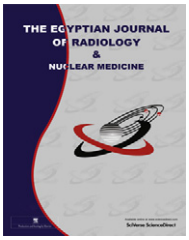
The Egyptian Journal of Radiology and Nuclear Medicine (2012) **43**, 25–31

Egyptian Society of Radiology and Nuclear Medicine

The Egyptian Journal of Radiology and Nuclear Medicine

www.elsevier.com/locate/ejrnm
www.sciencedirect.com



ORIGINAL ARTICLE

Prediction of motor outcome in ischemic stroke involving the pyramidal tract using diffusion tensor imaging

Gehan Gouda Ali *, Abeer Maghawry Abd Elhameed

Department of Radiodiagnosis, Faculty of Medicine, Ain Shams University, Cairo, Egypt

Received 26 July 2011; accepted 26 November 2011
Available online 22 December 2011

KEYWORDS

Diffusion tensor imaging (DTI);
Diffusion tensor tractography (DTT);
Corticospinal tract (CST);
Fractional anisotropy (FA)

Abstract *Background and purpose:* Early evaluation of the pyramidal tract is a prerequisite in patients with ischemic stroke in order to decide the optimal treatment or to assess appropriate rehabilitation. The aim of this study was to predict motor outcome using quantitative and qualitative diffusion tensor parameters and their correlations with severity of stroke as defined by the National Institutes of Health Stroke Scale (NIHSS).

Materials and methods: Twenty-one patients presenting with ischemic stroke were studied with DTI. All patients had diffusion measurements such as FA values of the affected and unaffected regions and the FA ratio between them. Color FA maps of the pyramidal tract were constructed and the degree of infarctions was classified into groups according to the involvements of the pyramidal tracts. The motor performance of the upper and lower extremities was assessed using the NIHSS on the day of patients' admission and discharge. The motor outcomes were correlated with the FA values of the pyramidal tract.

Results: The FA values of the affected pyramidal tracts were significantly lower as compared with the unaffected side (p-value < 0.01). The reduction in the FA values of the affected side was significantly correlated ($r = 0.41$ and p-value < 0.001) with the degree of pyramidal tract involvements that were significantly correlated with the motor outcome on patients' discharge day.

* Corresponding author. Mobile: +20 0105070242.
E-mail addresses: gehan_gouda@hotmail.com (G.G. Ali), abeermaghawry@gmail.com (A.M.A. Elhameed).

Peer review under responsibility of Egyptian Society of Radiology and Nuclear Medicine.
doi:10.1016/j.ejrnm.2011.11.004

ELSEVIER **Production and hosting by Elsevier**

Conclusions: Quantitative (FA values) and qualitative (the diffusion tensor tractography) diffusion parameters have potential to predict motor outcome in patients with ischemic stroke.

1. Introduction

Stroke is one of the leading causes of death worldwide, especially in the elderly population. As a broad clinical term, it includes patients with arterial ischemic infarcts, intracranial hemorrhage, subarachnoid hemorrhage, and venous infarction. Many recent research and clinical studies have focused on the application of the newer magnetic resonance (MR) techniques of diffusion weighted imaging (DWI) and perfusion imaging in acute stroke to identify the areas at risk for infarction (1,2).

The corticospinal tract (CST) is the most important motor pathway that functions in human motor control. The preservation or recovery of the CST is mandatory for good recovery of impaired motor function in patients with brain injury. The accurate estimation of the CST state after brain injury would enable us to predict the sequelae of motor weakness or to set up a scientific management strategy. This information also could be useful in accurate surgical planning for patients with brain tumor or vascular anomaly (3,4).

Few studies have however addressed the problem of applying MR techniques to study the outcome of this group of patients (1,5). Conventional MR imaging cannot provide reliable information about the integrity of white matter tracts, thereby limiting the ability to predict clinical outcome. However, with DTI, the microstructural organization of white matter tracts can be obtained and provides important information about their integrity as well as orientation (1,6).

The information provided by DTI acquisitions allows the quantification of various metrics as well as the generation of 3-dimensional (3D) white matter fiber tractography; these measures provide unique information about central nervous system tissue microstructure. Diffusion tensor imaging and fiber tractography may prove useful in clinical neuroradiology practice, with application to several categories of disease (7).

