Title: **The potential use of Diffusion Tensor Imaging in level diagnosis of multilevel Cervical Spondylotic Myelopathy**

Runing title: Level diagnosis of CSM

Xiang Li, MD; Jiao-Long Cui, BS; Kin-Cheung Mak, FRCS (Ed), FHKAM (Orth); Keith Dip-Kei Luk, FRCSE, FRCSG, FRACS, MCh(Orth), FHKAM(Orth); Yong Hu*, PhD

Department of Orthopaedics and Traumatology, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Pokfulam, Hong Kong.

"*" Correspondence Author
Dr Yong Hu
Dept. Of Orthopaedics and Traumatology, The University of Hong Kong
Address: 12 Sandy Bay Road, Pokfulam, Hong Kong
Email address: yhud@ hku.hk;
Tel: (852) 29740359; Fax: (852) 29740335

The study is supported by the General Research Fund of the University Grant Council of Hong Kong (771608M/774211M). The study was approved by the authors' Institutional Review Board (UW 04-104T/246).

Abstract

Study Design. Prospective study on a series of consecutive patients.

Objective. To investigate the use of diffusion tensor imaging (DTI) and orientation entropy (OE) in level localization in patients diagnosed with multilevel cervical spondylotic myelopathy (CSM).

Summary of Background Data. Multilevel CSM presents complex neurological signs make level localization difficult. DTI is recently found to be able to assess the microstructural changes of the white matter caused by cord compression.

Methods. Sixteen CSM patients with multilevel compression were recruited. The level(s) responsible for the clinical symptoms were determined by detailed neurological examination, T2-weighted (T2W) magnetic resonance imaging (MRI) and DTI. On T2W MRI, anterior-posterior compression ratio (APCR) and increased signal intensities (ISI) were used to determine the affected level(s). The level diagnosis results from T2W MRI, ISI, DTI and combination method were correlated to that of neurological examination on a level-to-level basis respectively. The accuracy, sensitivity and specificity were calculated.

Results. When correlated with the clinical level determination, the weighted OE based DTI analysis was found to have higher accuracy (82.76% versus 75.86%) and sensitivity (84.62% versus 76.92%) than those of the APCR. The ISI has the highest specificity (100.00%) but the lowest accuracy (58.62%) and sensitivity (53.85%). When combined level diagnosis result of APCR and DTI, it demonstrated the highest accuracy and sensitivity which were 93.10% and 96.15% respectively, and equal

specificity (66.67%) with using them individually.

Conclusion. DTI can be a useful tool to determine the pathological spinal cord levels in multilevel CSM. This information from OE based DTI analysis, in addition to conventional MRI and clinical neurologic assessment, should help spine surgeons in deciding the optimal surgical strategy.

Key words: Diffusion tensor imaging, Level diagnosis, Cervical spondylotic myelopathy, Multilevel compression

*Key Points (3-5 main points of the article)

Key points:

1. Orientation entropy (OE) based diffusion tensor imaging (DTI) analysis reached higher accuracy and sensitivity than anatomic MRI with equal specificity.

2. OE based DTI analysis combining with anatomic MRI showed better accuracy and sensitivity than using them individually with the same specificity.

3. OE based DTI analysis can be a useful tool to determine the pathological spinal cord levels in multilevel CSM with its capacity of detecting axon integrity.

4. OE based DTI analysis, in addition to anatomic MRI, should help the spine surgeons in deciding the optimal surgical strategy.

*Mini Abstract (50 words)

Mini Abstract/Précis

Orientation entropy (OE) based diffusion tensor imaging (DTI) analysis was used to indicate affected levels in multilevel CSM. The level diagnosis result from anatomic MRI and DTI was compared with that of neurological signs. OE based DTI analysis, in addition to anatomic MRI, should help the spine surgeons in deciding the optimal surgical strategy.

Abstract

Study Design. Prospective study on a series of consecutive patients.

Objective. To investigate the use of diffusion tensor imaging (DTI) and orientation entropy (OE) in level localization in patients diagnosed with multilevel cervical spondylotic myelopathy (CSM).

Summary of Background Data. Multilevel CSM presents complex neurological signs make level localization difficult. DTI is recently found to be able to assess the microstructural changes of the white matter caused by cord compression.

Methods. Sixteen CSM patients with multilevel compression were recruited. The level(s) responsible for the clinical symptoms were determined by detailed neurological examination, T2-weighted (T2W) magnetic resonance imaging (MRI) and DTI. On T2W MRI, anterior-posterior compression ratio (APCR) and increased signal intensities (ISI) were used to determine the affected level(s). The level diagnosis results from T2W MRI, ISI, DTI and combination method were correlated to that of neurological examination on a level-to-level basis respectively. The accuracy, sensitivity and specificity were calculated.

Results. When correlated with the clinical level determination, the weighted OE based DTI analysis was found to have higher accuracy (82.76% versus 75.86%) and sensitivity (84.62% versus 76.92%) than those of the APCR. The ISI has the highest specificity (100.00%) but the lowest accuracy (58.62%) and sensitivity (53.85%). When combined level diagnosis result of APCR and DTI, it demonstrated the highest

accuracy and sensitivity which were 93.10% and 96.15% respectively, and equal specificity (66.67%) with using them individually.

Conclusion. DTI can be a useful tool to determine the pathological spinal cord levels in multilevel CSM. This information from OE based DTI analysis, in addition to conventional MRI and clinical neurologic assessment, should help spine surgeons in deciding the optimal surgical strategy.

Key words: Diffusion tensor imaging, Level diagnosis, Cervical spondylotic myelopathy, Multilevel compression

Key points:

1. OE based DTI analysis could better correlate with clinical level diagnosis with higher accuracy and sensitivity than conventional MRI.

2. OE based DTI analysis combining with conventional MRI showed better accuracy and sensitivity than using them individually.

3. OE based DTI analysis can be a useful tool to determine the pathological spinal cord levels in multilevel CSM with its capacity of detecting axon integrity.

4. OE based DTI analysis, in addition to conventional MRI, should help the spine surgeons in deciding the optimal surgical strategy.

