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ORIGINAL RESEARCH

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BACKGROUND AND PURPOSE: The present standard for staging intervertebral disk degeneration is a discrete scale, consisting usually of 5 stages. The purpose of this pilot study was to investigate the use of T2 measurements as a continuous measure of intervertebral disk degeneration.

METHODS: We obtained images in 5 volunteers with a 3D fast spin-echo sequence modified for the purpose of calculating T2 relaxation times from multiple echoes in the echo train. Disks were classified on the basis of conventional criteria into one of the 5 stages of disk degeneration. Average T2 values were calculated for stage II, III, and V disks, which were identified in the volunteers. Differences between the disk levels were analyzed with analysis of variance and differences between stages tested with a Student *t* test with significance set at the 0.01 level.

RESULTS: In the 5 volunteers, 20 stage II, 4 stage III, and a single stage V disk were found. Contour plots showed the highest T2 values in the nucleus pulposus near the vertebral endplates and lower T2 values in the intranuclear cleft region and peripheral annulus fibrosus. Average T2 values were significantly lower in the type III and V disks than in the normal disks.

CONCLUSIONS: The study suggests that intervertebral disks can be characterized and classified accurately by means of T2 values. More studies are warranted to determine the range of T2 values for normal disks.

With current clinical MR imaging techniques, changes in intervertebral disks due to degeneration or repair can be detected only when new morphologic features appear. To detect intervertebral changes that are not accompanied by a new morphologic feature, no suitable imaging methods have been developed.

The current strategy used to quantify disk degeneration by MR is the use of morphologic criteria.[1,2] Specific findings such as clefts in the annulus fibrosus, decreased signal intensity, and loss of height are used to stage degeneration. Such scales, which typically include 5 stages, fail to identify lesser degrees of progression or regression of degeneration in the disk. To evaluate new novel therapies for treatment of intervertebral disk degeneration such as gene therapy a more sensitive technique is required. A reliable continuous scale is needed to track the progression and regression of disk degeneration.

One potential tool for studying disk degeneration is a T2 relaxometry of the disk. T2 measurements have been used in studies of the intervertebral disk.[3-11] The feasibility of detecting degeneration with T2 measurements has been demonstrated, with relatively long acquisitions and low field strengths.[3,4] In one more recent study, the T2 was measured in intervertebral disks in patients subjected to trauma.[5] Other examples of the use of T2 relaxometry for studying the intervertebral disk include measuring changes in disk water due to diurnal variation[6,7] and due to the effects of spinal loading.[8]

In these studies, spatial variation of T2 in the intervertebral disk has not generally been considered. Hypothetically the T2 relaxation of the disk varies among different regions within the disk as does signal intensity. Because the amorphous region in the intervertebral disk near the endplate has greater signal intensity than the "intranuclear cleft" region or the annulus fibrosus,[12] T2 likely varies from one region to another.[13] Furthermore, the T2 relaxation time of the disk may be characterized by combinations of slower and faster components. The effect of this variation on the T2 measurement as an index of disk integrity has, not to the best of our knowledge, been reported.

The value of T2 measurements as a measure of disk degeneration deserves more study. Potentially, the T2 measurement may identify early disk degeneration before the loss of signal intensity is sufficiently conspicuous that the inspection of the image will detect it. Hypothetically, normal-appearing disks with lower than average T2 values are more likely to demonstrate degenerative changes over time than disks with average T2 values. The purpose of this pilot study is to measure the variation of T2 through the disk and estimate the effect of this variation on different strategies for determining a standardized T2 value for a disk.

Methods

We developed a method to measure T2 based on a 3D fast spin-echo (FSE) sequence. In phantom studies, the precision of the method was 2.4% for 3 separate trials (J. Perry, unpublished data).

Three men and 2 women voluntarily consented for this study. The age range of the volunteers was 28–46 years. Three of the volunteers had no history of back pain, and 2 had chronic low back pain (>6 months) without radiating pain and without previous surgical therapy. Approval to obtain images in volunteers with the pulse sequence was obtained from the institutional review board.

