

ARTICLE



Clinical application of diffusion tensor tractography to postoperative C5 palsy

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STUDY DESIGN: Diagnostic study.

OBJECTIVE: Although C5 palsy is a well-known potential complication after cervical procedure, the exact pathophysiology remains uncertain. Diffusion tensor tractography (DTT) has recently been proposed as a useful tool to examine quantitatively and non-invasively the pathology of spinal cord disorders. The purpose of this study is to determine the clinical interest of DTT in patients with C5 palsy after cervical laminoplasty.

SETTING: Single university hospital.

METHODS: Five patients with C5 palsy out of 108 patients after cervical laminoplasty were subjected to DTT using a 1.5 Tesla magnetic resonance imaging in our hospital between 2010 and 2012. For the tractography, two regions of interest (ROI) were placed at the C5 segmental level and the bilateral C4/5 intervertebral foramen level.

RESULTS: The postoperative number of tract fibers at the C5 segmental spinal cord level was significantly increased compared to the preoperative number, despite the C5 palsy. Analyses of two ROIs (at the C5 segmental level and the C4/5 intervertebral foramen level) showed that the number of tract fibers at the palsy side was significantly decreased compared to the intact side. Furthermore, in the patient who spontaneously recovered from C5 palsy within postoperative 6 months, a gradual augmentation of tract fibers was identified at the palsy side.

CONCLUSIONS: Our findings suggest that DTT can document C5 palsy in detail, as the anatomical region between C5 segmental level and C4/5 intervertebral foramen level was potentially damaged in patients with C5 palsy after laminoplasty.

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INTRODUCTION

C5 palsy is a well-known potential clinical complication in ~5–10% [1–3] of cervical spine surgeries. Of the nerve roots contributing to the brachial plexus from the C5–T1 segment, postoperative segmental palsy is most frequently observed in the C5 nerve root. C5 palsy is defined as de novo or aggravating muscle weakness occurring mainly at the C5 region with slight or no sensory disturbance after cervical spine surgery [4]. It typically occurs unilaterally but can rarely present bilaterally. The exact pathophysiology remains uncertain, but it has been attributed to iatrogenic nerve injury during surgery, tethering of the C5 nerve from shifting of the spinal cord [5], spinal cord ischemia, or reperfusion injury of the spinal cord [6, 7].

Diffusion tensor tractography (DTT) is a magnetic resonance imaging (MRI) technique that is based on the diffusion of extracellular water molecules within nerve fibers [8, 9]. DTT analyses allow evaluating the orientation of nerve fibers along specific tracts quantitatively. Furthermore, DTT has been recently applied to the evaluation of spinal cord disorder within primates [10] and human and could enable the assessment of damaged lumbar nerve root under the condition of foraminal stenosis [11]. However, to the best of our knowledge, there are no studies using

DTT to examine the status of nerve fibers in C5 palsy after cervical decompression surgery. In the present study, we analyzed the C5 nerve fibers in five individuals developing postoperative C5 palsy after cervical laminoplasty utilizing DTT and performed the correlation analysis between DTT parameters and post-surgical clinical symptoms.

METHODS

Participants

We analyzed a total of 108 consecutive individuals [88 males and 20 females; the mean age (SD) was 66.1 (11.7) years] who had undergone expansive open-door laminoplasty in our hospital from 2010 to 2012. Eighty-two persons presented cervical spondylotic myelopathy (CSM), while 26 presented ossification of posterior longitudinal ligament (OPLL). The incidence of C5 nerve palsy for the group was five out of 108 (4.6%). Though both C5 and C6 innervate the deltoid, the patients with C6 palsy tend to involve not only shoulder abduction and external rotation but also elbow flexion, and forearm supination [12]. In this study, C5 palsy was defined as weakness of grade 1 or more of the deltoid muscle only by manual muscle test (MMT) without any deterioration of myelopathic symptoms within 1 month after surgery. Among these five patients, four had CSM, one had OPLL. All five cases with C5 palsy were male. Those with

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Table 1. Summary of the demographic data of the five patients with C5 palsy.