Mini Abstract/Précis

OE based DTI analysis was used to indicate affected levels in multilevel CSM. The level diagnosis result from conventional MRI and DTI was compared with that of neurological signs. OE based DTI analysis, in addition to conventional MRI, should help the spine surgeons in deciding the optimal surgical strategy.

Introduction

Cervical spondylotic myelopathy (CSM) is a degenerative disease of cervical spine, which is usually of extensive range of lesion involving multiple segments[1,2]. Multilevel affected CSM is complex with clinical manifestation and difficult to precisely localize all the involved levels by neurological examination[3]. Although conventional magnetic resonance imaging (MRI) can detect anatomic compression on spinal cord, the disproportion between the spinal cord compression presenting on MRI and neurological deficit is frequently seen[4]. If spinal cord damage could be detected pathologically on each level, it would be great supplemental information for evaluating the tissue impairment among affected levels in multilevel CSM.

Differing from conventional MRI, diffusion tensor imaging (DTI) could evaluate the integrity of nerve fibre tracts and assess the functional status of the spinal cord by detecting the diffusion of water molecular within axons[4-7]. As a parameter derived from DTI images, orientation entropy (OE) could reflect the distribution of the dominant orientation of diffusion in the assessment of microstructure properties and has been reported that could represent the distribution of compressive levels in single and multilevel CSM[4]. However, its efficacy in indicating affected levels in multilevel CSM remains unexplored. This study aims to test the reliability of OE based DTI analysis in indicating symptomatically affected levels in multilevel. It may provide evidence for further clinical trials that involves DTI in the consideration of surgical strategy.

Materials and Methods

Subjects

Twenty-nine patients with confirmed diagnosis of CSM were recruited. In order to distinguish the multilevel cases, T2-weighted (T2W) MRI images of all the patients were measured with anterior-posterior[8] (AP) and transverse diameter. Anterior-posterior compression ratio (APCR) was calculated for each disc level from C3 to C7 by the formula that AP diameter divided by transverse diameter[9] (Figure 1). Meanwhile, 47 healthy volunteers' (twenty-four males, twenty-three females, aged 42 ± 20 years) T2W MRI images were used to define the normal range of APCR. The mean and standard deviation (SD) of APCR were calculated for each disc level of healthy volunteers. Mean±2*SD was defined as the normal range of APCR. Any disc level that had lower value of APCR than the minimum value of normal range (mean-2*SD) was marked as compression level.

In the 47 healthy volunteers, 14 of them (seven males, seven females, aged 46±16 years) that have done DTI scan were employed to establish normal range of OE value.

Localization from neurological examination

Neurological test was performed to patients preoperatively by skilled clinicians and independent of MRI and DTI review. Neurological examination consisted of investigation of sensory disturbance areas, deep tendon reflexes and manual muscle testing (MMT). Sensory disturbance was defined as either perceived numbness or sensory deficit detected by light touch or pinprick.

We employed the index that developed by Seichi et al.[10] to define the topography of sensory disturbance, levels of segmental motor innervation and localization of the reflex center, and made level diagnosis from sensory disturbance, tendon reflexes and MMT respectively and combined the results from each aspect.

MRI data acquisition

All images were acquired with a 3.0T MR scanner (Achieva, Philips, Netherlands). Fast spin echo sequence (FSE) was used for T2W images acquisition. Diffusion MRI images were acquired using pulsed sequences: spin-echo echo-planar imaging (SE-EPI). Diffusion gradients in 15 directions were applied with b-value = 600s/mm^2. The imaging parameters were as follow: resolution = 1 × 1.26 × 7.0 mm^3, TE/TR = 60 ms/5 heartbeats. FOV, recon resolution and image slice planning was the same as the anatomical axial T2W images[11-13].

Localization from measurement of T2-MR images

AP and transverse diameter on the cross-section of T2W images were measured (Figure 1) with Image J software (National Institute of Health, USA). APCR was calculated as aforementioned in each disc level from C3 to C7[9].

Forty-seven healthy volunteers' (twenty-four males, twenty-three females, aged 42 ± 20 years) T2W images were employed to establish a normal range of APCR to quantitatively detect the abnormality of the APCR. Mean±2*SD was defined as the normal range of the APCR. Any disc level from C3 to C7 with lower value of APCR than the minimum value of normal range (mean-2*SD) was marked as compression

level.

Localization from increased signal intensities (ISI) on T2-MR images

ISI within the spinal cord was observed on the sagittal plane of the T2W images. Disc levels with ISI were recorded (Figure 2).

Data analysis of DTI and Localization from pure OE and weighted OE value

Diffusion measurement was performed using DTI Studio software (Version 2.4.01 2003, Johns Hopkins Medical Institute, Johns Hopkins University, Baltimore, MD). Image J software (National Institute of Health, USA) was used to define the region of interest (ROI) by B0 images to cover the whole spinal cord. Eigenvector was derived from diffusion tensor to calculate the OE (Figure 3). For color coding of the eigenvector map in DTI Studio, each voxel is composed of three orthogonal direction components in an image reference frame: (r, g, b)—(*v*x, *v*y, *v*z), where r, g and b represent red, green, and blue components of the voxel color, and (*v*x, *v*y, *v*z) is the normalized principal eigenvector, which points towards the coronal, axial and sagittal directions respectively[14]. The calculation of OE and least squares method (LSM) was performed using MATLAB (MathWorks, Natick, MA, USA) with the same method as our previous study[4]. The OE was defined in our study by

$$H = -\sum_{i=1}^{K} \frac{p(i) log_2[p(i)]}{log_2 N}$$

where *p(i)* was the probability density that the eigenvector direction fell into the *i*th angle band.

Fourteen healthy volunteers' DTI data was employed to establish the normal range of OE value. The mean and SD of OE value were calculated for each disc level. Mean±2*SD was defined as the normal range of OE value. Any disc level of the patients from C3 to C7 with higher OE value than the maximum value of normal range (mean+2*SD) was regarded as affected levels.

