



# Decreased Value of Highly Accurate Fractional Anisotropy Using 3-Tesla ZOOM Diffusion Tensor Imaging After Decompressive Surgery in Patients with Cervical Spondylotic Myelopathy: Aligned Fibers Effect

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■ **BACKGROUND:** Diffusion tensor imaging (DTI) is widely used; however, most of the prior studies have resulted in presurgical decreased fractional anisotropy (FA) values in patients with cervical spondylotic myelopathy (CSM). We used ZOOM DTI and could acquire highly accurate FA values during perioperative periods, which indicated different insights than preceding studies. The objective of this study was to assess the perioperative FA change in patients with CSM and determine the prognostic factor.

■ **METHODS:** Twenty-eight patients with CSM and healthy control subjects were enrolled in this study. Twenty patients (71%) had intracordal high intensity before surgery. All patients underwent decompressive surgery. ZOOM DTI and the Japanese Orthopaedic Association (JOA) assessment were performed before and after surgery. The region of interest was manually contoured to omit the surrounding cerebrospinal fluid. The axial plane of the most stenotic cervical level was assessed.

■ **RESULTS:** FA values before surgery and at 1 week after surgery, and FA values at 1 week after surgery and at 6 months after surgery differed significantly as determined. The FA values of patients with intracordal high intensity significantly decreased after surgery and significantly increased from 1 week to 6 months, whereas those of patients without intracordal high intensity did not significantly change. JOA scores at 6 months after surgery (13.1)

improved significantly compared with JOA scores before surgery (10.8). Only FA values at 1 week after surgery had a significant positive relationship with JOA scores presurgery and at 6 months after surgery.

■ **CONCLUSIONS:** The presurgical FA value in patients with CSM did not differ from that of normal control subjects, but significantly decreased after surgery, and significantly increased 6 months after surgery. We concluded that the postsurgical FA value approximates the proper state of the damaged cord and the presurgical FA value includes a masked effect as an aligned fiber effect because of compression by degenerative construction. Only the FA value at 1 week had a significant positive relationship with the JOA score presurgery and at 6 months, which established that the postsurgical FA value may be a more accurate prognostic factor than the presurgical FA value.

## INTRODUCTION

Cervical spondylotic myelopathy (CSM) is the most common cause of spinal cord dysfunction. Conventional magnetic resonance imaging (MRI) reveals compression of the spinal cord or root at the level of the lesion only. Intracordal high intensity on T2-weighted imaging may be a prognostic factor;

### Key words

- Cervical degenerative spondylosis
- Diffusion tensor imaging
- Fractional anisotropy
- Prognostic factor
- Tractography

### Abbreviations and Acronyms

- CSM:** Cervical spondylotic myelopathy
- DTI:** Diffusion tensor imaging
- FA:** Fractional anisotropy
- FOV:** Field-of-view
- JOA:** Japanese Orthopaedic Association
- MRI:** Magnetic resonance imaging

**ROI:** Region of interest

**SCI:** Spinal cord injury

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however, the signal does not always indicate the irreversible state of the cervical spinal cord lesion nor correlate with clinical outcomes.<sup>1,2</sup>

Tractography using diffusion tensor imaging (DTI) is frequently performed to assess the localization of motor fibers in patients with a space-occupying lesion, such as a brain tumor or hematoma, which can compress or damage the neural fibers. Visualization of the winding corticospinal tract helps surgeons to avoid the loss of such fibers during surgery.

To date, similar trials for the spinal cord using 1.5-Tesla MRI have been performed; however, the smaller cross-sectional area of the cord and the environmental disadvantage of being surrounded by tissues that have a variety of magnetic susceptibilities can lead to questionable study results, particularly regarding the accuracy of the acquired values. High-resolution DTI of the cervical spinal cord prolongs the scan time, which is not preferable in the clinical setting, but lower-resolution scans reduce the accuracy of fractional anisotropy (FA) value measurement. Given this information, novel techniques such as ZOOM DTI in 3-Tesla MRI (Philips, Amsterdam, The Netherlands) have been developed. The advantages of cervical spinal DTI with ZOOM DTI are as follows. First, small field-of-view (FOV) imaging reduces the readout scan time; therefore, the artifacts caused by off resonance are also reduced. Second, the phase encode step is reduced and no phase wrap is required because of the limited FOV excited with noncoplanar spin echo and outer volume suppression. In our previous study, we demonstrated that ZOOM DTI yielded better visibility than conventional DTI.<sup>3</sup> We also found that the FA value of the cervical spinal cord was approximately 0.6, which decreased at lower levels. In another study, we observed no significant difference between elderly and young healthy volunteers regarding cervical FA values at each spinal cord level despite mild cervical degenerative changes in the elderly persons.<sup>4</sup>

