ASSESSMENT OF NORMAL VALUES OF FRACTIONAL ANISOTROPY AND MEAN DIFFUSIVITY OF MOBILE LUMBAR SPINE NERVE ROOTS BY DIFFUSION TENSOR MR IMAGING: COMPARISON BETWEEN 1.5 AND 3T

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Purpose: To assess the normal values of fractional anisotropy (FA) and mean diffusivity (MD) of L4, L5 and S1 nerve roots using diffusion tensor imaging (DTI) in healthy volunteers.

Materials and methods: 37 subjects without previous history of lumbalgia or radiculalgia were prospectively examined: 27 at 1.5T and 10 at 3T MRI. The protocol included standard anatomical sequences and a DTI acquisition. Nerve root fibers were semi automatically extracted from DTI tractography. FA and MD values were measured at 4 key portions along each L4, L5 and S1 nerve roots.

Results: At 1.5T MRI, FA and MD were 0.221 ± 0.011 and 460.9 ± 35.5 mm².s^{-1} respectively; at 3T MRI, FA and MD were 0.216 ± 0.01 and 480.1 ± 36.1 mm².s^{-1} respectively, which may be considered as normal values for mobile lumbar spine nerve roots, independently of intersomatic space level ($p = 0.06$) and nerve root portion ($p = 0.08$) or magnetic field ($p = 0.06$).

Conclusion: Normal FA and MD values can be measured along lumbar mobile spine nerve roots in healthy subjects. These values were not dependent on intersomatic space level, side or anatomical portion of the nerve root or magnetic field.

Key words: Magnetic resonance (MR), diffusion study – Spine, MR.

Diffusion tensor imaging (DTI) can provide non-invasive, quantitative data to evaluate neural pathways in the central and peripheral nervous systems in vivo (1-5). This technique explores the anisotropic microscopic Brownian motions of water molecules along the preferential direction of fibers (6, 7). In each voxel, the diffusion tensor allows the calculation of eigenvalues, which are used to characterize the anisotropy, as reflected by fractional anisotropy (FA), and the mean diffusivity (MD, average of the 3 eigenvalues) of the middle. The degree of anisotropy and the average diffusion lead to the determination of the main diffusion direction in each voxel of the explored tissue (8), reflective of the orientation of the tissular components, e.g. axonal fibers.

DTI has been mostly used in neuroradiology in order to study neural connectivity in white matter. It is a tool to approach microstructural networks, capable to provide a three-dimensional visualization tool of nerves and muscles fibers (4).

The feasibility of DTI and tractography of human peripheral nerves (9, 10) was recently demonstrated in the carpal and ulnar tunnel syndromes (9-11). In lumbar spine, few studies reported fiber tracking of the nerve roots. Compression of lumbar nerve root consecutive to disc herniation has been associated to modifications of the diffusion parameters, namely FA and MD (12). DTI fiber 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 the nerve root (11-13). 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 undergone by compressed nerve roots. However, only few studies (1, 12, 13) established normal values of FA and MD of lumbar nerve roots at 1.5T MRI and none at 3T MRI, according to demographic data (14). More, inter individual variations of normal diffusion parameters may exist, as well as physiological variations according to the level and the portion of the considered nerve root.

Because of the growing importance of DTI in lumbar imaging and its clinical implications, we are interested in determing normative diffusion tensor parameters and to assess whether these normative findings differ according to the magnetic field strength.

Consequently, the purposes of our study were to confirm the feasibility of the DTI technique in the exploration of nerve roots of the mobile lumbar spine and to define normal values of FA and MD in healthy subjects at 1.5T and to compare them with results at 3T.

Material and methods

Patients

Thirty-seven volunteers without previous clinical history of lumbalgia or lumbar radiculalgia (BD, JL) were included prospectively in our single center study from April 2011 to January 2012. Written inform consent was obtained from each subject before inclusion.