Additionally, we calculated the weighted OE (wOE) value based on the least squares method (LSM) for weighted estimation that used in our previous study[4]. The probability of pathogenic level was estimated by the proportion of wOE of each level among all the investigated levels. We set the threshold of probability at 5% and levels that have higher proportion than 5% were marked as affected levels.

Reliability of MRI evaluation

The MRI evaluation was done with observation of ISI and measuring APCR and OE by two experienced radiologists independently without knowing the clinical manifestation of the patients. The concordance rate and k-coefficient between two observers were 91.10% and 0.82 for ISI, 91.07% and 0.81 for APCR and 91.07% and 0.88 for OE. The two observers established the final result for ISI by consensus. The value of APCR and OE was defined as the mean value of two observers.

Statistical analysis

Level diagnosis result of APCR, ISI, OE and wOE was compared with that of the neurological signs on level-to-level basis. If a disc level of a patient presented with imaging findings that corresponded with the neurological exam, it was defined as a

true positive level. Due to the possible symptom overlap of higher affected level with the lower ones, the neurological signs may be only able to detect the highest impaired level, and sometimes one or two severely impaired levels underneath. Hence, we only regarded the levels above the highest diagnosed level as the normal level in the neurological level diagnosis. For those levels that diagnosed positively by APCR, ISI, OE and wOE yet negatively by neurology, if they were under the highest level that diagnosed by neurological signs, we didn't count them as false positive levels in the comparison.

Furthermore, we combined the level diagnosis result of wOE with that of APCR and use the combination to compare with neurology. Subsequently, comparison was made and accuracy, sensitivity and specificity were calculated.

Results

The demographic information of patients and healthy volunteers is summarized in Table 1, in which inclusion and exclusion criteria are listed. Fifteen patients were excluded because of single level compression, C2/3 or C7/T1 compression and lack of clinical findings. Fourteen patients (nine males, five females, aged 64±20 year-old) with multilevel compression were included in the study.

The neurological evaluation results of the fourteen patients were listed in Table 2. The value of APCR, OE and wOE of each patient was listed in Table 3 and 4. Level diagnosis was made from neurological signs, APCR, ISI, OE and wOE respectively. Level diagnosis result of imaging methods was compared with that of neurological

signs. The accuracy, sensitivity and specificity were calculated and shown in Table 5. APCR demonstrated the accuracy of 75.86% in the comparison with neurological signs, and sensitivity and specificity were 76.92% and 66.67%. ISI demonstrated the highest specificity, which was 100%, whereas lowest accuracy and sensitivity of 58.62% and 53.85% respectively. OE and wOE demonstrated higher accuracy (79.31% and 82.76%) and sensitivity (80.77% and 80.77%) than those of APCR and wOE demonstrated higher specificity (100%) than APCR (66.67%).

With the combination of level diagnosis result of APCR and wOE, it demonstrated the highest accuracy and sensitivity among all the methods, which were 93.10% and 96.15% respectively.

Discussion

Dermatomes and myotomes distribution in cervical spondylotic 'radiculopathy' was well demonstrated, while it's not applicable for cervical spondylotic 'myelopathy'. Accuracy of level diagnosis by neurological signs has been tested by many researchers in single level CSM[1-3,10]. Due to the different anatomic relationship of cord segments and spinal roots with regard to intervertebral levels, the cervical cord segments approximately correspond to one or two intervertebral levels above (Figure 4). However, for multilevel CSM, the complexity of neurological signs and intrinsic limitation of neurological examination hinder quantitative level diagnosis neurologically. In order to derive sufficient information for neurological level diagnosis, we used sensory disturbance, muscle weakness and tendon reflex to

indicate affected levels upon established criteria[10] and combined the result. Although it could not reveal the whole picture of myelopathy along cervical cord segments, it is capable to build a benchmark to be compared by other level diagnosis methods.

Conventional MRI is advanced in presenting anatomic deformation of cervical spine including soft tissues. Intramedullary ISI on T2W MRI has been thought to reflect a wide range of pathological lesion within spinal cord, such as myelomalacia, cystic necrosis or edema. Its appearance with corresponded T1 signal change suggests severe impairment of spinal cord and predicts adverse neurological outcome[8,15-19]. However, it may not be able to detect minor damage within the cord sensitively and variations among different observers make it not practical for level diagnosis. On the other hand, the discrepancy between anatomic compression and neurological deficit makes level diagnosis challenging in some cases.

DTI was more sensitive in detecting microstructure disorganization by means of disclosing abnormal water molecule movement within spinal cord[5,6,20-23]. After spinal cord compression, neural impairment could further lead to neurologic dysfunction and present with clinical symptoms and signs. Hence, theoretically, DTI possesses closer correlation with clinical manifestation than conventional MRI and may detect subtle lesion within spinal cord that conventional MRI can’t reveal. As a DTI parameter, OE reflects the uniformity of water molecule movement direction within white matter and is superior in detecting pathological changes of the spinal cord with its consistent distribution along the cervical spinal cord[24]. From the result, we found OE based DTI

analysis demonstrated higher accuracy and sensitivity than T2W MRI methods. It suggests that OE based DTI could better correlate with patients' clinical manifestation than the deformity or ISI on T2W images. For instance, as shown in Figure 2, case 5 is a multi-level case with two levels compression (C4/5 and C5/6) detected by anatomical MRI. OE based DTI analysis demonstrates major abnormality in C5/6 and minor abnormality in C4/5 which is consistent with anatomical MRI. Moreover, it shows significant abnormality in level C3/4, which is consistent with the neurological evaluation. Another example showing in Figure 3, case 9 has four levels compression (C3/4-C6/7) detected by T2W MRI. In DTI analysis, C3/4 and C4/5 show major abnormalities, while C5/6 and C6/7 show minor ones. This result is consistent with the level diagnosis result of both the neurological evaluation and anatomical MRI. Moreover, with the weighted OE estimation we could diminish the interaction among multiple compression levels and the probability of pathogenic level could be learnt and the distribution of lesion along the cord could be delineated. Furthermore, the combination of APCR and wOE demonstrated higher accuracy and sensitivity than using them individually. It indicates that with the microstructure information from OE based DTI analysis we could achieve more comprehensive evaluation of pathological impairment along cervical spinal cord in CSM patients upon conventional MRI. Especially for multilevel CSM patients with complex symptoms and signs, the surgical decompression for multilevel CSM often involves a wide range of cervical spine segments, which may cause 'over-killing', and the decision making that 'how

many levels to decompress and which level to compress' is still upon experience. If the contribution of each compressed level in the overall pathological lesion and functional deficit could be estimated, selective decompression would be feasible.

