BMJ Neurology Open

Diffusion tensor imaging in peroneal neuropathy: a prospective, single-centre study

Christophe Oosterbos ,[1,2] Ahmed M Radwan ,[3] Stefan Sunaert,[4,5] Sophie Hoornaert,[2,6] Anais Van Hoylandt,[2,6] Robin Lemmens ,[7,8] Tom Theys[2,9]

To cite: Oosterbos C, Radwan AM, Sunaert S, *et al*. Diffusion tensor imaging in peroneal neuropathy: a prospective, single-centre study. *BMJ Neurology Open* 2025;**7**:e000876. doi:10.1136/bmjno-2024-000876

► Additional supplemental material is published online only. To view, please visit the journal online (https://doi.org/10.1136/bmjno-2024-000876).

CO and AMR contributed equally.

Received 17 August 2024
Accepted 22 December 2024

For numbered affiliations see end of article.

Correspondence to
Dr Christophe Oosterbos; christopheoosterbos@gmail.com

ABSTRACT

Objective Diffusion tensor imaging (DTI) showed promising results in diagnosing upper limb neuropathies, but its value in patients with foot drop due to peroneal neuropathy has not yet been investigated. We aim to establish reference values for DTI metrics of the healthy peroneal nerve and to evaluate differences in DTI metrics between patients and healthy controls.

Methods Diffusion-weighted images (DWI) from 22 pathological nerves, 14 asymptomatic patients' nerves and 65 healthy peroneal nerves were processed for quantitative assessment of fractional anisotropy (FA), radial diffusivity (RD), axial diffusivity and mean diffusivity. Clinical baseline and follow-up data were prospectively collected for all patients.

Results Mean patient FA values (0.40, SD 0.08) were significantly lower compared with healthy controls (mean FA 0.44, SD 0.06). Mean patient RD values (0.98 10^{-3} mm^2/s, SD 0.21 10^{-3} mm^2/s) were significantly higher compared with healthy controls (mean RD 0.85 10^{-3} mm^2/s, SD 0.16 10^{-3} mm^2/s). FA values were significantly lower in patients with severe foot drop (mean FA 0.40, SD 0.06) compared with non-severe foot drop (mean FA 0.48, SD 0.05).

Conclusion Based on these results, DTI appears to aid in the differential diagnostic process of patients with peroneal neuropathy. Future studies should focus on automation of DWI processing, confirm the results in larger patient groups and try to establish reliable cut-off values for DTI metrics.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Previous research on diffusion tensor imaging (DTI) in upper limb neuropathies was promising, with high sensitivity being reported. Thus far, the added value of DTI in patients with foot drop due to peroneal neuropathy has not been studied.

WHAT THIS STUDY ADDS

⇒ This preliminary study showed significant differences in DTI metrics of the peroneal nerve (fractional anisotropy (FA), radial diffusivity) between patients and healthy volunteers. FA values of the peroneal nerve could discriminate between a healthy nerve and a pathological nerve.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Further research should validate these findings and establish cut-off values. These results suggest that DTI can be of value in the diagnosis of patients with peroneal neuropathy.

INTRODUCTION

Peroneal neuropathy is the most common mononeuropathy in the lower limbs[1] and a well-known cause of foot drop and subsequent gait difficulties.[2] Diagnosis is routinely made based on typical clinical findings[1] and confirmatory electrodiagnostics (EDX).[3] This approach is limited by the absence of nerve visualisation and further lesion-type characterisation.[4] Consequently, EDX is increasingly supplemented with MRI[5] allowing for the detection of morphological abnormalities and further diagnostic finetuning based on increased cross-sectional area (CSA) measurements, increased T2 signal intensity and assessment of muscle denervation patterns.[6–8] Previous research[9] revealed important limitations of routine MRI of the peroneal nerve. CSA measurements and the assessment of T2 signal intensity were subjected to important intraobserver and interobserver variability and CSA cut-off values had a relatively low sensitivity and specificity. Routine MRI analysis is dependent on visual inspection of the image and therefore potentially subjective.[10]

Diffusion tensor imaging (DTI) is an advanced, quantitative MRI technique, capable of measuring the direction and magnitude of diffusion in neural tissue[11] and enables a more objective diagnostic approach compared with routine MRI.[10] In physiological circumstances, diffusivity is the largest in the fibre direction and therefore highly anisotropic in peripheral nerves.[12] Several parameters were defined to quantify diffusivity in peripheral nerves based on DTI. Among these measurements of diffusivity are fractional anisotropy (FA), mean diffusivity

(MD), radial diffusivity (RD) and axial diffusivity (AD). The FA value reflects the degree of anisotropy and varies between 0 and 1 with 1 reflecting perfect anisotropic diffusion. FA is considered a general biomarker of nerve tissue integrity.[13] A decrease might reflect tissue microstructure damage, demyelination or axonal loss.[13–15] MD is a measurement of global diffusion. An increase in MD is compatible with swelling, oedema and inflammation.[16] RD reflects diffusion orthogonal to fibre direction whereas AD measures diffusion in the fibre direction.[12] A decrease in AD might reflect axonal neuropathy whereas an increase in RD might reflect myelin sheath damage.[15]

DTI of white matter tracts is well known and researched with known limitations and drawbacks.[17] In contrast to the complex white matter tracts of the brain, peripheral nerves are comparatively simpler structures (orientation of nerve fibres along the same axis), potentially more suitable for diffusion assessment. Thus far, DTI has mostly been studied in frequent mononeuropathies of the upper limb including carpal tunnel syndrome[18] and cubital tunnel syndrome[19–21] with DTI values in healthy upper limb peripheral nerves being reported.[22] Some authors[19] conclude that DTI is a highly sensitive technique for the detection of peripheral neuropathy. The added value of DTI in patients with peroneal neuropathy is unknown.

