Diffusion tensor imaging in the assessment of ossification of the posterior longitudinal ligament: a report on preliminary results in 3 cases and review of the literature

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Ossification of the posterior longitudinal ligament occurs in 25% of patients with CSM,9 which is the most common form of acquired spinal cord dysfunction11 and is present in more than 60% of the population older than 40 years of age.4 Thickening and calcification of the posterior longitudinal ligament play a role in CSM through narrowing of the spinal canal, leading to cord compression. Resultant spinal cord ischemia and trauma are purported mechanisms of injury underlying CSM.2 The MR imaging findings indicative of CSM, such as increased signal (hyperintensity) of the spinal cord on T2-weighted imaging, typically occur late in the disease process and predict poor neurological outcome despite decompression.12,25 Diffusion tensor imaging is a relatively new technique in spinal imaging, with the sensitivity potentially to detect minor SCI prior to irreversible CSM. We describe its application in the preoperative evaluation of patients with cervical spinal stenosis due to OPLL, where signal artifact from calcification further complicates image acquisition.

Pathophysiological Features of CSM in OPLL

Narrowing of the anteroposterior diameter of the cervical spinal canal is correlated with the degree of CSM in OPLL.8,19 As the spinal cord becomes compressed by ossified or hypertrophied ligament and bone spurs, the cushioning effect of CSF is lost. In a series of 200 patients seeking treatment for CSS, 63 (31.5%) reported an episode of minor trauma in the preceding 2 weeks.29 Physiological neck motion, as well as abnormal motion due to cervical instability, which is often associated with spondylosis,22 predisposes the spine to repeated microtrauma.23 Tension applied by dentate ligaments preferentially stretches the lateral aspect of the spinal cord on neck flexion,27 which corresponds to lateral column atrophy noted in autopsy studies. Segmental OPLL has been shown to permit abnormal mobility between adjacent VB segments, with a range of motion > 35° at C1–7 associated with progressive myelopathy.20

Other investigators have postulated an ischemic origin. Ito et al.16 studied the spines of 7 patients with CSM at autopsy and found a characteristic pattern of lesion progression, beginning with atrophy and neuronal degeneration of the anterior horn and intermediate zones, followed by atrophy of the lateral and posterior funiculi. End-stage disease was marked by cell death throughout the gray

Abbreviations used in this paper: CSM = cervical spondylotic myelopathy; CSS = cervical spinal stenosis; DT = diffusion tensor; FA = fractional anisotropy; mJOA = modified Japanese Orthopaedic Association; OPLL = ossification of the posterior longitudinal ligament; SCI = spinal cord injury; VB = vertebral body.
matter and severe degeneration of the lateral funiculi. Although vascular occlusion or compression was not identified, the pattern of degeneration appeared consistent with generalized hypoperfusion. The authors postulated that increased intraspinal pressure may have reduced spinal perfusion to the stenotic region. Spinal hypoperfusion has been demonstrated in animal models, in which posterior compression resulted in reduced blood flow to the central gray matter through intramedullary branches. Turnbull et al. examined histological sections through the human spinal cord and noted that the small arteries and veins of the lateral columns and gray matter became stenotic on cord compression in the anteroposterior plane. Vessels supplying the anterior and posterior columns, on the other hand, remained patent. This correlates with the pattern of degeneration in CSM. Nevertheless, the relative contributions of trauma and ischemia have yet to be fully elucidated in live human subjects. Noninvasive MR perfusion and vascular permeability techniques being developed in step with spinal DT imaging protocols may provide more definitive evidence. Regardless of the mechanism, reproducible patterns of neural degeneration are found on imaging modalities such as DT studies.

**Diffusion Tensor Imaging**

Water molecules in a solution move freely and randomly in a process termed Brownian motion. Such isotropic diffusion lacks preference in any particular direction. The gray matter of the brain approximates this situation, because normal cell membranes allow for isotropic diffusion of water in this region. Myelin and axonal membranes of white matter, in contrast, present barriers to water diffusion in directions perpendicular to their long axis. Water moves anisotropically; that is, much more freely within the axonal plane than across it. Application of a directional diffusion gradient to heavily T2-weighted echo planar MR imaging sequences measures the spin of protons in water and can be used to track their movement over time. This principle forms the basis of DT imaging, in which diffusion of protons is tracked in 3 perpendicular orientations (x, y, and z) or eigenvectors. The principal eigenvector denotes the orientation of greatest diffusion and is subtracted from the 2 orthogonal middle and minor eigenvectors to calculate FA. The mean diffusivity value is an average of the 3 eigenvectors, analogous to apparent diffusion coefficient values in conventional diffusion-weighted images.

