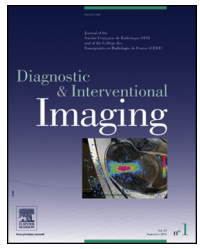
Diagnostic and Interventional Imaging (2014) **95**, 63—68



ORIGINAL ARTICLE / *Neuroradiology*

Clinical relevance of diffusion tensor imaging parameters in lumbar disco-radicular conflict

B. Dallaudière [a,b,c,*], J. Lincot [a], A. Hess [a,c], V. Balbi [d,e], F. Cornelis [f], A. Larbi [g], J.-P. Laissy [a,c], A. Cotten [d,e], E. Schouman-Claeys [a,c]

[a] *Service de Radiologie, Centre Hospitalier Universitaire Bichat—Claude-Bernard, 46, rue Henri-Huchard, 75018 Paris, France*
[b] *Inserm U698, Centre Hospitalier Universitaire Bichat—Claude-Bernard, 46, rue Henri-Huchard, 75018 Paris, France*
[c] *Faculté de Médecine Xavier-Bichat, Université Paris-7, Paris, France*
[d] *Service de Radiologie Ostéo-Articulaire, Centre Hospitalier Régional Universitaire Roger-Salengro, Lille, France*
[e] *Faculté de Médecine, Université Lille 2, Lille, France*
[f] *Service d'Imagerie Diagnostique et Interventionnelle de l'Adulte Groupe Hospitalier Pellegrin, place Amelie-Raba-Leon, 33076 Bordeaux cedex, France*
[g] *MSK Department Imaging, Cliniques Universitaires Saint-Luc, avenue Hippocrate 10, 1200 Bruxelles, Belgique*

KEYWORDS
Spine;
Lumbar;
Discoradicular conflict;
Diffusion tensor imaging;
Tractography

Abstract
Purpose: To measure the fractional anisotropy (FA) and the mean diffusivity (MD) values of L4, L5 and S1 nerve roots using diffusion tensor imaging (DTI) and to correlate them with four different clinical patterns.
Patients and methods: Fifty-six human participants were prospectively included and divided between four groups: healthy subjects, patients with clinical symptomatic nerve root pain with and without anatomical discoradicular conflict and patients with incidental anatomical disco-radicular conflict seen on magnetic resonance imaging (MRI). MRI protocol included anatomical sequences (sagittal T1- and T2-weighted, axial T2-weighted) and a 25 directions DTI sequence. FA and MD values were measured in consensus by two readers and compared between the four groups.
Results: Mean FA and MD values were significantly different for patients with clinically symptomatic nerve root pain ($n = 27$) both with ($n = 16$) (FA = 0.187 ± 0.015; MD = 510 ± 40) and without ($n = 11$) (FA = 0.193 ± 0.011; MD = 490 ± 30.5) anatomical discoradicular conflict compared

* Corresponding author. Service de Radiologie, Centre Hospitalier Universitaire Bichat—Claude-Bernard, 46, rue Henri-Huchard, 75018 Paris, France.
E-mail address: benjamin.dallaudiere@gmail.com (B. Dallaudière).

2211-5684/$ — see front matter
http://dx.doi.org/10.1016/j.diii.2013.08.019

to healthy subjects ($n = 29$) (FA = 0.221 ± 0.011; MD = 460.9 ± 35.5) including 2 subjects with incidental anatomical discoradicular conflict (FA = 0.211 ± 0.013; MD = 450.8 ± 41.2) on MRI ($P = 0.003$).

Conclusion: Measurement of FA and MD values of L4, L5 and S1 nerve roots using DTI could be useful in lumbar nerve root pain assessment. Further studies with different image processing methods are needed.

Abbreviations

DTI	Diffusion tensor imaging
FA	Fractional anisotropy
MD	Mean diffusivity
VAS	Visual analogic scale

Introduction

Degenerative discal herniation in the mobile lumbar spine is a common pathology, mostly explored by MRI. However, discordance between clinical nerve root pain and lumbar spine MRI findings is not rare and may be an issue for diagnostic and therapeutic management [1].