We obtained images of the lumbar spine on the volunteers on a 1.5T scanner with a spine coil. After obtaining routine localizer images, we prescribed a midline sagittal image by placing a cursor on the coronal image and angling it if necessary. A sagittal image with a 3D FSE sequence in the prescribed plane with a 3D FSE sequence was obtained. This FSE sequence was modified to enhance the precision and accuracy of the T2 calculation. Rectangular composite 180° refo-

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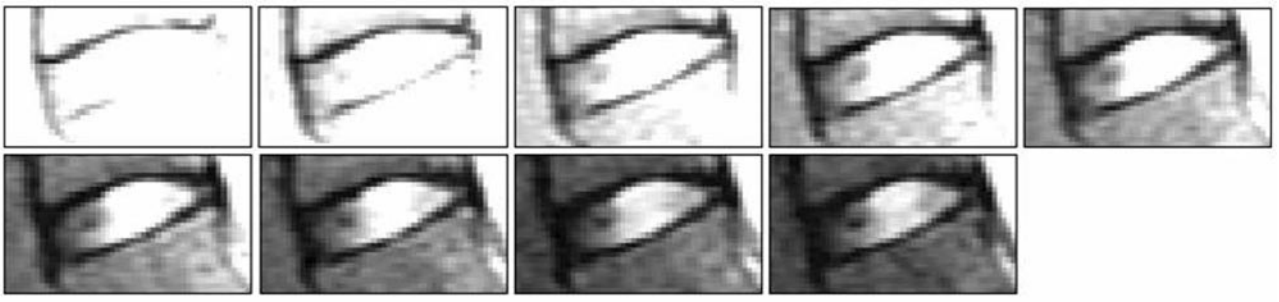

Fig 1. Images of successive echoes in the FSE echo train of an L4/5 disk classified as stage II. The images progress from the first echo on the upper left to the ninth echo in the lower right.

cusing pulses were used to minimize the effects of spatial heterogeneities in the RF B_1 field.[14] A series of crusher gradients with alternating sign and descending amplitude were added to bracket each 180° refocusing pulse to eliminate the contributions from stimulated echoes and signals from outside the selected section.[15] We used a 256 × 128 matrix, 24-cm field of view, 7.6-mm section, one average, echo train length of 32, TE of 9.3 milliseconds, and TR of 3 seconds, resulting in a 6:30 scan time.

We calculated T2 for each voxel by fitting the signal intensity for each TE to both mono- and multiexponential decay models by using a non-negative least-squares algorithm implemented in Matlab (MathWorks, Inc. Natick, Mass). We fit the signal intensity in the first 16 echoes, to capture 85% of the signal intensity decay. Our custom software preserved the spatial location of each voxel in the image by storing the data in matrices, which enabled us to create spatially accurate T2 maps. For this study, we did not consider the short T2 components separately.

Images of each of the first 12 echoes were inspected by a neuroradiologist for evidence of morphologic abnormalities, loss of disk height or anomalies in the spine. For each intervertebral disk, a stage from I to V was assigned on the basis of Pfirrmann et al's[2] criteria for grading intervertebral disk degeneration. For this study, disks were classified as stage II if the nucleus pulposus and inner annulus fibrosus had normal height and signal intensity equal to other disks lacking signs of degeneration, stage III if the nucleus and inner annulus had diminished signal intensity at least 70% of normal, stage IV if the nucleus and inner annulus had the same signal intensity as the outer annulus and disk height was at least 30% of normal, and stage V if the disk space had collapsed. Criteria for stage I disks (found only in subjects in the first 2 decades of life) were not used for this study which included only adult subjects.

One investigator outlined each intervertebral disk on the ninth image, drawing a cursor manually to include the disk and the low signal intensity within the upper and lower vertebral endplates and the anterior and posterior peripheral annulus fibrosus. The area of the high-signal-intensity region in the disk was calculated as the number of voxels with signal intensity >100 on the image of the ninth echo (T2 >38 ms). 3D maps of the T2 values were created with color coding. Excluding T2 values <38 ms, we calculated the means and SDs, as well as the 10th, 25th, 50th, 75th, 90th, and 99th percentiles, for the T2 values of each disk. A rank plot of the T2 values within each disk was created by sorting and plotting the values in ascending order. For the rank plot, a linear trend line was fitted to the data by least squares. The slope and intercept of the resulting line were tabulated and the closeness of the fit of T2 values to the line was assessed by visual inspection. The means, percentiles, slopes, and intercepts of the T2 values between disks of different degeneration stages were compared. Differences between disk levels were tested as well. We used analysis of variance at alpha = 0.01 to compare differences in T2 between disk levels. We tested for differences between different stages by using a Student *t* test with significance set at the 0.01 level.

