Readout-segmented diffusion tensor imaging for assessing sciatic nerve invasion by soft tissue tumor

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Abstract

There are few publications regarding feasibility of readout-segmented diffusion tensor imaging (rsDTI) in assessing nerve invasion by soft tissue tumor. 64 patients with soft tissue mass in upper leg suspected of sciatic nerve invasion underwent rsDTI. Nerve invasion was confirmed in 28 cases by operation or electromyogram. The sciatic nerve was better depicted with diffusion weighted map versus $b = 0$ map of rsDTI. Inter-reader agreement in using rsDTI to rate nerve invasion was excellent. Sensitivity and specificity of rsDTI in identifying nerve invasion were 93% (26/28) and 92% (33/36) respectively. Apparent diffusion coefficient (ADC) was significantly higher in invaded nerves versus normal nerves ($1.45 \pm 0.67 \times 10^{-3} \text{mm}^2/\text{s}$ vs. $1.39 \pm 0.46 \times 10^{-3} \text{mm}^2/\text{s}$, $P=0.05$). DTI derived FA was significantly lower in invaded nerves versus normal nerves (0.22 ± 0.11 vs. 0.37 ± 0.13 , $P=0.05$). Readout-segmented DTI was feasible in assessing sciatic nerve invasion by soft tissue tumor in selected patients.

Introduction

Soft tissue mass of leg usually invades adjacent vessels and nerves.^{1,2} Computed tomography angiography (CTA) is the first-line test in revealing arterial invasion by tumor.² Magnetic resonance angiography (MRA) serves as an alternative to CTA.² However, CTA and MRA have difficulty in identifying nerve invasion by tumor.³ In recent years, fast spin echo (FSE) T2 weighted imaging (T2WI) was found useful in depicting peripheral nerve.^{4,5} However, conventional T2 MR provides no quantitative parameter of nerve besides signal intensity.⁶ Quantitative MR parameters are still urgently required to reflect the intrinsic character of nerve.

Diffusion weighted (DW) MR is considered as a quantitative sequence. Diffusion weighted imaging (DWI) and diffusion tensor imaging (DTI) are widely used in clinical practice. However, conventional DW MR was limited in extremities due to image distortion and susceptible artifacts.⁷ In recent years, readout-segmented method was frequently used for diffusion weighted MR to overcome distortion and artifacts.^{8,9} By using multiple readout segments, depiction of lesions of limb can be significantly improved.^{10,11}

It is well established water molecular motion is more restricted in nerve versus muscle. DWI and DTI thus have the potentiality to separate peripheral nerve from background muscles.^{12,13} Compared to DWI, DTI uses more diffusion directions, and provides fraction of anisotropy (FA) besides apparent diffusion coefficient (ADC). FA was widely used in central nervous system; however, there are few publications regarding FA of peripheral nerve invaded by tumor. We here hypothesize sciatic nerve could be identified in DTI images. The purpose of the study is therefore to investigate the feasibility of readout-segmented DTI (rsDTI) in assessing sciatic nerve invasion by soft tissue mass.

Methods

All methods were carried out in accordance with relevant guidelines and regulations.

Study Design And Participants

This prospective study was approved by the Ethics Commission of Hospital (TJ-2015-075). Each patient signed an informed consent before inclusion of study.

Inclusion criterion was patients with soft tissue mass in upper leg suspected of sciatic nerve invasion. Exclusion criteria were: 1) standard contraindication to MR examination (such as claustrophobia); 2) metal internal fixator in upper leg; 3) underwent chemotherapy or radiotherapy before MR; 4) nerve invasion not confirmed by surgical operation or electromyogram (EMG). From September 2016 to October 2020, 88 patients with soft tissue mass in upper leg suspected of nerve invasion were enrolled in the study. 24 patients were excluded due to the following reasons: claustrophobia (n = 1); metal internal fixator (n = 3); chemotherapy or radiotherapy (n = 7); no confirmation of nerve invasion (n = 13). The remaining 64 patients who underwent rsDTI were finally analyzed.