Diffusion tensor imaging (DTI) has been widely used in brain imaging for tracking of white matter tracts and the evaluation of brain connectivity [2—5]. This technique explores the anisotropic microscopic Brownian motions of water molecules along the preferential orientation of nervous fibres. In each voxel, the diagonalization of the diffusion tensor allows the calculation of eigen values, which are used to characterize the anisotropy and diffusivity, as reflected by two parametric values: fractional anisotropy (FA) and mean diffusivity (MD), respectively. The degree of anisotropy and the average diffusion lead to the determination of the main diffusion direction, which reflects the orientation of the tissular components, e.g. white matter tracts or nerve roots [3]. This technique has also shown interest in carpal tunnel syndrome and acute transverse myelitis assessment [6—8].

Few preliminary studies reported fibre tracking of the lumbar nerve roots using DTI. Studies measuring FA and MD in healthy subjects at different intersomatic space levels of the mobile lumbar spine and different segments of L4, L5 and S1 nerve roots seems to allow the determination of reliable and reproducible normal values [7,9]. However, according to MRI field, acquisition parameters and software, using these values data can be variable [10].

Significant changes in compressed lumbar nerve roots diffusion parameters have been reported for patients suffering from disc herniation or lumbar foraminal stenosis [7,9].

Thereby, the modification of diffusion parameters of lumbar nerve roots according to clinical symptoms or MRI findings may be considered as a potential diagnostic tool to treat precisely pathologic nerve root pathway, based on parametric rather than anatomical information in case of clinical and imagery unconformity.

To our knowledge, no previous study has assessed the relation between FA and MD values of lumbar nerve roots, anatomical discoradicular conflict seen on MRI and symptoms of nerve root pain. Consequently, the aim of this study was to measure FA and MD values of L4, L5 and S1 nerve roots using DTI and to correlate them with different clinical patterns: clinically healthy subjects, including patients with anatomical incidental discoradicular conflict seen on MRI, and patients with clinical symptomatic nerve root pain with or without anatomical discoradicular conflict.

Materials and methods

Patients

We conducted a monocentric prospective study on a cohort counting 56 human participants (38 men and 18 women) consecutively included from April 2011 to January 2012. Informed consent was obtained from each participant before inclusion. Twenty-seven (19 men and 8 women) were patients presenting with a L4, L5 or S1 nerve root pain confirmed by clinical examination and DN4 score ≥ 4 [11]. Those were then classified in two groups according to the anatomical MRI results: (1) no anatomical discoradicular conflict concordant with the nerve root pain; and (2) anatomical discoradicular conflict concordant with clinical symptoms. Twenty-nine healthy subjects (18 men and 11 women) without prior history of low back pain or nerve root pain and with DN4 score ≤ 4 [11] were also included. Those were also classified in two groups according to anatomical MRI results: (1) no anatomical discoradicular conflict; and (2) clinically asymptomatic incidental discoradicular conflict seen on MR images. Anatomical discoradicular conflict was defined as mass effect due to disc herniation with deviation or non-visualization of a compressed nerve root segment. Mean age was 63 years (range, 43—86). Pain was also evaluated using a visual analogic scale (VAS) for each study participant. Exclusion criteria for both groups were a previous history of spinal trauma, surgery, or neurological disease and classical contraindication to MRI (pregnancy, metallic implants, and claustrophobia).

MRI

MRI scans were performed on a single 1.5 T GE system (GE Healthcare, Chalfont St. Giles, United Kingdom) the day of the inclusion. We used a six elements phased array spine coil. Images were acquired in supine position. A standard MRI protocol was performed, which included T1-weighted TSE (TR, 660 ms; TE, 9.5 ms; number of averages (NEX), 1; field of view (FOV), 380 × 380 mm; matrix, 512 × 512; slice count, 12; slice thickness, 4 mm; slice gap, 0.4 mm; acquisition time 2 min 53 s) and T2-weighted TSE (TR, 2960 ms; TE, 70 ms; NEX, 2; 380 × 380 mm; matrix, 512 × 512; slice count,

12; slice thickness, 4 mm; slice gap, 0.4 mm; acquisition time, 3 min 21 s) sequences both imaging the lumbar spine in the sagittal plane and a T2-weighted TSE (TR, 5680 ms; TE, 123 ms; FOV, 200 × 200 mm; matrix, 512 × 512; NEX, 2; slice count, 30; slice thickness, 3 mm; slice gap, 0; acquisition time, 3 min 40 s) acquisition performed in the axial plane and exploring the last two mobile levels of the lumbar spine.