The aim of this study was to predict the neuromotor outcome of patients with ischemic stroke by using DTI with its two tools which are the metric FA values and DTT and correlate their findings with the stroke outcome to show if it can affect therapeutic decision-making and eventually patient outcome.

2. Materials and methods

2.1. Patient selection

In total, 21 patients were recruited for this study (14 men and 7 women), their age ranged from 41 to 76 years. The study was done in a private hospital, in Cairo, Egypt in the period from June 2010 to April 2011. The inclusion criteria were as follows: (1) ischemic stroke diagnosed by conventional MRI and DWI; (2) motor deficit on admission; (3) no previous history of stroke or brain injury on MR imaging, or of other neurologic disease. An informed consent was provided by all patients.

2.2. Clinical assessment

The motor performances of the upper and lower extremities were assessed using the NIHSS for all patients at the first day of admission either in the acute phase or early sub acute phase (< 3 days after the onset of symptoms) and were evaluated again on day of discharge of the patients from hospital (motor outcome: within 1 month of onset of symptoms). The estimated values of the NIHSS for all patients at admission and discharge day (the range is 15–30 days after onset of symptoms with the average is 20 day and SD 0.57) were summed as seen in Table 1.

NIHSS is a widely used scale to evaluate neurological impairment in a patient experiencing an acute stroke. NIHSS is calculated by examining 11 parts, with 13 specific tests. The NIHSS examines for level of consciousness, vision and gaze, facial palsy and extremity weakness, limb ataxia, sensory loss, language and dysarthria, and neglect. It is designed to be conducted over 7 min. A patient with a completely normal neurological exam and normal mental status will have an NIHSS of 0. The maximum recordable NIHSS score is 42. However, since acute ischemic stroke causes unilateral paralysis and blindness, the maximum score actually is 31 for a stroke patient with complete hemiparesis, hemianopia, hemineglect, and aphasia (8).

2.3. DTI

DTI was conducted using a 1.5 T whole-body scanner (Philips, Achivia R 2.5) and 16 multichannel head coil (sense 8). The DTI sequence consisted of single-shot spin echo-planar imaging with the following parameters: acquisition matrix 112×110, reconstruction matrix is 128×128; field of view 224 mm for the anteroposterior and from right to left while it is 120 mm for the craniocaudal direction; slice thickness 2 mm; number of slices 60; TR 10,000 ms; TE 80 ms; *b*-value 1000 s mm^{-2} and the gradient directions were 16 (encoding gradient). Scan time was 9.47 min.

2.4. Data processing and post processing

The DTI data sets were transferred to a workstation (Philips Achivia R 2.5 Version: 1 Level: 1) for processing. Small regions of interest (ROI) were manually drawn in the stroke area on the affected side as well as the corresponding area on the unaffected side on the DTT color image. The average values of the FA were compared in the affected and unaffected sides. Additionally, the ratio of the FA (rFA) between the affected side and the unaffected side was calculated ($rFA = FA_{affected\ side}/FA_{unaffected\ side}$). The lower limit for FA is 0.3 (scale is from 0 to 1) and the angle for reconstruction is above 60 if below the reconstruction will stop.

Fiber tracking using the two ROI DTT methods was performed on the basis of the DWI following the anatomical location of the pyramidal tract and especially the corticospinal tract according to the anatomical atlas by (9), two- and three-

Table 1 Summary of the clinical and radiological data of the 21 patients included in the study.