We aim to investigate DTI metrics of the peroneal nerve in both patients and healthy volunteers and to compare results to clinical characteristics. This study focuses on differences within patients (between the symptomatic and asymptomatic peroneal nerve) and on differences between the nerves of patients and those of healthy individuals. We hypothesise that, in comparison to healthy controls, patients would have lower FA and AD values of the peroneal nerve and higher RD and MD values.

MATERIAL AND METHODS

Ethics approval statement

Obtaining diffusion-weighted imaging (DWI) in patients with peroneal neuropathy was a substudy within a larger imaging study involving both MRI and ultrasound.[9]

Participant data

Patients with EDX-confirmed peroneal neuropathy and motor impairment for less than 6 months were recruited at the outpatient clinic of a tertiary, neuromuscular reference centre (University Hospitals Leuven). Recruitment started in the COVID-19 pandemic and occurred between March 2021 and February 2023. Patients were eligible if they had no history of recurrent foot drop, polyneuropathy, critical illness polyneuropathy, hereditary neuropathy with liability to pressure palsies and had no surgical treatment prior to imaging. Trial participation was only considered in the absence of MRI contraindications. No exclusion based on aetiology occurred. Baseline data and clinical follow-up data were collected for all patients during standard-of-care follow-up. In case of incomplete motor recovery at the last clinical follow-up, patients were contacted by telephone to assess recovery. Recovery was defined as a clinically assessed normal Medical Research Council (MRC) score for ankle dorsiflexion muscle strength or the absence of subjective loss of strength and gait difficulties (telephone interview).

Healthy controls were recruited in the same period through advertisement and communications at the University Hospitals Leuven. Participants were considered healthy in the absence of a history of any neurological disease, diabetes mellitus, thyroid disease or musculoskeletal disorders at the level of the knee.

Imaging protocol

MR acquisition was done using a 3.0 Tesla whole-body MRI scanner (Achieva dStream, Philips Healthcare, Best, The Netherlands) and the dedicated dStream 16 channels knee receive coil. Patients were placed in a supine position, proximal fibular head positioned at the centre of the knee coil. Spin-echo echo-planar imaging (EPI) diffusion MRI (dMRI) data for peripheral nerve imaging was obtained with 16 directions and b-value=800 s/mm^2 in the axial plane using acquisition parameters as described in online supplemental table 1. The scanning protocol extended beyond the scope of this paper and included axial T1 weighted images, coronal and axial T2 weighted images with fat suppression and axial short τ inversion recovery sequences.[9] Detailed technical specifications are available in the supplementary materials of previous work.[9]

EDX studies

All patients underwent both nerve conduction studies (NCS) and electromyography (EMG) prior to imaging. All EDX studies were performed by residents, supervised by experienced neurologist–neurophysiologists with over 5 years of experience. For a peroneal NCS, we recorded the extensor digitorum brevis (EDB) muscle with stimulation at the typical sites: at 8 cm from the EDB muscle, distal and proximal to the fibular head. Typically, we also recorded the peroneal nerve at the contralateral side for comparison. The temperature in the room was controlled at 25°Celsius. Based on clinical findings (ie, temperature measurements on indication), heating of extremities was performed. Anterior tibial muscle recordings were documented during needle EMG. Following reference values were used during EDX evaluation: onset latency<6 ms, peroneal nerve conduction velocity≥40 m/s, ratio compound motor action potential (CMAP) amplitude proximal of the fibular head over CMAP amplitude distal of the fibular head≥70% and normal EDB muscle peak to peak value≥5 mV.

Imaging analysis

DTI postprocessing and quantitative analysis were performed by an experienced neuroradiologist (AMR) using MRtrix3 (V.3.0.3) and FSL (V.6.0.5.1). The raw dMRI data files underwent conversion from their original DICOM format to NIFTI using the dcm2niix tool.

Subsequently, files were transformed to the .mif format via the mrconvert function, ensuring the preservation of gradient and b-value information. Both healthy volunteers and patients' data sets underwent a series of processing steps.[23] Initially, the dwidenoise function was employed for denoising, aiming to mitigate noise in the diffusion data through the Marchenko-Pastur PCA technique.[24–26] Next, the mrdegibbs function ran to rectify Gibbs ringing artefacts.[27] The mean of the DWI was extracted with the dwiextract and mrmath functions.[23] The data sets then underwent preprocessing with the dwifslpreproc function to correct for Eddy current-induced distortions and potential subject motion, leveraging the Eddy command of FSL.[28] The dwibiascorrect function, paired with the ANTs option, addressed intensity inhomogeneities in the diffusion data.[29] Tensor estimation was done using dwi2tensor with default settings, and various diffusion metrics (FA, RD, AD and MD) were computed with tensor2metric.[23]