Results

The FSE images in each of the 5 volunteers were considered technically adequate. No abnormalities of the bony structure were evident. The consecutive echoes in the FSE sequence revealed differences in the contrast between the high- and low-signal-intensity regions of the disk (Fig 1). In the first image, little contrast was evident between the central disk, peripheral disk, and vertebrae. Contrast increased through the first 9 images. In the ninth image, the central portions of the disk (nucleus pulposus and inner annulus fibrosus) had conspicuously higher signal intensity than the peripheral disk (outer annulus fibrosus).

The 3 volunteers without back pain had stage II disks at each lumbar level. In one of these 3 subjects (volunteer 3), the intranuclear cleft at the L5/S1 disk was less conspicuous than in other stage II disks. In another asymptomatic volunteer, a small oval focus of high signal intensity in the posterior annulus fibrosus suggested a concentric tear.

In the volunteers with back pain, 5 disks were classified at stage II (L1/2 in both, L2/3 in both, and L3/4 in one), 4 as stage III (L3/4 in one subject, L4/5 in both subjects, and L5/S1 in one subject) and one as stage V (L5/S1). In one stage III L5/S1 disk, images suggested a partial tear in the posterior annulus fibrosus.

The 3D contour plots of the stage II intervertebral disk demonstrated nonuniform T2 relaxation (Fig 2). In the typical stage II disk, the T2 in the sagittal section of the disk peaked in the region of the most amorphous cartilage near the endplates and had lower values corresponding to the region on the intranuclear cleft and the peripheral annulus fibrous. Boundaries between the regions are indistinct rather than sharp. In the L5/S1 disk of volunteer 3, the intranuclear cleft was less evident in the contour and color plots than it was in the image (Fig 3).

The contour and color plots of T2 values in stage III and V disks demonstrated differences between annulus fibrosus and nucleus pulposus but no obvious differences between the intranuclear cleft region and the rest of the disk (Fig 4).

In stage II disks, the T2 values in the inner annulus and nucleus of the normal intervertebral disks ranged from 38 to 215 milliseconds, whereas the values in stage III and V disks