Pt. No.	Sex	Age	Side	Site of the infarction	Degree of involvement of the pyramidal tract	NIHSS score on admission	NIHSS score at discharge (15–30 days after onset of symptom)	Time to DTT MRI in days	Motor outcome
1	M	57	RT	Corona radiata	Partially	9	6	2	Good
2	M	76	RT	Internal capsule	Totally	17	11	3	Poor
3	M	43	RT	Centrum semi-ovale	Intact	0.5	0	1.2	Good
4	M	51	RT	Corona radiata	Partially	7	4	2	Good
5	F	49	RT	Internal capsule	Intact	3	0.5	1.7	Good
6	M	63	RT	Corona radiata	Totally	19	9.5	3	Poor
7	M	62	RT	Subcortical	Intact	2	0	0.8	Good
8	F	45	LT	Temporo-parietal	Intact	3	0	1	Good
9	F	46	LT	Internal capsule	Partially	11	7	2	Good
10	M	60	LT	Centrum semi-ovale	Totally	19	8	3	Poor
11	M	57	LT	Corona radiata	Partially	9	4	2	Good
12	M	47	RT	Temporo-occipital	Totally	23	18	3	Poor
13	F	50	RT	Subcortical	Intact	2	0	1.7	Good
14	M	41	RT	Thalamus	Intact	0.5	0	1	Good
15	F	56	LT	Corona radiata	Totally	16	11	3	Poor
16	F	64	LT	Subcortical	Intact	3	0.5	0.9	Good
17	M	61	RT	Thalamus	Intact	5	1	1.8	Good
18	M	51	RT	Corona radiata	Intact	1	0	1	Good
19	M	51	RT	Centrum semi-ovale	Partially	10	6	1.8	Good
20	M	57	LT	Pons	Totally	19	13	3	Poor
21	F	64	RT	Corona radiata	Partially	13	7	2	Good

dimensional tractographic images were then created to localize the infarction in relation to the CST. By analyzing the lesion location with regard to the CST on the tractographic images, the infarctions were visually classified into three subgroups based on the extent of pyramidal tract involvement by the infarct: in Group 1 lesions the CST was in close proximity to the infarction but did not pass through it, in Group 2 lesions the pyramidal tract partly passed through the lesion (CST partial involvement), and in Group 3 lesions the long lesions were centered in the pyramidal tract or involved a whole part of it.

2.5. Statistical analysis

A group comparison was made by using the Wilcoxon rank sum test. The comparison of the FA ratio and the clinical scores and between the three groups of patients according to pyramidal tract involvement on DTT image and the motor outcome as calculated by NIHSS score was also done.

3. Results

The clinical features of the included 21 patients, the anatomical sites of the ischemic areas as seen on the DWI and conventional MRI images, the time in days from onset of symptoms to the day of DTT study, and the NIHSS for all stroke patients on admission and discharge days as well as their motor outcomes as evaluated by the neurologist are all shown in Table 1.

The locations of lesions were in the corona radiata in 7 patients, the thalamus in 2 patients, internal capsule in 3 patients (Fig. 1), centrum semi-ovale in 3 patients, pons in 1 patient (Fig. 2), temporo-occipital in 1 patient (Fig. 3), temporo-parietal in 1 patient and subcortex in 3 patients (Fig. 4).

The FA values in affected areas were significantly decreased ($p < 0.01$) in comparison to the unaffected areas as their mean value was 0.427 ± 0.133 while in the unaffected side, the mean value was 0.557 ± 0.168. Also the FA ratio ($FA_{affected\ side}/FA_{unaffected\ side}$) was calculated and their mean was 0.766 ± 0.183.

It was found that in all patients in whom the FA ratio was under 0.8 at the admission day, motor function showed poor recovery at day of discharge. When FA ratio was over 0.8, the motor function at discharge day (within 1 month of onset of symptoms) showed good recovery.

Significant correlation between the reduction in the FA values and the degree of pyramidal tract involvement was found ($r = 0.41$ and p-value < 0.001) as the patients with intact tract had within normal FA values in comparison to the healthy contralateral side while those with interruption of the normal course of the tract showed variable degrees of reduction of the FA values.

DTT of the pyramidal tract was successful in all 21patients. The patients were classified according to the degree of pyramidal tract involvement into three groups as seen in Table 2: Group 1 infarctions (intact type), in which the pyramidal tract was in close proximity to the infarction but did not pass through it, included 9 patients (Fig. 4), Group 2 (partial involvement type), in which the pyramidal tract partly passed through the infarction, included 6 patients (Fig. 3), and Group 3 (whole involvement type), in which long lesions were centered in the pyramidal tract or involved a whole part of the pyramidal that, included 6 patients (Figs. 1 and 2).