Initial tractography attempts were conducted automatically but results were often contaminated by muscle fibres being reconstructed (in the absence of sufficient spatial constraints). Automated derivation of such a constraint relied on the mean DWI image to derive a mask of the most restricted structures in the data. This was based on the notion that nerves should normally be more restricted than muscles. However, this also suffered from inaccuracies due to the contamination of the resulting maps by fat-signal-related artefacts. Thus, we settled on an iterative tractographic approach where the initial automated results were subjectively scrutinised for anatomical accuracy and specific orientational priors in the form of manually defined inclusion and exclusion volumes-of-interest (VOIs) were defined by consensus between AMR and CO. Manual VOIs were used to create final, more accurate tractograms for each subject and to sample the corresponding voxels from scalar maps (FA, AD, RD and MD) for further statistical analysis. Tractography used tckgen with the probabilistic tensor method[30] with empirically determined parameters of 20 000 streamlines, a minimum length of 50 mm and a maximum angle threshold of 4 degrees. Initial tractography used the DWI-mean derived nerve mask for streamline seeding and inclusion, while final tractography used the manually defined inclusion and exclusion VOIs for simultaneous seeding and inclusion without masking. All resulting tractograms were also filtered for outlier streamlines using the Scilpy (V. 1.1) scil_outlier_rejection.py command. The dMRI and tractography processing pipeline are summarised in figure 1.

Statistical analysis

All statistical analyses were performed using IBM SPSS statistics V.25. Demographic parameters were compared using the Mann-Whitney U test (Shapiro-Wilk test showed no normal distribution for age and body mass index (BMI) only) and the χ^2 test for continuous and categorical variables, respectively. Analysis of differences in DTI measurements between the several types of nerves scanned (symptomatic nerve of patient, asymptomatic nerve of patient and healthy nerve of control) was done using linear mixed regression with random intercepts per patient. Age and BMI were modelled as covariates since they are known to explain some variability in DTI metrics.[13] Additionally, footedness was modelled as a covariable. Receiver operating characteristic curves were used to assess the area under the curve (AUC) and optimal cut-off points to discriminate between a pathological and healthy peroneal nerve (in case significant differences for that DTI metric were observed). Differences in DTI metrics between patient groups with severe and non-severe foot drop and patients that did and did not recover were assessed using an analysis of covariance with age, BMI and footedness as covariates. Foot drop severity and recovery were coded as binary categorical variables. A severe foot drop was defined as an MRC score for ankle dorsiflexion≤3/5. A non-severe foot drop was defined as an MRC score for ankle dorsiflexion of 4/5. Two patients with bilateral disease were excluded from the analysis. Recovery was defined as a clinically assessed normal MRC score for ankle dorsiflexion muscle strength or the absence of subjective loss of strength and gait difficulties (telephone interview). Four patients were excluded from the recovery analysis. Two patients who were treated surgically were excluded from this analysis to exclude variability introduced by different treatments. One patient who died very soon after diagnosis was excluded from this analysis. The fourth patient had bilateral disease and was excluded as well. All post hoc pairwise comparisons were corrected for multiple testing using the Holm-Bonferroni method. Correlation between FA and EDX parameters (% of the drop in CMAP, CMAP size proximal and distal to the fibular head and velocity decrement (m/s) were assessed with the Pearson R correlation coefficient in case of normally distributed data (FA, % of CMAP amplitude drop) and with Spearman's Rho in case of skewed data distribution (velocity decrement). Two patients with bilateral disease were excluded from the analysis since no data on velocity decrement or CMAP amplitude drop was available). Scatterplots were used to visualise the correlations.

RESULTS

Participants

In total, 22 patients and 38 healthy volunteers were included. DWI from 22 pathological nerves, 14 asymptomatic patients' nerves and 65 healthy nerves were suited for analysis (figure 2). The median duration between foot drop onset to first clinical examination and MRI was respectively 15 days (IQR: 3–42 days) and 45 days (IQR: 29–65 days).

Patients were older than healthy controls and more patients were male (see table 1).

18 patients had a severe foot drop. In total, 15 foot drops recovered within a period of 6 months (68.2%). All but two patients were treated conservatively. Two patients with severe foot drop underwent neurolysis of