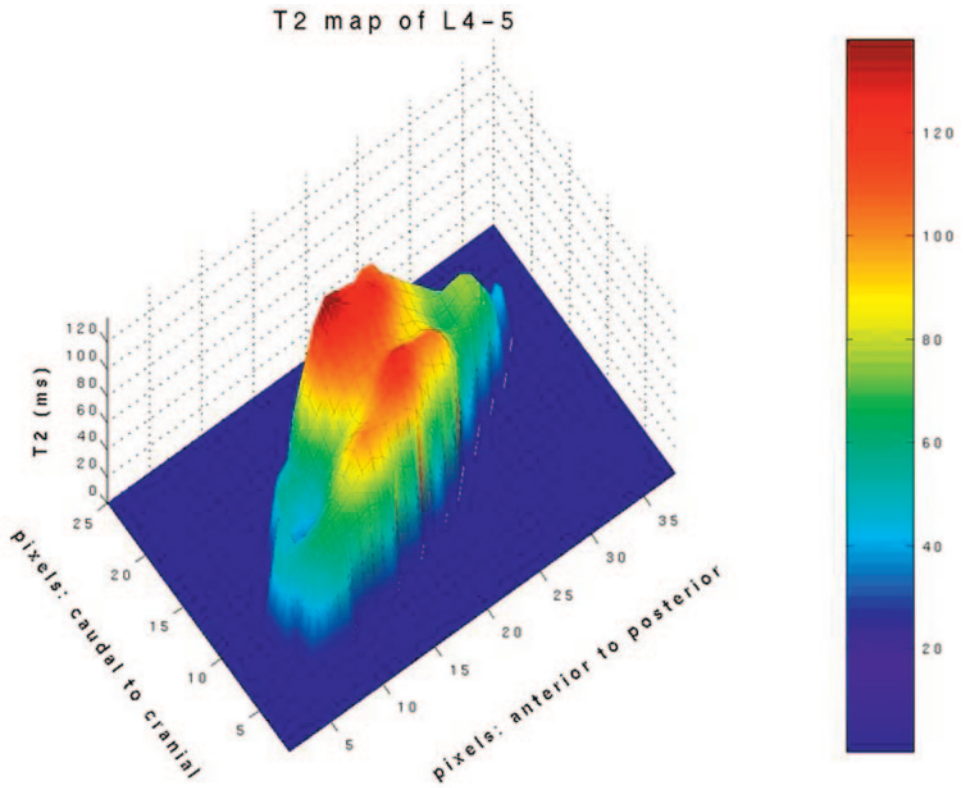

Fig 2. 3D contour plot of the disk shown in Fig 1. The anterior portion of the disk is to the reader's left and superior portion toward the top of the page. The inclination of the disk in the 3D plot is due to the angulation of the intervertebral disk from the axial plane. Notice the intranuclear cleft is clearly distinguished from the more amorphous regions of the nucleus pulposus because of its lower T2 values.

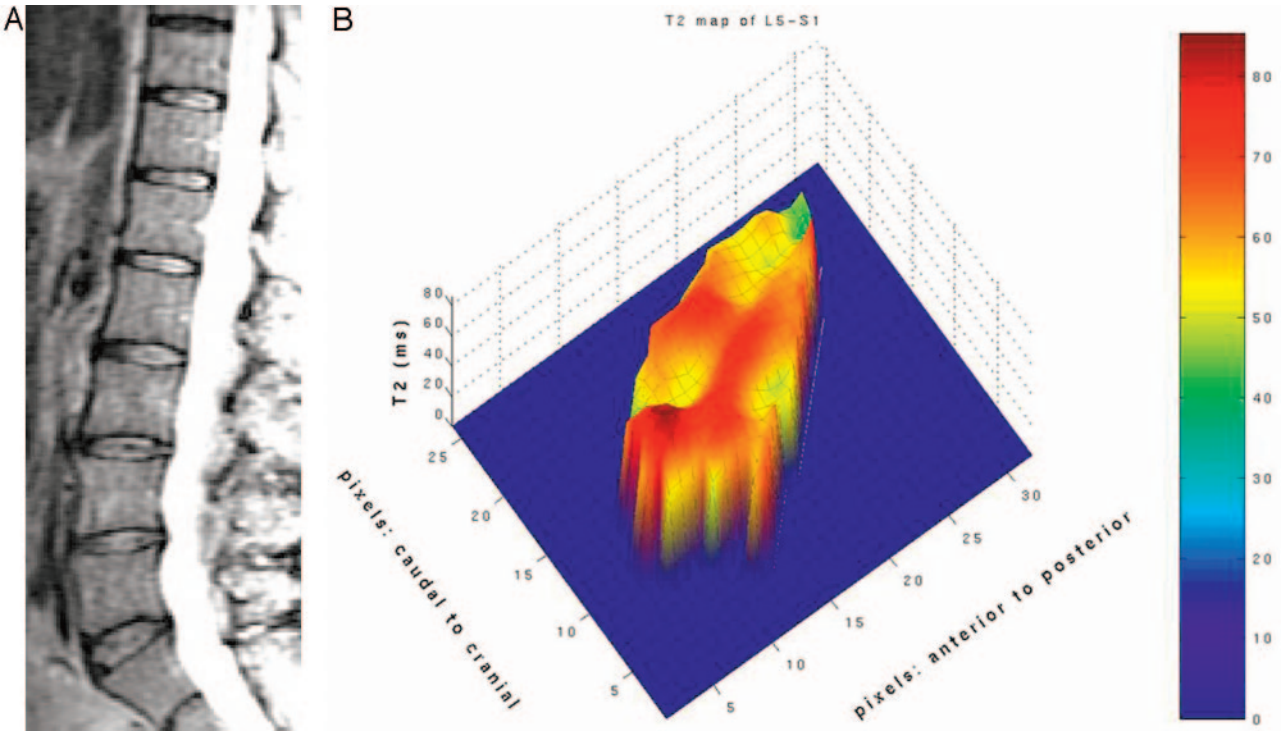

Fig 3. Sagittal MR image (ninth echo; *A*) and contour plot (*B*) of the L5/S1 disk in volunteer 3. This volunteer had a less-conspicuous intranuclear cleft at L5-S1.