In addition to these previous sequences, single-shot echo-planar spin-echo DTI sequence was performed in axial plane from L4—L5 to L5—S1 intersomatic spaces with the use of the following parameters: TR, 8400 ms; TE, 85.1 ms; FOV, 200 × 200 mm; matrix, 256 × 256; NEX, 4; slice count, 30; slice thickness, 3 mm; slice gap, 0; b value, 900s/mm^2; motion probing gradients applied in 25 non-collinear directions; acquisition time, 9 min 12 s.

Data analysis

All MRI scans were reviewed in consensus by two radiologists blinded to clinical data (JL and BD), both with a good experience in spine imaging. Image analysis was independently performed for each participant, immediately after the acquisition for qualitative assessment and secondly for data extraction. Mean delay between image acquisition and data extraction was 24 days (range: 13—35 days).

A neurography was obtained using the diffusion volume (b value, 900 s/mm^2), which was visualized as maximum intensity projection, in order not to include obviously artifacted images. First, image processing was performed using MedINRIA® (Sofia Antipolis, France).

Anatomical axial T2 and DTI images were merged. The following parameters were defined for automatic fibre tracking across the whole study DTI volume: FA threshold 1 and 2, 0.1; minimum fibre length, 10 mm; smoothness, 20. No ROI was used to initiate the fibre tracking. Once reconstructed, L4, L5 and S1 fibre bundles were manually segmented on each side for all participants. We considered as being significant at least five fibres for each nerve root. Anatomical fusion between the axial T2 sequence and the DTI reconstructions was performed to allow better visualization of the different anatomic spaces. FA color maps were displayed using the classic three-directional color code: blue for fibres running in the cephalocaudal direction, green for those running in the anteroposterior direction and red for those running right to left [9]. Matching between the encoded color maps and the T2-weighted images was also manually verified (Fig. 1). Global FA and MD values were obtained for each nerve root fibre bundle. Processing with FiberViewer® (http://www.ia.unc.edu/dev) software allowed automatic segmental FA and MD measurement along each fibre bundle at the root emergence, in the lateral recess, in the foramen and in the extra foraminal portion, except for L4 nerve root whose emergence was not in the exploration volume.

FA and MD values were obtained at the level of the discoradicular conflict for clinically symptomatic and incidental asymptomatic patients with positive anatomical MRI. In case of clinically symptomatic nerve root pain without anatomical discoradicular conflict on MRI, the measures were performed along the path of the clinically symptomatic nerve root and averaged. For these two groups, FA and MD values of normal asymptomatic contralateral nerve root were also collected. For healthy subjects without disco-radicular conflict, FA and MD values were measured on both sides for L4, L5 and S1 nerve roots and averaged (Fig. 2).

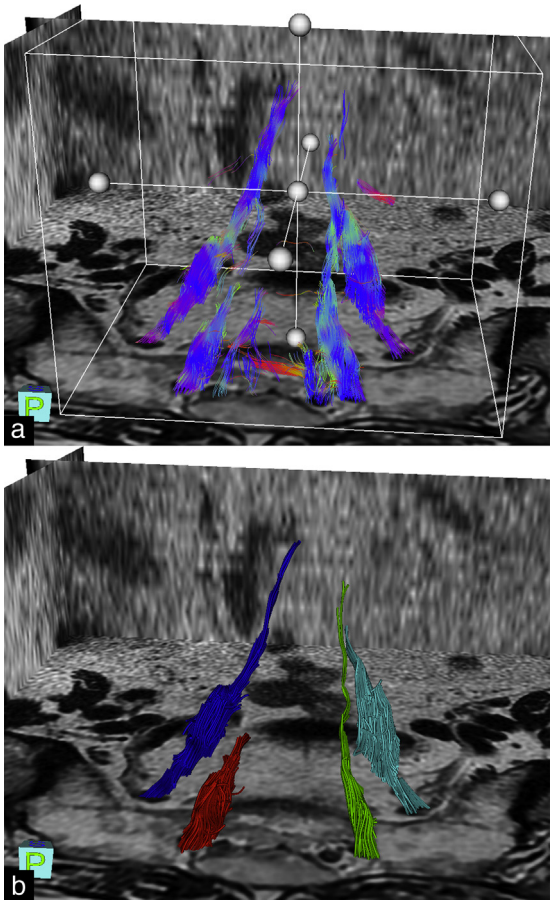


Figure 1. A 55-year-old control male; image fusion of diffusion tensor tractography and T2-weighted acquisition; a: unprocessed tractography across the entire acquisition volume showing the lombosacral roots as polylines within the cropping box; b: processed tractography showing individualized radicular fiber bundles as polytubes (color code: red, right S1; green, left S1; blue, right L5; cyan; left L5).

