



<b>Title</b>	<b>Potential use of diffusion tensor imaging in level diagnosis of multilevel cervical spondylotic myelopathy</b>
<b>Author(s)</b>	<b>Li, Xiang; Cui, Jiaolong; Mak, Kincheung; Luk, Keith Dip Kei; Hu, Yong</b>
<b>Citation</b>	<b>Spine, 2014, v. 39, n. 10, p. E615-E622</b>
<b>Issued Date</b>	<b>2014</b>
<b>URL</b>	<b><a href="http://hdl.handle.net/10722/205809">http://hdl.handle.net/10722/205809</a></b>
<b>Rights</b>	<b>This is a non-final version of an article published in final form in Spine, 2014, v. 39, n. 10, p. E615-E622</b>

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

Running 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](mailto: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:**

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/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.

## 1 Introduction

2 Cervical spondylotic myelopathy (CSM) is a degenerative disease of cervical spine,  
3 which is usually of extensive range of lesion involving multiple segments<sup>1,2</sup>.

4 Multilevel affected CSM is complex with clinical manifestation and difficult to  
5 precisely localize all the involved levels by neurological examination<sup>3</sup>. Although  
6 conventional magnetic resonance imaging (MRI) can detect anatomic compression on  
7 spinal cord, the disproportion between the spinal cord compression presenting on MRI  
8 and neurological deficit is frequently seen<sup>4</sup>. If spinal cord damage could be detected  
9 pathologically on each level, it would be great supplemental information for  
10 evaluating the tissue impairment among affected levels in multilevel CSM.

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

## 1 **Materials and Methods**

### 2 *Subjects*

3 Twenty-nine patients with confirmed diagnosis of CSM were recruited. In order to  
4 distinguish the multilevel cases, T2-weighted (T2W) MRI images of all the patients  
5 were measured with anterior-posterior<sup>8</sup> (AP) and transverse diameter.

6 Anterior-posterior compression ratio (APCR) was calculated for each disc level from  
7 C3 to C7 by the formula that AP diameter divided by transverse diameter<sup>9</sup> (Figure 1).

8 Meanwhile, 47 healthy volunteers' (twenty-four males, twenty-three females, aged 42  
9  $\pm$  20 years) T2W MRI images were used to define the normal range of APCR. The  
10 mean and standard deviation (SD) of APCR were calculated for each disc level of  
11 healthy volunteers. Mean $\pm$ 2\*SD was defined as the normal range of APCR. Any disc  
12 level that had lower value of APCR than the minimum value of normal range  
13 (mean-2\*SD) was marked as compression level.

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

### 16 *Localization from neurological examination*

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

1 We employed the index that developed by Seichi et al.<sup>10</sup> to define the topography of  
2 sensory disturbance, levels of segmental motor innervation and localization of the  
3 reflex center, and made level diagnosis from sensory disturbance, tendon reflexes and  
4 MMT respectively and combined the results from each aspect.

#### 5 ***MRI data acquisition***

6 All images were acquired with a 3.0T MR scanner (Achieva, Philips, Netherlands).  
7 Fast spin echo sequence (FSE) was used for T2W images acquisition. Diffusion MRI  
8 images were acquired using pulsed sequences: spin-echo echo-planar imaging  
9 (SE-EPI). Diffusion gradients in 15 directions were applied with b-value =  
10  $600\text{s/mm}^2$ . The imaging parameters were as follow: resolution =  $1 \times 1.26 \times 7.0 \text{ mm}^3$ ,  
11 TE/TR = 60 ms/5 heartbeats. FOV, recon resolution and image slice planning was  
12 the same as the anatomical axial T2W images<sup>11-13</sup>.

#### 13 ***Localization from measurement of T2-MR images***

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

17 Forty-seven healthy volunteers' (twenty-four males, twenty-three females, aged  $42 \pm$   
18 20 years) T2W images were employed to establish a normal range of APCR to  
19 quantitatively detect the abnormality of the APCR. Mean $\pm$ 2\*SD was defined as the  
20 normal range of the APCR. Any disc level from C3 to C7 with lower value of APCR  
21 than the minimum value of normal range (mean-2\*SD) was marked as compression

1 level.