Case No.	Age (y)/Gender	Lesion	Level	Days from surgery C5 palsy onset	MMT grade preoperation at onset FU	Palsy side	Months to recovery	Days from surgery DTT analysis
1	62/M	CSM	C3-6	7	5 1 3	Right	12	29
2	73/M	CSM	C2-7	5	5 1 5	Left	12	133
3	56/M	CSM	C3-6	4	5 2 5	Right	6	8
4	40/M	CSM	C4-6	5	5 1 5	Right	9	9
5	67/M	OPLL	C3-7	2	5 1 4	Right	6	15

CSM indicates cervical spondylotic myelopathy.

OPLL ossification of posterior longitudinal ligament, MMT manual muscle testing, FU follow-up.

postoperative C5 palsy underwent DTT immediately after obtaining their consent. The MMT of the deltoid muscle was used to determine the clinical motor neurological status of C5 nerve root (Table 1).

DTT and data analysis

All five individuals with C5 palsy underwent MRI with a 1.5 Tesla-imaging unit with phased-array cervical coils, both before and after surgery. First, conventional sagittal T1-weighted images [repetition time (TR) 460 ms; echo time (TE) 8.2 ms; slice thickness 4 mm; focus of volume (FOV) 24 × 24 cm²] and T2-weighted images (TR 5000 ms; TE 96.3 ms; slice thickness 4 mm; FOV 24 × 24 cm²) were obtained for general evaluation of the lesions. Diffusion tensor imaging was performed using a spin echo-based echo planar diffusion imaging sequence, covering the whole cervical cord with 4-mm-thick gapless axial sections (TR 9000 ms; TE 84.9 ms; FOV 30 × 30 cm²; imaging matrix 128 × 128, number of excitations (NEX) 5; motion probing gradient orientations 7 axes; *b*-value 1000 s/mm²). Diffusion tensor tractographic images were computed using the Diffusion Toolkit and TrackVis software (Massachusetts General Hospital, MA, USA). The diffusion tensor can be represented as an ellipsoid, where a proton at the center of the voxel has an equal probability of diffusing to any point in that ellipsoid. Fiber tracking was initiated from a manually selected region of interest (ROI), from which tracking lines were propagated bidirectionally according to the principal eigenvector in each voxel. Fiber tracts were generated by placing the ROIs at the level of the C5 segmentation (C3/4 cervical spine level) [13] and the intervertebral foramen of the C5 nerve root (C4/5 cervical spine foramen) with reference to the sagittal MR images, with the threshold fractional anisotropy (FA) value set to 0.3.

Statistical analysis

Statistical analysis was performed using GraphPad Prism (version 9.0), and significance tests were two-sided at a 5% significance level. We compared the number of long tracts at the C5 segmental level before and after surgery, and the number of the C5 nerve root at the intact and the palsy side in the same patients. Data normality was checked using the Shapiro-Wilk test and the Kolmogorov–Smirnov test, and each data was confirmed parametric in these two tests. A paired *t*-test was used to evaluate statistical significance in the number of long tracts and the C5 nerve root in the same patient.

RESULTS

We conducted a retrospective review of five patients (4.3% of individuals that had undergone expansive open-door laminoplasty in our hospital from 2010 to 2012) with C5 palsy (Table 1). To validate the positive surgical outcome for cervical long tracts of the cord, we compared the preoperative number of tract fibers at the C5 segmental level with the postoperative one by setting one ROI at the C5 cord area. The postoperative number of tract fibers was significantly increased compared to the preoperative, despite the C5 palsy (Fig. 1A, B; *p* = 0.0099), suggesting that expansive open-door laminoplasty succeeded in decompressing the cervical cord. To investigate the condition of the C5 nerves in individuals with C5 palsy, analyses at two ROIs (at the C5 segmental level and at the C4/5 intervertebral foramen level) were performed at postoperative status with C5 palsy. Analyses at one ROI (at the C4/5 intervertebral foramen level) showed that the tract fiber of C5 nerve root could not be depicted accurately. The number of tract fibers at the palsy side was significantly decreased compared to the intact side (Fig. 2A, B; *p* = 0.0166). Furthermore, the evaluation of the preoperative C5 nerve root showed that there was no significant difference in the number of the preoperative C5 tract fibers between the postoperative palsy and the intact side within the same patients with C5 palsy (Supplementary Fig. 1; *p* = 0.295).

