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Cervical spondylosis: Evaluation of microstructural changes in spinal cord white matter and gray matter by diffusional kurtosis imaging

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ABSTRACT

Introduction: We investigated microstructural changes in the spinal cord, separately for white matter and gray matter, in patients with cervical spondylosis by using diffusional kurtosis imaging (DKI).
Methods: We studied 13 consecutive patients with cervical myelopathy (15 affected sides and 11 unaffected sides). After conventional magnetic resonance (MR) imaging, DKI data were acquired by using a 3 T MR imaging scanner. Values for fractional anisotropy (FA), apparent diffusion coefficient (ADC), and mean diffusional kurtosis (MK) were calculated and compared between unaffected and affected spinal cords, separately for white matter and gray matter.
Results: Tract-specific analysis of white matter in the lateral funiculus showed no statistical differences between the affected and unaffected sides. In gray matter, only MK was significantly lower in the affected spinal cords than in unaffected spinal cords (0.60 ± 0.18 vs. 0.73 ± 0.13, $P = 0.0005$, Wilcoxon's signed rank test).
Conclusions: MK values in the spinal cord may reflect microstructural changes and gray matter damage and can potentially provide more information beyond that obtained with conventional diffusion metrics.

1. Introduction

Cervical spondylosis is a common degenerative disease that causes several types of motor and sensory dysfunction. Routine clinical magnetic resonance (MR) imaging (for example, T2-weighted imaging) to evaluate pathological changes in this disease is of limited use because the correlation between the MR findings and clinical symptoms is weak [1].

Diffusion tensor imaging (DTI) has been added to conventional MR imaging in many investigations of the spinal cord to evaluate microstructural changes [2]. Changes in DTI signals depend on the diffusivity of water molecules in a particular environment. DTI-derived quantitative metrics such as the fractional anisotropy (FA) and apparent diffusion coefficient (ADC) show promise as biomarkers in evaluating the microstructural pathology of the cervical spinal cord. For example, reduced FA and increased ADC have been reported at damaged spinal cord regions regardless of whether abnormal signal intensity in the spinal cord was observed on conventional MR images [3–5]. Moreover, a recently introduced extension of the DTI technique called diffusional kurtosis imaging (DKI) [6,7] has shown greater promise than DTI in evaluating the microstructure and pathologic condition of neuronal tissue [8–14], especially gray matter [15,16]. For evaluation of the spinal cord, DKI can provide a more comprehensive characterization of lesions and changes of white or gray matter in patients with multiple sclerosis [17]. Furthermore, as noted in a recent study [18], the mean diffusional kurtosis (MK) can provide additional information on the spinal cord in patients with cervical spondylosis. However, white matter and gray matter were not analyzed separately in the report and were treated as a single unit when setting regions of interest (ROIs). Tract-specific analysis by using white matter tractograms

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Table 1
Demographic characteristics of subjects.

Sex (male: female)	5: 8
Mean Age (SD)	54.9 (10.8)
Symptoms*	
Muscle weakness	12
Numbness	11
Pain	9
Hypalgesia	4
Apraxia	3
Neck stiffness	1

* Multiple symptoms were reported by some patients.

enables more precise measurements and better anatomical localization of white matter.

The purpose of this study was to investigate the use of MK to estimate changes in the spinal cord, separately for white matter and gray matter, in patients with early cervical spondylosis.

2. Materials and methods

2.1. Participants

Thirteen consecutive patients diagnosed with cervical myelopathy by clinical signs and symptoms participated in this study. Their demographic characteristics are summarized in Table 1. Prior to the study, the research protocol was approved by the institutional review board, and informed consent was obtained from each patient. The exclusion criteria were as follows: the presence of other intraspinal diseases such as tumors, a history of neck surgery for any disease, or unsatisfactory image quality for calculating diffusion metrics.