Data Collection

All MR examinations were performed on a 3T whole-body scanner (Siemens, Skyra). The region of interest (ROI) in the portion of leg was covered with an 18-element body coil. Fat-suppressed FSE T2WI was performed with the following parameters for the purpose of localizing mass: TR/TE, 4000/80 ms; matrix, 320; field of view, 320 mm or greater; slice thickness, 4 mm; slice number, 20 or more. Readout-segmented DTI was performed in the transverse plane covering the soft tissue mass with the following parameters: TR/TE, 5500/78 ms; matrix, 240; field of view, 240 mm × 240 mm or greater to fit of mass size; phase direction, anterior-posterior; slice thickness, 4 mm; slice number, 24 or more; b-value, 0 and 800; average for b = 0, 3; average for b = 800, 1; directions, 20; readout segments, 5; scanning time, 6 ~ 8 minutes. ADC map and FA map were automatically generated by the scanner.

Data analysis

Two radiologists with 7 and 9 years' experience in diagnosing peripheral nerve diseases in consensus assessed the depiction of sciatic nerve on b = 0 map, diffusion weighted (DW) map, ADC map and FA map. Subjective score was given to each map according to the following scale: 0 = poor depiction of nerve, identification from background impossible; 1 = moderate depiction, with nerve identification and ROI assessment possible; 2 = good depiction of nerve, adequate nerve-to-background contrast; 3 = excellent depiction of nerve.

Two radiologists with 8 and 11 years' experience in diagnosing peripheral nerve diseases separately assessed the invasion of sciatic nerve using all rsDTI maps. A subjective score was given to each case according to the following scale: 0 = nerve free from tumor; 1 = tumor very close to nerve, nerve boundary clear; 2 = no gap between tumor and nerve, part of nerve boundary not clear; 3 = nerve boundary not seen, separation of nerve from tumor impossible. In the current study, invasion score 0 and 1 were considered as nerve non-invasion, while score 2 and 3 as nerve invasion. The two radiologists separately measured FA and ADC of sciatic nerve by drawing ROI. ROI was drawn at five consecutive slices where soft tissue

mass and sciatic nerve were closest. ROI was drawn on DW map first, and then transferred to FA map and ADC map. ROI analysis of nerve was abandoned if separation of sciatic nerve from tumor impossible. The two readers also measured FA and ADC of soft tissue mass by drawing ROI at the slices where mass size was the largest. Necroses, vessels and fat were asked to be avoided when drawing ROI on mass. Values from multiple slices were averaged.

Statistical analysis

All statistical analysis was performed using SPSS 22.0. The score of nerve depiction was compared between rsDTI maps using a Wilcoxon sign-rank test. Cohen kappa coefficient was used to determine the inter-reader agreement in rating nerve invasion. Intra-class correlation coefficient (ICC) was calculated to determine the inter-reader reproducibility in measurement of DTI parameters. ICC ≥ 0.7 was considered excellent inter-reader reproducibility, thus data from two readers could be averaged. A Mann Whitney test was used to compare DTI parameters of sciatic nerve between nerve invasion cases and non-invasion cases. Receiver operator characteristic (ROC) curve was constructed for further evaluation. P value less than 0.5 was considered as statistical significance.

Results

From September 2016 to October 2020, 64 patients (male: female = 34:30; mean age = 43.4 years; age range = 17 ~ 71) underwent rsDTI for assessing sciatic nerve invasion by soft tissue mass. Sciatic nerve invasion was confirmed in 28 out of 64 cases (15 by operation, 13 by EMG), while non-invasion was confirmed for the other 36 cases (22 by operation, 14 by EMG).

Soft tissue sarcoma (n = 23) was the most common tumor in the study, including: fibrosarcoma, n = 5; synovial sarcoma, n = 3; myofibrosarcoma, n = 3; leiomyosarcoma, n = 3; epitheliosarcoma, n = 3; rhabdomyosarcoma, n = 2; liposarcoma, n = 4. Soft tissue sarcoma was followed by vascular anomalies (n = 15) and lipoma (n = 6). Main clinical information of the cohort of patients was provided in Table 1.