**Acquisition of DT Imaging for the Cervical Spine**

Diffusion-weighted imaging has proven utility in brain MR imaging for the assessment of acute ischemia and to identify fiber tracts preoperatively. However, spinal applications have lagged behind, in large part due to technical difficulties involving image acquisition. The spinal cord is a small structure relative to the brain and has a limited signal-to-noise ratio. Pulsations of CSF, breathing, and patient movement contribute to motion artifacts. Surrounding bone and calcified ligament, especially in the context of OPLL, produce susceptibility artifacts that further degrade image quality. However, the prevalence of 3-T magnets, with an increased signal-to-noise ratio compared with 1.5-T units, has accelerated acquisition time and reduced artifacts through parallel imaging and periodically rotated overlapping parallel lines with enhanced reconstruction (also known as PROPELLER) techniques. This has enabled performance of DT imaging protocols on most clinical MR imagers. Software bundled with MR imagers and available free over the internet, such as DTI Studio (http://lbam.med.jhmi.edu/DTIuser/DTIuser.asp), can process raw data into useful representations for evaluation by the neurosurgeon.

**Clinical Application of DT Imaging**

Fractional anisotropy values have demonstrated superior sensitivity in detecting SCI compared with increased T2 signal intensity in studies of patients with CSM. This raises the possibility of using DT imaging to distinguish patients with permanent myelopathic injury, reversible myelopathic injury, and absence of myelopathic change. Budzik et al. correlated mJOA scores with DT imaging results in 20 patients with CSM and found lower FA values in those with worse clinical function. The mean upper- and lower-extremity mJOA scores of 76.1 and 63.4, respectively, in this mildly affected population underscore the high sensitivity of DT imaging in detecting white matter damage. Measurements of T2 signal hyperintensity, on the other hand, did not show a relationship with regard to function. Correlation coefficients between FA values and mJOA score were not reported, however, and follow-up clinical data after surgery are also missing from this study. Facon et al. conducted a similar study of 6 patients with CSM and reported confirmatory results. Statistically significant reductions in FA between patients and healthy controls (p = 0.012) were noted with a sensitivity of 73.3% compared with a sensitivity of 46.7% with T2 signal hyperintensity. Myelopathy was qualitatively assessed by simply noting “motor deficit” or “sensory deficit.”

Sensitivity may be improved further by parsing eigenvectors and analyzing major, middle, and minor vectors separately. Axonal edema and protein degradation associated with compressive demyelination have been shown to increase middle and minor eigenvectors while sparing the major vector in animal models. Preliminary studies by Hesseltine et al. have shown this dissociation in 11 patients with CSM. Biomarkers specific for myelin breakdown may have prognostic value, because remyelination plays a role in functional improvement following decompression. A larger study of 84 patients found similar discrepancies between eigenvectors in mild CSS with effacement of the subarachnoid space alone, whereas cord compression resulted in reduced FA values. Unfortunately, a clinical correlation was not performed.

The practice of comparing DT imaging to T2 hyperintensity, a measure with poor sensitivity and weak prognostic value, underscores the lack of a clinical or imaging gold standard when assessing CSS. Currently, it is not known whether DT imaging can distinguish patients with permanent myelopathic injury, reversible myelopathic injury, and absence of myelopathic change. A prospective
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trial addressing this issue is currently under way at our institution.

Illustrative Cases

Case 1

This 57-year-old woman was evaluated at our institution for neck and bilateral upper-extremity pain. Neurological examination revealed grip strength of 4/5 bilaterally, with numbness in her hands and feet. The Babinski sign was positive bilaterally. Her mJOA, Nurick, and Oswestry scores prior to surgery were 8, 3, and 62, respectively. An admission CT scan of the cervical spine revealed continuous OPLL between the C-3 and C-4 VBs and posterior to C-5, with mild to moderate central canal stenosis at C3–4 and C4–5 (Fig. 1). Standard anatomical MR imaging of the cervical spine showed multilevel disc disease, with severe central canal stenosis at C4–5 accompanied by signal abnormality within the spinal cord (Fig. 2A). Diffusion tensor images were highly suggestive of axonal injury, with greater than 50% loss of FA in the left corticospinal tract (Fig. 2C). At 3 months after C4–6 anterior cervical discectomy and fusion and C3–T2 posterior spinal fusion, the patient’s mJOA and Oswestry scores improved to 12 and 49, respectively. Her Nurick score remained the same.