In terms of spinal cord injury (SCI) or motor neuron diseases such as amyotrophic lateral sclerosis, apparent destruction or degeneration of fibers results in a marked decrease in the FA value.<sup>5,6</sup> In addition, most of the prior research on CSM concluded that the FA value of patients before surgery was significantly lower

than that of healthy control subjects.<sup>7-10</sup> We yielded highly accurate perioperative FA values in patients with CSM using ZOOM DTI and therefore examined the perioperative changes of acquired values.

## METHODS

Informed consent was obtained from all study participants for this research.

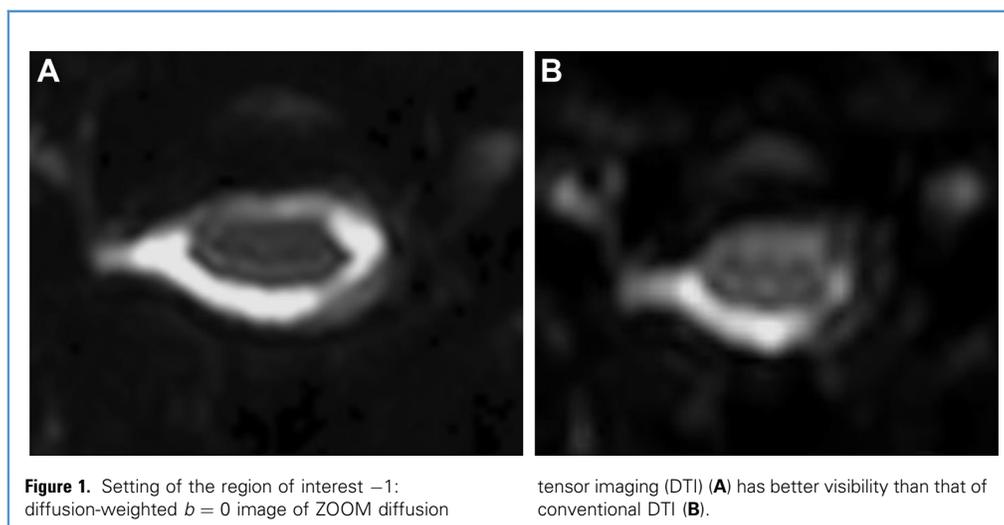
### Subjects

Twenty-eight patients with CSM were enrolled in this study. The group consisted of 15 men (54%) and 13 women (46%), with ages ranging from 42 to 92 years (mean,  $71.3 \pm 12.7$  years). Twenty patients (71%) had intracordal high intensity before surgery. All patients underwent decompressive surgery, including 16 anterior cervical discectomies/corpectomies and fusions (57%) using 11 polyether ether ketone, 3 titanium-coated polyether ether ketone, or 2 titanium mesh cages, and 12 laminoplasties (43%). We used the Japanese Orthopaedic Association (JOA) assessment as the patient's functional evaluation instrument, which includes upper and/or lower extremity function, sensory function, and bladder function. ZOOM DTI and JOA assessment were performed before surgery and at 1 week, 6 months, and 1 year after surgery. Twelve normal control subjects were also included in this study for comparison with the patients with CSM.

### Imaging Parameters and Quantitative Analysis

On 3-Tesla ZOOM DTI, the imaging parameters were as follows: repetition time 4500 milliseconds, echo time 81 milliseconds, FOV  $70 \times 47 \text{ mm}^2$ , matrix  $70 \times 47$ , number of sample average 10, and scan time 10 minutes and 35 seconds. Suppression slabs were implemented by successive quadratic phase radiofrequency pulses<sup>11</sup> followed by crusher gradients.