ranged from 38 to 86 milliseconds (Table). The high-signal-intensity area of disks ranged in size from 92 voxels to 235 voxels in stage II disks and 37 voxels to 100 voxels in stage III and V disks. The average T2 value in stage II disks was 85 milliseconds and for stage III and V disks 53 milliseconds. The average for the 90th percentile was 114 milliseconds for stage II disks and 63 milliseconds for stage III and V disks. The values for the 10th percentile were 55 milliseconds for stage II disks and 43 milliseconds for stage III and IV disks. The percentiles, means, and intercepts differed significantly between stage II and other disks (P values 2.5×10^{-5} to 0.0055). T2 values of stage II intervertebral disks tended to increase progressively from L1–2 to L4–5. The trends were not statistically significant in the 20 disks.

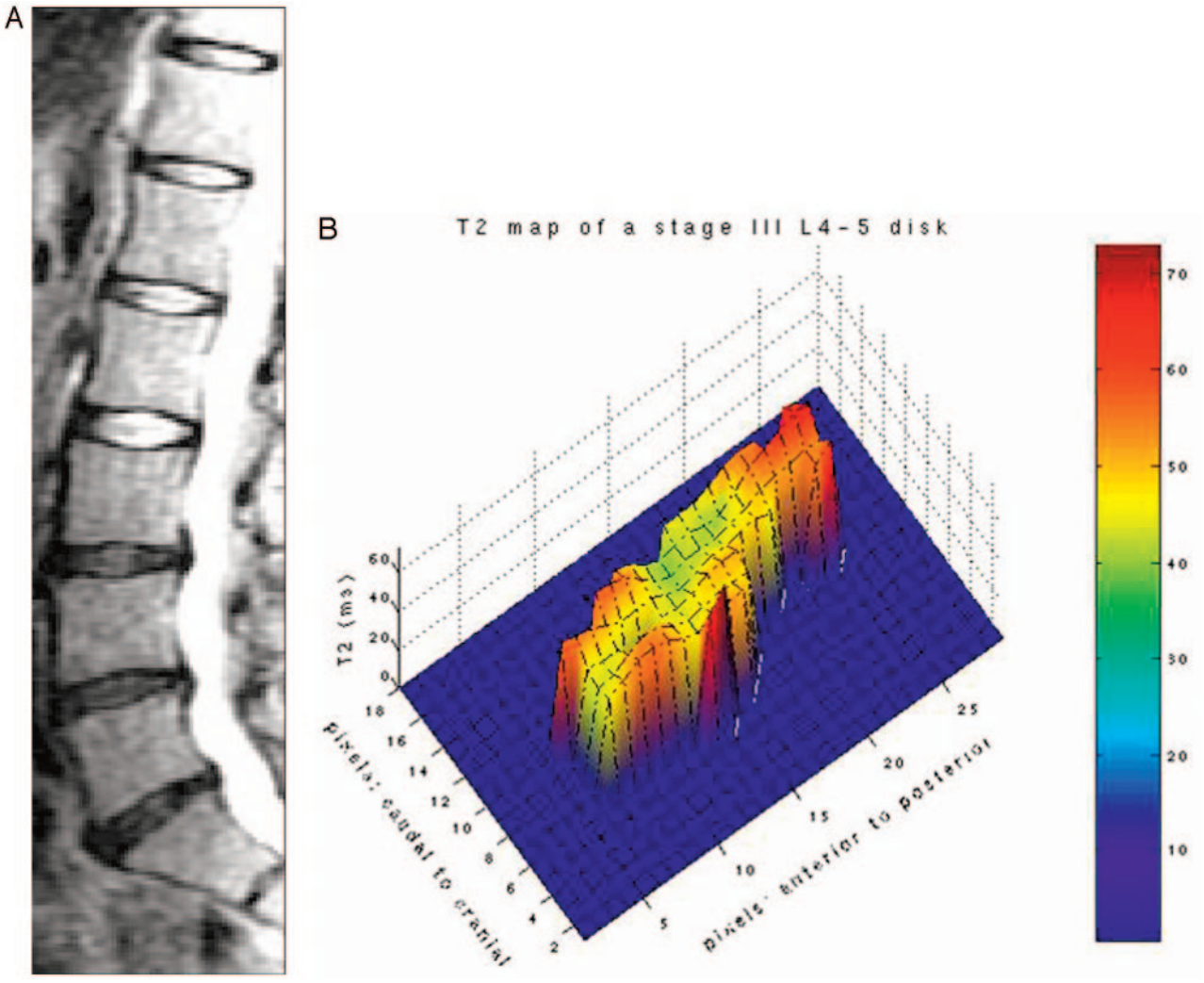

Fig 4. Sagittal MR image (9th echo; *A*) and contour plot (*B*) of an L4–5 stage III intervertebral disk. The intranuclear cleft region is not distinguished in the image or the plot.

Areas, means, percentiles, and slopes and intercepts for trendlines in a rank plot for T2 values in stage II and III disks in 5 volunteers

	Disk Stage		
Parameter	*II*	*III,V*	*P* value*
No. of disks	20	5	
Area (pixels)	161	65	
Mean T2 (ms)	84	53	.0025
SD of T2 (ms)	22	8	.014
10th percentile (ms)	55	43	2.5E-05
5th percentile (ms)	66	47	.00026
50th percentile (ms)	85	52	.0032
75th percentile (ms)	103	57	.0035
90th percentile (ms)	114	63	.0041
99th percentile (ms)	131	73	.0033
Slope of ranked T2 values	−0.48	−0.44	.76
Intercept of ranked T2 values	123	66	.0055

