Original Article

Role of Diffusion Tensor Imaging Scores in Patients with Spinal Trauma

Ankur Malhotra, Mohini Chaudhary, Arjit Agarwal, Shruti Chandak, Deepak Singla

Department of Radiodiagnosis, Teerthanker Mahaveer Medical College and Research Centre, Moradabad, Uttar Pradesh, India

Abstract

Background: Many patients of spinal trauma who have an apparently normal conventional magnetic resonance imaging (MRI) scan ultimately progress to neurological degradation in the long run. Diffusion tensor imaging (DTI) can play a vital role in such patients and can be used to assess the true extent of injury. **Aims:** The aims are to study the utility of DTI in detecting abnormalities in patients with spinal cord trauma and to obtain DTI scores. **Materials and Methods:** The study comprised 30 individuals including 20 cases and 10 apparently healthy controls who underwent conventional MRI, followed by DTI of involved spine. Fractional anisotropy (FA) and apparent diffusion coefficient (ADC) values were obtained by planning three regions of interest in the spinal cord at, above, and below the level of trauma. **Results:** Signal changes in the cord on conventional MRI were seen in 8 cases and were absent in 12. A significant difference was observed in mean FA values at the level of injury in cases without any change in signal intensity in the cord on conventional MRI (0.391 ± 0.12) as compared to controls (0.65 ± 0.165) as well as in mean ADC values in cases (1.534 ± 0.511) and controls (1.132 ± 0.616). **Conclusions:** DTI is an invaluable modality in assessment of the spinal cord following traumatic injury because it can detect subtle disruption of white matter leading to significant difference in the FA and ADC values.

Keywords: Apparent diffusion coefficient, diffusion tensor imaging, fractional anisotropy, magnetic resonance imaging, spinal cord trauma

Introduction

Spinal trauma is one of the important causes of morbidity throughout the world. The increasing number of high-speed Road Traffic Accidents has led to a drastic rise in number of patients with traumatic spinal cord injury (TSCI). TSCI leads to potentially upsetting consequences regarding physical, emotional, social, and vocational conditions of the patients. It has a very significant impact over lives of not only the injured persons but also their families as well. Without timely treatment and proper rehabilitation, there is the risk of lifelong complications of motor, sensory, and autonomic dysfunction. The prognosis of neurological recovery following TSCI is difficult and uncertain.

Radiography and multidetector computed tomography are the investigations used for detection of bony spinal injuries. Magnetic resonance imaging (MRI) is indispensable for the assessment of injuries involving the spinal cord and soft tissues and is being extensively used as an ideal noninvasive technique for evaluation of patients with TSCI.[1] However, there are many patients of spinal trauma who have an apparently normal conventional MRI scan and ultimately progress to neurological degradation in the long run. Diffusion tensor imaging (DTI), being a relatively newer MRI technique, has the property of noninvasively producing quantitative information regarding the direction as well as integrity of the white matter tracts and to detect pathology in those areas that are apparently normal on the conventional MRI.[2-4] The role of DTI to detect abnormalities in the spinal cord which appears normal on conventional MRI has been proposed previously, and thus, it can be used to assess the true extent of injury.[5]

In this study, we aim to obtain DTI parameters in patients with spinal trauma and to compare them with apparently healthy

Address for correspondence: Dr. Shruti Chandak, Department of Radiodiagnosis, Teerthanker Mahaveer Medical College and Research Centre, Moradabad - 244 001, Uttar Pradesh, India.
E-mail: chandakshruti@yahoo.com

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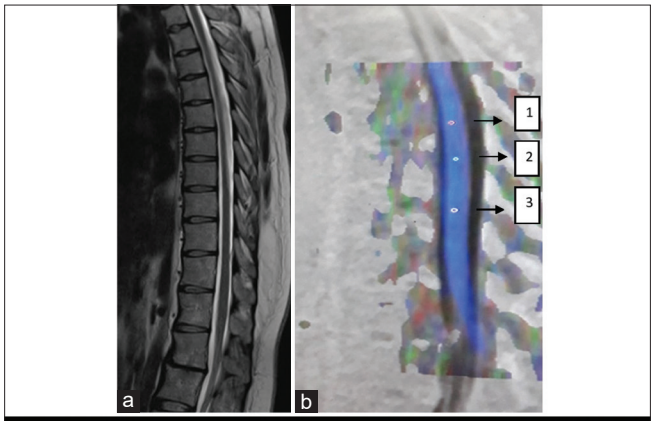
controls and also to find the correlation between conventional MRI spine and DTI scores in patients of traumatic spinal injury.