There were a few limitations in the present study. First, due to the selection for multilevel cases our small sample size is small and further validation of the results has to be confirmed using larger sample size. Secondly, the age of healthy control and CSM patients does not perfectly match. However, since APCR is a ratio involving both anterior-posterior diameter and transverse diameter, it doesn't depend on the absolute size of spinal cord which may relate to age, gender or ethnic. Besides, due to the limitation of neurological level diagnosis, we could only probe few true negative levels and it also accounts for the low specificity in the comparison. In addition, it is of interest that high OE value in C67 level existed in 9 out of 14 cases, whereas only 4 of them were detected by APCR. Due to the limitation of neurological level diagnosis, we can't assure that it was attributed to the pathological degeneration of the cord. But this phenomenon doesn't happen in healthy or single level CSM cases. It may be because of the longitudinal degeneration of afferent and efferent fiber tracts along the spinal cord beside the epicenter of compression[9] and unique vascular system of cervical spinal cord that makes the funiculus cuneatus of C5-C8 more vulnerable to ischemic-hypoxic damage secondary to high cervical cord compression[25-27]. Additionally, C6/7 is the lowest cord segment we investigated and DTI images were more likely to be affected by motion artifact due to respiratory[28]. Further investigation

is needed to fully reveal the underlying pathophysiological mechanism.

*References (cited in order of appearance)

Reference

1. Hirabayashi K, Satomi K, Wakano K. Level diagnostic neurology of cervical spondylotic myelopathy. Retrospective study of cases treated by single level interbody fusion. *Neuro-orthopedics* 1991;12:125-34.
2. Kokubun S. Neurological localization of the symptomatic level of lesion in cervical spondylotic myelopathy. *Rinsho Seikeigeka* 1984;19:417-24.
3. Matsumoto M, Ishikawa M, Ishii K, et al. Usefulness of neurological examination for diagnosis of the affected level in patients with cervical compressive myelopathy: prospective comparative study with radiological evaluation. *Journal of neurosurgery. Spine* 2005;2:535-9.
4. Cui J-L, Wen C-Y, Hu Y, et al. Orientation entropy analysis of diffusion tensor in healthy and myelopathic spinal cord. *NeuroImage* 2011;58:1028-33.
5. Fujiyoshi K, Konomi T, Yamada M, et al. Diffusion tensor imaging and tractography of the spinal cord: From experimental studies to clinical application. *Experimental neurology* 2012.
6. Kara B, Celik A, Karadereler S, et al. The role of DTI in early detection of cervical spondylotic myelopathy: a preliminary study with 3-T MRI. *Neuroradiology* 2011;53:609-16.
7. Rajasekaran S, Kanna R, Shetty A. Diffusion tensor imaging of the spinal cord and its clinical applications. *The Journal of bone and joint surgery. British volume* 2012;94:1024-31.
8. Mehalic T, Pezzuti R, Applebaum B. Magnetic resonance imaging and cervical spondylotic myelopathy. *Neurosurgery* 1990;26:217.
9. Ogino H, Tada K, Okada K, et al. Canal diameter, anteroposterior compression ratio, and spondylotic myelopathy of the cervical spine. *Spine* 1983;8:1-15.
10. Seichi A, Takeshita K, Kawaguchi H, et al. Neurologic level diagnosis of cervical stenotic myelopathy. *Spine* 2006;31:1338-43.
11. Morgan P, Bowtell R, McIntyre D, et al. Correction of spatial distortion in EPI due to inhomogeneous static magnetic fields using the reversed gradient method. *Journal of magnetic resonance imaging : JMRI* 2004;19:499-1006.
12. Andersson J, Skare S, Ashburner J. How to correct susceptibility distortions in spin-echo echo-planar images: application to diffusion tensor imaging. *NeuroImage* 2003;20:870-958.
13. Chuang T-C, Huang T-Y, Lin F-H, et al. PROPELLER-EPI with parallel imaging using a circularly symmetric phased-array RF coil at 3.0 T: application to high-resolution diffusion tensor imaging. *Magnetic resonance in medicine : official journal of the Society of Magnetic Resonance in Medicine / Society of Magnetic Resonance in Medicine* 2006;56:1352-60.
14. Jiang H, van Zijl P, Kim J, et al. DtiStudio: resource program for diffusion tensor computation and fiber bundle tracking. *Computer methods and programs in biomedicine* 2006;81:106-16.
15. Matsuda Y, Miyazaki K, Tada K, et al. Increased MR signal intensity due to cervical myelopathy. Analysis of 29 surgical cases. *Journal of neurosurgery* 1991;74:887-92.
16. Takahashi M, Yamashita Y, Sakamoto Y, et al. Chronic cervical cord compression: clinical significance of increased signal intensity on MR images. *Radiology* 1989;173:219-24.
17. Wada E, Yonenobu K, Suzuki S, et al. Can intramedullary signal change on magnetic resonance imaging predict surgical outcome in cervical spondylotic myelopathy? *Spine* 1999;24:455.
18. Okada Y, Ikata T, Yamada H, et al. Magnetic resonance imaging study on the results of surgery for cervical compression myelopathy. *Spine* 1993;18:2024-9.
19. Matsumoto M, Toyama Y, Ishikawa M, et al. Increased signal intensity of the spinal cord on