An illustrative case

This 67-year-old man, who had been complaining of gait disturbance and bilateral hand clumsiness, was referred to our hospital for surgery. His cervical MR images showed spinal cord compression at the level of C3-6, and he was consequently

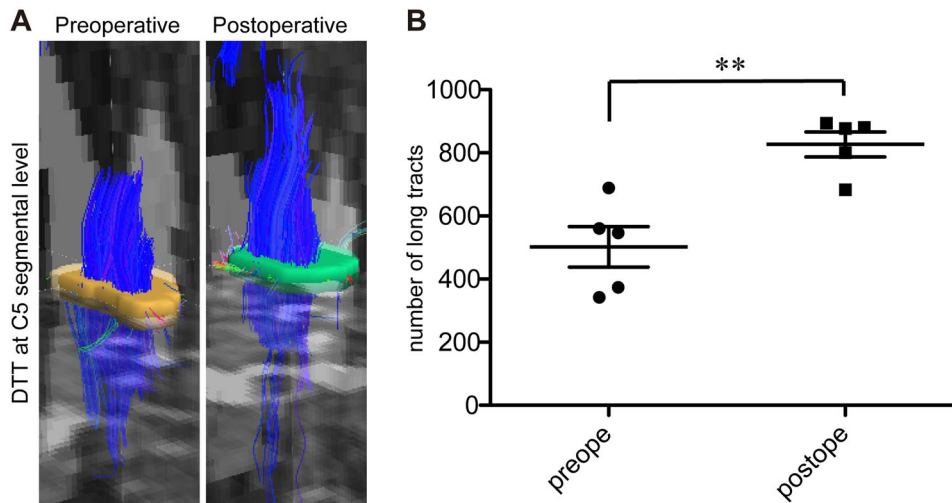


Fig. 1 Comparison of the number of long tracts between preoperative and postoperative patients with C5 palsy. **A** The tract fibers were generated by placing the ROI at the C5 segmental level. **B** There was a significant difference in the number of long tracts between preoperative and postoperative patients. $**p < 0.01$.

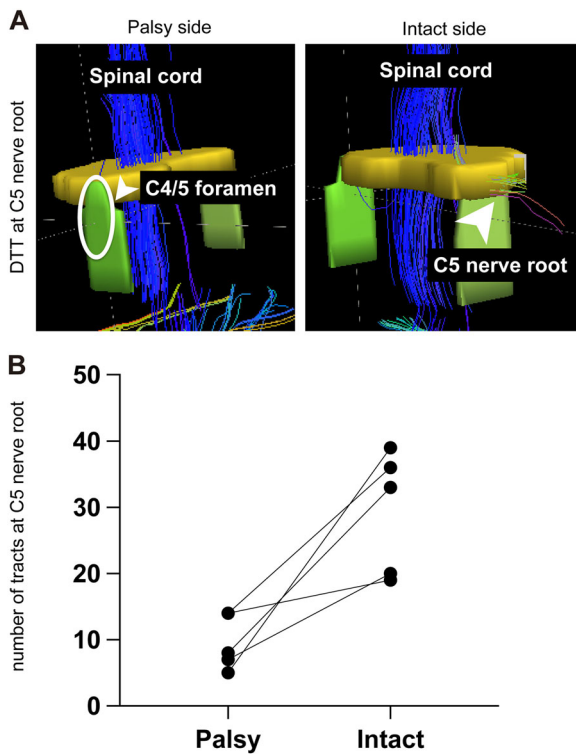


Fig. 2 Comparison of C5 nerve roots between palsy side and intact side in patients with C5 palsy. **A** The tract fibers of C5 nerve roots were generated by setting dual ROIs at the C5 segment and the C4/5 vertebral foramen. **B** There was a significant difference in the number of the C5 tract fibers between the palsy and intact side within patients with C5 palsy (paired comparison: $*p < 0.05$).

diagnosed with CSM. Based on these neurological and imaging assessments, he underwent expansive open-door laminoplasty at the level of C3-6 (Fig. 3A). At 2 days after surgery, he exhibited postoperative C5 palsy on his right upper extremity. We performed DTT analyses and found that the number of tract fibers in his right C5 nerve root was decreased compared with the intact side. Furthermore, along with the spontaneous recovery of his C5 palsy within 6 months after surgery, the

gradual recovery of the number of tract fibers was detected on quantitative DTT evaluation at the palsy side (Fig. 3B, C).

