

Segmental Quantitative MR Imaging Analysis of Diurnal Variation of Water Content in the Lumbar Intervertebral Discs

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Objective: To investigate the changes in water content in the lumbar intervertebral discs by quantitative T2 MR imaging in the morning after bed rest and evening after a diurnal load.

Materials and Methods: Twenty healthy volunteers were separately examined in the morning after bed rest and in the evening after finishing daily work. T2-mapping images were obtained and analyzed. An equally-sized rectangular region of interest (ROI) was manually placed in both, the anterior and the posterior annulus fibrosus (AF), in the outermost 20% of the disc. Three ROIs were placed in the space defined as the nucleus pulposus (NP). Repeated-measures analysis of variance and paired 2-tailed *t* tests were used for statistical analysis, with $p < 0.05$ as significantly different.

Results: T2 values significantly decreased from morning to evening, in the NP (anterior NP = -13.9 ms; central NP = -17.0 ms; posterior NP = -13.3 ms; all $p < 0.001$). Meanwhile T2 values significantly increased in the anterior AF (+2.9 ms; $p = 0.025$) and the posterior AF (+5.9 ms; $p < 0.001$). T2 values in the posterior AF showed the largest degree of variation among the 5 ROIs, but there was no statistical significance ($p = 0.414$). Discs with initially low T2 values in the center NP showed a smaller degree of variation in the anterior NP and in the central NP, than in discs with initially high T2 values in the center NP (10.0% vs. 16.1%, $p = 0.037$; 6.4% vs. 16.1%, $p = 0.006$, respectively).

Conclusion: Segmental quantitative T2 MRI provides valuable insights into physiological aspects of normal discs.

Index terms: Spine; Intervertebral disc; T2 mapping; Quantitative MRI

INTRODUCTION

Body height actually shows a diurnal variation by becoming shorter during the day and recovering during

the night. The change in body height is attributed to the diurnal variation in water content of the intervertebral disc (IVD) compartments. The annulus fibrosus (AF) in lumbar IVDs, consists of type I collagen fibers (low in water content) and functions as a rigid containment for the nucleus pulposus (NP). However, NP with its gelatinous structure consists mostly of ionized water and has a low collagenous content. By generating free water and proteoglycan (PG)-associated water, the disc maintains a balance between externally applied loads and internal osmotic pressure over the course of daily activities (1). A diurnal change of the water exuded and reabsorbed plays an important role in the fluctuation of disc hydration. Previous studies have shown that the total water content in normal lumbar discs in human will decrease by 5–10% throughout the day (1, 2).

Calculation of the T2 relaxation on quantitative T2-mapping MR technique provides information on IVD tissue

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composition, particularly the water content (3-5). Normal discs show periodical diurnal changes in T2 values, which significantly decrease with aging and degeneration (4-7). However, the aforementioned studies considered the entire vertebral disc as a single volume-of-interest, in order to investigate the diurnal changes of water content in normal IVDs (8, 9). The theoretical basis of such study does not correlate well with the distribution of biomechanical function of the discs, because the degeneration of the NP occurs earlier than the AF, and the posterolateral parts of the AF are the weakest and easily avulsed.

Thus, a precise regionally-segmented investigation of IVDs will provide a better understanding of the changes to biological function of the spine. Consequently, the detailed information will be valuable for early prediction, detection and intervention in patients, particularly for younger populations with disc disease at the first stage. The purpose of this study was to investigate the diurnal T2 value changes in different compartments of the discs after the normal daily activity load, by using quantitative T2-mapping MR imaging.

MATERIALS AND METHODS

Patient Population

The study was approved by the Institutional Review Board, and written informed consent was obtained from all volunteers before MR examinations. The study group consisted of 20 healthy volunteers (10 men, 10 women; mean age, 24.7 ± 2.3 years; age range, 23-31 years). None of the volunteers suffered from any known spine-related disease or relevant low back pain. The participants were examined by MR imaging twice: less than 30 minutes after rising in the morning and on finishing their daily work/activities in the evening, with a time interval of 12 hours. The subjects were mainly sedentary. They were requested to continue with normal activity and not to bear weights over 5 kg on the day of MR imaging.