Materials and Methods

The institutional ethical committee approved the study. All the patients involved in our study were enrolled only after obtaining written informed consent. The study population comprised 30 individuals including 10 apparently healthy age- and sex-matched controls for comparison purpose. Patients with spinal trauma (within 2 weeks of injury) coming to the radiology department for spinal MRI were included in the study as cases. Patients undergoing spinal MRI for other indications such as low backache who had a normal conventional MRI were taken as controls. Patients having contraindication for undergoing MRI were excluded from the study. All patients underwent MRI of the spine using 1.5 Tesla Siemens Avanto machine using spine coils. Conventional MRI images were obtained first, followed by DTI of the involved spine. Apparent diffusion coefficient (ADC) and fractional anisotropy (FA) values were obtained by planning region of interest in the spinal cord at, above, and below the level of trauma in cases as well as controls [Figure 1]. Signal intensity was considered increased in conventional MRI T2-weighted sequence if there was a hyperintense signal in the cord at the site of injury as compared to the unaffected spinal cord.

The data were entered in Microsoft Excel sheet (2010 version, Microsoft Corporation, Redmond, Washington, USA). Statistical analysis was performed using SPSS analyzer (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp). Mean and standard deviation were obtained. The results were considered to be "statistically significant" if the *P* values were below 0.05.



ID	FA Mean	FA SDev	FA Size / Min / Max	ADC Mean	ADC SDev	ADC Size / Min / Max	TraceW Mean	TraceW SDev	TraceW Size / Min / Max	Anat Mean	Anat SDev	Anat Size / Min / Max
1	529.0	0.0	1 / 529 / 529	948.0	0.0	1 / 948 / 948	69.0	0.0	1 / 69 / 69	2011.0	0.0	1 / 2011 / 2011
2	378.0	0.0	1 / 378 / 378	887.0	0.0	1 / 887 / 887	69.0	0.0	1 / 69 / 69	2011.0	0.0	1 / 2011 / 2011
3	686.0	0.0	1 / 686 / 686	861.0	0.0	1 / 861 / 861	48.0	0.0	1 / 48 / 48	2031.0	7.5	4 / 2023 / 2039

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Figure 1: (a) Magnetic resonance imaging T2-weighted sagittal image in a healthy control showing normal spinal cord. (b) Diffusion tensor imaging image showing placement of three regions of interest. (c) Chart showing normal fractional anisotropy and apparent diffusion coefficient values at the three regions of interest

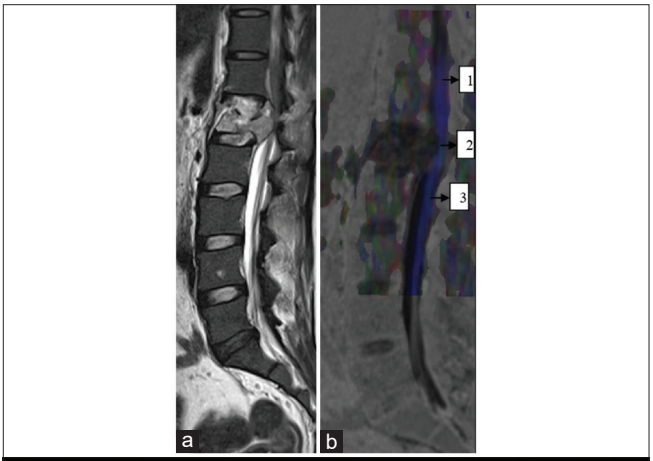
Results

The study consists of 30 individuals, with 20 cases and 10 controls. The mean age of the cases was 38.8 years and that of controls was 40.4 years.

The mean ADC value between cases and controls was compared using the unpaired Student's *t*-test [Table 1]. No significant difference in mean ADC values was noted above and below the level of trauma among cases and controls. However, the mean ADC value at injury level among cases (1.58 ± 0.52) was significantly more as compared to values in controls (1.132 ± 0.616). The mean FA value was also similarly compared between cases and controls [Table 2]. The mean FA value at the level of trauma among cases (0.334 ± 0.155) was significantly lesser than that of controls (0.65 ± 0.165) [Figure 2].