The NIHSS at discharge day of patients of Group 1 were significantly lower than those of Group 2 ($U = -5.447, p < 0.01$), and those of Group 2 were significantly lower than those of Group 3 ($U = -6.083, p < 0.01$). Therefore, the NIHSS scores

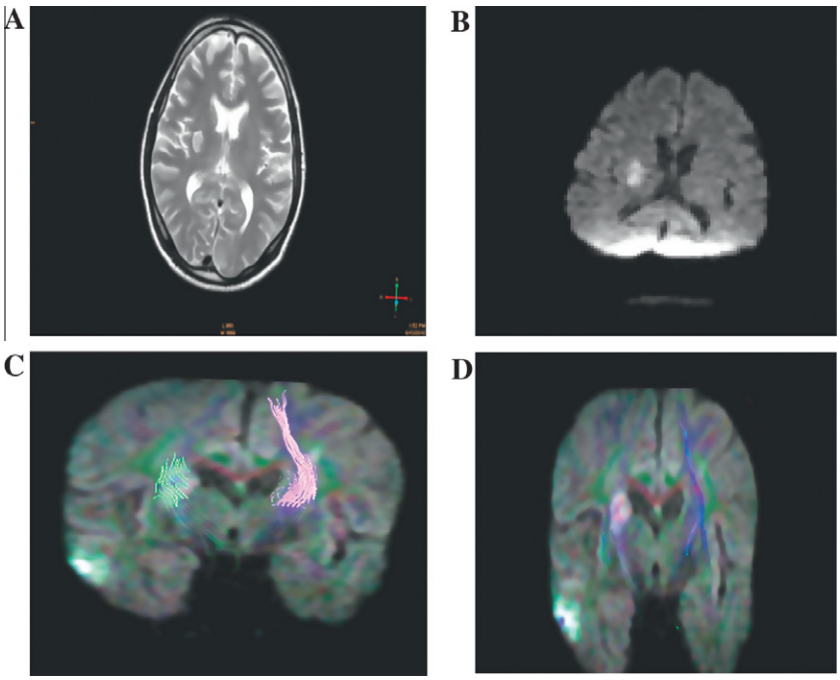


Fig. 1 Patient # 2 presented with left sided weakness. (A and B) Axial T2 weighted and DWI image displaying a hyperintense zone of an early subacute infarction in the posterior limb of the right internal capsule. (C and D) The DTT colored images superimposed on the coronal DWI showing total disruption of the pyramidal tract fibers of the affected right side in comparison to the contralateral healthy side associated with poor motor outcome of this patient.