Image Acquisition

All MR examinations were performed with a 1.5-tesla system (Signa, GE Medical Systems, Milwaukee, WI, USA) using a dedicated 8-channel spine coil. The standard MR protocol of the spine included sagittal T1-weighted fast spin echo (T1WI FSE; repetition time [TR]/echo time [TE], 350/7.0 ms; matrix, 352 x 256; number of excitation [NEX], 4; bandwidth, 62.5 kHz; field-of-view [FOV], 34 cm;

thickness, 4 mm; gap, 1 mm), and sagittal T2-weighted FSE (TR/TE, 2050/1200 ms; matrix, 416 x 256; NEX, 4; bandwidth, 62.5 kHz; FOV, 34 cm; thickness, 4 mm; gap, 1 mm no fat saturation) for morphologic evaluation of the spine. For the measurement of T2 relaxation time, a multiecho spin echo (SE) sequence was performed in the sagittal plane with imaging parameters: TR/TEs, 2000/13.9, 27.8, 41.6, 55.5, 69.4, 83.3, 97.2, and 111 ms; matrix, 320 x 256; NEX, 1; bandwidth, 19.23 kHz. The acquisition time for this sequence was 5 minutes 12 seconds. Sagittal T2 maps were calculated from image series of a multiecho SE sequence. During MR scan, the subject was positioned in supine posture with the back against the bed to prevent any errors from lumbar lordosis.

Image Analysis of Conventional MR Imaging

All image evaluations were performed by 2 radiologists (with 12- and 6-year experience of musculoskeletal radiology, respectively), in consensus. Two readers were blinded to the participants' personal information and imaging time of the 2 datasets (in the morning and evening). The distance between the upper anterior edges of the first lumbar spine (L1) and the first sacral spine (S1) was measured on the sagittal T2-weighted FSE images (Fig. 1). The 5 IVDs of the lumbar spine (L1/L2 to L5/S1) for each subject were analyzed according to the criteria used by Weishaupt et al. (10). Grade 1 and 2 were grouped together as normal. Other grades were grouped together as degeneration.

T2-Mapping Analysis

Five equally-sized rectangular regions of interest (ROIs) were placed manually from the anterior AF (ROI1) to the posterior AF (ROI5) in each IVD, on the middle slice of the sagittal T2-mapping image matched with conventional T2-weighted sagittal MR image (Fig. 2). Each ROI was 20% of the midline disc diameter. The outermost 20% of each disc was defined as AF tissue (anterior and posterior AF corresponded to ROI1 and ROI5); the area between the anterior and posterior AF was defined as NP; the anterior NP, the central NP and posterior NP tissues corresponded to ROI2 to ROI4 (11). The mean number of pixels for each ROI was approximately 50. Exemplary color-encoded T2 maps of the lumbar spine imaged in the morning and in the evening, respectively, were shown in Figure 3. Based on the 2 images obtained, the percentage of T2 value change was calculated as the difference of T2 values between evening

and morning, divided by the T2 values in the morning. The degree of T2 variation in the IVDs over the day was calculated using the following formula: the degree of T2

variation (relative changes percent) = $([T2 \text{ value in the evening}] - [T2 \text{ value in the morning}]) / ([T2 \text{ value in the morning}] \times 100\%$. Comparison of the changes in magnitude between multiple ROIs, were from the absolute values and presented as mean \pm standard deviation.

