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SHORT COMMUNICATION

Is diffusion tensor imaging useful in the assessment of the sciatic nerve and its pathologies? Our clinical experience

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Objective: To evaluate the usefulness of diffusion tensor imaging (DTI) in the clinical setting as a complementary tool to conventional MRI in the study and assessment of the sciatic nerve and its pathologies.

Methods: 17 patients diagnosed with different types of sciatic neuropathy and 10 healthy controls underwent a conventional MRI and a DTI study in a 3-T MR scanner (Achieva® 3-T X-Series; Philips Healthcare, Netherlands).

Results: In the control group, we were able to track and visualize the common sciatic nerve and its main branches from hip to foot. In the patient group, the affected sciatic nerves presented statistically significant lower fractional anisotropy values and higher apparent diffusion coefficient values when compared with controls, suggesting

nerve damage. In all cases, DTI offered complementary information for diagnosis and/or confirmation of the suspected pathology. When compared with conventional MRI, DTI showed higher sensitivity for nerve damage detection.

Conclusion: DTI offers a significant improvement and an important complement to visualize the sciatic nerve and its main branches. In patients with sciatic nerve pathology DTI allows to a better detection and characterization of the nerve damage.

Advances in knowledge: DTI enables *in vivo* dissection of the sciatic nerve white matter fibres; its use offers a significant improvement and complement to conventional MRI.

INTRODUCTION

Sciatic neuropathy can be caused by a large number of aetiologies, affect any level of the nerve and result in numerous symptoms.¹ The diagnosis is based on the patient's history, clinical findings and electrodiagnostic tests.² The most common are nerve conduction studies (NCSs) and electromyogram (EMG). However, these techniques present some limitations such as limited ability to assess proximal nerve lesions, exact location of the lesion or aetiology determination.³

MRI has been widely employed to study the normal or pathological anatomy of peripheral nerves and the associated muscle denervation.⁴ Peripheral nerves could be differentiated from the surrounding fat tissue with fat-saturated T_2 weighted imaging (T2WI) sequences.^{4,5} However, its utility is restricted in some ways including specificity for regeneration, detection of the underlying disease or exposure of the relationship between a tumour and its original nerve root.

Some of these limitations may be overcome by the application of diffusion tensor imaging (DTI). DTI allows the assessment of axonal integrity in neural tissues by using the diffusion motion of water molecules. It provides quantitative indices of the structural and orientation features of tissues,⁶ such as fractional anisotropy (FA), eigenvalues, eigenvectors and the apparent diffusion coefficient (ADC). Potential links between DTI parameters and nerve fibre integrity have been suggested by several studies focusing on axon degeneration.⁷

Because of the particularities of the DTI technique and the information that it may provide, we have systematically evaluated its utility in a group of 27 subjects as a complementary tool to conventional MRI in the clinical setting.

METHODS AND MATERIALS

Participants

Participants were selected from the neurology departments of the Hospital General Universitario de Alicante and Hospital Vega Baja (Alicante, Spain).

17 consecutive patients diagnosed with sciatic neuropathy were included (10 males, 7 females; age 51.11 ± 14 years). 15 patients presented damage in the common sciatic nerve (CSN) and 2 patients presented lesions affecting the tibial and peroneal branches (Patients 16 and 17, see Table 1). In these patients, only tractography was performed for clinical assessment. The average time between initial diagnosis and MRI was 10.6 ± 4.4 months.

For the control group, 10 volunteers (6 females, 4 males; age 51 ± 12 years) without any familiar or personal antecedents of interest were selected.

The protocol was approved by the institutional review board, and all participants gave their written informed consent before entering the study.

MR procedure

MR studies were performed with a 3-T scanner (Achieva® 3-T X-Series; Philips Healthcare, Netherlands), in supine position,

with the 16-channel Torso-XL phased-array coil for the pelvis and lower limb studies, and the 8-channel knee coil for studies at the knee level. The examined extremity was immobilized with cushions.

The MRI protocol included high-resolution axial T_1 weighted imaging (T1WI) [echo time (TE) <20 ms, repetition time (TR) <650 ms], T2WI (TE >90 ms, TR >6000 ms) and fat-saturated proton density-weighted images (PD-WI) (TE = 30 ms, TR >1000 ms); and coronal short tau inversion recovery (STIR; TE = 20 ms, TR >6000 ms, inversion time = 220 ms) and T1WI (TE <20 ms, TR <650 ms). For contrast images, patients received intravenous administration of 0.1 mmol/kg of gadobutrol (Gadovist, Gd-BT-DO3A, Schering, Berlin, Germany) in a bolus injection through a peripheral vein.