magnetic resonance images in cervical compressive myelopathy. Does it predict the outcome of conservative treatment? *Spine* 2000;25:677-82.
20. Boden S, McCowin P, Davis D, et al. Abnormal magnetic-resonance scans of the cervical spine in asymptomatic subjects. A prospective investigation. *The Journal of bone and joint surgery. American volume* 1990;72:1178-84.
21. Teresi L, Lufkin R, Reicher M, et al. Asymptomatic degenerative disk disease and spondylosis of the cervical spine: MR imaging. *Radiology* 1987;164:83-8.
22. Matsumoto M, Fujimura Y, Suzuki N, et al. MRI of cervical intervertebral discs in asymptomatic subjects. *The Journal of bone and joint surgery. British volume* 1998;80:19-24.
23. Sato T, Horikoshi T, Watanabe A, et al. Evaluation of cervical myelopathy using apparent diffusion coefficient measured by diffusion-weighted imaging. *AJNR. American journal of neuroradiology* 2012;33:388-92.
24. Lee J, Kim J, Park J, et al. Diffusion tensor imaging and fiber tractography in cervical compressive myelopathy: preliminary results. *Skeletal radiology* 2011;40:1543-94.
25. Kerkovský M, Bednarík J, Dušek L, et al. Magnetic resonance diffusion tensor imaging in patients with cervical spondylotic spinal cord compression: correlations between clinical and electrophysiological findings. *Spine* 2012;37:48-56.
26. Demir A, Ries M, Moonen C, et al. Diffusion-weighted MR imaging with apparent diffusion coefficient and apparent diffusion tensor maps in cervical spondylotic myelopathy. *Radiology* 2003;229:37-43.
27. Mamata H, Jolesz F, Maier S. Apparent diffusion coefficient and fractional anisotropy in spinal cord: age and cervical spondylosis-related changes. *Journal of magnetic resonance imaging : JMRI* 2005;22:38-43.
28. Turnbull I, Brieg A, Hassler O. Blood supply of cervical spinal cord in man. A microangiographic cadaver study. *Journal of neurosurgery* 1966;24:951-65.
29. Chang M, Liao K, Cheung S, et al. "Numb, clumsy hands" and tactile agnosia secondary to high cervical spondylotic myelopathy: a clinical and electrophysiological correlation. *Acta neurologica Scandinavica* 1992;86:622-5.
30. Voskuhl R, Hinton R. Sensory impairment in the hands secondary to spondylotic compression of the cervical spinal cord. *Archives of neurology* 1990;47:309-11.
31. Junqian X, Joshua SS, Eric CK, et al. Improved in vivo diffusion tensor imaging of human cervical spinal cord. *NeuroImage* 2013;67.

Tables

Table 1. Patients' gender, age and level diagnosis result from neurology, APCR(anterior-posterior compression ratio), ISI(increased signal intensities), OE(orientation entropy) and wOE(weighted OE)

	Patients (n=29)		Healthy volunteers (n=47)	
	n	Percent	n	Percent
Age, years				
20-40	0	0	17	36.1
41-60	11	37.9	28	59.5
61-80	16	55.1	2	4.2
>80	2	6.8	0	0
Mean(yr)	62.6		43.8	
Gender				
Male	22	75.8	24	51.0
Female	7	24.1	23	48.9
Ethnicity				
Southern Chinese	29	100	47	100
*Exclusion**				
Single level	9	31.0		
C2/3 or C7/T1 compression	4	13.7		
Few symptom and sign	2	6.8		

*Inclusion and exclusion criteria:

Inclusion criteria: A clinical diagnosis of cervical spondylotic myelopathy including the signs of corticospoinal lesions together with the appropriate radiographic findings.

Exclusion criteria: Acute spinal cord injuries, prior spinal intervention, claustrophobia, single level compression (determined by anterior-posterior compression ratio), C2/3 or C7/T1 compression and cases with few symptom and sign.

Table 2. Neurological evaluation result of the patients

Case no.	Neurologic Examination		
	Sensory disturbance	Reflex	Uppermost muscle with weakness
1	Bilateral whole hands	BTR↑,TTR↑	Deltoid
2	Bilateral whole arms	BTR→,TTR→,F.F.↑	Deltoid
3	Bilateral whole hands	BTR→,TTR↑	Deltoid
4	Bilateral whole arms	BTR↑,TTR↑	Deltoid
5	Right whole hand	BTR↑,TTR↑	-
6	Bilateral whole hands	BTR↑,TTR↑	Deltoid
7	Bilateral whole hands	BTR→,TTR↑	Deltoid
8	-	TTR↓, F.F.↑	EDC
9	Right whole hand	BTR↑,TTR↑	Biceps
10	Bilateral whole hands	BTR↑,TTR↑	Biceps
11	Bilateral ulnar aspect of forearm and hands	BTR↑,TTR↑	Biceps
12	Bilateral whole hands	BTR↑,TTR↑	-
13	Bilateral whole arms	BTR→,TTR↑	Deltoid
14	Bilateral whole hands	BTR↓,TTR↑	EDC

BTR = deep tendon reflexes of biceps; EDC = extensor digiti communis; FF = finger flexor reflex; TTR = deep tendon reflexes of triceps

Table 3. Anterior-posterior compression ratio of the patients

Case no.	Anterior-posterior compression ratio			
	C3/4	C4/5	C5/6	C6/7
1	0.3625	0.2300	0.3872	0.4524
2	0.5547	0.4275	0.3066	0.4979
3	0.2729	0.2549	0.4971	0.5597
4	0.3402	0.3803	0.5438	0.5958
5	0.4574	0.2472	0.1753	0.4451
6	0.4341	0.2651	0.3933	0.4296
7	0.1813	0.3343	0.3534	0.3615
8	0.5264	0.3583	0.4452	0.4297
9	0.2145	0.1356	0.3320	0.4008
10	0.3299	0.4732	0.5162	0.4076
11	0.3465	0.2640	0.2713	0.2858
12	0.4434	0.2953	0.3819	0.3704
13	0.1808	0.3133	0.4590	0.5152
14	0.4338	0.3064	0.2228	0.4394
Normal range (Mean±2*SD)	0.5574±0.1249	0.5193±0.1205	0.5275±0.1147	0.5297±0.1241