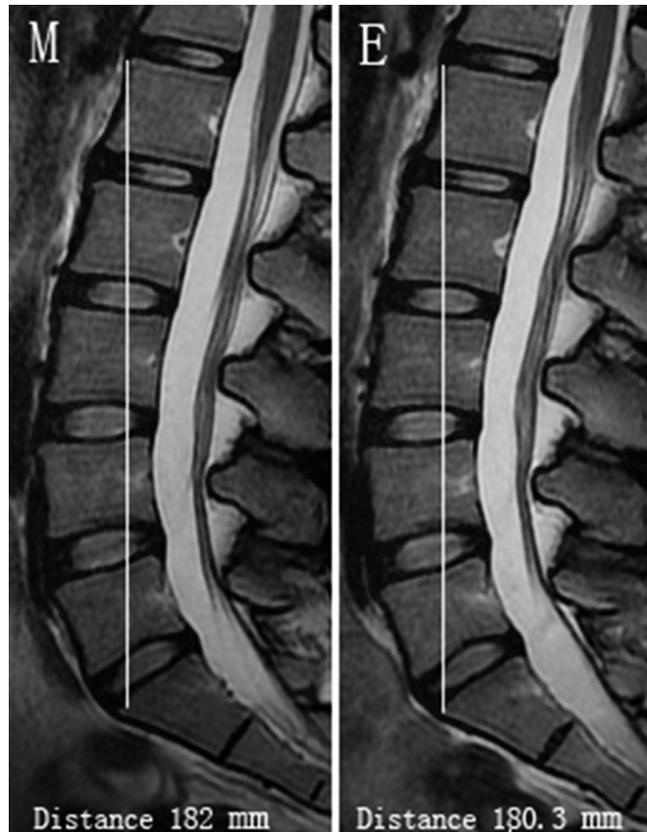


Fig. 1. Height from upper anterior edges of L1 to S1 in morning (M) and evening (E) was measured on sagittal T2-weighted images.

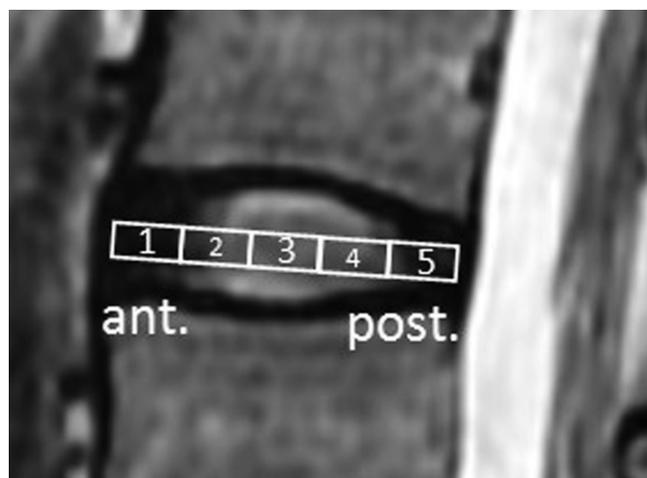


Fig. 2. Subregional segmentation of intervertebral disc. Disc was divided into 5 equal portions from anterior to posterior in mid-sagittal plane. Each region-of-interest (ROI) measured about 20% of disc diameter. ROI1 was placed on anterior annulus fibrosus (AF), ROI5 on posterior AF, and ROIs 2 to 4 on anterior nucleus pulposus (NP), central NP, and posterior NP, respectively.

Statistical Analysis

Statistical and graphical analyses were performed with SPSS 18.0 (IBM SPSS Statistics, Armonk, NY, USA). Paired 2-tailed *t* tests were performed for the differences in the length of the L1–S1, and changes of T2 relaxation times between the paired samples (morning vs. evening; and low vs. high basal central NP [CNP] T2). The data set was split into 3 equal portions according to the numerical values, to compare the discs with high and low CNP T2 values; the highest and lowest portions were analyzed. The degree of T2 variation in the same ROI of all 5 discs (from L1/2 to L5/S1) in each person was calculated, to obtain a mean value for the comparisons of the degree of variation among all 5 ROIs. Differences in the degree of variation among all 5 ROIs were analyzed by repeated-measures analysis of variance, and Fisher's least significant difference method was performed for the multiple comparisons if necessary. Differences with a *p* value < 0.05 were considered as statistically significant.