*Differences in stage II and III disks.

The rank plots of T2 values in intervertebral disks revealed a strikingly linear pattern. T2 values in stage II disks were in close proximity to the linear trend line, except at the highest values in the disk which deviated in an upward direction (Fig 5). In 2 of the asymptomatic volunteers, the rank plots for each level tended to coincide closely. In asymptomatic volunteer 3, the rank plots for the 5 levels were not as consistent (Fig 6).

In stage III and V disks, the T2 values also had close proximity to a linear trend line (Fig 7). The linear trend lines for the stage II and the stage III disks were conspicuously different. Stage II differed from III or V disks in the number of voxels with high signal intensity and tended to differ in the slope of the trend lines. The slope of the trend line in the stage II disks averaged 0.5 and in III and V disks it averaged 0.4. The difference was not significant.

Discussion

With a 6.5-minute FSE acquisition modified for the purpose, T2 values of the lumbar intervertebral disks can be assessed accurately. The T2 values show regional variation, theoretically because of variations in water content across the disk. The T2 values can be analyzed in various ways. These pilot studies suggest that the T2 measurements provide a continuous measure of intrinsic disk structure that can be applied clinically or in research. For example, the T2 measurements might be applied to measuring the effect of aging and of degeneration on the intervertebral disk. It could potentially be applied to measure the effect of exper-