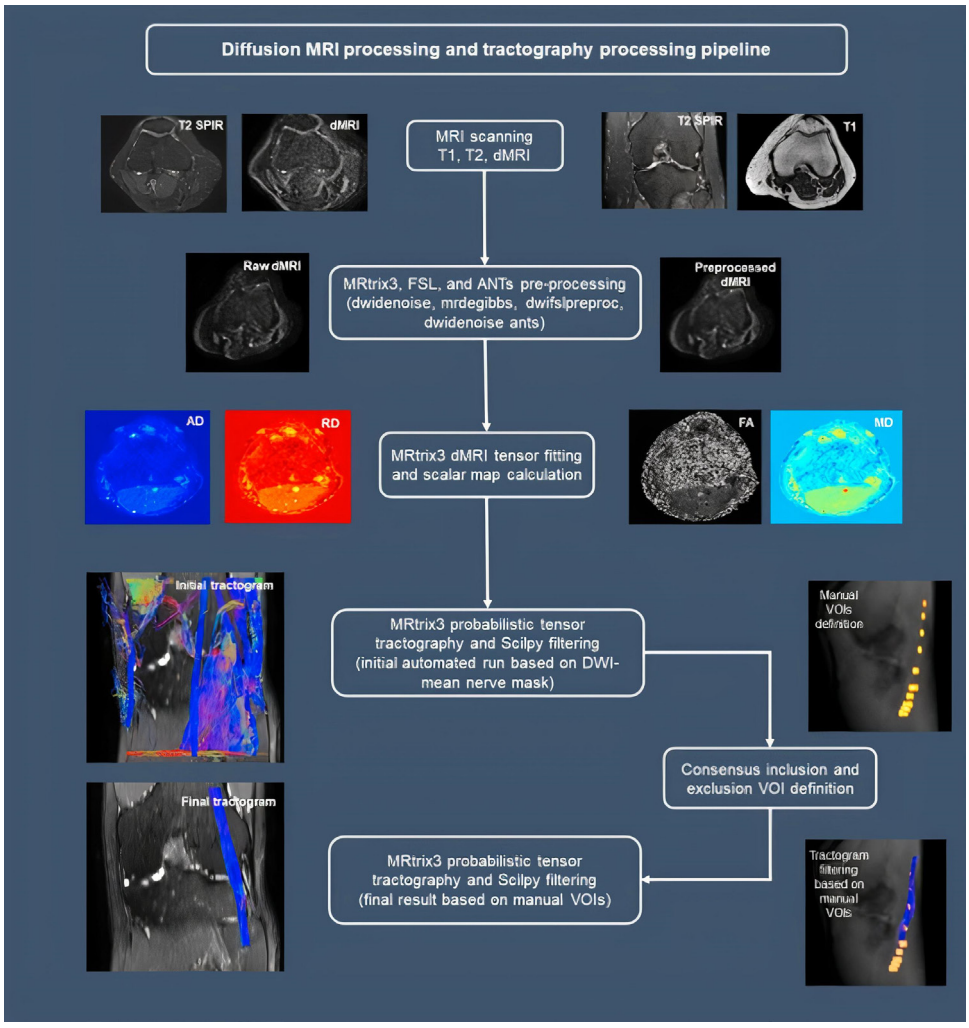

Figure 1 Diffusion MRI and tractography processing pipeline. AD, axial diffusivity; dMRI, diffusion-weighted MRI; DWI, diffusion-weighted imaging; FA, fractional anisotropy; MD, mean diffusivity; RD, radial diffusivity; SPIR, spectral presaturation with inversion recovery; VOI, volume-of-interest.

the peroneal nerve in a multicentre study comparing surgical and non-surgical treatment.[31]

Footedness

Within the healthy peroneal nerve sample, significant differences in mean FA, RD, AD and MD were observed between the peroneal nerve of the dominant and non-dominant foot (see online supplemental table 2). Based on these findings, footedness was modelled as a binary covariate in further analysis.

Differences in DTI metrics between patients and healthy volunteers

DTI metrics for (a) symptomatic patient's nerves and healthy volunteers were reported in table 2. Mean values for FA, RD, AD and MD of the healthy volunteers taking age and BMI into account are available in the online supplemental table 3.

Significant differences in mean RD and FA values were observed between healthy controls and symptomatic nerves (table 3). In comparison to healthy controls RD was significantly higher and FA significantly lower in patients with foot drop due to peroneal neuropathy. The AUC for FA was 0.636 (p=0.06). An FA value≤0.43 had a sensitivity of 63.6% and a specificity of 50.8% (Youden index 0.14). The AUC for RD was 0.666 (p=0.02). An RD value≥0.92 10^{-3} mm^2/s had a sensitivity of 68.2% and a specificity of 60.0% (Youden index 0.28). We observed no differences in DTI metrics when comparing pathological versus asymptomatic nerves in patients or when comparing asymptomatic patients' nerves versus healthy controls.

DTI and foot drop severity/foot drop recovery

14 patients had a severe foot drop at the time of imaging, 4 patients had a non-severe foot drop. The mean FA values of patients with a severe foot drop (0.40) were significantly lower (p=0.04) compared with the mean FA values of patients with a non-severe foot drop (0.48). Mean values for RD, AD and MD were not significantly different between patients with a severe and non-severe foot drop (table 4A).