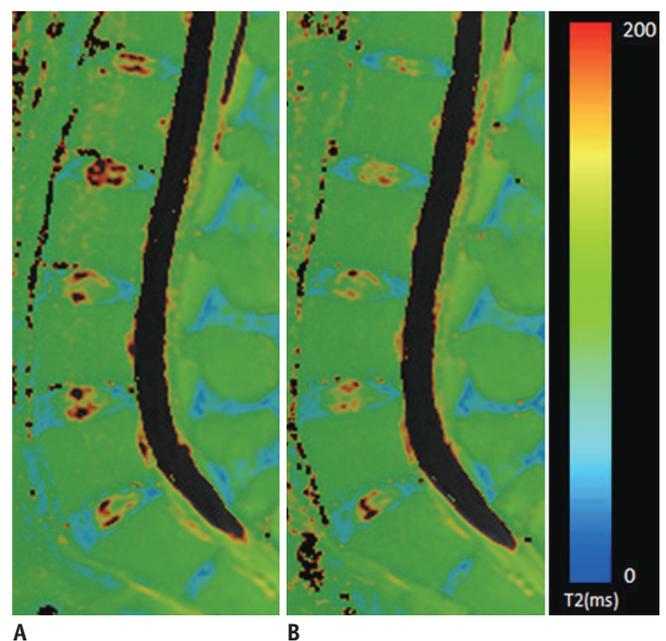


Fig. 3. Colored T2 maps of lumbar intervertebral discs in morning (A) and evening (B) show evident change of T2 values in central parts of lumbar vertebral discs from morning to evening.

RESULTS

The average distance between the upper anterior edges of L1 and S1 were 183.8 ± 6.3 mm in the morning and 179.9 ± 5.9 mm in the evening, respectively (Table 1). This

Table 1. The Height of L1 to S1 of Lumbar Spine in Morning and Evening

Cases	Morning (mm)	Evening (mm)	Difference (mm)
1	186.0	180.0	6.0
2	196.7	190.9	5.8
3	176.3	171.7	4.6
4	178.0	173.7	4.3
5	188.3	183.5	4.8
6	177.8	175.2	2.6
7	182.0	180.3	1.7
8	175.5	172.6	2.9
9	174.9	171.9	3.0
10	183.2	181.4	1.8
11	179.3	176.7	2.6
12	188.3	183.7	4.6
13	184.0	179.4	4.6
14	189.6	187.0	2.6
15	180.7	177.8	2.9
16	189.7	185.4	4.3
17	189.9	185.2	4.7
18	181.3	176.6	4.7
19	193.9	190.3	3.6
20	179.8	175.2	4.6
Mean \pm SD	183.8 ± 6.3	179.9 ± 5.9	$3.8 \pm 1.2^*$

Note.— * $p < 0.001$. SD = standard deviation

corresponded to a mean percentage decrease in height of 2.1%, relative to the morning measurement. The length of L1 to S1 was significantly decreased after daily activities by 2.1% ($p < 0.001$), as illustrated in Figure 1.

Three degenerative IVDs according to the Weishaupt's criteria were excluded from the measurements of T2 relaxation times. One hundred and ninety four discs were included for further measurements. From the morning to evening, there was a significant decrease of T2 values in the anterior NP (ROI2, -13.9 ms; 95% confidence interval [95% CI], -16.5 to -11.2; $p < 0.001$), in the CNP (ROI3, -17.0 ms; 95%CI, -21.4 to -12.6; $p < 0.001$), as well as in the posterior NP (ROI4, -13.3 ms; 95% CI, -17.0 to -9.6; $p < 0.001$). However, we found a significant increase of T2 values in the anterior AF (ROI1, +2.9 ms; 95% CI, +0.38 to +5.5; $p < 0.05$) and in the posterior AF (ROI5, +5.8 ms; 95% CI, +4.0 to +7.6; $p < 0.001$). Detailed results and illustration were provided in Table 2 and Figure 4.