The Chi-square test was used to analyze the signal changes in the cord on conventional MRI, and this was compared between the cases and the control group [Table 3]. Signal intensity changes in the spinal cord on conventional MRI were seen in 8 cases and were absent in 12.

The DTI values were also compared at the level of trauma in cases without cord signal changes and controls [Table 4]. The



ID	FA Mean	FA SDev	FA Size / Min / Max	ADC Mean	ADC SDev	ADC Size / Min / Max	TraceW Mean	TraceW SDev	TraceW Size / Min / Max	Anat Mean	Anat SDev	Anat Size / Min / Max
1	566.0	0.0	1 / 566 / 566	736.0	0.0	1 / 736 / 736	69.0	0.0	1 / 69 / 69	2037.2	1.6	13 / 2035 / 2040
2	268.0	0.0	1 / 268 / 268	1575.0	0.0	1 / 1575 / 1575	28.0	0.0	1 / 28 / 28	2030.3	13.7	11 / 2008 / 2048
3	438.0	0.0	1 / 438 / 438	1491.0	0.0	1 / 1491 / 1491	37.0	0.0	1 / 37 / 37	2015.7	8.9	10 / 2000 / 2025

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Figure 2: (a) Magnetic resonance imaging T2-weighted sagittal image in a trauma patient showing compression fracture of lumbar vertebra. (b) Diffusion tensor imaging image showing placement of three regions of interest at, above, and below the level of injury. (c) Chart showing reduced fractional anisotropy and raised apparent diffusion coefficient values at injury level

Table 1: Comparison of mean apparent diffusion coefficient value between cases and controls

ADC value	Groups	Mean ADC±SD	Mean difference	*t*-test	*P*
Above the level of injury	Case	1.02±0.29	−0.11	−0.969	0.341
	Control	1.13±0.61			
At the level of injury	Case	1.58±0.45	0.43	2.390	0.024*
	Control	1.13±0.61			
Below the level of injury	Case	0.99±0.20	−0.13	-0.684	0.499
	Control	1.13±0.61			

Unpaired *t*-test. *Significant difference. ADC: Apparent diffusion coefficient, SD: Standard deviation

Table 2: Comparison of mean fractional anisotropy value between cases and controls

FA value	Groups	Mean±SD	Mean difference	*t*-test	*P*
Above	Case	0.599±0.153	−0.016	−0.160	0.874
	Control	0.616±0.164			
At the level	Case	0.334±0.155	−0.282	−5.140	0.001*
	Control	0.616±0.164			
Below	Case	0.593±0.166	−0.023	−1.457	0.156
	Control	0.616±0.164			

Unpaired *t*-test. *Significant difference. FA: Fractional anisotropy, SD: Standard deviation

Table 3: Comparison of cord intensity changes on conventional magnetic resonance imaging sequences in cases and controls

Signal intensity changes in spinal cord on conventional MRI sequences	Case	Control	Total
Absent	12 (60.0)	10 (100.0)	22 (73.3)
Present	8 (40.0)	0 (0.0)	8 (26.7)
Total	20 (100.0)	10 (100.0)	30 (100.0)
P		0.020*	