The FA map was calculated on ZOOM DTI and conventional DTI. The FA value and apparent diffusion coefficient of the spinal cord were measured. The setting of the region of interest (ROI) is provided in **Figure 1**. The ROI was manually contoured around the



**Figure 1.** Setting of the region of interest –1: diffusion-weighted  $b = 0$  image of ZOOM diffusion

tensor imaging (DTI) (**A**) has better visibility than that of conventional DTI (**B**).

**Table 1.** Summary of Patient Characteristics

Characteristic	Normal Control Subjects	Patients
Mean age at surgery $\pm$ SD (years)	73.8 $\pm$ 11.5	71.3 $\pm$ 12.7
Female/male	7/5	13/15
Intracordal high signal	0	20
Level of responsible lesion		
C3-4		5
C4-5		9
C5-6		11
C6-7		3
Total		28

Values are number or as otherwise indicated.

whole spinal cord without distinction of gray and/or white matter and was made to be as large as possible; however, the surrounding cerebrospinal fluid was omitted by checking a 3-dimensional ROI cube. All operations were performed using Fiber Track (Philips, Andover, Massachusetts, USA), which is the software in the MRI scanner. This procedure was repeated from the C3-4 level to the C6-7 level in all patients and control subjects.

The axial plane of the most stenotic (compressed) cervical level, which was the area of the target lesion in all patients, was used for assessment.

For statistical analysis, a repeated-measures design and the Tukey-Kramer method were used for comparison between each time point ( $P < 0.05$ ) with JMP 13 software (SAS Institute Inc., Cary, North Carolina, USA).

This study was approved by the institutional review board (30–009).

## RESULTS

The patients' demographic data are provided in [Table 1](#).

### Perioperative Change in FA Values

Because of the small number of patients with CSM ( $n = 3$ ) in whom the target lesion occurred at the C6-7 level, we excluded this

level. The titanium cages used for anterior cervical discectomies/corpectomies and fusions did not disturb the ROI contouring via the presence of metal artifacts.

The mean FA values of patients and control subjects at each level are provided in [Table 2](#), and there was no significant difference between patients and normal control subjects. The mean FA values at presurgery, 1 week after surgery, and 6 months after surgery of all patients were  $0.569 \pm 0.114$ ,  $0.485 \pm 0.096$ , and  $0.556 \pm 0.103$ , respectively. There were significant differences between FA values at presurgery and 1 week ( $P = 0.0076$ ) and between FA values at 1 week and 6 months ( $P = 0.0442$ ) in the patient group as determined by the Tukey-Kramer method. The perioperative FA changes at each cervical disk level are also provided in [Table 2](#). The chronological FA change in patients with intracordal T2-weighted imaging high signal was significantly different compared with that of patients without intracordal high signal throughout the follow-up period (repeated-measures design,  $P = 0.0031$ ); however, the FA value presurgery in patients with intracordal high intensity did not differ from that in patients without intracordal high intensity ( $P = 0.3728$ ). The FA value of the intracordal high-intensity group significantly decreased after surgery ( $P = 0.0049$ ) and significantly increased from 1 week to 6 months after surgery ( $P = 0.0390$ ), whereas the FA value of patients without intracordal high intensity did not undergo any significant changes ([Table 3](#)).

### Prognostic Assessment

The JOA score at 1 year (14.3) and 6 months (13.1) improved significantly compared with the JOA score presurgery (10.8) ( $P < 0.0001$  and  $P = 0.0002$ , respectively).

Only the FA value at 1 week after surgery had a significant positive relationship with the JOA score at presurgery and 6 months ( $R^2 = 0.339$  and  $R^2 = 0.258$ ,  $P = 0.0049$  and  $P = 0.0263$ , respectively) ([Table 4](#)). The JOA score at 1 year also had a tendency for a positive relationship with the FA value at 1 week; however, it did not have significance ( $P = 0.0593$ ).