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

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

## 5 ***Data analysis of DTI and Localization from pure OE and weighted OE value***

6 Diffusion measurement was performed using DTI Studio software (Version 2.4.01  
7 2003, Johns Hopkins Medical Institute, Johns Hopkins University, Baltimore, MD).  
8 Image J software (National Institute of Health, USA) was used to define the region of  
9 interest (ROI) by B0 images to cover the whole spinal cord. Eigenvector was derived  
10 from diffusion tensor to calculate the OE (Figure 3). For color coding of the  
11 eigenvector map in DTI Studio, each voxel is composed of three orthogonal direction  
12 components in an image reference frame: (r, g, b)—(vx, vy, vz), where r, g and b  
13 represent red, green, and blue components of the voxel color, and (vx, vy, vz) is the  
14 normalized principal eigenvector, which points towards the coronal, axial and sagittal  
15 directions respectively<sup>14</sup>. The calculation of OE and least squares method (LSM) was  
16 performed using MATLAB (MathWorks, Natick, MA, USA) with the same method as  
17 our previous study<sup>4</sup>. The OE was defined in our study by

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

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

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

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

### 11 ***Reliability of MRI evaluation***

12 The MRI evaluation was done with observation of ISI and measuring APCR and OE  
13 by two experienced radiologists independently without knowing the clinical  
14 manifestation of the patients. The concordance rate and k-coefficient between two  
15 observers were 91.10% and 0.82 for ISI, 91.07% and 0.81 for APCR and 91.07% and  
16 0.88 for OE. The two observers established the final result for ISI by consensus. The  
17 value of APCR and OE was defined as the mean value of two observers.

### 18 ***Statistical analysis***

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

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

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

## 12 **Results**

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

18 **The neurological evaluation results of the fourteen patients were listed in Table 2.** The  
19 value of APCR, **OE and wOE** of each patient was listed in Table 3 and 4. Level  
20 diagnosis was made from neurological signs, APCR, ISI, OE and wOE respectively.

21 Level diagnosis result of imaging methods was compared with that of neurological

1 signs. The accuracy, sensitivity and specificity were calculated and shown in Table 5.

2 APCR demonstrated the accuracy of 75.86% in the comparison with neurological

3 signs, and sensitivity and specificity were 76.92% and 66.67%. ISI demonstrated the

4 highest specificity, which was 100%, whereas lowest accuracy and sensitivity of

5 58.62% and 53.85% respectively. OE and wOE demonstrated higher accuracy (79.31%

6 and 82.76%) and sensitivity (80.77% and 80.77%) than those of APCR and wOE

7 demonstrated higher specificity (100%) than APCR (66.67%).

8 With the combination of level diagnosis result of APCR and wOE, it demonstrated the

9 highest accuracy and sensitivity among all the methods, which were 93.10% and

10 96.15% respectively.

## 11 **Discussion**

12 Dermatomes and myotomes distribution in cervical spondylotic ‘radiculopathy’ was

13 well demonstrated, while it’s not applicable for cervical spondylotic ‘myelopathy’.

14 Accuracy of level diagnosis by neurological signs has been tested by many

15 researchers in single level CSM<sup>1-3,10</sup>. Due to the different anatomic relationship of

16 cord segments and spinal roots with regard to intervertebral levels, the cervical cord

17 segments approximately correspond to one or two intervertebral levels above (Figure

18 4). However, for multilevel CSM, the complexity of neurological signs and intrinsic

19 limitation of neurological examination hinder quantitative level diagnosis

20 neurologically. In order to derive sufficient information for neurological level

21 diagnosis, we used sensory disturbance, muscle weakness and tendon reflex to



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

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

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

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

1 many levels to decompress and which level to compress' is still upon experience. If  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60  
61  
62  
63  
64  
65

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

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

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60  
61  
62  
63  
64  
65

1 is needed to fully reveal the underlying pathophysiological mechanism.

2

## 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.

**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
<i>Age, years</i>				
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
<i>Gender</i>				
Male	22	75.8	24	51.0
Female	7	24.1	23	48.9
<i>Ethnicity</i>				
Southern Chinese	29	100	47	100
<i>Exclusion*</i>				
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 corticospinal 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 $\pm$ 2*SD)	0.5574 $\pm$ 0.1249	0.5193 $\pm$ 0.1205	0.5275 $\pm$ 0.1147	0.5297 $\pm$ 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 $\pm$ 2\*SD): C3/4, 0.6998 $\pm$ 0.1207; C4/5, 0.7182 $\pm$ 0.0954; C5/6, 0.7128 $\pm$ 0.1492; C6/7, 0.7193 $\pm$ 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.

1 **Figure legends:**

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

4

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

7

8 **Figure 3:** The representative images show the sagittal T2W (A), cross-sectional B0, FA and principal  
9 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  
10 multilevel CSM patient (case no. 9). The region of interest (ROI) was drawn manually and defined by  
11 B0 image to cover the whole spinal cord.

