data with the study of Cook et al., we can postulate that there is a correlation between the hydration state and the mobility of the disc (for LB and AT).

This tendency was inverted for the mean delta (difference between morning and afternoon) with the lowest value in L3 and L4. Thus the more hydrated is a disc, the less water it will lose during the day.

An important limitation in our study is the analysis of the annulus fibrosus. The placements of the ROIs (region of interest) were difficult due to the convex shape of the disc. In some cases, the ROI had to be really small to fit between the two endplates. A small ROI will be easily influenced with little displacement or misplacement. It could be a problem for reproducibility and that should be consider for further evaluation. Another question is the studied population (mostly students) that may not be representative of the current population (no practical worker for instance) and could be a bias.

Inversion recovery technique used for this study is time consuming and may not be applicable in daily practice. It still has to be proven if using less IR times to shorten the protocol and gain precious time is accurate enough.

To our best actual knowledge, our study is the first one to investigate intervertebral disc T1 relaxation time using inversion-recovery. This work only evaluates discs of asymptomatic volunteers and the next step will be the analysis of pathologic discs in symptomatic patients. A correlation between the T1 values and the Pfirrmann grades should be found but still to be demonstrated. This method also seems promising for longitudinal analysis, for instance for the follow up of discs after spine dynamic fixation surgery. Potential use in sport medicine also seems interesting, for example in analyzing the impact of different training techniques or materiels (i.e. shoes) in long distance running.

In conclusion, T1 relaxation time measurement using different inversion recovery times seems promising for the evaluation of (patho)physiological changes of the intervertebral discs and shows potential for further evaluation.

## Conflicts of interest

The authors whose names are listed immediately below certify that they have NO affiliation with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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