## DISCUSSION

In the brain and spinal cord white matter, cellular membranes and myelin sheaths act as natural barriers to molecular diffusion, including the movement of water molecules, which affects isotropy.<sup>12</sup> There are fewer reports on spinal DTI than on brain DTI,

**Table 2.** Fractional Anisotropy Value at Each Level

Level	FA at Presurgery: Normal Control Subjects	FA at Presurgery: Patients	FA at 1 Week: Patients	FA at 6 Months: Patients
C3-4	0.646 $\pm$ 0.078	0.625 $\pm$ 0.138	0.480 $\pm$ 0.078	0.613 $\pm$ 0.032
C4-5	0.630 $\pm$ 0.088	0.566 $\pm$ 0.100	0.487 $\pm$ 0.064	0.553 $\pm$ 0.096
C5-6	0.563 $\pm$ 0.081	0.571 $\pm$ 0.090	0.505 $\pm$ 0.116	0.531 $\pm$ 0.091
Mean value of all 3 levels		0.569 $\pm$ 0.114	0.485 $\pm$ 0.096*	0.556 $\pm$ 0.103*

Values are mean  $\pm$  SD.  
FA, fractional anisotropy.  
\*Significant difference by repeated-measures design.

**Table 3.** Fractional Anisotropy Change of Patients with and without Intracordal High Signal

T2-Weighted Image	Number	FA Presurgery	FA at 1 Week	FA at 6 Months
With intracordal high signal	20	0.558 ± 0.116	0.459 ± 0.071*	0.537 ± 0.093*
Without intracordal high signal	7	0.601 ± 0.088	0.560 ± 0.110	0.633 ± 0.022

Values are mean ± SD or as otherwise indicated.  
FA, fractional anisotropy.  
\*Significant difference by repeated-measures design.

and most used conventional 1.5-Tesla MRI. ZOOM DTI is a recently developed method for the estimation of fiber tracts.<sup>13</sup> In particular, in small organs, such as the spinal cord, finer spatial resolution that can clearly distinguish the boundary between the target and the surrounding tissue is preferable. ZOOM DTI has previously been demonstrated to yield better visibility than conventional DTI.<sup>3</sup>

Of note, fluctuation of the FA and apparent diffusion coefficient values was strongly influenced by cerebrospinal fluid. To acquire accurate values, drawing and setting the 3-dimensional ROI contour along the cervical curvature should be performed with care to omit the surrounding cerebrospinal fluid<sup>14</sup> to avoid a decreased FA value (Figures 1 and 2).<sup>9,11</sup> The decrement of the FA values at the C5-6 level in normal control subjects illustrates the difficulty associated with excluding the cerebrospinal fluid influence when setting the ROI around the apex of the cervical cord sagittal curvature. Not only cerebrospinal fluid involvement, but also susceptibility and motion artifacts at lower levels, particularly C5-6 and C6-7, cannot be ignored even in ZOOM DTI. Therefore, in our previous study, the cervical spinal cord FA values gradually decreased and the apparent diffusion coefficient values increased toward the lower levels.<sup>3</sup> Furthermore, there was no significant difference between elderly and young volunteers despite the mild cervical degenerative changes in elderly persons.<sup>4</sup>