12

13 **Figure 4:** Anatomical discrepancy between the bony level, cord level and root level. Bony level is  
14 determined by vertebral body; spinal cord segment is represented by black block (■); the nerve root  
15 is represented by arrow (↙).

16

Figure1  
[Click here to download high resolution image](#)

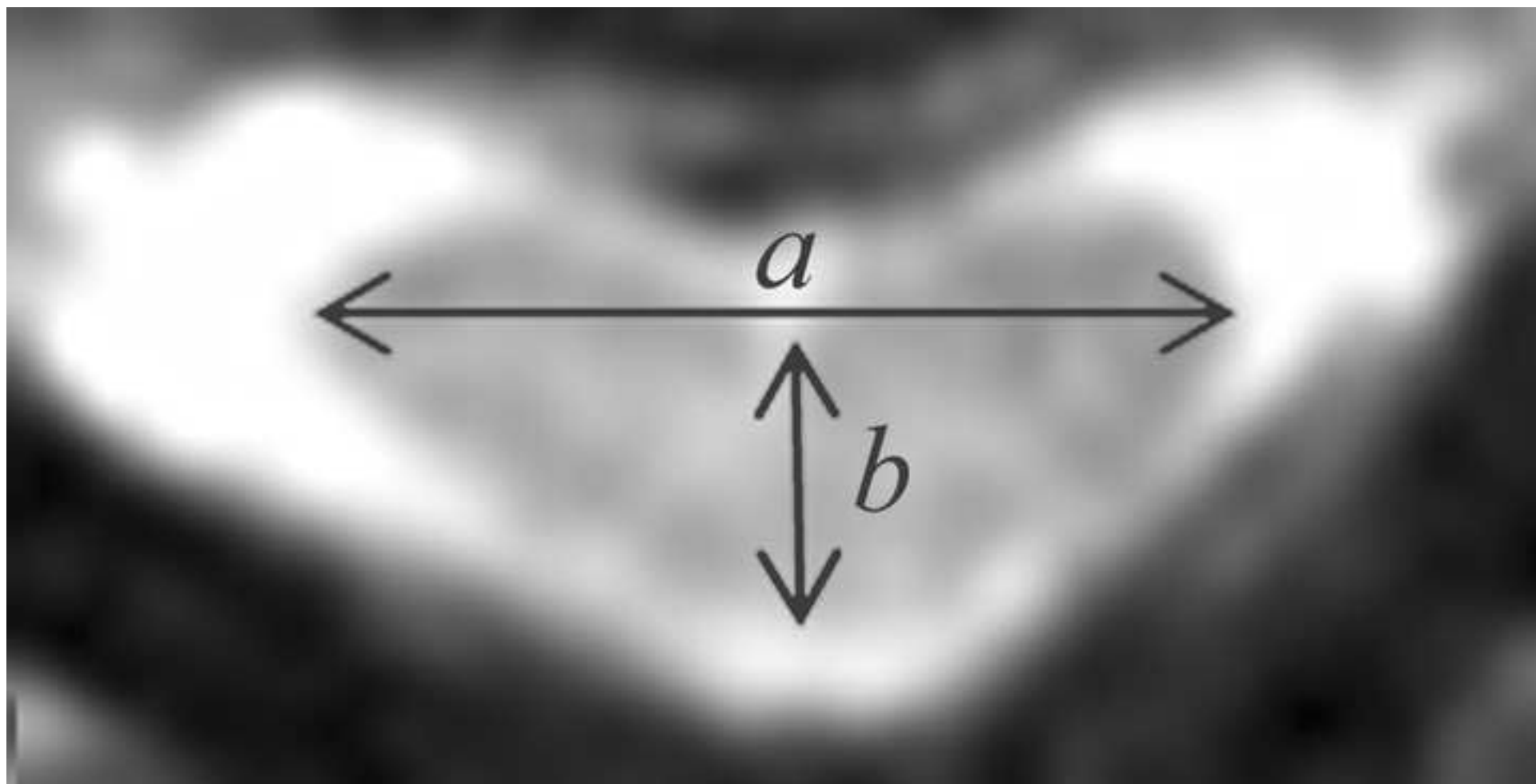


Figure 2  
[Click here to download high resolution image](#)