The biggest change in degree was found in the posterior AF (ROI5), and the smallest was in the posterior NP (ROI4) (Fig. 5). However, no statistical difference was found among the 5 ROIs ($p = 0.414$). Compared to those discs with high CNP T2 values, IVDs with low CNP T2 values had a smaller degree of T2 variation in the anterior NP (ROI2, 10.0% vs. 16.1%, $p = 0.037$), as well as in the CNP (ROI3, 6.4% vs. 16.1%, $p = 0.006$). Although there appeared to be an increasing trend for the IVDs with low CNP T2 values, no significant difference in the degree of T2 time variation in the AF (ROI1 and ROI5) was observed (Fig. 6).

Table 2. Mean T2 Values of Different ROIs of Lumbar Intervertebral Discs in Morning and Evening Respectively

ROIs	Mean	SD	95% CI	P
ROI1 (anterior AF)				0.025*
Morning	56.0	15.3	52.9	59.0
Evening	58.9	11.3	56.6	61.1
ROI2 (anterior NP)				< 0.001*
Morning	106.3	24.9	101.4	111.3
Evening	92.4	21.8	88.1	96.8
ROI3 (central NP)				< 0.001*
Morning	149.1	23.8	144.4	153.9
Evening	132.1	23.8	127.4	136.9
ROI4 (posterior NP)				< 0.001*
Morning	125.5	27.9	119.9	131.0
Evening	112.2	22.8	107.6	116.7
ROI5 (posterior AF)				< 0.001*
Morning	44.6	9.5	42.7	46.5
Evening	50.5	11.0	48.3	52.7

Note.— *Statistically significant. AF = annulus fibrosus, NP = nucleus pulposus, ROI = regions-of-interest, SD = standard deviation, 95% CI = 95% confidence interval

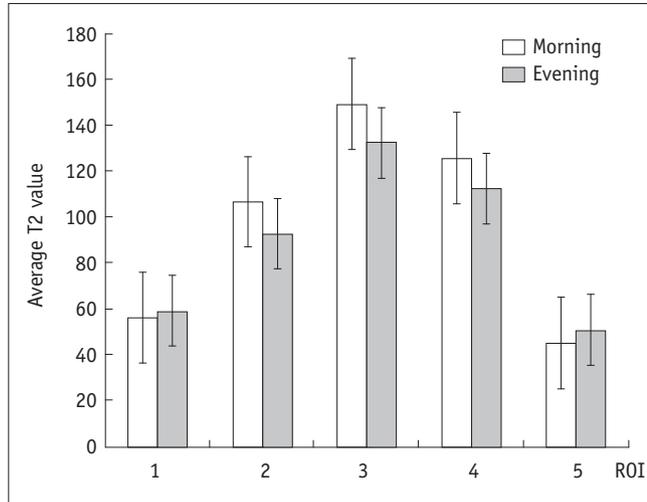


Fig. 4. Mean T2 values (milliseconds) for different ROIs of IVDs. From morning to evening after daily activities, average T2 values were significantly decreased in ROI2 to ROI4 (NP portion of disc), and significantly increased in ROI1 and ROI5 (AF portion of disc). AF = annulus fibrosus, IVDs = intervertebral discs, NP = nucleus pulposus, ROI = region-of-interest