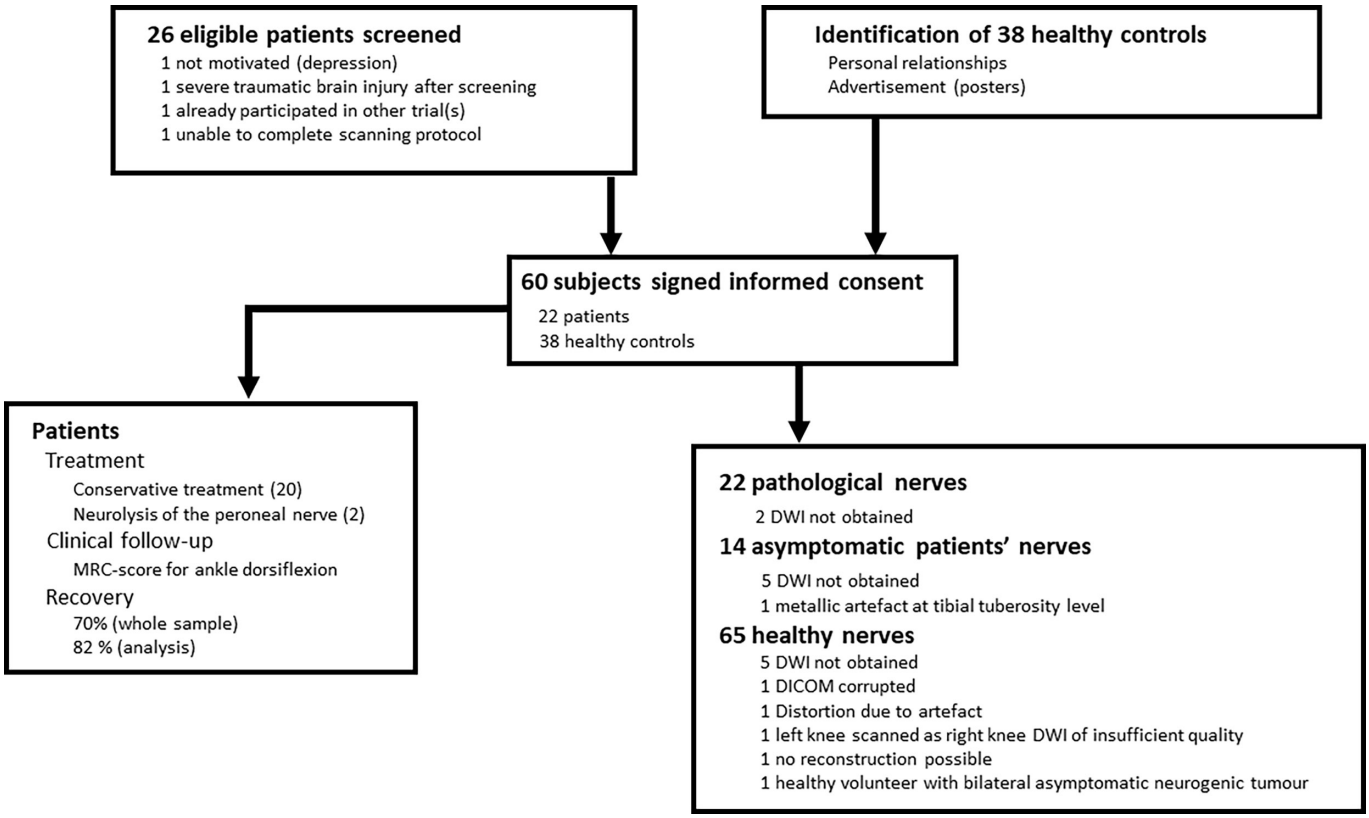

Figure 2 Trial flow. DWI, diffusion-weighted imaging; MRC, Medical Research Council.

Foot drop from 14 out of 17 patients included in the analysis recovered (82%). No significant differences in mean values for FA, RD, AD and MD were observed between patients who did and did not recover (table 4B).

Correlation between DTI metrics and neurophysiology

There was no correlation between FA values and the percentage of drop in CMAP across the fibular head (Pearsons R −0.086, p=0.73) or between CMAP size in mV and FA values (Pearsons R 0.231, p=0.356 for CMAP size proximal to the fibular head; Pearsons R 0.354, p=0.149 for CMAP size distal to the fibular head). No correlation between FA values and velocity decrement across the fibular head (Spearman's rho 0.140, p=0.58) was established. See online supplemental figure 1-4.

DISCUSSION

This proof-of-concept study reported DTI metrics of the peroneal nerve in both patients and healthy controls. To our knowledge, this was the first study investigating DTI metrics of the peroneal nerve in patients with foot drop due to peroneal neuropathy.

In both ulnar neuropathy and carpal tunnel syndrome, previous work indicated that diffusion is more isotropic in patients compared with healthy controls.[18 21] This shows the potential for DTI in the detection of peripheral mononeuropathies. Based on our study results, FA and RD values of the peroneal nerve differ significantly between patients with foot drop due to peroneal neuropathy and healthy individuals. These results indicate a decrease in peroneal nerve integrity and myelin sheath damage in patients with foot drop due to peroneal neuropathy. Our results adhere closely to those of Griffiths *et al*,[21] investigating differences in DTI metrics of the ulnar nerve between healthy volunteers and patients with cubital tunnel syndrome. Differences in FA and RD between patients and healthy controls were reported but not for MD and AD values. Differences in DTI metrics were not limited to the cubital tunnel alone but appeared throughout the length of the ulnar nerve as studied. As is

Table 1 Participant demographics (patients and healthy volunteers)

	Patients (n=22)	Healthy volunteers (n=65)	P value
Age in years (mean, (SD))	55.8 (16.1)	43.6 (12.0)	0.00
Sex (% male)	86.3	43.1	0.00
BMI (kg/m^2) (mean, SD)	25.8 (3.0)	24.1 (4.8)	0.09

BMI, body mass index.

Table 2 DTI metrics for the peroneal nerve of patients (both asymptomatic and symptomatic nerve) and healthy volunteers

	FA	MD	RD	AD
	(0–1)	(10^{-3} mm^2/s)	(10^{-3} mm^2/s)	(10^{-3} mm^2/s)
Symptomatic patient's nerve (n=22)				
Mean	0.4	1.27	0.98	1.86
SD	0.08	0.22	0.21	0.29
Minimum–maximum	0.24–0.53	1.17–1.37	0.59–1.39	1.22–2.32
Asymptomatic patient's nerve (n=14)				
Mean	0.44	1.19	0.88	1.81
SD	0.06	0.26	0.21	0.38
Minimum–maximum	0.36–0.53	0.70–1.46	0.58–1.25	1.23–2.44
Healthy control (n=65)				
Mean	0.44	1.16	0.85	1.73
SD	0.06	0.2	0.16	0.32
Minimum–maximum	0.33–0.62	0.70–1.61	0.42–1.12	1.17–2.27