Chi-square test. *Significant difference. MRI: Magnetic resonance imaging

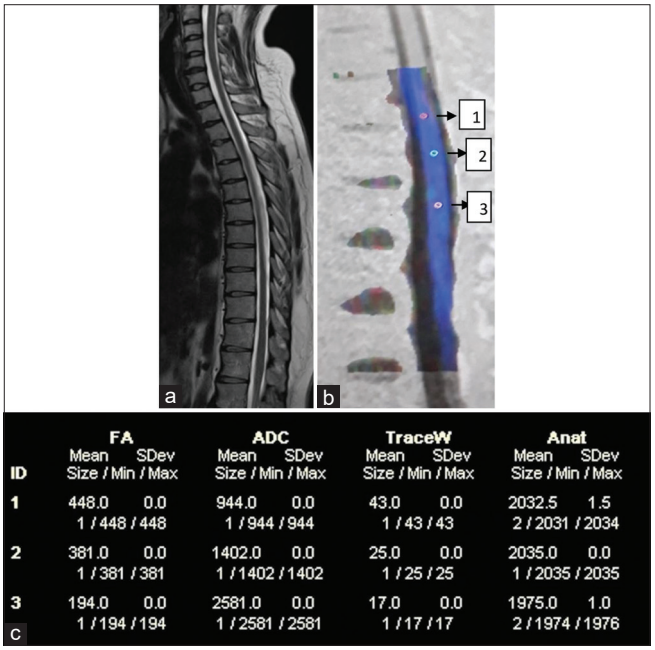

Figure 3: (a) Magnetic resonance imaging T2-weighted sagittal image in traumatic injury patient showing normal signal intensity of the spinal cord. (b) Diffusion tensor imaging image showing placements of three regions of interest. (c) Chart showing reduced fractional anisotropy and raised apparent diffusion coefficient values in the cord despite normal conventional magnetic resonance imaging

mean FA value at injury level in cases without any cord intensity changes on standard MRI (0.391 ± 0.12) was significantly lesser compared to controls (0.65 ± 0.165). The mean ADC value at injury level among cases without any changes in the cord signal intensity (1.534 ± 0.511) was significantly higher as compared to controls (1.132 ± 0.616) [Figure 3].

Discussion

Detection and assessment of spinal trauma is primarily dependent on diagnostic imaging. Tremendous changes have occurred in the imaging evaluation of these patients in the last few years. MRI is presently modality of choice for evaluating patients after TSCI, especially among cases of Spinal Cord Injury without Radiographic Abnormality (SCIWORA), which has been defined "as clinical symptoms of traumatic myelopathy with no radiographic or computed tomographic features of spinal fracture or instability."[6] Nowadays, conventional MRI is routinely performed to delineate injuries to the spinal cord, ligaments, and other soft tissues. The numerous benefits of MRI such as better contrast resolution, multiplanar imaging, and different sequences make it an excellent modality to diagnose spinal injuries more precisely.[7-9]

Conventional MRI is based mainly on signal intensity alteration for portrayal of abnormality.[10] Past studies reveal uncertainty about the association of MRI findings and the extent of neurological injury, although spinal cord edema and hemorrhage may help to forecast neurologic outcome.[11-13] On the other hand, some authors propose that myeloedema and hemorrhage may not effectively estimate the actual functional neurological deficit.[14]

DTI has been estimated to be an innovative MRI sequence which evaluates the integrity of microstructure of nerve fiber tracts. It relies on the molecular diffusion of water molecules in tissues. Within neural tissues, the diffusion is anisotropic since the mobility of water molecules is limited to one specific

Table 4: Comparison of diffusion tensor imaging values in cases without signal intensity changes and controls

	Groups	Mean ± SD	Mean difference	*t*-test	*P*
ADC at the level of injury	Cases without signal intensity changes	1.53±0.51	380.65	2.153	0.045*
	Controls	1.13±0.61	380.65		
FA at the level of injury	Cases without signal intensity changes	0.391±0.12	−359.05	−5.896	0.001*
	Controls	0.65±0.16	−359.05		

Unpaired *t*-test. *Significant difference. ADC: Apparent diffusion coefficient, SD: Standard deviation, FA: Fractional anisotropy

route by biological barricades such as cellular membranes and myelin sheath. Any disruption or modification of this facilitated molecular diffusion anywhere along the neuronal path can herald a disturbance in the physiology which explains why DTI is most sensitive to initial changes, even earlier than the appearance of gross physical changes on conventional MRI sequences.[15,16] DTI is presently the only noninvasive technique for evaluation of integrity of white matter tracts in living beings.[17,18]

The diffusion pattern is indicated by FA which ranges from 0 to 1. Totally isotropic diffusion is indicated by a value of 0, whereas extremely anisotropic diffusion is indicated by 1. The ADC quantifies the diffusion magnitude with increased values of ADC indicating smaller amount of restriction which, in turn, implies less amount of undamaged fibers.[19]

It is imperative to know alterations in normal values of DTI regarding factors which may potentially influence them to deliver a consistent interpretation of parameters of DTI among patients. Previous studies conducted by Ellingson *et al*.,[3] Lindberg *et al*.,[20] Mamata *et al*.,[21] Song *et al*.,[22] and Vedantam *et al*.[23] have reported that FA decreases linearly in the rostrocaudal direction. This has been thought probably to be due to the variation in proportion of gray and white matter at different spinal levels.[24] Some differences could be due to interruption of the "directional coherence" of fibers by the exiting nerve roots of brachial plexus in the inferior cervical levels[24] and the varying diameters of axons at different spinal cord levels.[3] In our study, to overcome these variations, the measurement of DTI parameters was made using region of interests at three various anatomic sections of the spinal cord as performed by Ellingson *et al*. in their study.[2]