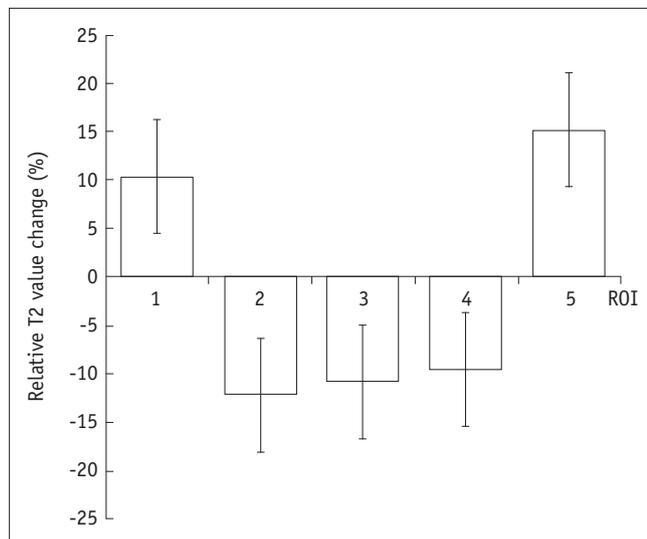


Fig. 5. Degree of T2 variation in different compartments of disc from morning to evening. Biggest change in degree was found in posterior AF (ROI5) and smallest was in posterior NP (ROI4). AF = annulus fibrosus, NP = nucleus pulposus, ROI = region-of-interest

DISCUSSION

We successfully investigated the diurnal changes in the length of the lumbar spine and T2 values in IVDs based on regional segmentation. For all volunteers, the lumbar spine became shorter after daily activity. There was a significant decrease in T2 values of NP and a remarkable increase in T2 values of AF. Although there was no statistical significance among the 5 ROIs, ROI5 (posterior AF) had the highest

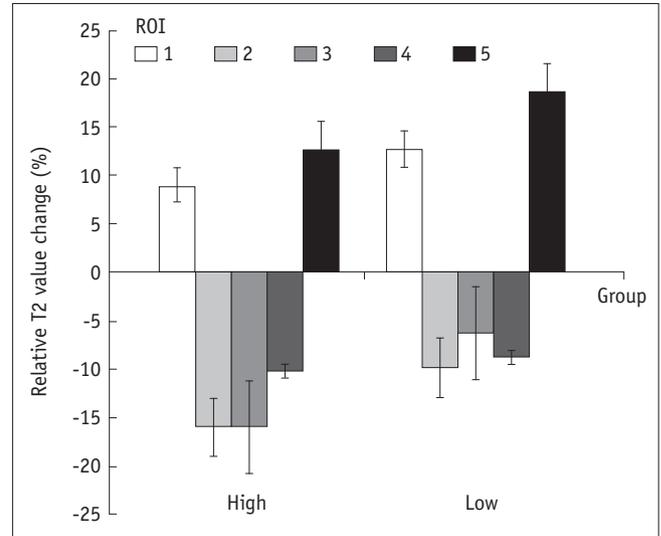


Fig. 6. Relative variation in discs with low and high CNP T2 values from morning to evening. Compared to those discs with high CNP T2 values, discs IVDs with low CNP T2 values, showed smaller degree of T2 variation in NP and increasing trend in degree of T2 time variation in AF. AF = annulus fibrosus, CNP = central nucleus pulposus, IVDs = intervertebral discs, NP = nucleus pulposus, ROI = region-of-interest

degree of variation in T2 values. Compared to the IVDs with higher CNP T2 values, the ROI2 (anterior NP) and ROI3 (CNP) with lower CNP T2 values had a smaller degree of T2 variation.

The fluid flow is mainly a governing factor for the change in length (or height) of the lumbar spine, which is controlled by the ability of PG to hold the fluid internally. This ability ensures the exchange of nutrition and waste products. A decrease in the variation of disc length may serve as an important predictor for early degeneration of the IVDs. So far, several *in vivo* studies have demonstrated the height or volume variations of IVDs due to diurnal load by MR imaging (2, 12, 13). For example, Malko et al. (2) found that the volume of IVD increased by 10.6% during overnight bed rest, which corresponds to a resorption of about 0.9 cm³ of fluid; Ludescher et al. (12) investigated the length change of the lumbar spine in 6 male subjects, and found that the difference ranged from 0.1 mm to 0.6 mm. The decrease in lumbar length by 2.1% (mean, -3.8 mm) after daily activity demonstrated in our study, was consistent with previous studies.