Exclusion criteria were a previous history of spinal trauma, surgery, or neurological disease and contraindication to MRI (pregnancy, metallic

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implants, and claustrophobia).

We collected clinical data including age and gender whereas ethnic group or sports habits were not considered.

MRI

The MRI scans were performed on the day of inclusion on GE systems (GE Healthcare, Milwaukee, WI) in random order: on a 1.5T unit in 27 subjects and on 3T unit in the remaining 10 volunteers. We used a 6 elements phased array spine coil with the patient in supine position.

The standardized MRI protocol (with non-use of parallel imaging) typically included T1 weighted FSE (for 1.5T: TR, 660ms; TE, 9.5ms; 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 min53 s; for 3T: TR, 973 ms; TE, 8ms; NEX, 1; FOV, 360 × 360 mm; matrix 512 × 512; slice count, 8, slice thickness, 3 mm; slice gap, 0.3 mm; acquisition time 3min23s) and T2 weighted TSE (for 1.5T: TR, 2960 ms; TE, 70ms; NEX, 2; 380 × 380 mm; matrix, 512 × 512; slice count, 12; slice thickness, 4 mm; slice gap, 0.4 mm; acquisition time, 3 min21 s; for 3T: TR, 3781ms, TE, 57.4ms,NEX, 1.5;FOV, 360 × 360 mm; matrix, 512 × 512; slice count, 8; slice thickness, 3 mm; slice gap, 0.3 mm, acquisition time, 3min06) sequences of the lumbar spine both in the sagittal plane and a T2 weighted TSE (for 1.5T: 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 min40 s; for 3T: TR, 3769 ms; TE, 116.7 ms; NEX, 1.5; FOV, 200 × 200 mm; matrix, 512 × 512; slice count, 30; slice thickness, 3 mm; slice gap, 0; acquisition time, 3min18) sequence in the axial plane in the last 2 mobile levels L4-L5 to L5-S1 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: for 1.5T: TR, 8400ms; 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, 900 s.mm^{-2}; motion probing gradients applied in 25 non-collinear directions; acquisition time, 9 min12 s; for 3T: TR, 4500 ms; TE, 83.5 ms; FOV, 200 × 200 mm; matrix, 256 × 256; NEX, 4; slice count, 30; slice thickness, 3 mm; slice gap, 0; b value, 900 s.mm^{-2}; motion probing gradients applied in 25 non-collinear directions; acquisition time, 7 min53.

Data analysis

All MRI scans were reviewed in consensus by 2 readers (JL and BD), with respectively 2 and 4 year experience in spine imaging, blinded to clinical data. Image analysis was performed for each subject, immediately after the acquisition for qualitative assessment and secondly for data extraction (24 days later in mean; range, 13-35 days).

A coregistration of DTI and axial T2-weighted images was systematically performed to increase the anatomical resolution of DTI images.

A "neurography" was obtained using the diffusion volume (b value, 900 s.mm^{-2}) which was visualized as maximum intensity projection, to evaluate neurograms, before tractography color maps, in order not to include obvious artifacts. Indeed, Diffusion-weighted magnetic resonance imaging postprocessed by maximum-intensity projection reportedly demonstrates the nerve roots (15, 16).

Image processing was first performed using MedINRIA v1.9.4 software (©Sofia Antipolis, France).

The following parameters were defined for automatic fiber tracking across the whole study DTI volume: FA threshold, 0.1; minimum fiber length, 10 mm. No ROI was used to initiate the fiber tracking. L4, L5 and S1 fiber bundles were manually segmented on each side for all subjects. Anatomical fusion between the axial T2 sequence and the DTI reconstructions was performed to allow better visualization of the different anatomic spaces. Once reconstructed, L4, L5 and S1 fiber bundles were manually segmented on each side (Fig. 1). We considered as being significant at least 5 fibers for each nerve root. FA color maps were displayed using the classic three-directional color code: blue for fibers running in the cephalocaudal direction, green for those running in the anteroposterior direction and red for those running right and left (12). Matching between the encoded color maps and the T2-weighted images was also manually verified. Processing with FiberViewer v1.2.3 (©University of North Carolina, http://www.ia.unc.edu/dev/) software permitted automatic FA and MD values measurement for each fiber bundle at the root emergence, in the lateral recess, in the foramen and in the extra foraminal portion, except for L4 nerve roots in which origin part was not in the exploration field on 1.5T (Fig. 2). No ROI was used.