FA and MD values were statistically compared between each group.

Statistical analysis

We described FA and MD data as mean, median, minimal and maximal values and standard deviation for each patient. Association between diffusion parameters, clinical data and measurement topography was assessed using non-parametric tests as Wilcoxon tests. Data were analyzed using MedCalc® v11.0 software. Statistical testing was done at the two-tailed alpha level of 0.05.

Results

Clinical conflict levels for the 27 patients with clinical nerve root pain were: right L4 ($n = 2$), left L4 ($n = 1$), right L5 ($n = 10$), left L5 ($n = 6$), right S1 ($n = 5$) and left S1 ($n = 3$) roots.

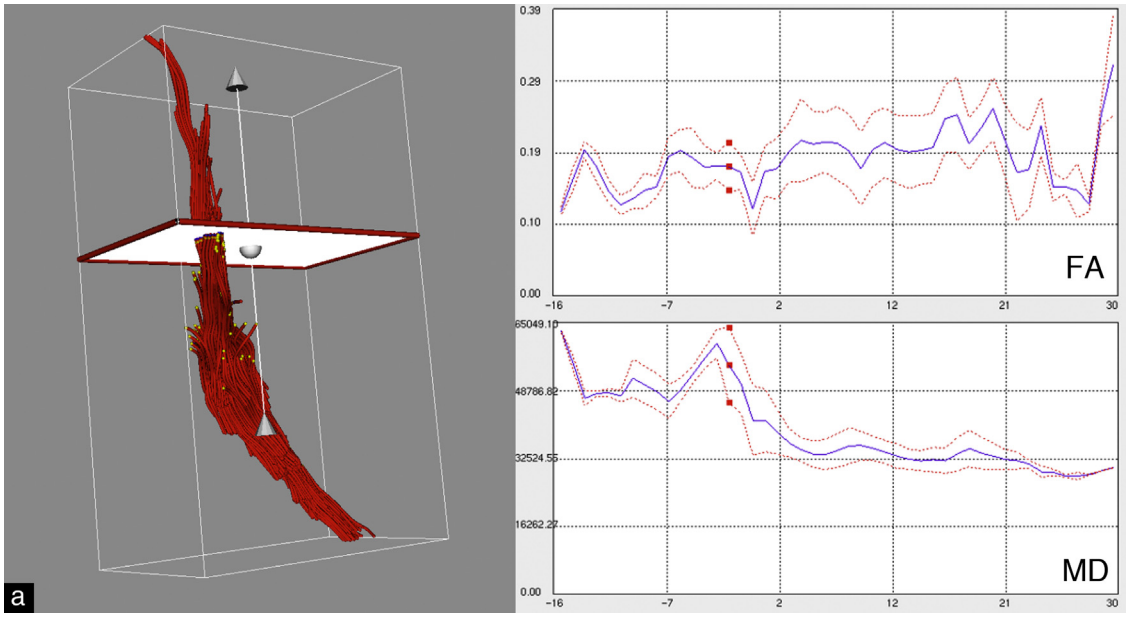


Figure 2. Same control subject as in Fig. 1; left S1 root fiber bundle processed by FiberViewer© software; a: fiber bundle as shown within the cropping box with crossing analysis plane; FA and MD are respectively, the fraction of anisotropy and the mean diffusivity graphs along this fiber bundle with red squares marking the level of the crossing analysis plane.

Among those patients, no anatomical discoradicular conflict concordant with clinical nerve root pain was found in 11 patients, whereas concordant anatomical discoradicular conflict was present in 16 patients on MRI images.

Among the 29 healthy subjects without clinically symptomatic nerve root pain, 27 did not have anatomical discoradicular conflict whereas two subjects had an incidental discoradicular conflict found on MRI.

Anatomical conflict levels were right L4 ($n=1$), left L4 ($n=1$), right L5 ($n=6$), left L5 ($n=2$), right S1 ($n=4$) and left S1 ($n=2$) roots in symptomatic patients and right L5 ($n=2$) root in healthy subjects. Anatomical symptomatic conflict root segments were in root emergence ($n=7$), in the lateral recess ($n=4$), in the foramen ($n=4$) and in the extra foraminal portion ($n=1$) for symptomatic patients and in the lateral recess ($n=2$) for healthy subjects.