2.2. Image acquisition

All images were acquired on a 3 T MR scanner (Achieva; Philips Medical Systems, Best, The Netherlands). The imaging parameters for DKI were as follows: repetition time/echo time, 10758/88 ms; number of excitations, two; slice thickness/gap, 4/0 mm; number of slices, 32; field of view, 64 × 64 mm; matrix, 128 × 128 reconstructed; imaging time, approximately 13 min; and four *b*-values (0, 700, 1400, and 2100 s/mm^2) with diffusion encoding in 6 directions for each *b*-value. The gradient length (δ) and time between the two leading edges of the diffusion gradient (Δ) were 9.8 and 44.1 ms, respectively. A reduced field-of-view technique was used to improve image quality [19,20]. Before DKI, conventional turbo spin-echo T1- and T2-weighted sagittal and axial images were obtained. The imaging parameters for sagittal images were as follows: repetition time/echo time, 400/10 ms for T1-weighted imaging (T1WI) and 3246/128 ms for T2-weighted imaging (T2WI); echo train length, 4 for T1WI and 36 for T2WI; number of excitations, two; slice thickness/gap, 3/0.3 mm; number of slices, 11; field of view, 250 × 250 mm; and matrix, 512 × 512. Imaging parameters for the axial images were as follows: repetition time/echo time, 726/10 ms for T1WI and 6196/93 ms for T2WI; echo train length, 5 for T1WI and 36 for T2WI; number of excitations, two; slice thickness/gap, 4/0.4 mm; number of slices, 24; field of view, 160 × 160 mm; and matrix, 512 × 512.

2.3. Analyses of DTI, tractography, and DKI

Analyses of DTI, tractography, and DKI were performed by using the free software dTV II FZRx and Volume-One 1.81 (Image Computing and Analysis Laboratory, Department of Radiology, The University of Tokyo Hospital, Tokyo, Japan) [21] on an independent Windows PC.

First, maps for FA, ADC, and MK were calculated. The FA and ADC maps were established on the basis of a conventional mono-exponential model that assumes a Gaussian probability diffusion function, by using data at *b*-values of 0 and 700 s/mm^2.

Next, we performed diffusion tensor tractography of the bilateral lateral funiculus with threshold values for the termination of fiber tracking set to FA > 0.18. We recognized the advantages of the use of multiple *b*-values or DKI tractography [22]; however, such advanced fiber tracking was not implemented in our software. Identification of fiber tracts was initiated by placing a seed ROI of 2 pixels in diameter in the lateral funiculus on axial FA maps at spinal canal levels C3–C4 (Fig. 1). A tractographic image of the lateral funiculus was then generated for each patient (Fig. 2). The tract was divided into spinal canal levels C1–C2, C2–C3, C3–C4, C4–C5, C5–C6, and C6–C7 by manually by referring to T1- and T2-weighted images, and each segment of the tractogram was voxelized. The ADC, FA, and MK values in coregistered voxels were then calculated and compared between the affected and unaffected sides, as diagnosed on the basis of clinical symptoms and findings.

A subgroup analysis was also performed for 7 patients in whom the damaged spinal level and affected side were clearly identified for the corresponding clinical symptoms. ROIs that conformed to the size and shape of the gray matter on T2-weighted images were placed manually on the gray matter near the tractogram of the

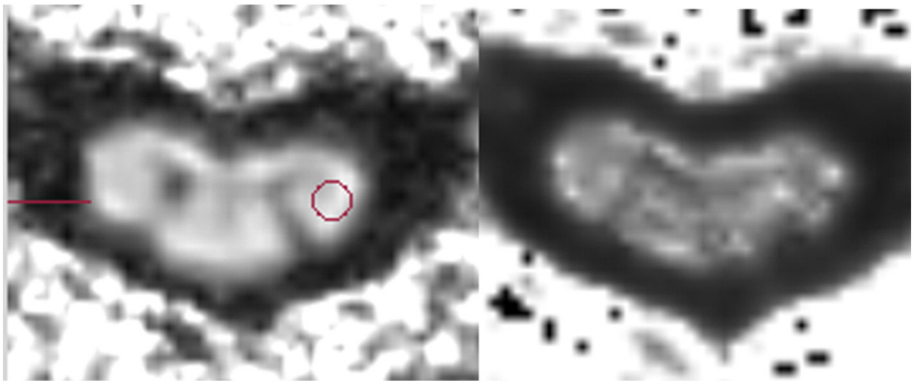

Fig. 1. Placement of ROIs in the lateral funiculus. A representative FA map with ROI (left) and the corresponding MK map (right).