FA and MD values were measured in both sides of L4, L5 and S1 nerve roots and compared between them.

Statistical analysis

We described FA and MD data generated by FiberViewer software as mean, median, minimal, maximal and standard deviation for continuous variables. Association between diffusion parameters and topography of the measure was attested using non-parametric tests (Wilcoxon test).

Time data extraction was also described as mean, minimal with standard deviation.

FA and MD data were compared and analyzed to clinical data using Medcalc© v11.0 software. Statistical testing was done at the 2-tailed alpha level of 0.05.

Results

Subjects

Thirty-seven subjects were included:

– 27 clinically healthy volunteers (17 men, 10 women) on 1.5T MRI
– 10 clinically healthy volunteers (5 men, 5 women) on 3T MRI

Mean age was 62 years old (range, 43-86; SD, 5.6).

Standard MRI and DTI analysis

The DTI sequence was interpretable in all cases, with a good depiction of L4, L5 and S1 nerve roots. Fusion between DTI and axial T2-weighted images permitted a good anatomical correlation in all cases. We insured that the entire path of the root was taken into account from its emergence to its extraforaminal portion by MedInria and Fiber Viewer softwares in 22 patients (132 nerve roots). In 26 nerve roots (11.7%) in 13 patients, fiber tracking was discontinuous in isolation on 1.5 T MRI and on 3 nerve roots (1.4%) in 2 patients on 3T MRI, the largest bundle gap measuring 5 mm.

At 1.5T, anatomical disruption were right lateral recess L4 (n = 4), right foraminal L4 (n = 1), left lateral recess L4 (n = 2); right spinal canal L5 (n = 2),right foraminal L5 (n = 1), left lateral recess L5 (n = 4); right spinal canal S1 (n = 3), right extra foraminal S1 (n = 3), left foraminal S1
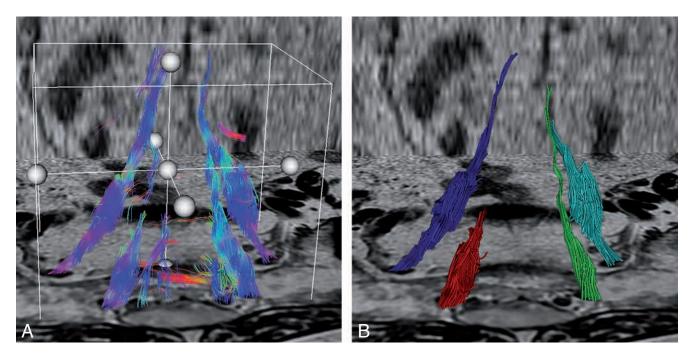
Fig. 1. — 55 year-old male; image fusion of diffusion tensor tractography and T2-weighted acquisition. A. Unprocessed tractography across the entire acquisition volume showing the lumbosacral roots as polylines within the cropping box; three-directional color code for fiber direction: blue, cephalocaudal; green, anteroposterior; red, transverse. B. Processed tractography showing individualized radicular fiber bundles as polytubes; color code: red, right S1; green, left S1; blue, right L5; cyan; left L5.

(n = 2) and left extra foraminal S1 (n = 4) roots.

At 3T, anatomical disruption were right lateral recess L4 (n = 1), left foraminal S1 (n = 2).

Fiber tracking can't be performed after changing parameters (threshold and/or minimum length) whose initial tracking was discontinuous. According to our experience, FA threshold, 0.1; minimum fiber length, 10 mm are optimal parameters for lumbar nerve roots fiber tracking.