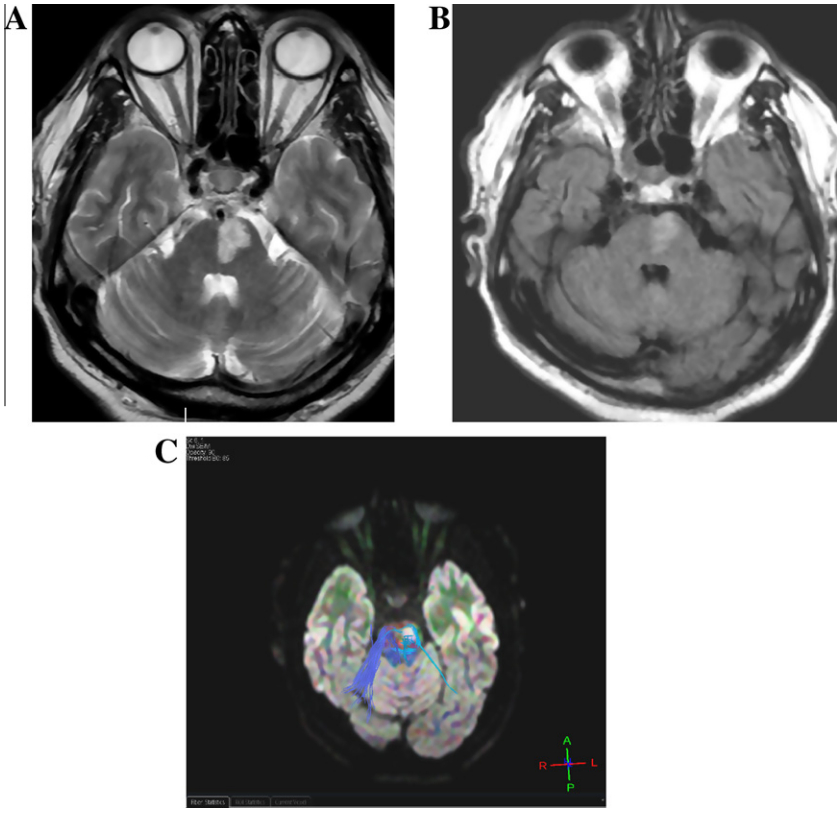


Fig. 2 Patient # 20. (A and B) The T2 weighted axial image and the corresponding FLAIR image showed hyperintense region of subacute infarction in the left side of the pons. (C) The DTT colored image based on DWI showed near total disintegration of the corticobulbar tract fibers on left side in comparison with the right sided tract associated with poor outcome of this patient.

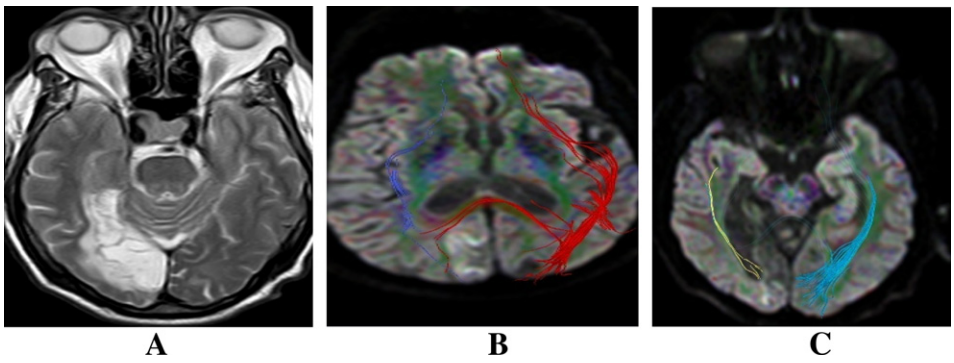


Fig. 3 Patient # 12 admitted with left sided weakness. (A) The axial T2 weighted image showed a wide hyperintense area of ischemic infarction is seen involving the right parieto-occipital region. (B and C) The diffusion directional colored image and the tractography colored image superimposed on the DWI showed thinning out of the inferior parieto-occipital fasiculus fibers on the affected right side in comparison to the left side. This patient had poor outcome with left sided hemiparesis on discharge.