The DTI sequence was interpretable in all cases, with a satisfying L4, L5 and S1 nerve root detection. Fusion between DTI and axial T2-weighted images allowed a good anatomical correlation in all cases. The whole radicular path from its rise to its extraforaminal segment was taken into account by MedINRIA® and FiberViewer® in 38/56 (71.4%) participants totalizing 228 nerve roots. In 18/56 participants (22.6%), representing 76 nerve roots, radicular fibre tracking was discontinuous, the largest bundle gap measuring 5 mm. This finding was due to disc herniation in five patients, representing five nerve roots (Fig. 3). In 13 other subjects, representing 71 nerve roots, this finding was isolated without a corresponding anatomical discoradicular conflict. In those cases, FA and MD measures were performed in either end of the interrupted nerve root tract.

Compression of the lumbar nerve root was visualized on both T2-weighted images and DTI fibre tracking reconstructions in all patients showing discoradicular conflict.

FA and MD values of healthy subjects, including patients with incidental discoradicular conflict, and those of symptomatic clinical nerve root pain with and without anatomical discoradicular conflict are reported in Table 1.

There is only one overlap of FA (L5), two overlaps in MD (L5, S1) between healthy subjects without and with anatomical disco-radicular conflict; and four overlap of FA (2 L5, 2 S1), five overlap (2 L5, 3 S1) in MD between patients with clinical nerve root pain without and with anatomical discoradicular conflict.

The mean values of FA and MD in the 27/56 healthy subjects without discoradicular conflict were not significantly different according to age ($P=0.09$), gender ($P=0.08$), intersomatic level ($P=0.06$) and nerve root segment ($P=0.08$). Mean FA and MD values were significantly different for patients with clinically symptomatic nerve root pain ($n=27$) both with ($n=16$) and without ($n=11$) anatomical discoradicular conflict compared to healthy subjects ($n=29$) including those two subjects with incidental anatomical discoradicular conflict seen on MRI ($P=0.003$). Conversely, no significant difference was found for FA and MD values in patients with clinically symptomatic nerve root pain with or without anatomical discoradicular conflict ($P=0.06$), neither for clinically healthy subjects with or without incidental anatomical discoradicular conflict ($P=0.06$).

Last, the mean values of FA and MD in 27 patients with nerve root pain were not significantly different according to VAS ($P=0.07$).

Discussion

DTI fibre tracking sequences have already demonstrated their feasibility for peripheral nerves (median and ulnar nerves notably, and more recently in lumbar nerve roots) [6—8].