Most previous studies investigated T2 value changes focusing on the entire vertebral disc, instead of detailed consideration of different substructures and subregional segmentations. However, Ludescher et al. (12) investigated the change of T2 values during the day, by using circular

ROIs with a diameter of 4 mm in the NP, AF and an intermediate area, respectively; in his study, a significant decrease of T2 values in the CNP and the intermediate area, as well as a marked increase of T2 values in the AF were demonstrated, which grossly agreed with our results. A major limitation to their findings was that they did not divide the disc into subregions of anterior/posterior NP and anterior/posterior AF. Distinguishing between anterior and posterior AF is clinically more important, given the fact that the posterior AF is weaker and more easily torn. Stelzeneder et al. (4, 14) applied a similar approach to characterize IVDs, by focusing on T2 relaxation time correlated with morphological grading, and short-term unloading variations of IVDs. They found a statistically significant decrease in the anterior NP and an increase in the posterior AF for T2 values.

T2 relaxation time reflects hydration of cartilaginous tissues, as well as collagen content and orientation (15-17). Many factors might influence relaxation times in the vertebral discs. A variation in water content and a change in the orientation of collagen fibers contribute to the diurnal change of T2 values, with the former more dominant (18, 19). The relative concentration of water decreases if water is exuded from the vertebral disc matrix, resulting in a shortened T2 relaxation time. Several studies have demonstrated a good correlation between T2 relaxation time and water content in the disc (3, 20, 21). Therefore, our result that a significant decrease of T2 values in the NP area after a diurnal load, supports the hypothesis that water is pressed out of the NP. The increase of T2 values in the AF indicates that the water moves to the periphery. The result that the biggest change was found in the posterior AF (ROI5) may be interpreted as a fluid shift from the anterior to the posterior portions of the disc during daily activity. The biomechanical forces acting on the lumbar lordosis may play a key role in this process.

The T2 values in the NP tend to decrease in response to the increasing degeneration. The reasons could be the lower water content and reduced PG in this area (22). Compared with the discs with high CNP T2 values, the discs with lower CNP T2 values have a decreased amount of PG and water content. The decrease in the PG/collagen ratio reduces not only the water holding capacity but also the ability to resorb the fluid under the biomechanical stress related to daily activities (7). Thus, the degree of T2 variation in the ROI2 (anterior NP) and in the ROI3 (CNP) was smaller in the discs with lower CNP T2 values. In the process of

physiological aging (after 35 years old) and consequent degeneration of IVDs, the diurnal variation of T2 values decreases gradually, due to the gradual deterioration in the hydration states. This information maybe helpful in identifying an early stage of IVD degeneration.

T2 values in the posterior AF increased from normal adolescent grade I to normal adult grade II discs (4). The increased T2 fluctuation in the AF (ROI1 and ROI5) in the discs with lower CNP T2 values indicates the weakness of micro-structures in the AF. There is a possibility of a decreasing trend in T2 changes in the AF with an advancing grade of disc degeneration. Diurnal change of T2 values in the degenerative IVDs should be further investigated in the future.

A major limitation to our study was that a control group with different weight bearing was not included. Furthermore, not all lumbar discs were measured for height change. Consequently the relationship between disc height change and diurnal T2 value change is still unclear, and should be determined in the future.

In conclusion, subregionally-segmented quantitative T2 mapping is valuable in providing distinct insights into physiological aspects of IVDs. This imaging modality combined with conventional MR imaging, shows a high sensitivity of detection for the component water changes and the distribution of biomechanical stress in different subregions of the IVD. It is a promising tool for early detection of changes in micro-structures and biological function of IVDs, particularly when those changes are not visible on conventional imaging.

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