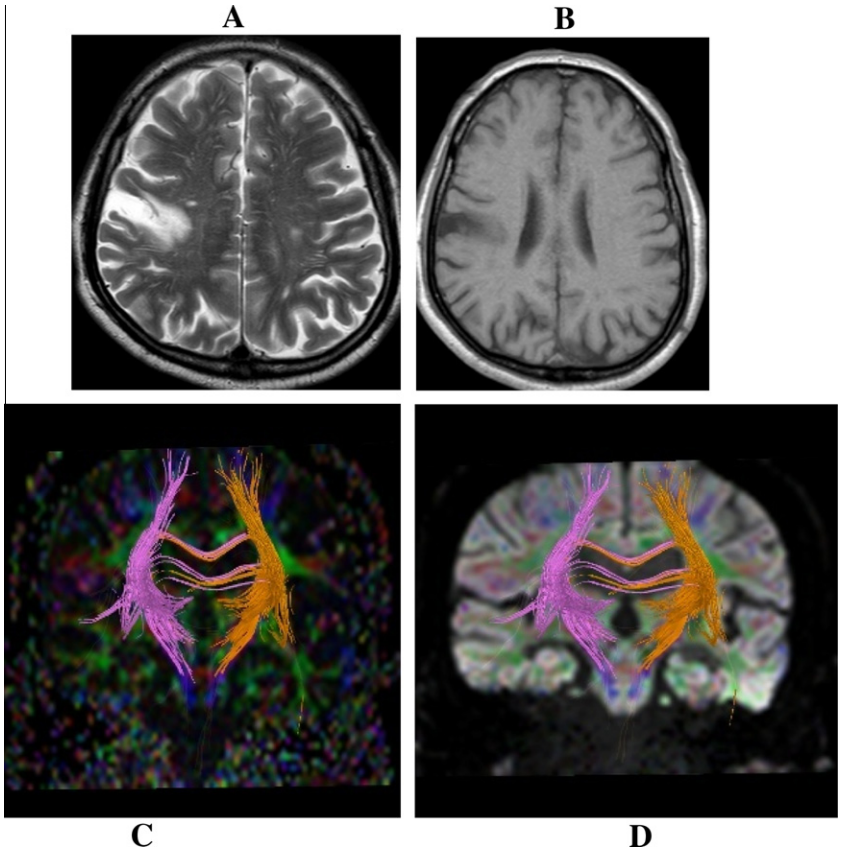


Fig. 4 Patient # 13 admitted with left sided heaviness. (A) The T2 weighted image of a patient with subacute ischemic infarction showed a right sided parietal subcortical hyperintense area which is seen as hypointense area on the T1 weighted image. (C and D) The axial directional colored image and the coronal tractography colored image based on DWI show intact pyramidal tracts as they are of the same caliber on both sides. The patient had good outcome on discharge.

of Group 3 at the time of discharge (outcome) were significantly higher than those of both Groups 1 and 2 (Table 2).

The NIHSS scores of each group gradually decreased from admission to the discharge day. Neurological improvement was statistically different among the three groups ($H = 17.5$, $p < 0.01$; $H = 24.9$, $p < 0.01$; $H = 33.5$, $p < 0.01$). All members of Group 1 showed a good recovery, members of Group 2 also showed a good recovery but sometimes kept some mild motor dysfunction, and members of Group 3 always showed minor improvement and had marked deficits (Table 2).

4. Discussion

Cerebral infarction and recovery of patients with stroke have been a topic of intense research recently. The recovery from stroke early in the disease has been implicated to the resolution

Table 2 The mean values of NIHSS scores in the three groups of patients.

Patients	Group 1	Group 2	Group 3
Number of patients	9	6	6
NIHSS score on admission	2.222	9.833	18.833
NIHSS score on discharge (outcome)	0.22	5.667	11.75

of tissue edema and mass effect associated with infarction and hemorrhage. However, for long-term recovery, relative preservation of the integrity and anisotropy of the white matter tracts (CST particularly) plays an important role and indicates a better clinical outcome (5,6).

In previous studies (3,10–12), the neuromotor outcome was found to correlate with conventional neuroimaging findings such as the size, the volume, and the extent of the infarction. Conventional imaging, however, does not give data about the microstructural organization of the white matter fiber tracts, which can be obtained from DTT. The information so obtained may prove more sensitive to assess tract damage than the volume estimation of signal abnormality on conventional imaging (3,10,11).

Diffusion anisotropy mirrors the fiber integrity and the degree of the fiber organization in the white matter tract (10,11). Axonal loss, gliosis, and an accompanying increase in the extracellular matrix have been generally considered to be the determinants of the decrease in diffusion anisotropy in wallerian degeneration (13). Diagnosing wallerian degeneration requires at least 4–5 weeks after the stroke when using T2 weighted images, the apparent diffusion coefficient, or other conventional MR imaging parameters, whereas the FA is more sensitive than these conventional MR imaging parameters for detecting wallerian degeneration (10,13).

In our study, we use both tools of the DTI which are the quantitative one represented by measuring the FA and rFA values in both the affected and unaffected sides of ischemic stroke and the other qualitative one by evaluating the anatomical location and the extent of pyramidal tract involvement within the infarcts as seen by DTT colored images superimposed on DWI.

The pyramidal tract usually represents both the corticospinal tract and the corticobulbar tract (14). The corticospinal tract is a large and highly anisotropic tract; on the other hand, the corticobulbar tract is easily affected by other fibers running in the anteroposterior projection (15). Moreover, the pyramidal tract does not run precisely perpendicular to the axial plane. Therefore, the FA in the cerebral peduncle may not exactly reflect the pyramidal tract. Diffusion spectrum imaging (16) or Q-ball imaging (17), which have recently been proposed, might overcome this issue (18) but are still far from clinical use because of their long acquisition times and data analyses (19). So in this study we depend mainly on measuring the FA ratio between the affected and unaffected sides more than the absolute value of the FA to reduce effect of this crossing-fiber problem.