Vedantam *et al*.[25] concluded that there was no significant correlation between age and DTI metrics in cases <55 years of age. However, in cases ranging between 55 and 85 years, they found a linear and negative association of FA values with age. Studies reported by Mamata *et al*.[21] and Petersen *et al*.[26] showed a substantial effect of age on DTI metrics. However, other researchers have demonstrated no link among these parameters.[27,28] Detailed evaluation of these studies showed that the age range was wider[21] and mean age higher[26] in studies showing a significant age correlation. In addition, a study reported by Lindberg *et al*. demonstrated a negative association of age with FA values in the lateral aspect of the cord.[20] Since our study population consisted mostly of younger individuals, we did not consider the impact of age in our study. The average age of the cases in our study was 38.85 ± 15.68 years and that of controls was 40.40 ± 12.80 years. Furthermore, the assessment of the impact of age on DTI parameters was out of the scope of our study.

Fractional anisotropy values

In recent times, FA has been proposed to be the most extensively used index of anisotropy which facilitates comparison with statistics from other studies. FA is the value which signifies the anisotropic part of diffusion and is the tendency of water molecules to diffuse in one direction and not randomly. FA is being used as anisotropy index due to its rotational invariance and good signal-to-noise ratio.[29]

In our study, we found that FA values were the most sensitive parameter of DTI for assessment of TSCI. We found that the mean FA values at injury level among cases (0.334 ± 0.155) were significantly lesser compared to controls (0.650 ± 0.165). This decrease could be due to the restriction of anisotropic diffusion in the traumatized spinal cord. Since FA values indirectly measure the extent of myelination, higher FA values indicate the integrity of spinal nerves.[10] No significant difference was observed in the mean FA values above or below the injury level in our cases as compared to controls.

Ellingson *et al*. also demonstrated a decrease in FA values in TSCI patients similar to our study. They could also distinguish between patients with complete or incomplete injuries with FA values. They also found that FA values measured at injury level were considerably reduced in patients with chronic TSCI, as compared to healthy controls.[2]

Czyz *et al*.[1] also found that FA values in cases with TSCI were considerably lower as compared to the controls (0.48 and 0.55, respectively). Similarly, Vedantam *et al*.[25] and Rao *et al*.[30] found decreased FA values in TSCI patients compared to neurologically intact volunteers (0.61 and 0.22, respectively).

Our study was also in accordance with the findings of Shanmuganathan *et al*. and Cheran *et al*. who again showed reduced FA values in patients with TSCI as compared to controls.[31,32]

Our study did not reveal any significant difference in mean FA values above or below the injury level, which was in concordance with the findings of D'souza *et al*.[10] who also found the same. However, Kamble *et al*.[33] in their study showed that the FA values in the cord above and below injury level were significantly reduced. They concluded that, as a result of trauma, there is resultant descending as well as

ascending Wallerian degeneration, and this fact leads to altered DTI metrics.

Similar findings were also found by Mohamed *et al*. who conducted a study on DTI in children with spinal trauma.[34] Few other studies have also demonstrated a reduction in FA values distant to the site of trauma or the lesion.[2,35-39] The reason for not finding any variation in DTI metrics above or below the level of injury in our study could probably be due to the timing of the imaging which was held soon after trauma in majority of our cases, whereas other studies have followed up the patients for a longer period of time.

Due to the significant difference in the FA values at the site of trauma among patients as compared to controls, it is logical to conclude that DTI is an invaluable instrument in assessment of the spinal cord following TSCI.

Apparent diffusion coefficient values

ADC is a measure of degree of motion of molecules of water.[40] ADC declines with increasing amount of barriers to arbitrary water motion such as myelinated axons, cellular membranes, and extracellular molecules.[41]

In our study, we determined that the mean ADC value at the level of injury among cases (1.58 ± 0.52) was significantly more as compared to values in controls (1.13 ± 0.61). No significant difference was observed in mean ADC values above or below injury level among the cases and controls.

