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In-vivo T2 Relaxation Times of Asymptomatic Cervical Intervertebral Discs

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Abstract

Limited research exists on T2 mapping techniques for cervical intervertebral discs and its potential clinical utility. The objective of this research was to investigate the in-vivo T2 relaxation times of cervical discs, including C2-C3 through C7-T1. Ten asymptomatic subjects were imaged using a 3.0 T MR scanner and a sagittal multi-slice multi-echo sequence. Using the mid-sagittal image, intervertebral discs were divided into five regions-of-interest (ROIs), centered along the mid-line of the disc. Average T2 relaxation time values were calculated for each ROI using a mono-exponential fit. Differences in T2 values between disc levels and across ROIs of the same disc were examined. For a given ROI, the results showed a trend of increasing relaxation times moving down the spinal column, particularly in the middle regions (ROIs 2, 3 and 4). The C6-C7 and C7-T1 discs had significantly greater T2 values compared to superior discs (discs between C2 and C6). The results also showed spatial homogeneity of T2 values in the C3-C4, C4-C5, and C5-C6 discs, while C2-C3, C6-C7, and C7-T1 showed significant differences between ROIs. The findings indicate there may be inherent differences in T2 relaxation time properties between different cervical discs. Clinical evaluations utilizing T2 mapping techniques in the cervical spine may need to be level-dependent.

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Conflict of Interest

No conflict of interest.

Keywords

T2 mapping; Cervical spine; Intervertebral disc; Magnetic resonance imaging; In-vivo

Introduction

Cervical intervertebral discs are multifaceted structures that facilitate complex neck motion and loading. Disc degeneration, which occurs naturally with age, can lead to both pain and neurologic conditions, such as radiculopathy and myelopathy¹⁻⁴. Currently, cervical intervertebral disc health is commonly evaluated based on morphological features obtained from diagnostic imaging⁵⁻⁹. This information often complements a clinical examination that assesses pain, sensation, and neck motion. However, these outcomes are relatively subjective and no standard evaluation method of cervical intervertebral disc health has been widely adopted¹⁰⁻¹⁴. Additionally, current clinical assessments of disc health do not help in detecting early signs of degeneration, which is thought to be marked by proteoglycan degradation and decreased disc water content^{15, 16}. Identification of initial degenerative stages may allow for potential disc preservation prior to subsequent intervertebral morphological deterioration via emerging regeneration technologies, such as cell injections, laser therapy, and tissue engineering¹⁶⁻²¹.

Recently, quantitative MRI protocols have been used to evaluate the intervertebral disc²²⁻³². T2 relaxation times have been shown to correlate strongly with disc biochemical composition, such that decreased T2 values indicate decreased disc water content^{33, 34}. This makes T2 mapping a potentially powerful tool in detecting early signs of disc degeneration. It also provides a non-invasive method to analyze disc composition, and examine the effects of age, disease, and treatment interventions. Further, T2 relaxation times of in-vivo lumbar intervertebral discs have been shown to correlate with the qualitative Pfirrmann grading^{22, 25, 27-29, 31, 32}. This suggests potential for T2 mapping techniques to objectively evaluate and stratify disc health in a clinical setting. Pfirrmann grading was established in assessing intervertebral discs of the lumbar spine, employing a rating system that assigns grades of I through V to discs based on sagittal T2-weighted MRI images with a rating of I indicative of a normal, healthy disc and a rating of V indicative of a highly degenerated disc³⁵. For lack of an established cervical disc grading equivalent, recent research on the cervical spine has employed Pfirrmann grading and modified forms of Pfirrmann grading to assess the state of cervical disc degeneration^{4, 23, 36}.

Limited research exists regarding in-vivo T2 relaxation times in cervical intervertebral discs³⁶. Considering the reported anatomical and biochemical differences between cervical and lumbar discs³⁷⁻³⁸, further research is warranted to investigate the potential clinical utility of T2 mapping. Therefore, the objective of this research was to investigate the in-vivo T2 relaxation times of asymptomatic cervical intervertebral discs, including C2-C3 through C7-T1. Establishing intervertebral disc T2 relaxation times in healthy, asymptomatic individuals may serve as a reference for future comparisons to patients with degenerative disc conditions. It will also help further our knowledge of potential level- and region-dependent composition properties of cervical discs.