The mean values of FA and MD for all subjects were respectively: FA, 0.221 ± 0.011; MD, 460.9 ± 35.5 mm^2.s^{-1} at 1.5T MRI; FA, 0.216 ± 0.01; MD, 480.1 ± 36.1 mm^2.s^{-1} at 3T MRI.

Mean values of FA and MD in the 37 healthy volunteers were not significantly different according to intersomatic space level (p = 0.06), nerve root portion (p = 0.08) and MRI magnetic strength (p = 0.06).

Discussion

We aimed to determine normal values of diffusion tensor parameters in lumbar nerve roots of asymptomatic volunteers without prior history of low back surgery or nerve root pain. In this study, FA was 0.221 ± 0.011, MD was 460.9 ± 35.5 mm^2.s^{-1} at 1.5T MRI; and FA was 0.216 ± 0.01, MD was

480.1 ± 36.1 mm^2.s^{-1} at 3T MRI, which might be considered as normal values for mobile lumbar spine nerve roots, independently of MRI field. Fiber tracking and measurement of diffusion parameters was successfully obtained in 86.9 % of the subjects, confirming the feasibility of DTI for lumbar nerve roots (12). Indeed, these disruptions couldn't be corrected because when we modify and particularly when we increase the parameters of automatic fiber tracking across the whole study DTI volume, too much artifacts like para vertebral musculature fibers were identified. Hence, according to our experience, the mentioned parameters seems to be the better compromise and permits reliable measurements, with a negligible gap.

Our values of FA on volunteers are consistent with those reported in the literature of 0.218-0.219 (12). Furthermore, FA and MD were measured and compared according to the same post-processing algorithms, software and readout procedure at 1.5 and 3T.

However, to our knowledge there are only few reports of normal diffusion parameters values for lumbar nerve roots in the literature and these findings have to be confirmed by further studies. The systematic co registration of axial T2 and DTI se-

quences permitted a good anatomic correlation. Measurements of FA and MD according to anatomical imaging probably contributed to the precision of our measurements (17). Determination of normal values of diffusion parameters in lumbar nerve roots may have further implications in the comprehension and the management of mechanical nerve root pain due to disc herniation. Some interesting reports (1, 12) have already demonstrated modifications of FA and MD values in case of compressed nerve root, emphasizing the importance of defining reliable and reproducible normal values in the healthy population.

We acknowledge that our study has several limitations. First, we focused on the last 2 intersomatic space levels since L4, L5 and S1 are the most frequently involved nerve roots in disc herniation or foraminal nerve root entrapment. In fact, exploration of the other intersomatic space levels would have implied an additional DTI sequence on 1.5T with substantial increase in the acquisition time. The exploration of the other intersomatic space levels was limited by the size of the FOV and the number of slices of the DTI sequence, fixed to optimize the spatial resolution and the acquisition time.

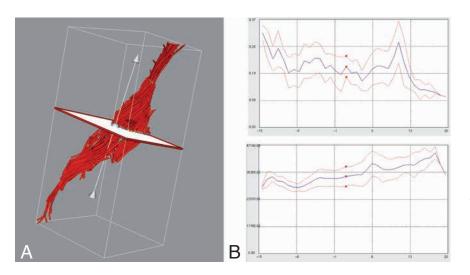Another important limitation concerns the small sample size of

Fig. 2. — Same patient as in Fig. 1. A. Right S1 root fiber bundle processed in Fiber-Viewer© software shown within the cropping box with crossing analysis plane. B,C: fractional anisotropy (FA) and mean diffusivity (MD) measurements along this fiber bundle with red squares on the graphs marking the level of the crossing analysis plane.

subjects included in our study, requiring confirmation of the results by further larger studies. Nevertheless, to our best knowledge we reported the largest series of lumbar nerve roots DTI and also the only one on 3T MRI and studied FA and MD measurements on 222 nerves roots.

In conclusion, our study shows that FA and MD are not subject to variations according to the magnetic field.

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