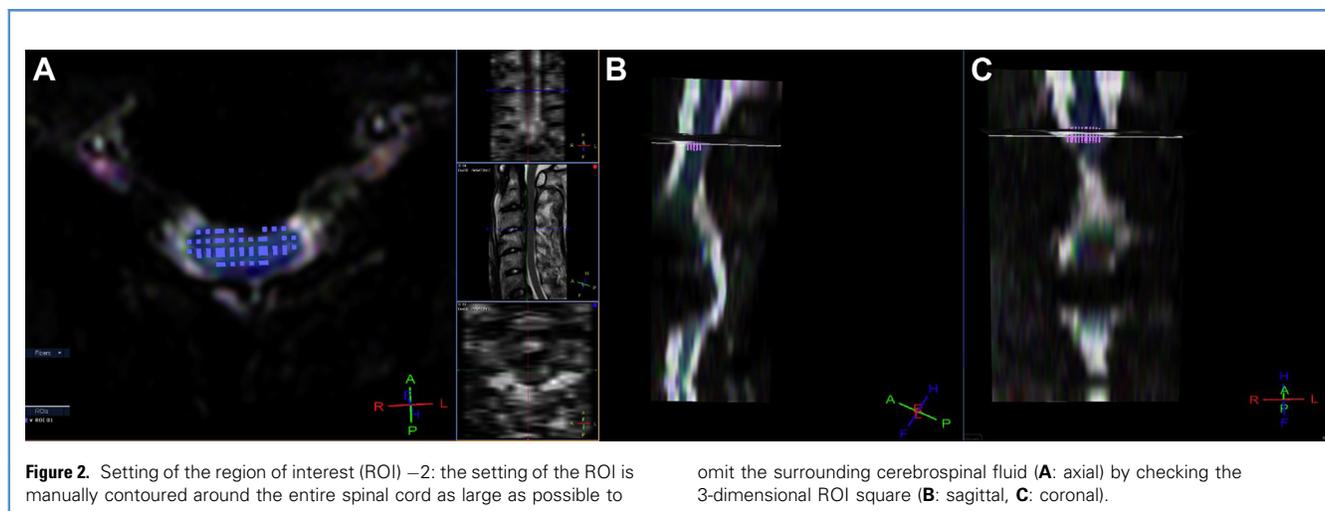
With respect to chronic traumatic SCI, Rao et al.<sup>5</sup> reported that all patients with SCI had significantly decreased FA values in both residual and remote normal fibers using 3.0-Tesla MRI. Wang et al.<sup>6</sup> also reported that patients with amyotrophic lateral sclerosis had significantly lower FA values than the control group. There is no doubt that the injured cord with edema has a decreased FA value. However, in patients with CSM, the neural fiber condition varies in its severity because of damage to the spinal cord;

therefore, it is possible that most of the fibers in patients with CSM avoid severe damage and most are only compressed, which can differ from the pathology of SCI or neurodegenerative disease without compression. Most of the previous studies reported that the preoperative FA value in patients with cervical spondylosis was low and that this was a prognostic factor.<sup>9,10,15,16</sup> Bhosale et al.<sup>16</sup> reported the reduction in FA at the stenotic level significantly improved after surgery; however, this study is performed by 1.5-Tesla MRI and there are no concrete numerical data of pre- and postsurgical FA values. Banaszek et al.<sup>17</sup> also reported a significant decrease in the FA value even in the presence of only subarachnoid space obliteration without any compression or T2-weighted imaging signal change in the spinal cord in 132 symptomatic patients with cervical spondylosis compared with control groups. However, this study used 1.5-Tesla MRI and includes radiculopathy, which can contradict itself. Although a few studies have used 3-Tesla MRI,<sup>7,18</sup> the signal-to-noise ratio and resolution of spinal cord DTI are still limited. In the systematic review of DTI in patients with CSM reported by Rindler et al., even though there were 4 reports using 3-Tesla MRI, most of FOV values were larger (approximately 200 × 200 mm<sup>2</sup>) than our study of the ZOOM DTI method (70 × 47 mm<sup>2</sup>). We reported that ZOOM DTI was superior to conventional DTI for inter- and intrarater reliability.<sup>3</sup> The visibility and distortion ratio were better, and the SD was smaller in ZOOM DTI; however, they were estimated in the same 3-Tesla MRI instrument. Regarding the size of the FOV, ZOOM DTI is the smallest in past reports (e.g., 53 × 140 mm<sup>2</sup> by Ellingson et al.<sup>19</sup>). They also assessed cervical stenosis and the average FA value at C1-2 was 0.61, whereas the average FA at the site of compression was 0.50, which was significantly lower. However, we have reported that the FA value at the lower cervical level of

**Table 4.** Prognostic Assessment by the Japanese Orthopaedic Association Assessment

JOA Score	Mean ± SD	Relationship with Each FA Value (P Value)		
		FA Presurgery	FA at 1 Week	FA at 6 Months
JOA score presurgery	10.8 ± 3.34	0.5646	0.0049*	0.6946
JOA score at 6 months	13.1 ± 2.75	0.4085	0.0263*	0.0650
JOA score at 1 year	14.3 ± 2.24	0.1721	0.0593	0.3938