Table 4. Orientation entropy, weighted orientation entropy value and probability of pathogenic level of the patients

Case no.	C3/4		C4/5		C5/6		C6/7	
	OE	wOE	OE	wOE	OE	wOE	OE	wOE
1	0.7800	0.1783(9.36%)	0.9356	0.4433(23.28%)	0.8369	0.7431(39.02%)	0.8322	0.5399(28.35%)
2	0.8099	0.3205(14.86%)	0.9040	0.8009(37.14%)	0.8793	0.5751(26.67%)	0.8308	0.4601(21.33%)
3	0.9325	0.424(27.16%)	0.9287	0.6864(43.96%)	0.7491	0(0%)	0.8028	0.4509(28.88%)
4	0.8875	0.8712(33.29%)	0.8883	0.5073(19.39%)	0.8376	0(0%)	0.9238	1.2384(47.32%)
5	0.8945	0.817(37.44%)	0.8582	0.4673(21.41%)	0.8324	0(0%)	0.8783	0.898(41.15%)
6	0.8524	0(0%)	0.8578	0.5607(31.20%)	0.8985	0(0%)	0.9042	1.2366(68.8%)
7	0.8423	0.2808(14.59%)	0.7990	0.2808(14.59%)	0.8212	0(0%)	0.8692	1.1152(57.93%)
8	0.6703	0(0%)	0.8274	0(0%)	0.9196	0.7791(100%)	0.7823	0(0%)
9	0.9266	0.4803(23.87%)	0.9392	0.312(15.51%)	0.8773	0.2642(13.13%)	0.8630	0.9554(47.49%)
10	0.8127	0.219(10.79%)	0.8337	0.4126(20.34%)	0.8631	0(0%)	0.9300	1.3974(68.87%)
11	0.8426	0.4748(19.16%)	0.9500	0.7285(29.39%)	0.8885	0(0%)	0.9083	1.2754(51.45%)
12	0.8484	1.0924(59.52%)	0.9634	0(0%)	0.7459	0(0%)	0.8878	0.7429(40.48%)
13	0.8792	0.007(0.47%)	0.8180	0.6376(43.01%)	0.8274	0(0%)	0.8306	0.8379(56.52%)
14	0.7582	0(0%)	0.7275	0(0%)	0.9167	0.916(83.18%)	0.8313	0.1852(16.82%)

Normal range of OE (Mean±2*SD): C3/4, 0.6998±0.1207; C4/5, 0.7182±0.0954; C5/6, 0.7128±0.1492; C6/7, 0.7193±0.1399. OE indicates orientation entropy; wOE, weighted orientation entropy.

Table 5. Statistical result of the comparison of APCR, ISI, OE, wOE and combination with neurology in level diagnosis

	True positive	False positive	False negative	True negative	Accuracy	Sensitivity	Specificity
APCR	20	1	6	2	75.86%	76.92%	66.67%
ISI	14	0	12	3	58.62%	53.85%	100.00%
OE	21	1	5	2	79.31%	80.77%	66.67%
wOE	21	0	5	3	82.76%	80.77%	100.00%
APCR+wOE	25	1	1	2	93.10%	96.15%	66.67%

APCR indicates anterior -posterior compression ratio; ISI, increased signal intensities; OE, orientation entropy; wOE, weighted orientation entropy.

Figure legends:

Figure 1: Transverse diameter (a) and anterior-posterior diameter (b) of spinal cord were measured on cross-section of T2-weighted MRI images. Anterior-posterior compression ratio (APCR) = b/a.

Figure 2: Increased signal intensity (ISI) on the disc level was observed on sagittal T2-weighted MRI image of a patient (case no. 5) and result was correlated to the diagnosed level by neurological signs.

Figure 3: The representative images show the sagittal T2W (A), cross-sectional B0, FA and principal eigenvector images of C3/4 (B, C, D), C4/5 (E, F, G), C5/6 (H, I, J) and C6/7 (K, L, M) level in a multilevel CSM patient (case no. 9). The region of interest (ROI) was drawn manually and defined by B0 image to cover the whole spinal cord.

Figure 4: Anatomical discrepancy between the bony level, cord level and root level. Bony level is determined by vertebral body; spinal cord segment is represented by black block (); the never root is represented by arrow (↙).