Case 2

This 52-year-old man presented with complaints of neck pain and left upper-extremity pain and numbness. Neurological examination revealed hyperreflexia of the bilateral upper extremities, positive Hoffman sign of the left upper extremity, and bilateral Babinski signs. Preoperatively, his mJOA, Nurick, and Oswestry scores were 7, 4, and 78, respectively. Standard MR imaging of the cervical spine (Fig. 3A) demonstrated multilevel spondylosis, worst at C6–7, where a disc-osteophyte complex resulted in moderate CSS. No signal abnormality within the spinal cord was noted. The DT imaging findings (Fig. 3B–E) included a marked reduction in FA at C6–7, below even the threshold of fiber tracking. The patient subsequently underwent a C4–7 anterior cervical discectomy and fusion, based primarily on clinical deterioration consistent with progressive CSM. His follow-up mJOA, Nurick, and Oswestry scores at 4 months improved to 10, 3, and 72, respectively.

Case 3

This 82-year-old man presented with neck pain radiating to his left upper extremity. Neurological examination demonstrated diffuse 3+/4 hyperreflexia and broad-based ataxic gait. His mJOA, Nurick, and Oswestry scores were 14, 1, and 34, respectively. An admission CT scan of the cervical spine revealed extensive continuous OPLL from C-3 to C-7, with moderate to severe spinal canal narrowing (Fig. 4). Standard MR imaging showed compression of the spinal cord and questionably associated signal abnormality within the cord at the level of the C-6 VB (Fig. 5A). The FA values at the level of worst stenosis, however, were suggestive of preserved white matter tracts (Fig. 5B). Despite the finding of severe stenosis on conventional MR imaging, the patient was only mildly symptomatic from CSM. Given his age and medical comorbidities, the patient is currently being monitored conservatively with serial neurological examination for his OPLL with cervical stenosis.

These illustrative cases describe how DT imaging...
might quantify the degree of SCI, yet a clinical trial with rigorous statistical analysis is necessary to confirm such anecdotal reports.

**Discussion**

Based on several experimental and early clinical studies, DT imaging of the cervical spine appears to manifest improved sensitivity in the detection of myelopathy compared with conventional anatomical MR imaging. By examining changes in FA levels, DT imaging can detect abnormal values seen early in the course of myelopathy that may be otherwise clinically asymptomatic or undetectable by standard MR imaging protocol. The increase in sensitivity to detect myelopathic changes by DT imaging can potentially improve clinicians’ ability to determine the most optimal treatment for patients with OPLL and other forms of cervical myelopathy. Patients who are mildly symptomatic or who harbor only mild to moderate stenosis on conventional MR imaging but who demonstrate FA values suggestive of axonal injury, may benefit from early surgical decompression. On the other hand, patients with severe stenosis who present with mild or no clinical myelopathy symptoms or signs and normal FA values on DT imaging can perhaps be monitored with serial neurological examination and imaging.

The ability to detect physiological changes accurately using noninvasive imaging modalities such as DT imaging can be particularly valuable in the management of OPLL. Although the incidence of OPLL is low compared with spondylotic myelopathy, complications from surgical treatment of OPLL are significantly higher. The ability to determine with accuracy the subgroup of patients who have incurred axonal injury from OPLL prior to major clinical manifestations may allow clinicians to select those who will benefit from prophylactic decompression prior to the onset of irreversible CSM. Conversely, undesired perioperative risks associated with OPLL may be avoided in patients without findings of axonal injury on DT imaging, despite the appearance of stenosis on conventional MR imaging.

At this time, DT imaging remains an experimental modality in the evaluation of cervical myelopathy. The advantage of this modality over conventional MR imaging is its ability to quantify minor axonal injury that is other-

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**Fig. 3.** A T2-weighted MR imaging study (A) of the cervical spine shows loss of lordosis and moderate CSS that is worst at C6–7 without signal change within the spinal cord. The DT imaging studies demonstrate a 35% decrease in FA values between the C2–3 and C6–7 levels (B–D). The FA values were below the threshold for fiber tracking, leading to a gap on the composite image (E).

**Fig. 4.** Sagittal CT scan of the cervical spine showing continuous OPLL with severe central spinal canal stenosis.
sults in 3 patients demonstrate that DT imaging is feasible in OPLL despite central canal narrowing and susceptibility artifact from the ossified ligament. Further studies are needed to better interpret FA and fiber tracking metrics by correlating the findings on DT imaging to the clinical symptoms. Clinical studies with larger patient cohorts designed to evaluate the sensitivity and specificity of DT imaging are needed to determine the utility of this modality to identify patients at risk for progressive myelopathy or possibly to predict treatment outcome. In conjunction with clinical findings, advanced MR techniques such as DT imaging may provide clinicians with the pertinent information needed to predict treatment outcome and determine optimal timing of surgical decompression.

**Disclosure**

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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