Previous studies have also shown an increase in ADC values (mean diffusivity) in patients with acute TSCI in accordance with our study.[20,22,42] Cheran *et al*.[32] have also reported higher ADC values at the site of the injury. They found ADC and FA values to be inversely related as in our study.

Our findings were also consistent with those of D'souza *et al*. who reported that ADC is significantly increased in patients with TSCI signifying disorganization within the spinal cord fibers. Lower ADC values indicate that the fiber tracts of the spinal cord are intact.[10]

Our findings differ from Shanmuganathan *et al*. who reported that ADC is significantly decreased in patients with acute TSCI and patients with spinal cord hemorrhage exhibiting the greatest decrease. This could be due to the different patient populations in their study. They included patients with hemorrhagic cord contusions, and the blood products could play a role in the ADC values hence obtained.[31]

In contrast to our study, Ellingson *et al*. have reported lower ADC values in the cervical cord of patients with chronic TSCI. They suggested that these low ADC values are suggestive of the fact that there is a decrease in overall diffusion magnitude away from the injury site due to restructuring of the axons and chronic widespread spinal cord degeneration, as proved in previous animal models.[2]

The substantial DTI variations at the site of injury possibly replicate the results of both the primary as well as secondary neuronal injury and the outcome of secondary neuronal degeneration. The distraction of coherent axonal architecture possibly reduces the FA values. The increased ADC values could possibly be due to the increased extracellular fluid in the damaged tissue.[42] Tsuchiya *et al*. have previously predicted that raised ADC values could be due to necrosis and cord edema in the early phase and myelomalacia changes in the late phase.[43]

Due to the significant difference in the ADC values at the site of trauma among patients as compared to controls, this parameter is also of great value in diagnosing and predicting the course of TSCI.

Diffusion tensor imaging parameters in patients without any signal changes on conventional magnetic resonance imaging

MRI is an ideal technique for the evaluation of acute spinal injuries because of its extremely high sensitivity in picking up injuries to the soft tissues. It is the ideal modality for assessment of the spinal cord, ligaments, disc, and soft tissues.[44,45] The usual protocol employed for spinal trauma consists of T1W image, T2W image, and short-tau inversion recovery sequences.

Previous reports state that SCIWORA accounts for 6%–19% and 9%–14% of spinal trauma in pediatric and adult patients, respectively, and MRI is an excellent tool for evaluation of the same.[46,47] Patients with SCIWORA who have normal MRI findings have been classified as "Spinal Cord Injury without Neuroimaging Abnormality (SCIWNA)."[48] The usefulness of "diffusion-weighted imaging (DWI)" has already been proved in clinical evaluation of SCIWNA, wherein hyperintense lesions in the spinal cord have been observed.[49] It has previously been predicted that DTI can be an indispensable imaging tool in patients with SCIWNA who do not show any signal abnormality on DWI,[50] and our study proves the same.

We found in our study that even though 12 patients did not show any spinal cord abnormality on conventional MRI, they showed reduced FA and raised ADC values. The mean FA value in these cases was 0.391, and the mean ADC value was 1.53 in these cases, which was significantly different from those of controls (mean FA value = 0.65 and mean ADC value = 1.13). This shows that DTI is of utmost importance to evaluate patients with spinal trauma, especially in those patients in whom altered signal intensity is not demonstrated on routine MRI sequences.

Therefore, we conclude that DTI shows great promise in predicting and diagnosing early cord injury even in those patients with spinal trauma who do not demonstrate any alteration in the signal intensity on conventional MRI sequences. This fact was proved in our study by the reduced FA and raised ADC values in patients with spinal trauma who showed an apparently normal spinal cord on conventional MRI as compared to the controls.

Conclusions

DTI is an invaluable instrument in assessment of the spinal cord following TSCI due to the significant difference in the FA and ADC values. FA values reflect the cord functionality, whereas ADC may serve as a potential prognostic factor. We also propose that a correlation between the quantitative parameters of diffusion such as FA and ADC can be used for monitoring the response to therapy. DTI parameters can also detect subtle disruption of white matter in patients with spinal trauma and thus can have a better clinical correlation with neurological deficit. Spinal cord DTI has a very high potential in forecasting the severity of spinal injury and is of high predictive value in the prognosis of neurological recovery. Our study also shows that DTI is indispensable for diagnosing cord injury even in those patients with apparently normal cord on conventional MRI sequences.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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