DISCUSSION

In the present study, we show that DTT could depict C5 palsy in detail after cervical decompression surgery. In the illustrative case, we could observe the chronological change of the tract fibers of C5 palsy side in accordance with the spontaneous recovery of the motor deficit in the deltoid muscle. DTT could be used to quantitatively measure C5 nerve fiber damage and appears as a useful tool for monitoring C5 palsy.

Some authors have reported that DTT could be a new diagnostic tool in cervical compression myelopathy after laminoplasty [14–17]. Nakamura et al. suggested that the postoperative DTT tract fibers of the cervical spinal cord correlated significantly with patients' recovery [18]. Kara et al. also reported that DTT could show the abnormalities in compressive spinal cord before the development of T2 hyperintensity on conventional MRI sequences in patients with CSM [19]. To determine the pathological significance of tract fibers of the cervical cord, we previously performed DTT in animal models of spinal cord injury and cervical spinal cord compression [10, 20, 21]. These reports showed that DTT was strongly correlated with nerve fibers-positive area and motor function, suggesting that DTT might reflect the severity of the damage to the axonal fibers.

Recently, some authors reported that DTT could be a diagnostic examination in the lesion of the nerve roots as well [22, 23]. Kitamura et al. showed that DTT demonstrated the compression of the L5 nerve root between the L5 transverse process and the S1 alar [24]. Eguchi et al. also reported that DTT could depict the disruption of the S1 nerve root caused by the disc herniation between the L5 and S1 discs [11]. Although DTT is thought to have great potential for detecting the lumbar root, it has been unclear how DTT would show the pathological change of the C5 palsy.

One of the more striking results of our study was that DTT could show the anatomical lesion (ventral root) of C5 palsy and quantitatively measure its degree. To the best of our knowledge, this is the first report to demonstrate the potential of DTT as a useful and diagnostic MRI tool to reveal the pathology of C5 palsy.

Our study has several limitations. First, the number of patients included in this study is small. It is difficult to increase the number