AD, axial diffusivity; DTI, diffusion tensor imaging; FA, fractional anisotropy; MD, mean diffusivity; RD, radial diffusivity.

the case in our study, these differences became apparent in a small study sample consisting of 13 patients and 14 healthy controls. Studies with larger patient samples are warranted to investigate differences in MD and AD values, since differences in MD values between patients and healthy controls were observed in other mononeuropathies like carpal tunnel syndrome.[32] In patients with peroneal neuropathy, some oedema and swelling can be expected, potentially translating to higher MD values. In our study, FA values were significantly lower in patients with a severe foot drop compared with patients with a non-severe foot drop. These findings reflect a more severe loss of nerve integrity in patients with a more severe neurological deficit (foot drop). These findings are not unique to peroneal neuropathy. Cao *et al*[33] showed a significant decrease in FA and AD values of the common peroneal nerve in patients with Guillain-Barre syndrome compared with healthy volunteers. Bulut *et al*[34] found differences in mean FA values of the median nerve between patients with mild, moderate and severe carpal tunnel syndrome. Overall, DTI findings in patients with peroneal neuropathy appear to correlate quite well with findings from other mononeuropathies. Future studies should aim at

Table 3 Pairwise comparisons of mean DTI metrics measurements between pathological nerve of the patient, healthy nerve of the patient, healthy nerve of the healthy control

		Lower 95% CI	Upper 95% CI	Adjusted P Value
Patient (pathological) versus patient (asymptomatic)				
Difference in mean FA	0.04	−0.09	0.01	0.18
Difference in mean RD (10^{-3} mm^2/s)	0.1	−0.05	0.25	0.31
Difference in mean AD (10^{-3} mm^2/s)	0.05	−0.23	0.32	1.00
Difference in mean MD (10^{-3} mm^2/s)	0.08	−0.1	0.26	0.81
Patient (pathological) versus volunteer (healthy)				
Difference in mean FA	0.04	−0.08	0	**0.04**
Difference in mean RD (10^{-3} mm^2/s)	0.13	0.02	0.24	**0.01**
Difference in mean AD (10^{-3} mm^2/s)	0.13	−0.07	0.33	0.38
Difference in mean MD (10^{-3} mm^2/s)	0.12	−0.01	0.25	0.08
Patient (asymptomatic) versus volunteer (healthy)				
Difference in mean FA	0	−0.05	0.04	1.00
Difference in mean RD (10^{-3} mm^2/s)	0.03	−0.16	0.1	1.00
Difference in mean AD (10^{-3} mm^2/s)	0.08	−0.32	0.16	1.00
Difference in mean MD (10^{-3} mm^2/s)	0.04	−0.2	0.12	1.00

Analysis: linear mixed regression. P values; Bonferroni corrected. Age, footedness and BMI were modelled as covariates.
AD, axial diffusivity; BMI, body mass index; DTI, diffusion tensor imaging; FA, fractional anisotropy; MD, mean diffusivity; RD, radial diffusivity.

Table 4 Analysis of differences in DTI metrics between patients A with severe and non-severe foot drop and B who did and did not recover

A. DTI and foot drop severity			
	Recovered (mean (SD))	Not recovered (mean (SD))	P value
FA	0.40 (0.06)	0.48 (0.05)	**0.04**
RD (10^{-3} mm^2/s)	0.91 (0.20)	0.94 (0.15)	0.72
AD (10^{-3} mm^2/s)	1.75 (0.29)	2.09 (0.17)	0.20
MD (10^{-3} mm^2/s)	1.19 (0.22)	1.32 (0.17)	0.73
B. DTI and foot drop recovery			
	Foot drop MRC≤3/5 (mean (SD))	Foot drop MRC 4/5 (mean (SD))	P value
FA	0.42 (0.07)	0.45 (0.06)	0.34
RD (10^{-3} mm^2/s)	0.93 (0.17)	0.82 (0.27)	0.65
AD (10^{-3} mm^2/s)	1.86 (0.31)	1.66 (0.31)	0.75
MD (10^{-3} mm^2/s)	1.24 (0.20)	1.10 (0.29)	0.70

Analysis: Analysis of covariance (ANCOVA) with DTI metrics as dependent covariable and foot drop severity as categorical independent variable. Age, BMI and footedness (dummy variable) were modelled as covariates. Only patients with unilateral disease were included. Patients who underwent surgery were excluded as well from the recovery analysis. Bonferroni corrected.
AD, axial diffusivity; BMI, body mass index; DTI, diffusion tensor imaging; FA, fractional anisotropy; MD, mean diffusivity; RD, radial diffusivity.

establishing cut-off values for DTI metrics to differentiate between a healthy and pathological peroneal nerve.

No meaningful correlation between FA values and velocity decrement across the fibular head was found. This stands in contrast to the findings of Bäumer *et al*[35] who found significant correlations between FA values and findings from ulnar NCS in patients with cubital tunnel syndrome. Since the evidence indicates that FA considerably depends on myelin sheath integrity, a correlation was expected (a proportional decrease in FA values and motor conduction velocities/CMAP amplitude).[19 36] The varying time between EDX and MRI and the small patient sample could explain some of these differences.