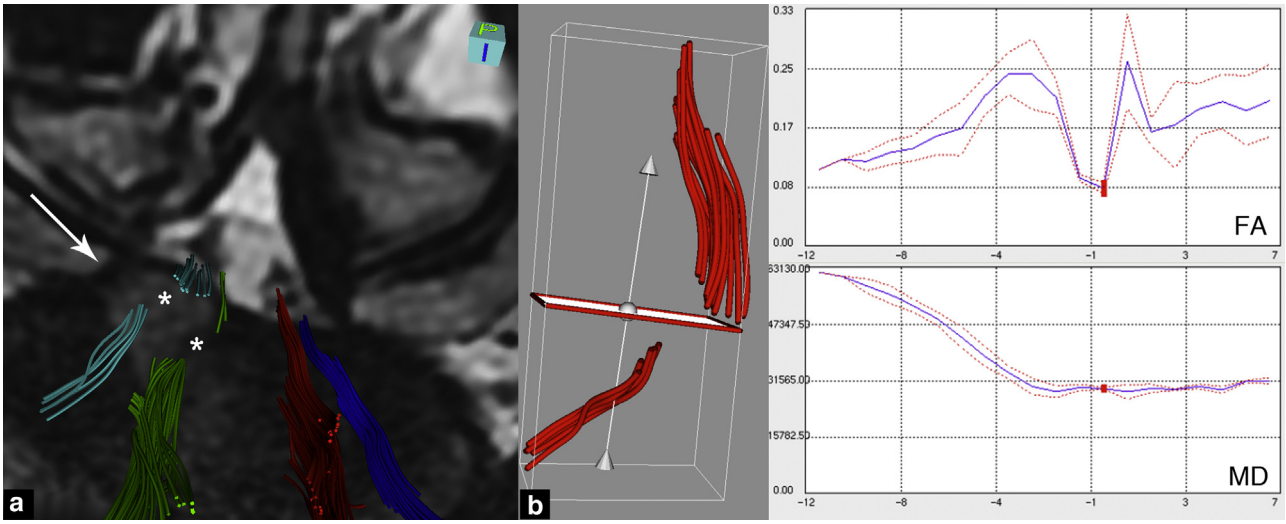


Figure 3. A 50-year-old male with medical history of discoradicular conflict; image fusion of diffusion tensor tractography and T2-weighted acquisition seen from below; a: processed tractography showing individualized roots as polytubes, fiber tracking interruption (asterisks) of left L5 and S1 roots at the level of a L4—L5 discal hernia lateralized in the left lateral recess of the spinal canal (color code: red, right S1; green, left S1; blue, right L5; cyan; left L5); b: left L5 root fiber bundle analysis processed in FiberViewer© software; FA and MD are respectively the fraction of anisotropy and the mean diffusivity graphs along this fiber bundle and show FA drop at the compression level and MD decrease along the bundle.

Normal FA and MD values have been determined in healthy subjects and seemed independent of age, gender, intersomatic space level, side and segment of the nerve root [9].

In case of clinical and MRI discoradicular conflict, FA and MD have been reported to be significantly lower for FA and increased for MD compared to healthy subjects with normal MRI [9].

However, to our knowledge, no previous study has focused on relation between diffusion parameters values, clinical symptoms of nerve root pain attested by a neuropathic pain scale (e.g. DN4 scale), visual analogic pain scale and discoradicular conflict seen on MR images.

In our study, we found associated FA decrease and MD increase in the symptomatic lumbar nerve root, with or without anatomical discoradicular conflict in opposition to healthy subjects and patients with incidental anatomical MRI discoradicular conflict, independently of age, gender and VAS, despite some overlap in 12 nerve roots between FA and MD. To our knowledge, this is the first clinical study showing modifications of diffusion parameters in patients suffering from nerve root pain without anatomical MRI discoradicular conflict, which has been previously suggested by experimental data [12,13]. Animal studies showed that nerve root injury might be independent of mechanical compression [12,13]. Diffusion tensor parametric MRI may provide a better concordance with clinical symptoms than anatomical MRI sequences solely, which can have applications notably in initial prognosis and in postoperative patients with recurrent nerve root pain. Moreover FA and MD values in healthy subjects included in our series did not seem different from those reported in recent literature [9].

Hence, DTI fibre tracking may reflect histological changes in the nerve root tissue secondary to the compression, independently of a patent discoradicular conflict seen on MRI. It may then be used as an additional diagnostic tool in clinical routine, particularly, in case of discordance between anatomical MRI and clinical symptoms. Indeed, increase in the vascular permeability with disruption of the nerve root barrier, intraneural edema, intra and perineural hyperaemia have been attributed to chronic compression of the nerve roots and may explain modifications of water diffusion along

Table 1 Mean FA and MD values in healthy subjects and patients with clinical nerve root pain.

Study participants	29 healthy subjects		27 patients with clinical nerve root pain	
	aDRc ($n=2$)	No aDRc ($n=27$)	aDRc ($n=16$)	No aDRc ($n=11$)
FA	0.211 ± 0.013	0.221 ± 0.011	0.187 ± 0.015	0.193 ± 0.011
MD (mm^2/s)	450.8 ± 41.2	460.9 ± 35.5	510 ± 40	490 ± 30.5
P values	0.003			
	0.06		0.06	
Patient overlap in FA	1		4	
Patient overlap in MD	2		5	

aDRc: anatomical disco-radicular conflict.

the nerve root [14—17]. Moreover, ischemia, demyelination and Wallerian degeneration may reduce anisotropy by increasing the distance between axons fascicles, thus, leading to a decrease in the FA value, as well as an increase in that of MD. Thereby, DTI evaluation of lumbar nerve roots may stand as a new imaging approach with more functional assessment of the microstructural changes underwent by compressed nerve roots.

However, our study has several limits. The first one concerns its small population size, requiring confirmation of these results over larger cohorts. Nevertheless, to our best knowledge we report the largest series of lumbar nerve roots assessed by DTI with correlation of MRI data with clinical patterns. Furthermore, MRI scans were performed in supine position, which can mask dynamic discoradicular conflict. In our opinion, it would be of interest to repeat this evaluation of clinical relevance of diffusion parameters in discoradicular conflict in stand-up position, should today's MR technology permit it.