DTI was acquired in transversal orientation using a single-shot echo planar imaging sequence with diffusion encoding in 32 directions (b -values 0 and 800 s mm^{-2} ; TR 7398; TE 70 ms; fat

Table 1. Clinical features of the patients diagnosed with peripheral neuropathy

Patient	Gender	Age (years)	Aetiology	Clinical presentation	NCS motor	NCS sensitive	Evolution time (months)	T2WI NH	MD-MRI
1	M	80	Diabetes I	P, PA (U)	BN	BN	2	Yes	No
2	M	56	Traumatic	H, PA, W (U)	NCB in CSN	DA in PS	6	No	Yes
3	M	57	Toxic	PA, P, W, PR (B)	NCB in both PN	BN	8	No	Yes
4	F	32	Nerve entrapment	P, PA (U)	NCB in PN and TN	BN	15	Yes	Yes
5	M	56	Traumatic	P, W, PA (U)	BN in PN	DA in PF	6	No	Yes
6	F	48	Nerve entrapment	P, W, MA, H (U)	NCB in CSN	DA in TN and PN	12	Yes	Yes
7	F	32	Autoimmune origin	P, W, FD (U)	NCB in CSN	BN	12	No	Yes
8	M	47	Nerve entrapment	P, PA (U)	NCB in CSN	DA TN and PN	8	No	No
9	M	41	Perineuroma surgery	P, C (U)	BN	DA TN and PN	12	Yes	No
10	M	80	Idiopathic	P, W (B)	NCB in left CSN	BN	14	Yes	Yes
11	F	32	Autoimmune origin	P, C, W, FD (U)	NCB in CSN	BN	9	No	No
12	M	57	Toxic	P, W (B)	NCB in both PN	BN	8	No	Yes
13	F	57	Traumatic	P, W, PA (U)	NCB in TN	N	15	Yes	Yes
14	F	58	Traumatic	P, W, H (U)	NCB in CSN	DA in TN and PN	9	Yes	Yes
15	F	44	Iatrogenic	P, W, H (U)	NCB in CSN	BN	10	Yes	Yes
16	M	45	Nerve entrapment	P (U)	N	N	15	No	No
17	M	47	Schwannoma	PA, W (U)	N	DA in PS	20	Yes	No

(B), bilateral limb involvement; (U), unilateral limb involvement; BN, below laboratory limits of normal; C, cramps; CSN, common sciatic nerve; DA, decreased amplitude; F, female; FD, foot drop; H, hypoesthesia; M, male; MA, muscle atrophy; MD-MRI, presence of muscle denervation pattern in the MRI study; N, normal; NCB, nerve conduction block; NCS, nerve conduction studies; P, pain; PA, paraesthesia; PF, peroneal fibular branch; PN, peroneal nerve; PR, paresis; PS, peroneal sural branch; T2WI NH, presence of nerve hyperintensity in the T_2 weighted imaging images; TN, tibial nerve; W, limb weakness.

saturation mode: selective partial inversion recovery; sensitivity encoding factor 1.9; field of view 220 mm; acquired voxel size $2 \times 2 \times 2 \text{ mm}^3$; 60 slices).

Diffusion tensor imaging analysis

Analyses were performed with the fibre track tool at the MR Extended Workspace (Philips Healthcare, Netherlands) after eddy current compensation by affine registration to B0 image. The axial T2WI sequences were co-registered geometrically to the DTI data and used as anatomical reference to identify peripheral nerves. For tractography, multiple regions of interest which covered the area under study were manually outlined. Tractography was performed based on the connection between the regions of interest to minimize the risk of including other tracts. Fibres were computed automatically by the software (minimum FA 0.3; maximum angle between fibres 27° ; and minimum fibre length 10 mm). FA and ADC values were obtained from the segmented nerve. For the CSN study, the proximal area was located at the sciatic notch, the medial in the gluteal region at the ischial intersection and the distal at the root of the thigh.

MRI and diffusion tensor imaging interpretation

MR analyses were performed by an experienced radiologist (SL-C) who evaluated the peripheral nerve size (focal or diffuse decrease or enlargement), signal intensity compared with skeletal muscle in T1WI, T2WI and STIR sequences, lesion presence, fascicular pattern, course (normal or deviated), abnormal contrast agent enhancement and indirect signs of muscle denervation (oedema, atrophy, fatty infiltration). Additionally, visual inspection of the DTI segmented nerve was also performed (assessment of nerve integrity, interruption, myelin damage or focal size changes).