Finally, age and BMI have been established as important covariates for DTI metrics.[13 16] Within our healthy control sample, we found that footedness also explained some variation in FA, RD, AD and MD. Our approach to footedness was somewhat reductive (subjects were asked if they were right or left-footed); but we believe that this is an argument in favour of DTI being able to detect subtle differences in peripheral nerve (patho)physiology.

LIMITATIONS

There are several important limitations to this study. Due to the single-centre study design and the low incidence of patients with peroneal neuropathy, the patient sample size is small. Important differences, not only in a number of subjects but also in baseline characteristics (age and sex), were observed between patients and healthy controls. Even though the statistical models are correct for age and BMI, the absence of an age-matched control cohort is another weakness of the study. Some follow-up data were collected through telephonic follow-up which is inferior to a clinical assessment (but this was not always possible throughout the COVID-19 pandemic). Study results should be confirmed in larger patient samples and normative values need to be defined before these results can be used in daily practice. Currently, the DTI processing pipeline is not standardised and involves manual nerve segmentation. Lastly, no correction for EPI distortion was applied during dMRI preprocessing. Adding this step can possibly increase overall sensitivity in future research.

CONCLUSION

DTI of the peroneal nerve in patients with foot drop due to peroneal neuropathy is feasible. This preliminary study shows promising results for the use of FA and RD as an add-on in the diagnosis of patients with peroneal neuropathy.

Author affiliations
[1]Neurosurgery, Ziekenhuis Oost-Limburg Campus Sint-Jan, Genk, Belgium
[2]Research Group experimental Neurosurgery and Neuroanatomy and the Leuven Brain Institute, KU Leuven, Leuven, Flanders, Belgium
[3]Imaging and Pathology, Translational MRI, KU Leuven, Leuven, Belgium
[4]Radiology, UZ Leuven, Leuven, Belgium
[5]Imaging and Pathology, Translational MRI, KU Leuven, Leuven, Flanders, Belgium
[6]Department of Neurosurgery, Katholieke Universiteit Leuven Universitaire Ziekenhuizen Leuven Campus Gasthuisberg Dienst Neurosurgery, Leuven, Flanders, Belgium
[7]Neurology, University Hospitals Leuven, Leuven, Belgium
[8]Department of Neurosciences, Experimental Neurology, KU Leuven, Leuven, Flanders, Belgium
[9]Neurosurgery, Katholieke Universiteit Leuven Universitaire Ziekenhuizen Leuven Campus Gasthuisberg Dienst Neurosurgery, Leuven, Flanders, Belgium

Contributors CO is the guarantor. CO and AMR analysed and interpreted the data and wrote the manuscript. SH and AVH aided in trial design, patient recruitment and data collection. SS supervised the study and advised in matters of diffusion tensor imaging scanning protocol and processing. RL and TT aided in trial design,

recruitment of patients, data interpretation and supervised the data processing and manuscript writing.

Funding This study was funded by the Fund for Academic Research of the University Hospitals Leuven (KOOR funding UZ Leuven)

Competing interests No, there are no competing interests.

Patient consent for publication Consent obtained directly from patient(s).

Ethics approval Approval from the Ethical Commission Research from University Hospitals Leuven was obtained in March 2021 (Belgian registration number B3222021000410). Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request.

ORCID iDs
Christophe Oosterbos http://orcid.org/0000-0003-2142-9941
Ahmed M Radwan http://orcid.org/0000-0002-4819-548X
Robin Lemmens http://orcid.org/0000-0002-4948-5956