Methods

Subject Selection

10 asymptomatic subjects (5 males, 5 females, average age: 41.8 ± 12.3 years, average BMI 23.6 ± 3.3 kg/m²) were recruited for this study, which was approved by the authors' Institutional Review Board. Prior to testing, informed consent was obtained and each subject was evaluated for the absence of cervical spine related pain and disorders.

MRI Image Acquisition

Subjects were imaged in a supine position using a 3.0 Tesla MR scanner (MAGNETOM Trio, Siemens, Germany) and a sagittal multi-slice multi-echo (MSME) sequence. All subjects were imaged in the morning to limit the potential for diurnal variation in disc composition^{41–43}. Imaging parameters included: TR: 1810 ms; TEs: 10.9, 21.8, 32.7, 43.6, 54.5, 65.4, 76.3, 87.2, 98.1, and 109.0 ms; field of view: 176×240 mm; slice thickness: 4 mm; spacing: 4 mm; number of slices: 256; bandwidth: 181 kHz; and scan time: 9.06 seconds. The mid-sagittal image was selected for analysis. The first echo of the sequence was removed to limit the effect of the stimulated echo^{28, 31, 36}. In addition, each subject was also scanned using a T2 sequence for evaluation of Pfirrmann grading of each discs. Imaging parameters included: TR: 2000 ms; TE: 98 ms; field of view: 176×240 mm; slice thickness: 4 mm; spacing: 4 mm; number of slices: 14; bandwidth: 303 kHz; and scan time: 7.48 seconds

Image Analysis to Calculate T2 Values

To objectively and reproducibly evaluate the intervertebral discs, each disc was divided into five equal-area rectangular regions-of-interest (ROIs), centered along the mid-line of the disc, using OsiriX software (version 5.8.5)⁴⁴ (Fig. 1). First, two lines were drawn to approximate the disc height and width (Fig. 1a). Six evenly spaced lines were then drawn from the edges of the vertebral bodies perpendicular to the disc width line, such that the distance between each line was 20% of the disc width (Fig. 1b). After determining the mid-point of each perpendicular line, a curved path was run through each mid-point (Figs. 1c and 1d). Perpendicular to the path at each mid-point, two new points above and below the mid-line were created at a distance that was 10% of the disc height (Fig. 1e). This allowed for the creation of five rectangular ROIs, each of which had a height of ~20% the disc height and a width of ~20% the disc width³² (Fig. 1f).

Average T2 relaxation time values were calculated for each ROI using a mono-exponential fit in OsiriX software (Fig. 2). The exponential decay of average ROI image signal intensity (SI) with increasing echo time (TE) was plotted and a least-squares best fit was applied. The best fit decay curve was modeled with the equation: $SI(TE) = M_0 e^{-(TE/T_2)}$, allowing for the calculation of the spin density ($M_0 = SI(0)$) and T2 relaxation time (T2) for the given ROI^{45, 46}.

Statistical Analysis

Analysis of variance (ANOVA) with repeated measures and Newman-Keuls post-hoc analysis were used to examine the differences between cervical discs across each ROI, and

to examine the differences between ROIs across each disc. T2 relaxation times of each ROI were also correlated with age and the Pfirrmann grading of the same disc. Statistical significance was set at $p < 0.05$. Statistical analysis was performed using commercial software (Statistica, Statsoft, Tulsa, OK).

Results

Segment-dependent

Figure 3 illustrates the differences in T2 relaxation times across cervical discs for each ROI. At ROI 1, no significant differences were observed between different levels. At ROIs 2 and 3, no significant differences were observed between C2-C3, C4-C5, and C5-C6. Additionally, no significant differences were observed between C6-C7 and C7-T1. However, discs between C6 and T1 had significantly higher T2 relaxation values than those between C2 and C6. At ROI 4, no significant differences in T2 relaxation values were observed between C2-C3, C4-C5, and C5-C6, or between C6-C7 and C7-T1. However, C6-C7 had significantly higher T2 relaxation values than C2-C3, C3-C4, and C5-C6, while C7-T1 was significantly higher than all discs between C2-C6. At ROI 5, C7-T1 had significantly higher T2 relaxation values than all other discs, with no significant differences observed between C2-C7.