This study revealed statistically significant reduction in the FA values on the affected sides compared with the unaffected sides with significant correlation between the FA ratio ($FA_{affected\ side}/FA_{unaffected\ side}$) and the motor outcome of the ischemic stroke patients these results were in agreement with other studies (20–22); however, they follow-up the FA values and the FA ratio in the affected sides several times after stroke insult and up to 3 months while in our study we make the correlation between the FA values that were measured on day of admission of the patient and the motor outcome at patient discharge (the range is 15–30 days from onset of symptoms and the average is 20 day and SD .057).

We defined the cutoff point of the rFA that classified the motor outcome as good and poor to be 0.8. This number was in agreement with that given in the previous study by Maeda et al. Measuring the FA in the very early phase of an ischemic stroke would be beneficial for patients to determine the best therapy or to design a suitable rehabilitation program.

With regard to the pyramidal tract involvement, all infarction lesions were divided into three subgroups, and the degree of pyramidal tract involvement was correlated with the severity of the patients' motor deficits outcome according to NIHSS scores and also with FA values and ratios. There was a good correlation between the location of the lesion, the degree of pyramidal tract involvement and the patient's motor deficit on day of discharge and correlated also with the FA values where significant reduction correlated well with pyramidal tract interruption and loss of anatomical continuity on the DTT colored images. These results also were in agreement with other results given by previous studies (20–23) but in this study, it was the first time to study both DTI tools which are the FA values and ratio as well as the degree of involvement of pyramidal tract on DTT.

DTT exquisitely depicts these changes in the involved white matter tracts. Our DTT results showed good correlation with the clinical outcome within one month of onset of symptoms. The predictability of our diffusion tensor tractography results compares favorably with the recent reports by other studies (20–24).

Our experience suggest that it is technically feasible to incorporate such a DTI sequence into the routine imaging protocol for stroke patients and that the relative preservation of white matter tracts results in subsequent good clinical recovery and could potentially be used as clinical markers. The advantage of DTT lies in the fact that it gives direct and superior visualization of the involved white matter tracts in vivo, which is currently not possible by conventional imaging and DWI.

There are however a few limitations in our study. First is the relatively small group of patients studied by this novel technique. Additionally, our current diffusion tensor tractography tool requires a good knowledge of the anatomical location of various white matter tracts, and operator (radiologist) selection of the ROI is required. Future availability of an automated algorithm for fiber tractography of the major tracts would greatly reduce operator dependence and the relatively time intensive and manually intensive nature of the procedure. Furthermore, future availability of standardized tractography maps in normative space, should allow direct comparison of results between groups.

In conclusion, our findings suggest that DTT can be performed within a relatively short time and can visualize and quantify the changes in the integrity and orientation of the white matter tracts that are transected by focal ischemic lesions, which are otherwise not shown on conventional MR imaging or even DWI scans. DTT can visualize the white matter tracts as being either displaced or disrupted due to

edema or infarction, and offers a potential tool for clinical-imaging correlation of the involved white matter tracts and patients' clinical recovery.

References

(1) Parmar H, Golay X, Lee EK, Hui F, Sitoh YY. Early experiences with diffusion tensor imaging and magnetic resonance tractography in stroke patients. Singapore Med J 2006;47(3):198–203.

(2) Wu O, Koroshetz WJ, Ostergaard L. Predicting tissue outcome in acute human cerebral ischemia using combined diffusion- and perfusion- weighted MR imaging. Stroke 2001;32:933–42.

(3) Kusano Y, Seguchi T, Horiuchi T, Kakizawa Y, Kobayashi T, Seguchi K, et al. Prediction of functional outcome in acute cerebral hemorrhage using diffusion tensor imaging at 3T: a prospective study. Am J Neuroradiol 2009;30:1561–5.

(4) Kim YH, Kim DS, Hong JH, Park CH, Hua N, Bickart KC, et al. Corticospinal tract location in internal capsule human brain: diffusion tensor tractography and functional MRI study. Neuroreport 2008;19:817–20.