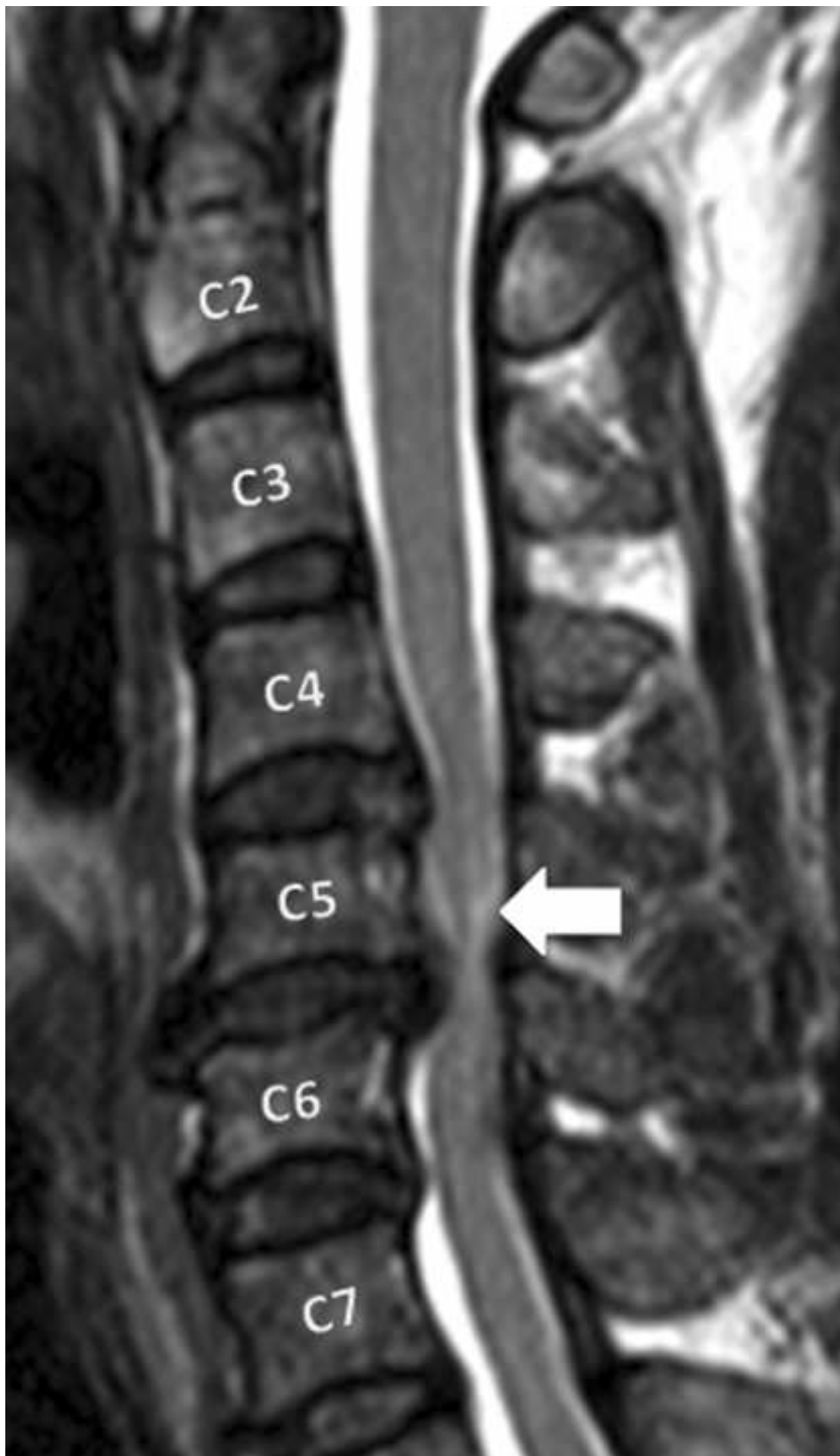


Figure3  
[Click here to download high resolution image](#)