REFERENCES

1 Poage C, Roth C, Scott B. Peroneal Nerve Palsy: Evaluation and Management. *J Am Acad Orthop Surg Jan* 2016;24:1–10.
2 Carolus A, Mesbah D, Brenke C. Focusing on foot drop: Results from a patient survey and clinical examination. *Foot (Edinb)* 2021;46:101693.
3 Marciniak C, Armon C, Wilson J, *et al*. Practice parameter: utility of electrodiagnostic techniques in evaluating patients with suspected peroneal neuropathy: an evidence-based review. *Muscle Nerve* 2005;31:520–7.
4 Kwee RM, Chhabra A, Wang KC, *et al*. Accuracy of MRI in Diagnosing Peripheral Nerve Disease: A Systematic Review of the Literature. *Am J Roentgenol* 2014;203:1303–9.
5 Agarwal A, Chandra A, Jaipal U, *et al*. Can imaging be the new yardstick for diagnosing peripheral neuropathy?-a comparison between high resolution ultrasound and MR neurography with an approach to diagnosis. *Insights Imaging* 2019;10:104.
6 Lee PP, Chalian M, Bizzell C, *et al*. Magnetic resonance neurography of common peroneal (fibular) neuropathy. *J Comput Assist Tomogr* 2012;36:455–61.
7 Bendszus M, Wessig C, Reiners K, *et al*. MR imaging in the differential diagnosis of neurogenic foot drop. *AJNR Am J Neuroradiol Aug* 2003;24:1283–9.
8 Bignotti B, Assini A, Signori A, *et al*. Ultrasound versus MRI in common fibular neuropathy. *Muscle Nerve* 2017;55:849–57.
9 Oosterbos C, Weerdt OD, Lembrechts M, *et al*. Diagnostic accuracy of ultrasound and MR imaging in peroneal neuropathy: A prospective, single-center study. *Muscle Nerve* 2024;70:360–70.
10 Hiltunen J, Suortti T, Arvela S, *et al*. Diffusion tensor imaging and tractography of distal peripheral nerves at 3 T. *Clin Neurophysiol* 2005;116:2315–23.
11 O'Donnell LJ, Westin C-F. An introduction to diffusion tensor image analysis. *Neurosurg Clin N Am* 2011;22:185–96.
12 Jeon T, Fung MM, Koch KM, *et al*. Peripheral nerve diffusion tensor imaging: Overview, pitfalls, and future directions. *Magn Reson Imaging* 2018;47:1171–89.
13 Kronlage M, Schwehr V, Schwarz D, *et al*. Peripheral nerve diffusion tensor imaging (DTI): normal values and demographic determinants in a cohort of 60 healthy individuals. *Eur Radiol* 2018;28:1801–8.
14 Tanitame K, Iwakado Y, Akiyama Y, *et al*. Effect of age on the fractional anisotropy (FA) value of peripheral nerves and clinical significance of the age-corrected FA value for evaluating polyneuropathies. *Neuroradiology* 2012;54:815–21.
15 Heckel A, Weiler M, Xia A, *et al*. Peripheral Nerve Diffusion Tensor Imaging: Assessment of Axon and Myelin Sheath Integrity. *PLoS One* 2015;10:e0130833.
16 Hiltunen J, Kirveskari E, Numminen J, *et al*. Pre- and post-operative diffusion tensor imaging of the median nerve in carpal tunnel syndrome. *Eur Radiol* 2012;22:1310–9.
17 Assaf Y, Pasternak O. Diffusion Tensor Imaging (DTI)-based White Matter Mapping in Brain Research: A Review. *J Mol Neurosci* 2008;34:51–61.
18 Rojoa D, Raheman F, Rassam J, *et al*. Meta-analysis of the normal diffusion tensor imaging values of the median nerve and how they change in carpal tunnel syndrome. *Sci Rep* 2021;11:20935.
19 Bäumer P, Pham M, Ruetters M, *et al*. Peripheral neuropathy: detection with diffusion-tensor imaging. *Radiology* 2014;273:185–93.
20 Iba K, Wada T, Tamakawa M, *et al*. Diffusion-weighted magnetic resonance imaging of the ulnar nerve in cubital tunnel syndrome. *Hand Surg* 2010;15:11–5.
21 Griffiths TT, Flather R, Teh I, *et al*. Diffusion tensor imaging in cubital tunnel syndrome. *Sci Rep* 2021;11:14982.
22 Wade RG, Lu F, Poruslrani Y, *et al*. Meta-analysis of the normal diffusion tensor imaging values of the peripheral nerves in the upper limb. *Sci Rep* 2023;13:4852.
23 Tournier J-D, Smith R, Raffelt D, *et al*. MRtrix3: A fast, flexible and open software framework for medical image processing and visualisation. *Neuroimage* 2019;202.
24 Veraart J, Fieremans E, Novikov DS. Diffusion MRI noise mapping using random matrix theory. *Magn Reson Med* 2016;76:1582–93.
25 Veraart J, Novikov DS, Christiaens D, *et al*. Denoising of diffusion MRI using random matrix theory. *Neuroimage* 2016;142:394–406.
26 Cordero-Grande L, Christiaens D, Hutter J, *et al*. Complex diffusion-weighted image estimation via matrix recovery under general noise models. *Neuroimage* 2019;200:391–404.
27 Kellner E, Dhital B, Kiselev VG, *et al*. Gibbs-ringing artifact removal based on local subvoxel-shifts. *Magnetic Resonance in Med* 2016;76:1574–81.
28 Jenkinson M, Beckmann CF, Behrens TEJ, *et al*. FSL. *Neuroimage* 2012;62:782–90.
29 Tustison NJ, Avants BB, Cook PA, *et al*. N4ITK: Improved N3 Bias Correction. *IEEE Trans Med Imaging* 2010;29:1310–20.
30 Jones DK. Tractography Gone Wild: Probabilistic Fibre Tracking Using the Wild Bootstrap With Diffusion Tensor MRI. *IEEE Trans Med Imaging* 2008;27:1268–74.
31 Oosterbos C, Rummens S, Bogaerts K, *et al*. A randomized controlled trial comparing conservative versus surgical treatment in patients with foot drop due to peroneal nerve entrapment: results of an internal feasibility pilot study. *Pilot Feasibility Stud* 2023;9:181.
32 Evans AG, Morgan MD, Aiken BA, *et al*. Can Diffusion Tensor Imaging Apparent Diffusion Coefficient Diagnose Carpal Tunnel Syndrome? A Systematic Review and Meta-Analysis. *Hand (NY)* 2023;18:91S–99S.
33 Cao J, He B, Wang S, *et al*. Diffusion Tensor Imaging of Tibial and Common Peroneal Nerves in Patients With Guillain–Barre Syndrome: A Feasibility Study. *Magn Reson Imaging* 2019;49:1356–64.
34 Bulut HT, Yildirim A, Ekmekci B, *et al*. The Diagnostic and Grading Value of Diffusion Tensor Imaging in Patients with Carpal Tunnel Syndrome. *Acad Radiol* 2014;21:767–73.
35 Bäumer P, Dombert T, Staub F, *et al*. Ulnar neuropathy at the elbow: MR neurography--nerve T2 signal increase and caliber. *Radiology* 2011;260:199–206.
36 Beaulieu C. The basis of anisotropic water diffusion in the nervous system – a technical review. *NMR Biomed* 2002;15:435–55.