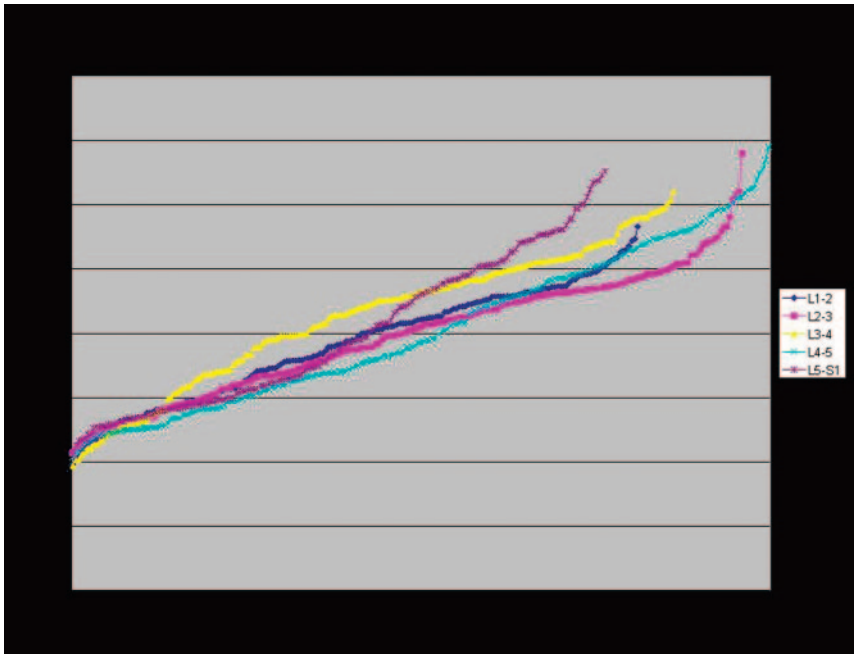

Fig 5. Rank plot of T2 values in a volunteer with 5 stage II disks. The T2 values are plotted in order of increasing value. Note that the plots for each level tend to coincide.

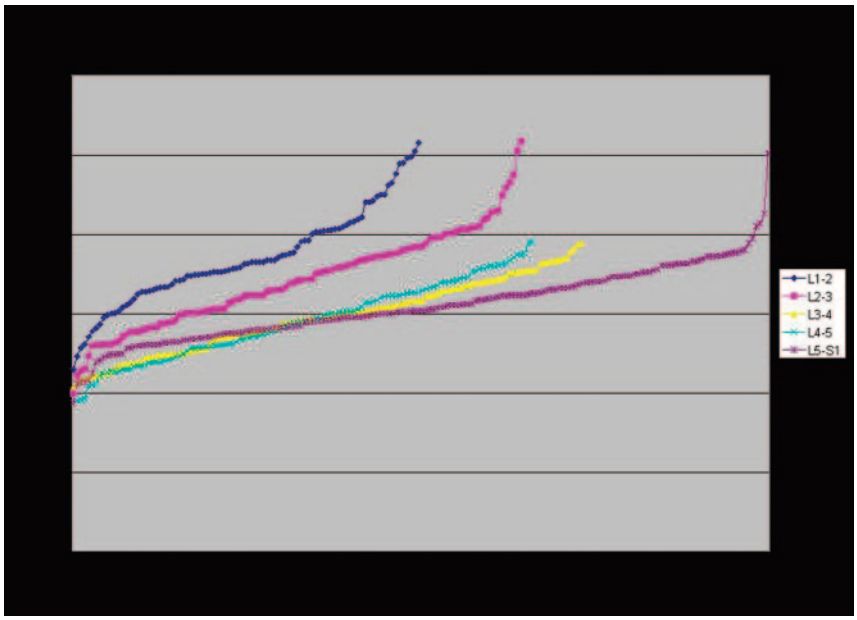

Fig 6. Rank plots of T2 values of disks in volunteer 3, who had a less-conspicuous intranuclear cleft at L5/S1. The rank plots show greater discrepancies than they did in the other 2 volunteers.

imental treatment on the intervertebral disk. It might be used to measure the effect of surgical instrumentation on the disks adjacent to the instrumentation.

The distribution of T2 through the human lumbar intervertebral disks is heterogeneous. The heterogeneity of the T2 values corresponds to the pattern described previously for the signal intensity in T2 weighted images. Regions with higher fiber content such as the intranuclear cleft and the peripheral annulus have lower T2 values, whereas the amorphous regions have higher T2. T2 values throughout the disk differed significantly between normal adult intervertebral disks (stage II) and those with changes attributed to degeneration (stage III). Some variability is noted in stage II disks, which suggests the possibility that T2 measurements may detect degenerative changes before conventional staging does.

Measuring the distribution and average of T2 values in the disk may be biased by the selection of the region of interest. Furthermore, including regions with low signal intensity reduces the accuracy of the T2 measurement. In previous measurements of disk T2, the region of interest was determined manually, introducing a possible bias in the size of the disk or the average T2. We disregarded the low signal intensity ($T2 < 38$ ms) in the periphery of the disk to reduce the risk of a reader bias. An automated program excluded these voxels, to reduce possible reader bias. The endplate containing bone and the peripheral annulus fibrous with high collagen content were thereby eliminated. The inner annulus and the nucleus pulposus were included. Because of the small magnitude and inconsistent presence of short T2 components in the disks we studied, we used a monoexponential transverse relaxation decay for analysis, disregarding the short T2 components. Also, the shorter T2 component is likely less relevant to water content in the disk.