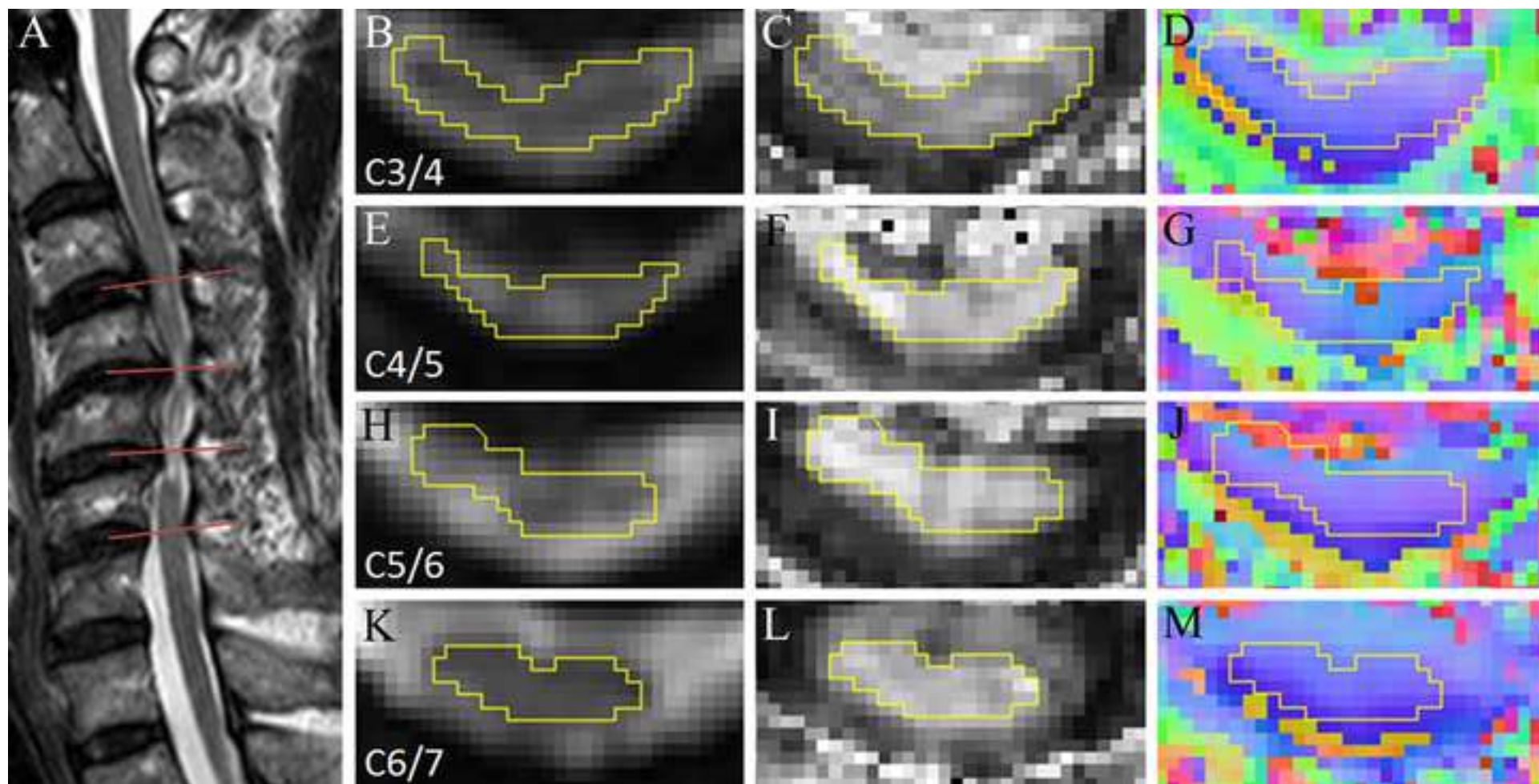
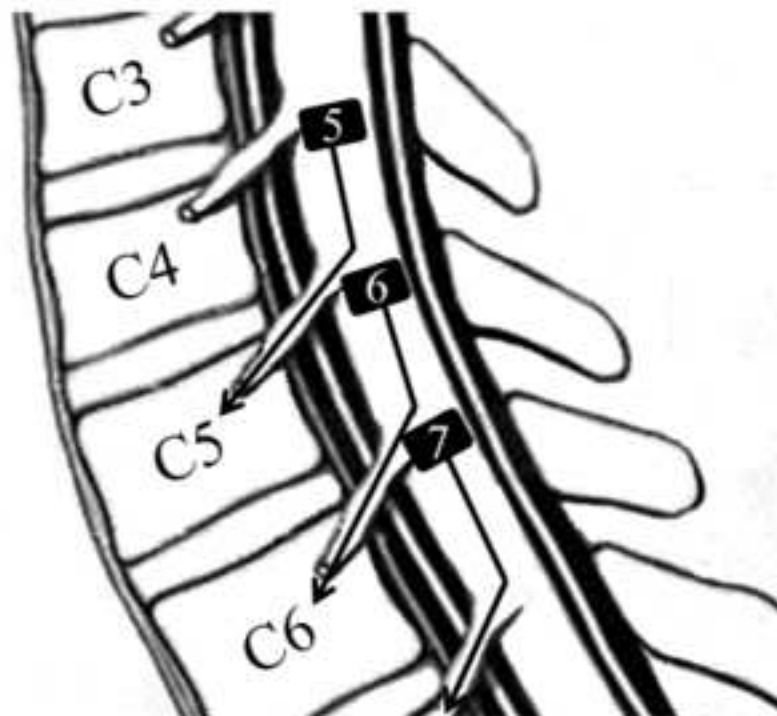


Figure 4

[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