Region-dependent

Figure 4 illustrates the differences in T2 relaxation times across ROIs for each cervical disc. At the C2-C3 disc, there were no significant differences between anterior ROIs nor were there significant differences between posterior ROIs. However, ROI 1 was significantly greater than ROI 5, while ROI 2 was significantly greater than both ROI 4 and ROI 5. Intervertebral discs C3-C4, C4-C5 and C5-C6 showed no significant differences between any ROIs. At C6-C7, there were no significant differences between ROI 2 and ROI 3, or between ROIs 1, 4, and 5. However, both ROI 2 and ROI 3 were significantly greater than ROIs 1, 4, and 5. At C7-T1, there were no significant differences between ROI 2, ROI 3, and ROI 4, or between ROIs 1 and 5. However, ROIs 2, 3, and 4 were significantly greater than ROIs 1 and 5.

Correlations

Table 1 displays the correlation results between T2 relaxation times and age. Increased age was correlated with a decrease in T2 relaxation times across many discs and ROIs. Significant correlations were mostly observed in the middle regions (ROIs 2, 3 and 4) of the C2-C3, C3-C4, C6-C7, and C7-T1 discs.

Table 2 contains the Pfirrmann grading of each disc, while Table 3 shows the correlation results between T2 relaxation times and the Pfirrmann grading of each disc. Increased Pfirrmann grading was correlated with a decrease in T2 relaxation times across many discs and ROIs. Significant correlations were mostly observed in the middle regions (ROIs 2, 3 and 4) of the C2-C3, C3-C4, C6-C7, and C7-T1 discs.

Discussion

In-vivo T2 relaxation times of asymptomatic intervertebral cervical discs (C2-C3 through C7-T1) were calculated. Significant differences in T2 values were found between different cervical discs and, at some levels, across ROIs of the same disc. Additionally, significant correlations were observed between T2 relaxation times and age, and between T2 relaxation times and Pfirrmann grading.

Many studies have investigated the in-vivo T2 relaxation times of lumbar intervertebral discs. Stepwise decreases in T2 relaxation times with increasing Pfirrmann grade and marked distinctions between middle (nucleus pulposus (NP)) and outer (annulus fibrosus (AF)) regions have been widely reported^{25, 27–29, 31, 32}. These studies suggest the ability of T2 mapping to objectively stratify lumbar intervertebral disc health and provide promise for the potential detection of early stage disc degeneration. A decrease in lumbar disc NP relaxation times with increasing age has also been found^{25, 30, 31}. This is further evidence of the natural changes in lumbar disc composition throughout the lifespan. Blumenkrantz et al. provided level-specific results of T2 relaxation times in lumbar discs²². A trend of decreasing relaxation times was observed from L1-2 to L5-S1. However, they investigated subjects with a wide range of age and disc health. It remains to be seen whether the observed trend was a result of the lower lumbar levels having a higher rate of degeneration, or whether there are inherent T2 relaxation time, and subsequent disc composition, differences between these discs.

Chen et al. reported on the T2 relaxation times of cervical intervertebral discs, including C2-C3 through C6-C7, in a young healthy population³⁶. Anterior AF, NP, and posterior AF regions for each disc were manually segmented. They found a stepwise decrease in T2 values of the NP with increasing Pfirrmann grade, as well as significant differences between the NP and AF areas in all discs. They also found no differences in T2 values of the NP or AF between males and females. While no significant differences in NP or AF T2 values between levels were reported, the C6-C7 NP showed the greatest relaxation times compared to other discs. However, Chen et al. limited their investigation to subjects between the ages of 18 and 25 years old. Given the natural composition changes of intervertebral discs throughout the lifespan, any direct comparisons to the results of our older subject population should be made with caution.