Statistical analyses

Statistical analyses were performed with SPSS software (SPSS® v. 15.0; IBM Corp., New York, NY; formerly SPSS Inc., Chicago, IL). For group comparisons, the Mann–Whitney test was used. For correlation analyses, a point biserial correlation test was used. Results were considered significant when $p < 0.05$.

RESULTS

Fractional anisotropy and apparent diffusion coefficient values

In the control group, FA and ADC values of the CSN remained stable, without any significant differences along the nerve values when compared with the controls (Table 2).

In the patient group, damage of the CNS resulted in a significant decrease of the global FA values and increase of the global ADC values when compared with the controls (Table 1). Furthermore, when studying the nerve at different levels (from proximal to distal), the proximal region did not show any significant differences in the FA and ADC values between groups. The main differences were located at the medial and distal regions within the nerve.

Statistical results did not show any correlation between the FA and ADC values with sex, age, time after diagnosis, nerve conduction

Table 2. Fractional anisotropy (FA) and apparent diffusion coefficient (ADC) values measured at different levels within the common sciatic nerve

	FA patients (<i>n</i> = 15)	95% CI	FA controls (<i>n</i> = 10)	95% CI	ADC patients (<i>n</i> = 15)	95% CI	ADC controls (<i>n</i> = 10)	95% CI	<i>p</i> -value
Proximal	0.47 ± 0.08	$0.36\text{--}0.62$	0.54 ± 0.03	$0.51\text{--}0.57$	0.93 ± 0.18	$0.66\text{--}1.42$	0.83 ± 0.03	$0.8\text{--}0.86$	0.16
Medial	0.43 ± 0.07	$0.34\text{--}0.59$	0.53 ± 0.03	$0.51\text{--}0.56$	1.1 ± 0.26	$0.6\text{--}1.53$	0.78 ± 0.06	$0.73\text{--}0.84$	0.011
Distal	0.43 ± 0.01	$0.32\text{--}0.72$	0.55 ± 0.03	$0.52\text{--}0.57$	1.04 ± 0.28	$0.4\text{--}1.43$	0.77 ± 0.09	$0.69\text{--}0.85$	0.02
Global	0.44 ± 0.08	$0.36\text{--}0.62$	0.54 ± 0.02	$0.51\text{--}0.56$	1.02 ± 0.2	$0.6\text{--}1.28$	0.79 ± 0.04	$0.75\text{--}0.83$	0.03

CI, confidence interval.

Values are given as mean $\pm$ standard deviation. *p*-values and CIs are shown.

Figure 1. Normal appearing tractography results merged with T_2 weighted imaging, in axial and coronal views of the common sciatic nerve in the pelvis and thigh in a healthy 24-year-old female (a-c), and distal level of the thigh (d, e) in a healthy 37-year-old female where peroneal and tibial branches are shown. Nerve colour is based on the orientation diffusion tensor imaging colour code.

study results or nerve hyperintensity in T2WI. Only a positive correlation between the NCS motor results and the presence of denervation pattern by MRI was observed ($p = 0.01$, Table 2).

Tractography

Healthy controls

With our experimental conditions, we were able to track the Sciatic Nerve (SN) and its main branches from hip to foot (Figures 1 and 2). At the pelvis, we were able to visualize the

main branches L4, L5, S1, S2 and S3 and their association to form the CSN (Figure 1a). At the thigh, DTI displayed the CSN and its tibial and peroneal branches (Figure 1b,c). This region was the easiest to study with tractography, as the nerve is wide and clear to identify on MRI. At the lower limb, tibial and peroneal nerves divide into several branches. These branches are thinner and therefore more difficult to track with DTI. When comparing peroneal to tibial branches, both tibial branches (deep and superficial) were easier to track than

Figure 2. Normal appearing tractography in a healthy 37-year-old female merged with T_2 weighted imaging in axial plane at the lower limb. Tibial branches (tibial and sural nerves) (a), peroneal branches (deep and superficial) (b), medial plantar (c) and sural (d) nerves, medial and lateral plantar nerves as well as some of its branches (e), and the digital nerves (f). Nerve colours are based on the orientation diffusion tensor imaging colour code.

Figure 3. Patient 17. A 47-year-old male with left lower limb Schwannoma located posterior to the lateral condyle of the femur (see white arrows). (a) T_1 weighted imaging (T1WI) showing the MRI appearance of tibial and peroneal nerves (red arrows) in the axial plane above the lesion. The lesion was hypointense in T1WI (b) and hyperintense on T_2 weighted imaging (c, d) and fat-saturated proton density-weighted images with spectral adiabatic inversion recovery sequence (PD-SPAIR) (h, f). Tractography results merged with axial T_1 weighted image (e), and axial PD-SPAIR (f) showed the existence of wrapping fibres from the sural cutaneous branch forming the tumour capsule (g). The external popliteal nerve was undamaged. Nerve colours have been changed to improve visualization.

peroneal. This is important when studying the lower limb with DTI because of its difficulties (the thinner the nerve, the more difficult to track with DTI).