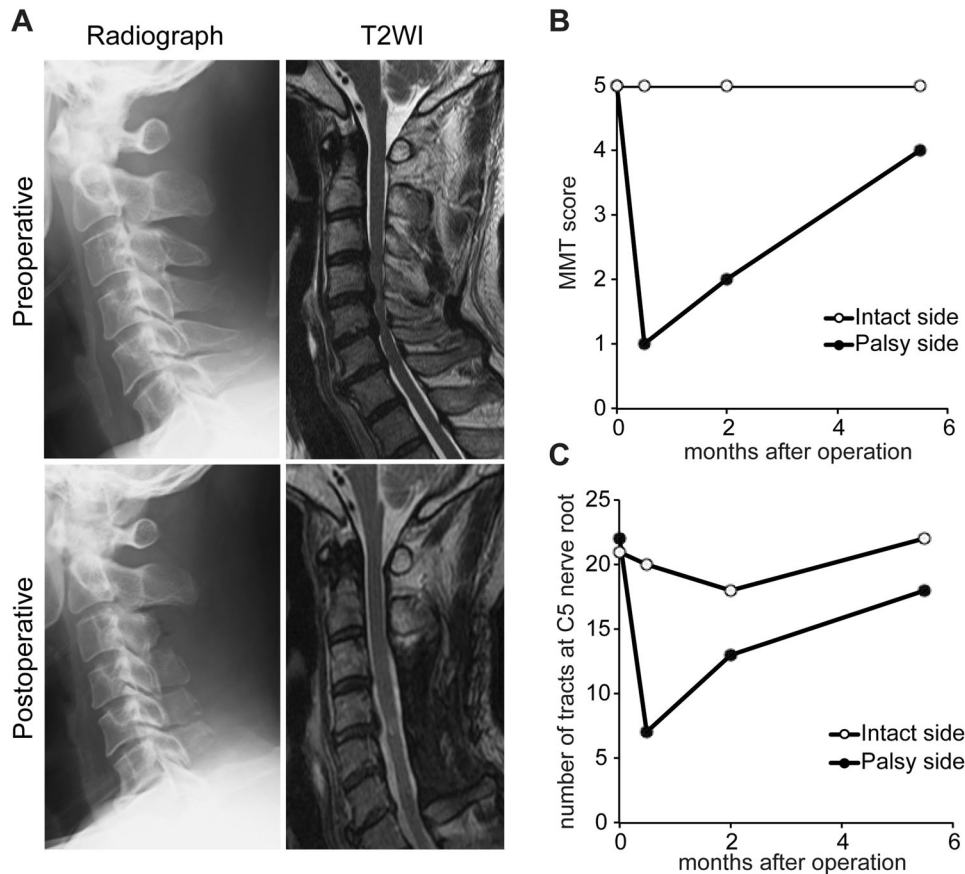


Fig. 3 Representative case: a 67-year-old man with OPLL. **A** Preoperative T2-weighted MRI (T2WI) showed spinal cord compression at the level of C3–6. C3 laminectomy and C4–6 expansive open-door laminoplasty were performed. **B, C** Time course of MMT and the number of tract fibers in bilateral C5 nerve root. As the MMT score spontaneously recovered, the number of tract fibers in the C5 palsy side increased during 6 months after the operation.

of cases with C5 palsy due to the low incidence of C5 palsy (~5%) and the inability to predict the occurrence of C5 palsy preoperatively [25]. Further studies are therefore needed to investigate whether our findings remain valid in a large population. Second, the spinal instrumentation such as mini-plate system could be an artifact for diffusion MRI technique. Although we did not use implants for the laminoplasty in this study, cervical surgeries will often be needed for the instrumentation. Kobayashi et al. reported that mini-plate fixation in cervical laminoplasty produced comparable clinical outcomes and significantly lowered the incidence of C5 palsy compared with suture suspension [26]. Further studies are needed to consider the conditions for the DTT of C5 palsy using spinal instrumentation. Third, while DTT data is available on the reliability and reproducibility of brain DTI [27, 28], there is little research on the reliability of ROI placement to quantify spinal cord. Although this study was evaluated by free hand ROI as previously reported [29], a robust method of DTT is needed to reduce operator variability in the future [30]. Fourth, while DTT analysis is a good method to evaluate the nerve fibers quantitatively and non-invasively, DTT may not be readily available everywhere like electromyography.

In conclusion, DTT could be clinically applicable to patients with C5 palsy after cervical laminoplasty. The major benefit of this imaging modality will allow the quantitative and selective analysis of human cervical spine nerve roots. Our findings also suggest that the anatomical region between the C5 segmental level and the C4/5 intervertebral foramen level was potentially damaged in patients with C5 palsy after laminoplasty.

DATA AVAILABILITY

The datasets generated during the current study are available from the corresponding author on reasonable request.

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AUTHOR CONTRIBUTIONS

Conceived and designed the experiments: MT, OT, KF, MM, MN, and KW. Performed the experiments: MT, OT, and KF. Analyzed the data: MT, OT, NN, KF, SN, SS, EO, and MY. Contributed reagents/materials/analysis tools: MM, MN, and KW. Wrote the paper: MT, OT, and KW.

COMPETING INTERESTS

The authors declare no competing interests.

ETHICS STATEMENT

The study protocol was conducted in accordance with the Declaration of Helsinki, and in compliance with ethical guidelines for medical and health research involving human subjects and approved by the Ethics Committee and Institutional Review Board of our institute. Written informed consent was obtained from all the participants included in the study.

ADDITIONAL INFORMATION

Supplementary information The online version contains supplementary material available at <https://doi.org/10.1038/s41394-021-00447-w>.

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