Table 1
Clinical information of 64 patients with soft tissue mass in upper leg suspected of sciatic nerve invasion. Readout-segmented DTI was performed for all patients. Nerve invasion was confirmed by operation or electromyogram.

	nerve invasion (n = 28)	non-invasion (n = 36)	total (n = 64)
age and gender			
age range (year)	19 ~ 71	17 ~ 69	17 ~ 71
mean age (year)	44.6	42.5	43.4
male: female	15: 13	19: 17	34: 30
invasion confirmation			
by operation	n = 15	n = 22	n = 37
by electromyogram	n = 13	n = 14	n = 27
ROI analysis			
available	n = 23	n = 36	n = 59
unavailable	n = 5	n = 0	n = 5
symptoms			
limb pain	n = 26	n = 9	n = 35
limb numbness	n = 23	n = 4	n = 27
muscle weakness	n = 18	n = 3	n = 21
pathology results			
soft tissue sarcoma	n = 20	n = 3	n = 23
vascular anomalies	n = 0	n = 15	n = 15
lipoma	n = 0	n = 6	n = 6
schwannoma	n = 3	n = 0	n = 3
neurofibroma	n = 4	n = 0	n = 4
leiomyoma	n = 0	n = 3	n = 3
angioleiomyoma	n = 0	n = 2	n = 2
tenosynovial giant cell tumor	n = 0	n = 3	n = 3

DTI = diffusion tensor imaging; ROI = region of interest.

	nerve invasion (n = 28)	non-invasion (n = 36)	total (n = 64)
metastasis	n = 1	n = 1	n = 2
fibroma	n = 0	n = 3	n = 3
DTI = diffusion tensor imaging; ROI = region of interest.			

In DW map, sciatic nerve depiction was excellent (score = 3) in 48% cases, while good (score = 2) in 44%. In b = 0 map, sciatic nerve depiction was poor (score = 0) in 33% cases, while moderate (score = 1) in 34%. Sciatic nerve was better depicted with DW map versus b = 0 map (mean score 2.3 vs. 1.0, $P < 0.05$, see Table 2).

Table 2

Depiction of sciatic nerve on each map of readout-segmented DTI was assessed by two radiologists in consensus according to the following scale: score 0 = poor depiction; score 1 = moderate depiction; score 2 = good depiction; score 3 = excellent depiction. A Wilcoxon sign-bank test was used to compare depiction score between two maps.

	Score 0	Score 1	Score 2	Score 3	mean score	versus b = 0 map	versus DW map	versus ADC map	versus FA map
b = 0 map	n = 21	n = 22	n = 20	n = 1	1.0		$P < 0.001$	$P = 0.46$	$P = 0.04$
DW map	n = 4	n = 1	n = 28	n = 31	2.3	$P < 0.001$		$P < 0.001$	$P < 0.001$
ADC map	n = 17	n = 21	n = 23	n = 3	1.2	$P = 0.46$	$P < 0.001$		$P = 0.03$
FA map	n = 32	n = 27	n = 5	n = 0	0.6	$P = 0.04$	$P < 0.001$	$P = 0.03$	
DTI = diffusion tensor imaging; DW = diffusion weighted.									

The inter-reader agreement in rating sciatic nerve invasion with rsDTI was excellent ($\kappa = 0.911 \pm 0.043$, $P < 0.001$, see Table 3). Divergence of invasion score occurred in 4 out of 64 cases (see Table 3). The nerves invasion rated by one reader was as follows: score = 0 (n = 19); score = 1 (n = 16); score = 2 (n = 25); score = 3 (n = 4). The nerves invasion rated by another reader was as follows: score = 0 (n = 18); score = 1 (n = 17); score = 2 (n = 24); score = 3 (n = 5). In the study, score 0 and 1 were considered as negatives (of nerve invasion), while 2 and 3 positives. The numbers of positives (n = 29) and negatives (n = 35) were thus the same for the two readers.

Table 3

Sciatic nerve invasion by soft tissue mass was assessed by two radiologists separately using readout-segmented DTI according to the following scale: 0 = nerve free from tumor; 1 = nerve close to tumor, nerve boundary clear; 2 = no gap between nerve and tumor, part of nerve boundary not clear; 3 = separation of nerve from tumor impossible.

		Reader 1			
		0	1	2	3
Reader 2	0	18	0	0	0
	1	1	15	1	0
	2	0	1	23	0
	3	0	0	1	4
DTI = diffusion tensor imaging.					

29 positives included 26 true-positives (score 2 or 3, invasion confirmed) and 3 false positives (score 2, confirmed non-invasion). 35 negatives included 33 true-negatives (score 0 or 1, non-invasion confirmed) and 2 false-negatives (score 1, confirmed invasion). The sensitivity and specificity of rsDTI for identification of sciatic nerve invasion were 93% (26/28) and 92% (33/36) respectively.