Our investigation into cervical intervertebral disc T2 relaxation times found distinct level- and region-dependent features. For a given ROI, the results show a trend of increasing relaxation times moving down the spinal column, particularly in the middle regions (Fig. 3). T2 values of ROIs 2, 3, and 4 were significantly greater in the C6-C7 and C7-T1 discs compared to superior discs (i.e., discs between C2 and C6), and approximately show a stepwise increase moving inferiorly from C3-C4 to C7-T1 (Fig. 3). The results also show that regions across the disc have more distinct relaxation times moving down the spinal column (Fig. 4). The middle regions of the C6-C7 and C7-T1 intervertebral discs showed significantly greater relaxation times than the outer regions. This feature was not apparent in more superior discs, which showed relatively similar T2 values. This suggests superior cervical discs may have more homogenous water composition compared to lower cervical

discs. The one exception to these trends was the C2-C3 disc, which showed relatively high T2 values in the anterior regions (ROI 1 and ROI 2). These differences may be due to the unique anatomy of the C2 vertebrae, which likely induces alterations in composition and lifespan changes compared to other discs.

The T2 values in this study were relatively similar in magnitude to those reported by Chen et al., and generally lower than those observed in the lumbar spine. This agrees with previous biochemistry reports of lower water content in cervical discs compared to lumbar discs^{39, 40}. However, spatial homogeneity of T2 values in discs C3-C4, C4-C5, and C5-C6 is in contrast to the findings of Chen et al. in their young subject population. Spatial disc homogeneity in T2 values has also not been reported in previous T2 mapping investigations of asymptomatic lumbar discs. Our findings may support those of Bland et al., who describes a transformation of a gel-like NP to a more rigid fibrocartilage disc center by age 40 and suggests the adult cervical disc is more “ligament-like” than “disc-like”³⁷. In our study population, spatial homogeneity in T2 values (water content) was observed for the mid-cervical discs, while C2-C3, C6-C7, and C7-T1 preserved region distinctions.

The findings of this research suggest potential considerations for the clinical application of T2 mapping techniques in the cervical spine. The results indicate there may be inherent differences in T2 relaxation time properties between different cervical intervertebral discs. Clinical evaluations utilizing T2 mapping may need to be level-dependent. Additionally, a negative correlation between T2 values and age was observed in many ROIs. Clinical analysis may also need to account for patient age. It should be noted, however, that the general trends observed in this study (an increase in T2 values and region distinction at the C6-C7 and C7-T1 intervertebral discs) were seen individually in almost all subjects throughout the age range. Finally, a wide range of inter-subject variability in the magnitude of T2 values was found. This inter-subject variability suggests the establishment of “normal” or “healthy” T2 values may be difficult, with T2 mapping potentially lending itself more effectively to individual longitudinal analysis.

Interestingly, a negative correlation between T2 values and Pfirrmann grading was also observed in many ROIs, similar to the findings of Chen et al.³⁶. While Chen et al. analyzed the correlation of T2 values with Pfirrmann grading and found a negative correlation by grouping all segments in the analysis, no significant correlation was found at the middle ROIs of C4-C5 and C5-C6 in our study. Since no correlations were found between age and T2 values in these two discs as well, they might have different biochemical and biomechanical features compared to other intervertebral discs. Future studies should recruit more subjects and investigate the characteristic features of these discs, as well as potential differences in disease etiologies, and compare the data with other cervical discs.

In this investigation, discs were divided into five equal area rectangular ROIs, slightly modifying the methods of many previous lumbar studies^{24, 27, 28, 32} to account for the anatomy and curvature of the cervical vertebrae. This segmentation method may allow for more robustness and reproducibility in analysis compared to manual segmentation of AF and NP tissues. This is especially true considering the potential challenges in identifying traditional anatomical structures in the cervical disc throughout the lifespan, such as the NP

and posterior AF^{37, 38}. While the segmentation described by Chen et al. may be appropriate for young healthy subjects, research or clinical applications of T2 mapping in older and pathological populations may find the method outlined in this study beneficial.