Conclusion

To conclude, measurement of diffusion parameters by DTI in lumbar nerve roots may take part in the radiological management of discoradicular disease. Adjunction of DTI parametric data to standard evaluation of lumbar nerve root pain may increase interobserver concordance. Indeed, FA and MD values seem correlated with clinical nerve root pain, independently of a visible anatomical discoradicular conflict on MR images. Our study can discuss the usefulness of this technique in second intention in case of discrepancy between the clinical and MRI anatomical data, in particular, in relation to the EMG, which is often asked by clinicians in this context.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

References

[1] Arana E, Royuela A, Kovacs FM, Estremera A, Sarasíbar H, Amengual G, et al. Lumbar spine: agreement in the interpretation of 1.5 T MR images by using the Nordic Modic Consensus Group classification form. Radiology 2010;254(3):809—17.

[2] Basser PJ, Pajevic S, Pierpaoli C, Duda J, Aldroubi A. In vivo fiber tractography using DT-MRI data. Magn Reson Med 2000;44(4):625—32.

[3] Le Bihan D, Johansen-Berg H. Diffusion MRI at 25: exploring brain tissue structure and function. Neuroimage 2012;61(2):324—41.

[4] Le Bihan D, Mangin JF, Poupon C, Clark CA, Pappata S, Molko N, et al. Diffusion tensor imaging: concepts and applications. J Magn Reson Imaging 2001;13(4):534—46.

[5] Tensaouti F, Lahlou I, Clarisse P, Lotterie JA, Berry I. Quantitative and reproducibility study of four tractography algorithms used in clinical routine. J Magn Reson Imaging 2011;34(1):165—72.

[6] Andreisek G, White LM, Kassner A, Sussman MS. Evaluation of diffusion tensor imaging and fiber tractography of the median nerve: preliminary results on intrasubject variability and precision of measurements. AJR 2010;194(1):W65—72.

[7] Eguchi Y, Ohtori S, Orita S, Kamoda H, Arai G, Ishikawa T, et al. Quantitative evaluation and visualization of lumbar foraminal nerve root entrapment by using diffusion tensor imaging: preliminary results. AJNR 2011;32(10):1824—9.

[8] Filippi CG, Andrews T, Gonyea JV, Linnell G, Cauley KA. Magnetic resonance diffusion tensor imaging and tractography of the lower spinal cord: application to diastematomyelia and tethered cord. Eur Radiol 2010;20(9):2194—9.

[9] Balbi V, Budzik JF, Duhamel A, Bera-Louville A, Le Thuc V, Cotten A. Tractography of lumbar nerve roots: initial results. Eur Radiol 2011;21(6):1153—9.

[10] Budzik JF, Verclytte S, Lefebvre G, Monnet A, Forzy G, Cotten A. Assessment of reduced field of view in diffusion tensor imaging of the lumbar nerve roots at 3 T. Eur Radiol 2013;23(5):1361—6.

[11] Bouhassira D, Attal N, Alchaar H, Boureau F, Brochet B, Bruxelle J, et al. Comparison of pain syndromes associated with nervous or somatic lesions and development of a new neuropathic pain diagnostic questionnaire (DN4). Pain 2005;114(1—2):29—36.

[12] Olmarker K, Nordborg C, Larsson K, Rydevik B. Ultrastructural changes in spinal nerve roots induced by autologous nucleus pulposus. Spine 1996;21(4):411—4.

[13] Takebayashi T, Cavanaugh JM, Cüneyt Ozaktay A, Kallakuri S, Chen C. Effect of nucleus pulposus on the neural activity of dorsal root ganglion. Spine 2001;26(8):940—5.

[14] Rydevik B, Brown MD, Lundborg G. Pathoanatomy and pathophysiology of nerve root compression. Spine 1984;9(1):7—15.

[15] Rydevik BL, Pedowitz RA, Hargens AR, Swenson MR, Myers RR, Garfin SR. Effects of acute, graded compression on spinal nerve root function and structure. An experimental study of the pig cauda equina. Spine 1991;16(5):487—93.

[16] Takahashi N, Yabuki S, Aoki Y, Kikuchi S. Pathomechanisms of nerve root injury caused by disc herniation: an experimental study of mechanical compression and chemical irritation. Spine 2003;28(5):435—41.

[17] Yoshizawa H, Kobayashi S, Morita T. Chronic nerve root compression. Pathophysiologic mechanism of nerve root dysfunction. Spine 1995;20(4):397—407.