We selected TR, TE section thickness, and other parameters to measure T2 accurately, but we have not performed studies to optimize imaging parameters for a quantitative study. The section thickness represents a compromise between spatial resolution and signal intensity to noise. We chose to use the sagittal plane for data analysis to minimize partial volume averaging errors. We analyzed only one sagittal section, so portions of the disk were not included in the analysis and possibly the closeness of the section to midline varied between

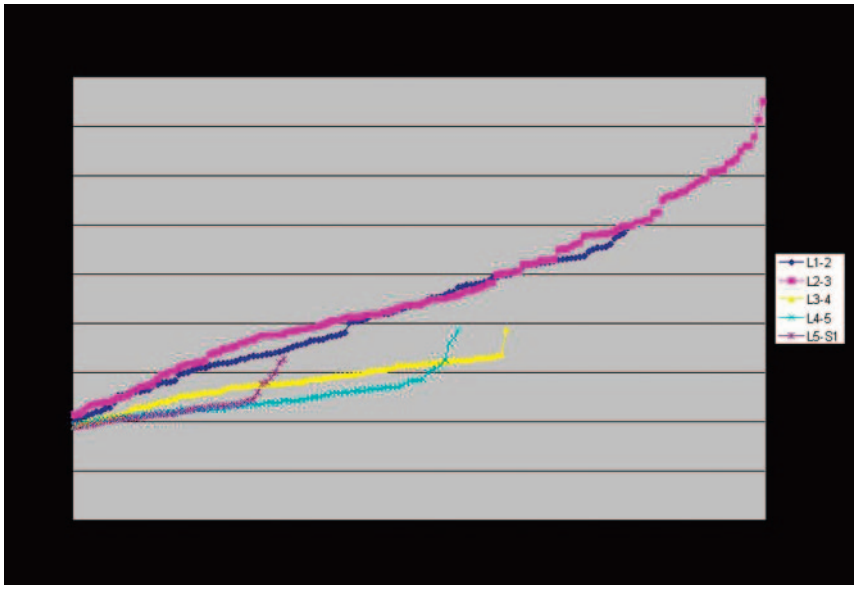

Fig 7. Rank plot of T2 values in a volunteer with stage II disks at L1–2 and L2–3 and stage III disks at L3–4, L4–5, and L5-S1. The stage II disks are clustered together, but the stage III disks are not.

subjects and disks. We did not control for diurnal variation in the disk or loading.

Our value for T2 is similar to previously published T2 values, considering the differences in measuring techniques. Kerttula et al published a *T* value of 80 milliseconds for T2 in the disks in their control group of normal young subjects.[5] They, however, use a TR of 2000 milliseconds and a region of interest set on the disk. Karakida et al[7] found that T2 averaged 75.6 milliseconds in normal disks and 53.5 milliseconds in degenerative disks. They used TR of 2000 milliseconds and a region of interest set on the center of the nucleus. Boos et al found an average T2 in normal disks of 58 milliseconds by using a region of interest larger than ours.[6] Tissue mapping was suggested by Isherwood et al[16] by using T1 probability. One study suggested that T2 might distinguish between symptomatic and asymptomatic disk herniations.[17]

The study shows that T2 measurements distinguish between normal adult and degenerative intervertebral disks. The method potentially can detect a change in the integrity of the disk before there is a change in the Thompson or Pfirrmann stage. The tool may potentially be used in experimental studies to determine the effect of therapy on the intervertebral disk degenerative process.

Conclusions

With a modified 3D FSE sequence, T2 maps of the disk may be obtained. The T2 maps show the internal structure of the disk, presumably because of the variations in water content in different portions of the disk. The pilot data suggest that T2 measurements may be useful to characterize temporal changes in intervertebral disks. Further studies are indicated to determine how the disk T2 changes due to aging, degeneration, or various disk or spine therapies. The possibility that early degeneration may be detected by identifying abnormal T2 values in otherwise normal-appearing disks could be studied.

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