At the foot, we were able to track both plantar nerves and some of its branches as well as most of the digital nerves (Figure 2c–f), which could be useful when studying lesions such as Morton's neuroma.

Figure 4. Patient 9. A 41-year-old male diagnosed with intraneural perineurioma of the left common sciatic nerve. After resection, the patient referred only mild sensory loss in the lower limb that affected the dorsal part of the feet and toes, and the distal lateral leg. Axial PD-SPAIR weighted images showing the lesion before surgery (a) and 12 months after surgery (f). Axial T_1 weighted images after contrast injection showing the location of the lesion before surgery (b) and 12 months after surgery (g, e). The lesional area presented an ill-defined contrast enhancement secondary to post-surgical changes. Post-surgical coronal T_1 weighted imaging (T1WI) turbo spin echo (TSE) (c) and short tau inversion recovery TSE (d) images; arrows point to the lesional area. (j–l) Tractography results performed 12 months after surgery merged with T_1 weighted images, in the axial and coronal views, showed the existence of an area with a lack of healthy myelin at the location of the surgery. This area was not observed in the T_1 weighted and T_2 weighted images (h, i). Nerve colour has been changed for better visualization, and arrows point to the lesion area.

Figure 5. Patient 16.A 45-year-old male with a clinical history of three different left ankle sprains during the period of 2 years. Physical examination showed a positive Tinel's sign, suggesting nerve entrapment. The nerve conduction study of the left tibial nerve did not show pathological findings in both sensitive and motor branches. Axial T_1 weighted (a), T_2 weighted (b) and PD-SPAIR (c) images showed an area of fibrosis at the medial malleolus (white arrows) caused by chronic sprains, in a medial impingement syndrome. Illustration of tractography results merged with T_2 weighted imaging in the axial plane (d), PD-SPAIR in the coronal plane (e, f) and T_1 weighted imaging in the sagittal plane (d, f) showed the region of the nerve entrapment (white arrows) which was related to the fibrosis area (a–c). The red arrows show the location of the tibial nerve. Nerve colour has been changed for better perception.

Peripheral neuropathy

Tractography results complemented the conventional MRI study allowing a more precise identification of the damaged nerve area, supplying information that was not available by conventional MRI.

Tractography allowed the identification of the relationship between the tumour and its nerve root (Figure 3). This information, which was not available by conventional MRI, was of value for surgery planning. In addition, DTI enabled the study of CSN integrity after tumour removal (Figures 4).

In entrapment neuropathy, tractography results displayed the region where the nerve was entrapped as well as the presence of nerve inflammation (Figures 5 and 6). In Patient 16, the nerve entrapment was caused by fibrosis triggered by chronic sprains (Figure 5a,b), where tractography allowed us to locate the entrapment region at the medial retromalleolar area.

In traumatic neuropathy, tractography results displayed the location and extension of the damaged area, which correlated with the electroneurography results (Figure 7). This information was useful for surgery planning, allowing minimizing the area under incision.

Finally, only in diffuse polyneuropathies, tractography results showed the presence of areas affecting both CSNs with regions

lacking healthy myelin showing a patched distribution (Figure 8). In this context, DTI allowed to picture the affected nerves and characterize the presence of local differences.

Diffusion tensor imaging vs MRI

All patients diagnosed with sciatic neuropathy presented DTI results suggesting nerve damage. When comparing DTI to conventional MRI results, we observed that in our patient group in eight cases (47%), the MRI appearance of the nerve was normal. Besides, six of these patients with normal nerve MRI appearance had pathological EMG results and five already had muscle atrophy.

DISCUSSION

One of the major difficulties in the management of patients with peripheral neuropathies is the lack of objective and non-invasive techniques to assess the integrity of the nerve. Despite MRI being routinely used in the clinical setting to provide information about the anatomy and injury of the peripheral nerves, its sensitivity and specificity are still unsatisfactory.