Figure1
Click here to download high resolution image

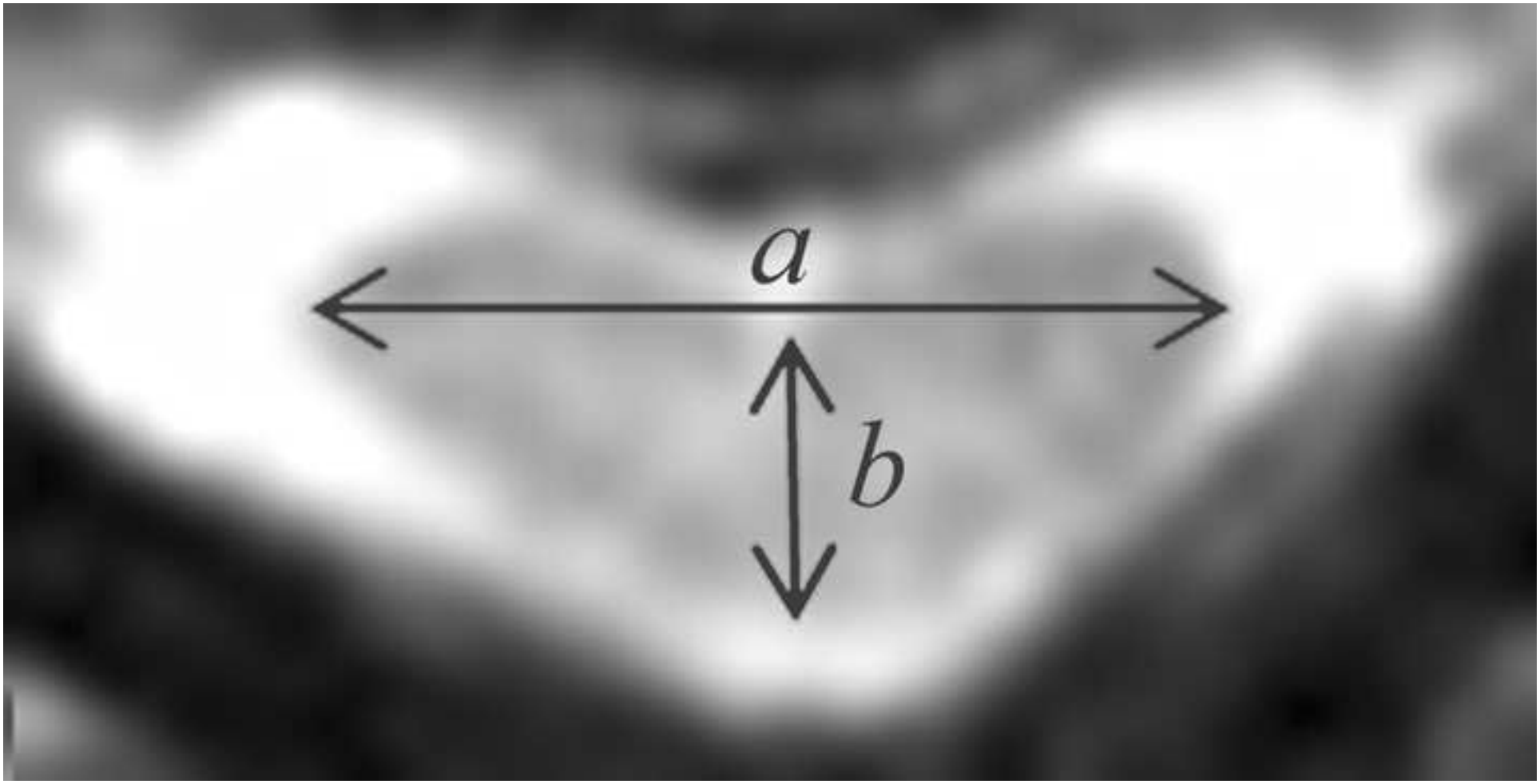


Figure2
Click here to download high resolution image

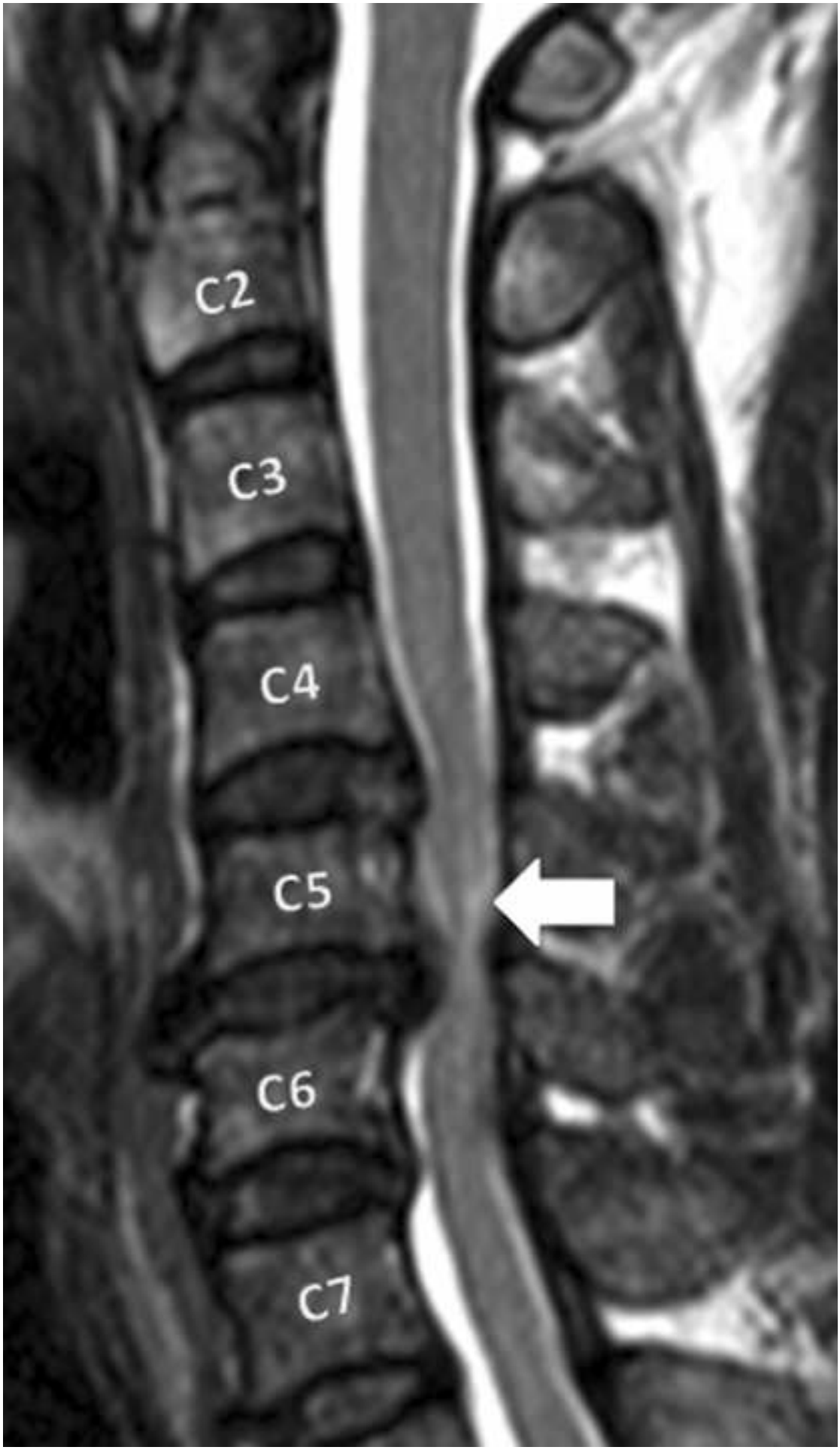


Figure3
Click here to download high resolution image