(5) Gillard JH, Papadakis NG, Martin K. MR diffusion tensor imaging of white matter tract disruption in stroke at 3T. Br J Radiol 2001;74:642–7.

(6) Laura ED, Nobue KI, David MT, Mary KF. Reliability of fiber tracking measurements in diffusion tensor imaging for longitudinal study. Neuroimaging 2010;49(2):1572–80.

(7) Assaf Y, Pasternak O. Diffusion tensor imaging (DTI)-based white matter mapping in brain research: a review. J Mol Neurosci 2008;34(1):51–61.

(8) Olavarria V, Delgado I, Hoppe A, Brunser A, Cárcamo D, Lavados D-TPM. Validity of the NIHSS in predicting arterial occlusion in cerebral infarction is time-dependent. Neurology 2011;79:14–7.

(9) Setsu W, Hang YJ, Lindia M, Van Zijl PC, Mori S. Fiber tract-based atlas of human white matter anatomy. Radiology 2004;230:77–87.

(10) Thomalla G, Glauche V, Koch MA. Diffusion tensor imaging detects early wallerian degeneration of the pyramidal tract after ischemic stroke. Neuroimage 2004;22:1767–74.

(11) Delsing BJP, Catsman-Berrevoets CE, Appel IM. Early prognostic indicators of outcome in ischemic childhood stroke. Pediatr Neurol 2001;24:283–9.

(12) Hsieh CT, Chen CY, Chiang YH. Role of diffusion tensor imaging in a patient with spontaneous intracerebral hematoma treated by stereotactic evacuation. Surg Neurol 2008;70:75–8.

(13) Pierpaoli C, Barnett A, Pajevic S. Water diffusion changes in wallerian degeneration and their dependence on white matter architecture. Neuroimage 2001;13:1174–85.

(14) Yokoyama K, Matsuki M, Shimano H. Diffusion tensor imaging in chronic subdural hematoma: correlation between clinical signs and fractional anisotropy in the pyramidal tract. Am J Neuroradiol 2008;29:1159–63.

(15) Aoki S, Iwata NK, Masutani Y. Quantitative evaluation of the pyramidal tract segmented by diffusion tensor tractography: feasibility study in patients with amyotrophic lateral sclerosis. Radiat Med 2005;23:195–9.

(16) Frank LR. Anisotropy in high angular resolution diffusion-weighted MRI. Magn Reson Med 2001;45:935–9.

(17) Tuch DS, Reese TG, Wiegell MR. Diffusion MRI of complex neural architecture. Neuron 2003;40:885–95.

(18) Alexander AL, Hasan KM. Analysis of partial volume effects in diffusion-tensor MRI. Magn Reson Med 2001;45:770–80.

(19) Masutani Y, Aoki S, Abe O. A new fiber tracking method based on vector field reconstruction excepting fiber crossing area in MR diffusion tensor images. Med Imag Technol 2004;22:243–9.

(20) Maeda T, Ishizaki K, Yura S. Can diffusion tensor imaging predict the functional outcome of supra-tentorial stroke. No To Shinkei 2005;57(1):27–32.

(21) Chen Z, Ni P, Zhang J, Ye Y, Xiao H, Qian G, et al. Evaluating ischemic stroke with diffusion tensor imaging. Neurol Res 2008;30(7):720–6.

(22) Lai C, Zhang Z, Liu HM, Zhou YB, Zhang YY, Zhang Q, et al. White matter tractography by diffusion tensor imaging plays an important role in prognosis estimation of acute lacunar infarctions. Br J Radiol 2007;80:782–9.

(23) Yamada K, Ito H, Nakamura H, Osamu K, Wataru A, Takao K, et al. Stroke patients' evolving symptoms assessed by tractography. J Magn Reson Imaging 2004;20:923–9.

(24) Kunimatsu A, Aoki S, Masutani Y, Abe O, Mori H, Ohtomo K. Three-dimensional white matter tractography by diffusion tensor imaging in ischaemic stroke involving the corticospinal tract. Neuroradiology 2003;45:532–53.