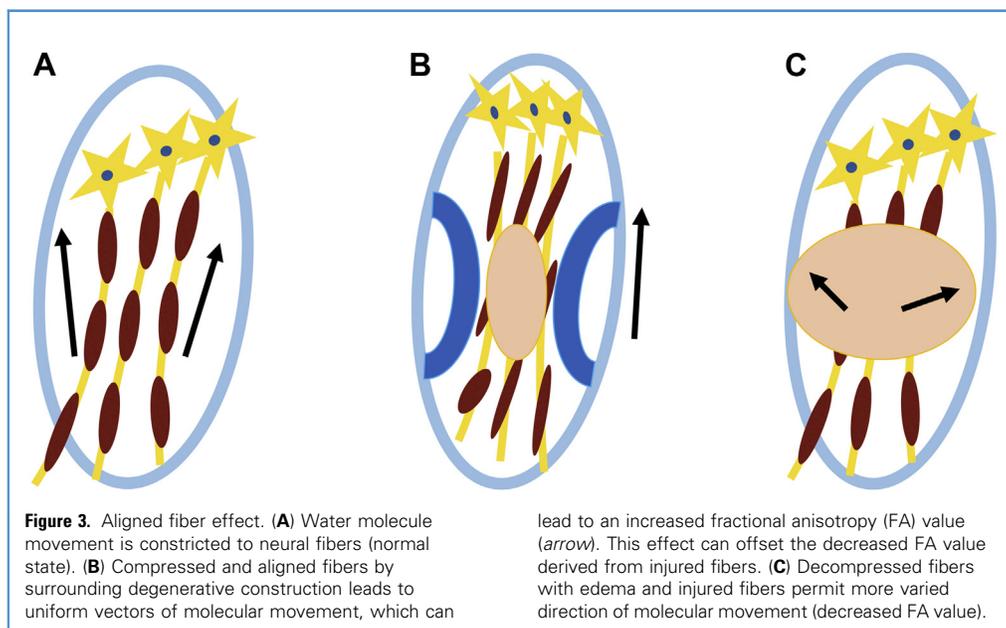
FA, fractional anisotropy; JOA, Japanese Orthopaedic Association.  
\*Significant difference by repeated-measures design.



normal control subjects is gradually decreased because of artifacts<sup>3</sup>; therefore, lower FA values in the same spinal cord can be a regular phenomenon.

Given these previous reports and our results, we concluded that the preoperative FA value in patients with CSM is not necessarily lower and in line with that of patients with a damaged cord without any compression. In our hypothesis, the vectors of the molecular movement in compressed and aligned neural fibers lead to a uniform direction that causes a slight increase in the FA value, which may be a masked effect by offsetting the dispersion of vectors in the damaged edematous spinal cord. The significant decrease in the FA value after decompression surgery of the intracordal high signal group indicates that the postoperative FA value approximates the proper

state of the cord by omitting the preoperative aligned fiber effect (**Figure 3**). The essential FA values without any compression in the intracordal high signal group should be lower because of its edema and fiber damage. That is, the preoperative FA value is determined by the balance between injury with edema and compression of the spinal cord. Therefore, the postoperative FA value can be a prognostic factor for patients with CSM. In our study, only the FA value at 1 week postsurgery had a significant positive relationship with the JOA score at presurgery and at 6 months after surgery, which confirms our hypothesis. In addition, because spinal cord edema disappears in the chronic stage, the FA value must be improved. The FA value at 6 months after surgery was higher than the FA value at 1 week after surgery in our results, which relates to the



clinical time course. The JOA score at 1 year after surgery did not have a significant positive relationship with the FA value at 1 week after surgery; however, most patients were older than 70 years old in our study. They had other complications, which might have affected the JOA score.

## CONCLUSIONS

The presurgical FA value in patients with CSM did not differ from the FA value of normal control subjects, but significantly decreased after cervical decompression surgery, and significantly increased 6 months after surgery, which was remarkable in intracordal high signal intensity patients. We concluded that the

postsurgical FA value approximates the proper state of the damaged cord and the presurgical FA value includes a masked effect as aligned fiber effect because of compression by degenerative construction. Only the FA value at 1 week after surgery had a significant positive relationship with the JOA score at presurgery and at 6 months after surgery, which established that the postsurgical FA value may be a more accurate prognostic factor than the presurgical FA value.

## DECLARATION OF COMPETING INTEREST

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