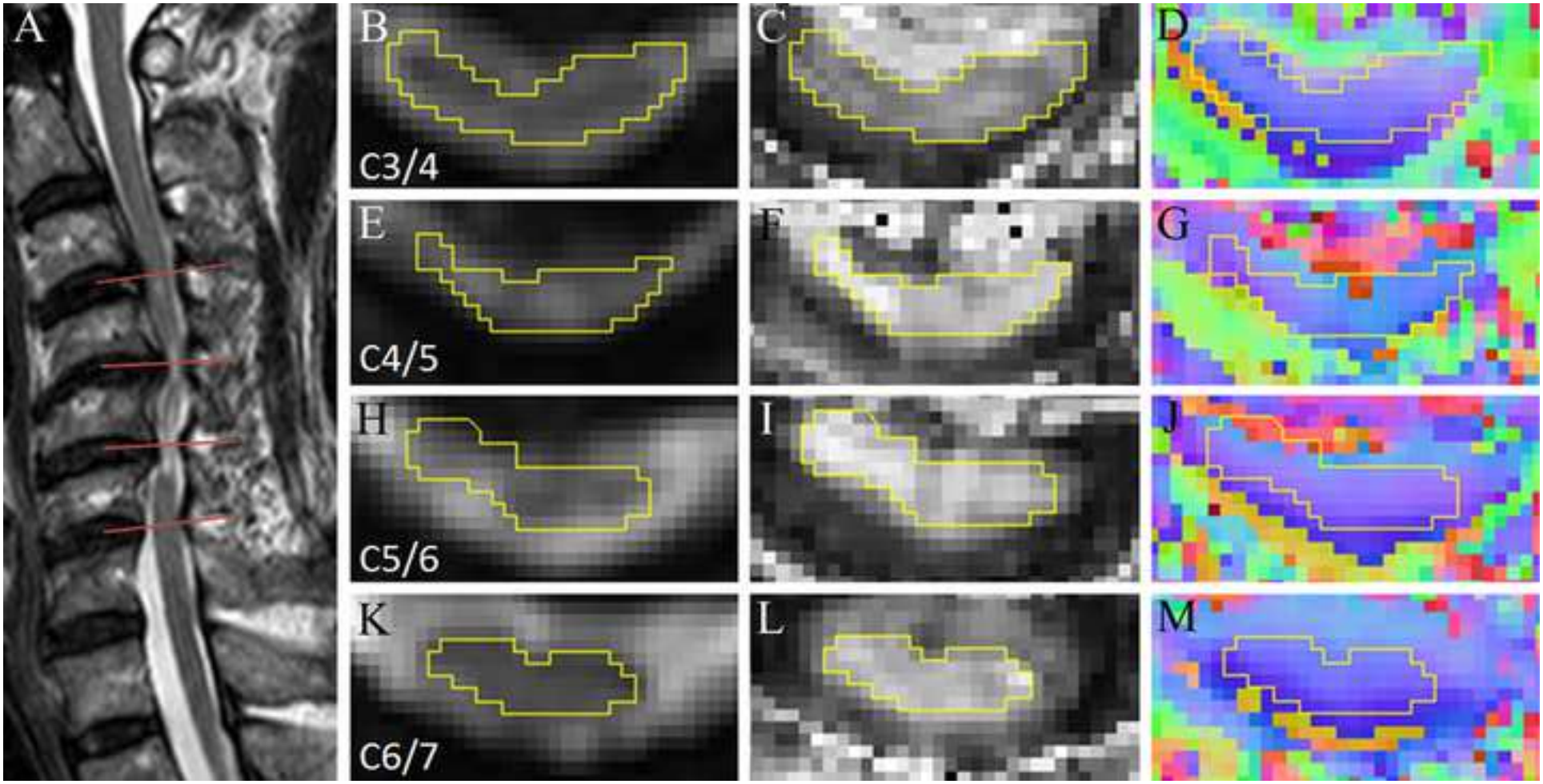
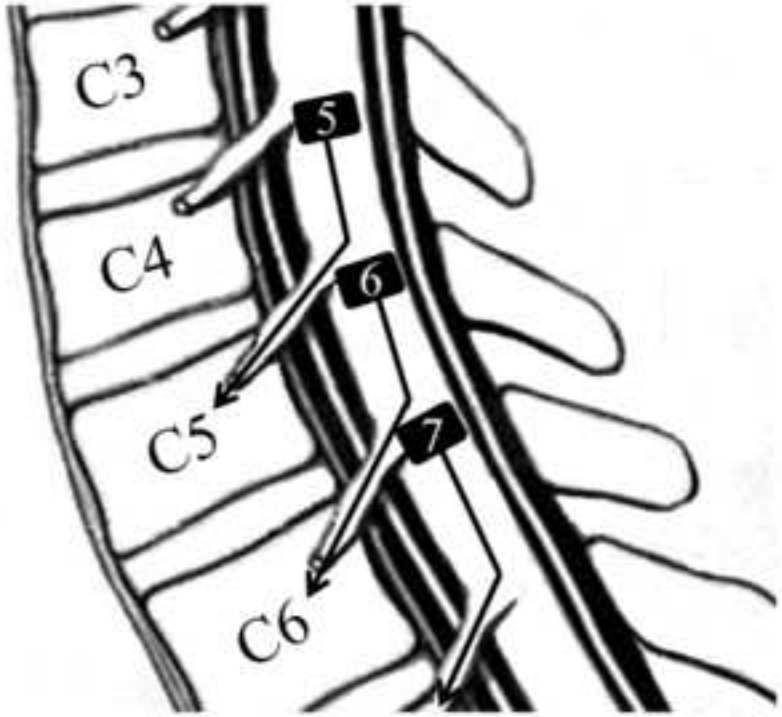


Figure4
Click here to download high resolution image



Bony Level	Spinal Cord Segment	Nerve Root
C3/4	C5	C4
C4/5	C6	C5
C5/6	C7	C6
C6/7	C8	C7