ICC for ADC and FA of sciatic nerve were 0.91 and 0.88 respectively. ICC for ADC and FA of soft tissue mass were 0.93 and 0.91 respectively. As all ICC above 0.7, data from the two readers were averaged. ADC of sciatic nerve was significantly different between non-invasion cases and nerve invasion cases ($1.39 \pm 0.46 \times 10^{-3} \text{mm}^2/\text{s}$ vs. $1.45 \pm 0.67 \times 10^{-3} \text{mm}^2/\text{s}$, $P=0.05$). Nerve FA was significantly lower in nerve invasion cases versus non-invasion cases (0.22 ± 0.11 vs. 0.37 ± 0.13 , $P=0.05$). Area under curve (AUC) for ADC and FA were 0.67 and 0.85 respectively.

ADC and FA were significantly lower in soft tissue sarcoma versus vascular anomalies (see Table 4). AUC for ADC and FA were 0.72 and 0.84 respectively in discrimination of tumor. Figure 1 shows a comparison among DTI maps for depiction of sciatic nerve. Figures 2, 3, 4 and 5 show nerve invasion score 0, 1, 2 and 3 respectively.

Table 4

DTI parameters of nerve were compared between nerve invasion cases and non-invasion cases using a Mann Whitney test. DTI parameters of mass were compared between soft tissue sarcoma and vascular anomalies, also using the Mann Whitney test.

	non- invasion (n = 36)	nerve invasion (n = 23)	P	soft tissue sarcoma (n = 23)	vascular anomalies (n = 15)	P
age	42.5	44.5	0.12	48.6	38.3	0.001
ADC($10^{-3}\text{mm}^2/\text{s}$)	1.39 ± 0.46	1.45 ± 0.67	0.04	1.34 ± 0.42	1.57 ± 0.55	0.03
FA	0.37 ± 0.13	0.22 ± 0.11	0.004	0.14 ± 0.06	0.35 ± 0.16	0.01
DTI = diffusion tensor imaging; ADC = apparent diffusion coefficient; FA = fraction of anisotropy.						

Discussion

In the current study, we investigated the feasibility of readout-segmented DTI in assessing sciatic nerve invasion by soft tissue mass. The most important findings were as follows: 1) sciatic nerve was best depicted with diffusion weighted map; 2) rsDTI had 93% sensitivity and 92% specificity in identification of sciatic nerve invasion; 3) FA value of invaded nerve decreased.

It is necessary to assess peripheral nerve invasion by tumor before producing treatment plan.^{14–16} In recent years, several MR sequences have been tried for peripheral nerve diseases.^{17–19} However, they fail to provide objective parameters to reflect intrinsic characteristics of nerve. Readout-segmented DTI was thus introduced by us as a new way to assess peripheral nerve, as it could provide quantitative parameters including FA and ADC.^{20–23}

The $b = 0$ map was T2 weighted. We actually found $b = 0$ map of rsDTI was similar to FSE T2WI image, which was valuable in assessing peripheral nerve diseases.^{24–26} However, we found FSE T2WI, as well as $b = 0$ map, failed to well depict sciatic nerve when nerve and background tissue had similar signal intensity (SI). In contrast, sciatic nerve and background generally had substantially different signal in diffusion weighted map. A possible explanation is that water molecular diffusion is more restricted in nerve versus background tissue.^{27,28} From $b = 0$ to $b = 800$, the signal decrease was less for nerve, so it was brighter than background on $b = 800$ map. Compared to T2 weighted image, diffusion weighted MR seemed more suitable for depicting peripheral nerve. On diffusion weighted map, nearly all soft tissue masses and nerves were hyperintensity, while background tissues were hypointensity or isointensity,

making it possible to assess the relationship of nerve and tumor. In fact, the inter-reader agreement of rsDTI in assessing nerve invasion was excellent ($\kappa = 0.911$).

Water molecular motion could be prevented by myelin sheath of nerve, resulting in diffusion difference in transverse and longitudinal directions, which is described with FA. For diseased nerve, destroy of myelin sheath is expected to cause FA to decrease.^{29,30} Our data seemed to support this hypothesis. We found FA was lower in invaded nerves versus normal nerves. Invaded and normal nerves also differed in ADC, which is not easy to explain. It is worth noting that AUC of FA was higher than that of ADC. DTI derived FA seemed more suitable than DWI derived ADC in identifying nerve invasion.