In our study, we have observed that there could be normal-appearing MR images in patients with symptomatic neuropathy. In these patients, although MRI was unable to detect nerve damage, DTI showed pathological results suggesting neuropathy in all cases. The characteristic MRI signal of peripheral neuropathy has been widely described in literature; the most

Figure 6. Patient 4. A 32-year-old female diagnosed with piriformis syndrome. Axial short tau inversion recovery (STIR) (a), T_1 weighted image (b), T_2 weighted image (c) and STIR images (f) suggested inflammation in the right common sciatic nerve. Tractography of both sciatic nerves merged with T_1 weighted imaging in the coronal view (d, e) showed an increase in the size of the right sciatic nerve in the area related to inflammation observed in the MRI study (white arrows). Nerve colours are displayed according to the orientation diffusion tensor imaging colour code.

common is nerve hyperintensity on T2WI, but the assessment of signal intensity may be subjective.^{4,8} In our study, the lack of ability to detect nerve damage by MRI in some patients could be related to the inherent characteristics of the peripheral nerves. The peripheral nerves are composed by nerve fibres embedded in the connective tissue (endoneurium) and grouped into fascicles (the smallest unit visualized by MRI) encircled by the perineurium. Fascicles are also embedded in the connective tissue (internal epineurium), which are also encircled by the epineurium thus comprising a peripheral nerve. Therefore, as we are mostly visualizing the connective tissues by MRI, abnormalities or damages in the myelin sheath may exist even in the case of normal-appearing MRI.

In our study, only the patients diagnosed with diffuse neuropathies presented areas with a patched distribution within the nerve suggesting a lack of myelin integrity. The distribution of these areas

was bilateral in all cases, affecting both CSNs. This result must be confirmed in further investigations. However, when tractography results show the presence of bilateral healthy myelin-lack areas with a patched distribution, a diffuse neuropathy might be suspected.

We have observed a correlation between electrophysiology results and the presence of muscle denervation in MRI. Denervation patterns can be differentiated by MRI. The last pattern is muscle fatty replacement, suggesting a long-standing denervation in which the involved muscle fibres are inevitably lost.⁹ This is vital information for the surgeon as a muscle with fatty infiltration is unlikely to recover after surgical nerve repair. In this context, the information provided by DTI before the presence of muscle fatty replacement may be of value.

One of the main limitations of this study is the small and heterogeneous cohort of patients. We believe that an increase in the

Figure 7. Patient 5. A 56-year-old male who suffered a traumatic lesion affecting the left peroneal nerve 6 months earlier. Physical exploration revealed left common peroneal nerve paralysis. Electroneurography (ENG) showed a partial severe lesion in the left peroneal nerve probably at the level of the fibular head. Coronal and axial T_2 weighted imaging (a, b), PD-SPAIR (e), short tau inversion recovery turbo spin echo (f) and T_1 weighted imaging (d) of the left lower limb showed MRI changes in the tibialis anterior, extensor digitorum longus and peroneus muscles, secondary to muscle atrophy and fatty replacement (white arrows). Tractography results of the peroneal nerve branches (deep and superficial) merged with T_1 weighted image in the axial and coronal views showed the area of the nerve damage at the head of the fibula which matched with the ENG results. The red arrows show peroneal nerve.

number of patients will give a better understanding of the putative role of FA and ADC values in aetiology characterization.

DTI has been lately considered as the most sensitive imaging technique for detection of white matter pathologies.⁶ It has been widely applied in the study of the brain white matter and lately has been used in the study of peripheral nerves although the literature is still

sparse.^{7,10–12} Some studies have highlighted its high reproducibility and feasibility in the clinical setting.^{13,14} For example, reproducibility studies in brachial plexus show an overall reproducibility between 81% and 92%, considering combined influence of the observer and of the repeated measurements.¹⁴ DTI does not have any specific requirements although the analysis requires experience, a good knowledge of the anatomy and is time consuming.

Figure 8. Patient 12. A 57-year-old male diagnosed with liver disease in 2010 and hepatic transplant in 2013. 4 months after initiation of the immunosuppressive therapy with tacrolimus, the patient started with progressive weakness in both lower limbs. Electromyogram/electroneurography results revealed multiple mononeuropathy in acute/subacute phase affecting both sciatic nerves at the peroneal branch with conduction blocks. The common sciatic nerve, peroneal and tibial branches presented a normal appearance in the T_1 weighted imaging turbo spin echo (TSE) and T_2 weighted imaging (T2WI) TSE (a, b, red arrows). T2WI showed a bilateral hyperintensity affecting both anterior tibialis and peroneus brevis muscles (c, white arrows). Tractography results showed the existence of a patched myelin damage affecting both sciatic nerves (d). Both peroneal branches were absent in the tractography results (e, f). Red arrows point to peroneal and tibial branches.

Our results suggest that DTI may complement MRI, by providing additional information about the white matter structures as well as quantitative data that could be used in longitudinal studies. From this perspective, we recommend to implement this technique as a clinical protocol in the MR units, especially in those cases where conventional MRI does not expose the real condition of the patient.

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