Several limitations of this study should be addressed. Most notably, the sample size of this investigation was small and did not allow for an in-depth examination of age and gender effects on T2 values. The subjects ranged in age from 30 to 59 years old, and given the composition changes that occur naturally during the lifespan^{5–7, 37, 39, 40}, future studies should investigate T2 values in narrower age subsets, and include the investigation of any gender effect. Our segmentation method was not anatomical and may have suffered from partial volume effects^{32, 36}. T2 values also provide only an indirect measurement of disc composition. Histology studies are necessary to confirm the findings of level-dependent composition properties. Future research should also investigate the morphological and kinematic characteristics of different cervical levels, and the potential relationship between segment-dependent biomechanical environments (loading and motion) and T2 properties^{47, 48}.

In summary, this study investigated the T2 relaxation times of asymptomatic cervical intervertebral discs. T2 values tended to increase moving down the spinal column. Further, lower cervical discs showed more distinct regions compared to superior discs. The results suggest evaluation of cervical disc T2 values may need to be level-specific. The findings may also serve as useful comparisons to patients with degenerative changes, both pre- and post-operatively. Additionally, this report provides further insight into the composition of cervical discs and echoes previous reports on differences compared to lumbar discs.

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Figure 1. Segmentation steps of intervertebral disc regions-of-interest (ROIs). Intervertebral discs were divided into five equal area rectangular ROIs (1–5), centered along the mid-line disc. ROI 1 is most anterior while ROI 5 is most posterior. Please refer to the text for a detailed description of each segmentation step.

Figure 2.

a) OsiriX T2 Fit Map plug-in with images and axes titles overlaid to illustrate the decrease in signal intensity (SI) with increasing echo time (TE). The plot includes mean, minimum, and maximum SI curves, as well as the best fit regression (red line). b) C6-C7 intervertebral disc, and the c) resulting T2 relaxation time distribution.

Figure 3.

T2 relaxation times were compared across cervical levels for each ROI. * indicates significant difference between levels ($p < 0.05$).

Figure 4.
T2 relaxation times were compared across ROIs for each cervical level. * indicates significant difference between ROIs ($p < 0.05$).

Table 1

Age vs. T2 relaxation time correlation results

		ROI 1	ROI 2	ROI 3	ROI 4	ROI 5
Age vs. C2-C3 T2 Times	r-value	-0.193	-0.653*	-0.435	-0.280	0.191
Age vs. C3-C4 T2 Times	r-value	-0.616	-0.758*	-0.566	-0.660*	-0.604
Age vs. C4-C5 T2 Times	r-value	-0.124	-0.441	-0.257	-0.127	0.555
Age vs. C5-C6 T2 Times	r-value	0.132	0.118	-0.082	-0.350	-0.026
Age vs. C6-C7 T2 Times	r-value	-0.321	-0.642*	-0.584	-0.513	-0.621*
Age vs. C7-T1 T2 Times	r-value	-0.460	-0.671*	-0.773*	-0.406	-0.490

r-value indicates Pearson correlation coefficient

* indicates statistically significant correlation (p < 0.05)

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Table 2

Pfirrmann Grading of each disc of the cervical discs

Disc	C2-C3	C3-C4	C4-C5	C5-C6	C6-C7	C7-T1
AVG±SD	2.5±0.6	2.6±0.6	2.4±0.4	2.4±0.4	2.2±0.5	2.0±0.4

Table 3

Pfirschmann Grading vs. T2 relaxation time correlation results

	ROI 1	ROI 2	ROI 3	ROI 4	ROI 5
Pfirschmann Grading vs. C2-C3 T2 Times	r-value -0.187	-0.344	-0.811 *	-0.638 *	-0.187
Pfirschmann Grading vs. C3-C4 T2 Times	r-value -0.055	-0.514	-0.687 *	-0.711 *	-0.684 *
Pfirschmann Grading vs. C4-C5 T2 Times	0.243	-0.371	-0.503	-0.253	0.280
Pfirschmann Grading vs. C5-C6 T2 Times	0.503	-0.088	-0.367	-0.103	0.636 *
Pfirschmann Grading vs. C6-C7 T2 Times	-0.361	-0.641 *	-0.806 *	-0.775 *	-0.731 *
Pfirschmann Grading vs. C7-T1 T2 Times	-0.741 *	-0.450	-0.772 *	-0.598	-0.406

r-value indicates Pearson correlation coefficient

* indicates statistically significant correlation ($p < 0.05$)