Soft tissue sarcoma is the most common malignant soft tissue tumor of leg, while vascular anomalies the most common benign soft tissue tumor. We performed a comparison in DTI parameter between the two tumors, and found ADC was lower in soft tissue sarcoma versus vascular anomalies, in consist with previous publications.³¹ Interestingly, we found FA was also lower in soft tissue sarcoma. A possible explanation is that tissue structure of soft tissue sarcoma is extremely disordered,³² resulting in similar diffusion in all directions. DTI derived FA seemed suitable for discrimination of soft tissue sarcoma and vascular anomalies, with AUC above 0.8.

Our study had some limitations. First, the sample size was small. Soft tissue tumor in leg was not a common disease. Large tumor with sciatic nerve invasion was not easy to collect. We only collected 64 cases during nearly four years. Multi-center large-size study is required to validate our results. Second, nerve depiction on diffusion weighted map was compared to that on $b = 0$ map, but not directly to FSE T2WI. We found $b = 0$ map of rsDTI was very similar to FSE T2WI, and nerve depiction was nearly the same on the two maps. Nerve depiction on rsDTI should be compared to other sequences in future study. Third, EMG is not a gold standard in determining nerve invasion. The accuracy of rsDTI in identifying nerve invasion may be influenced by this imperfect standard. Fourth, FA and ADC of nerve could not be obtained when separation of nerve and tumor was unavailable. Other MR sequences (such as contrast enhanced T1) are still required to separate nerve from tumor for such cases.

In conclusion, readout-segmented DTI was feasible to assess sciatic nerve invasion by soft tissue tumor in selected patients.

Declarations

Data availability

After publication, the data will be made available to others on reasonable requests to the corresponding author.

Competing interests

We declare no competing interests.

Author contributions

GW collected the epidemiological and clinical data. SW and CP summarized all data. GW drafted the manuscript. TW revised the final manuscript.

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Figures

Figure 1

Comparison of nerve depiction among maps of readout-segmented DTI. a, b, c and d were b=0 map, diffusion weighted map, ADC map and FA map respectively. T2 weighted b=0 map provided poor depiction of sciatic nerve. The sciatic nerve was well depicted on diffusion weighted map (b, arrows), and was brighter than background tissue. ADC map provided acceptable depiction of nerve (c, arrows), but FA map did not (d).

Figure 2

Score 0 of nerve invasion. Saggital FSE T2WI displayed hyperintensity masses (a, arrows) within gluteus. Neither axial FSE T2WI (b) nor b=0 map of readout-segmented DTI (c) well depicted sciatic nerve. It was difficult to determine whether sciatic nerve was invaded by tumor on b or c. Diffusion weighted map (d) could well depict sciatic nerve (d, arrows), which was free from tumor. ADC map (e) and FA map (f) provided poor depiction of nerve. The electromyogram for this patient was normal.

Figure 3

Score 1 of nerve invasion. a, b, c and d were FSE T1WI, fat-suppressed FSE T2WI, b=0 map and diffusion weighted map respectively. The lipoma was hyperintensity on T1WI, and hypointensity on fat-suppressed T2WI. Sciatic nerve was similar to adjacent muscle in T1 signal (a, arrows). On b=0 map (c) and diffusion weighted map (d), sciatic nerve was brighter than background (c, d, arrows). The clear nerve boundary indicated non-invasion, which was confirmed by operation.

Figure 4

Score 2 of nerve invasion. a, b and c were b=0 map, diffusion weighted map and ADC map of readout-segmented DTI respectively. Tumor and nerve were both hyperintensity on diffusion weighted map (b, arrows). There was no gap between tumor and nerve. Part of nerve boundary was not clear, indicating nerve invasion, which was confirmed by operation. The pathology result was schwannoma (d).

Figure 5

Score 3 of nerve invasion. a, b, c and d were respectively axial $b=0$ map, axial diffusion weighted map, coronal $b=0$ map and coronal diffusion weighted map. The tumor was hyperintensity on diffusion weighted map. Normal sciatic nerve in the right side could be seen on axial DTI (a, b, arrows). The beginning part of sciatic nerve in the left side was well depicted on coronal DTI (c, d, arrows), but it was impossible to separate other part of nerve from tumor. Nerve invasion was confirmed by operation. The pathology result was plexiform schwannomas (e).