Early experiences with diffusion tensor imaging and magnetic resonance tractography in stroke patients

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ABSTRACT

Introduction: Recent advances in magnetic resonance (MR) diffusion tensor imaging technique enable evaluation of the anisotropy of white matter tracts in-vivo, as well as the integrity of fibre tracts and their orientation. We describe our initial experiences with diffusion tensor imaging and MR tractography techniques to evaluate the structural degeneration of white matter tracts following stroke.

Methods: Diffusion tensor imaging data were acquired in 11 cases with stroke on a 3T MR imaging scanner, with three-dimensional diffusion tensor imaging-based colour maps and MR tractography performed offline. We evaluated the spatial relationships of the eloquent white matter tracts to the infarcts and areas of haemorrhage, and classified therewith the tracts as either disrupted or displaced. We compared these with the clinical severity of the neurological deficits and prognosis.

Results: A good correlation was found between tractography findings and patient's clinical recovery. All the patients with disruption of white matter tracts had residual deficits on clinical follow-up, whereas the patients with displaced tracts had near complete neurological recovery.

Conclusion: Diffusion tensor imaging and MR tractography provide a novel and useful method to directly visualise changes in the white matter tracts in stroke. This can potentially allow clinical-imaging correlation with prognostic potential.

Keywords: cerebrovascular accident, diffusion magnetic resonance imaging, echo planar imaging, magnetic resonance imaging, magnetic resonance tractography, stroke

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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 ischaemic infarcts, intracranial haemorrhage, subarachnoid haemorrhage, 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]. Few studies have however addressed the problem of applying MR techniques to study the outcome of this group of patients[3,4]. Conventional MR imaging cannot provide reliable information about the integrity of white matter tracts, thereby limiting the ability to predict clinical outcome. However, with diffusion tensor imaging (DTI), the microstructural organisation of white matter tracts can be obtained and provide important information about their integrity as well as orientation[5,6]. With DTI, quantification of anisotropy in the white matter tracts is obtained from the fractional anisotropy (FA) values[6].

Three-dimensional images of MR tractography can be generated to give visual depiction of the involved white matter tracts[7]. With higher field strength (3 Tesla) clinical scanners, the signal-to-noise ratio (SNR) and spatial resolution are significantly improved, with better visualisation of these fibre tracts[8]. Previously, DTI has been used to show involvement of white matter tracts adjacent to tumour[9,10] and in lacunar infarcts at the internal capsule level[11,12] on 1.5T scanners. We believe this is the first report to depict MR tractography of large white matter tracts in stroke, using a higher field strength magnet. We investigate the clinical utility of MR tractography in visualising the morphological correlate of dysfunctional pathways after cerebral infarction or haemorrhage at 3T, and its potential towards prognostication of patient recovery.

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Table I. Clinical and MR imaging details of the patients.

No.	Age/ sex	Clinical features	Time of MRI	MRI findings	% FA change in WMT	MRT findings	Clinical follow-up
1.	73/M	Rt hemiparesis, Dementia	>6 mths	Chronic Lt MCA infarct	-23	Disruption of Lt CST	Motor deficits persist at 12 mths
2.	56/F	Rt hemiparesis	>8 wks	Old Lt MCA infarct, wallerian degeneration	-13	Lt CST Small	Motor deficits persist at 12 mths
3.	72/M	Rt visual field defects	7 days	Acute Lt PCA infarct	-42	Disruption of Lt OR	Visual field defects persist at 6 mths
4.	47/M	Drowsiness, -GCS, Lt hemiparesis	4 days	Acute Rt MCA infarct, haemorrhagic conversion	Unaffected	Rt CST displaced	Complete recovery after 6 wks
5.	61/F	Giddiness, Lt knee weakness	>8 wks	Old infarcts in Rt ACA and Lt MCA territories	-6	Rt CST disrupted, LT CST normal	Residual weakness in Lt LL at 12 mths
6.	62/M	Vertigo, giddiness	1 day	Small acute infarct in Rt medulla and pons	Unaffected	CST not involved	No residual symptoms
7.	67/F	Lt sided weakness, Lt facial palsy	13 days	Subacute Rt MCA infarct, haemorrhagic conversion	-15	Rt distal CST disrupted	Residual weakness at 2 mths
8.	75/M	Lt sided hemiparesis	1 day	Acute large Rt. MCA infarct	-27	Rt CST disrupted	Patient expired due to AMI
9.	75/M	TIAs	>3 wks	Subacute Lt MCA with chronic Lt MCA infarct	Unaffected	CST not involved	No residual symptoms
10.	64/F	Headaches	>6 mths	Lt temporal haematoma	Unaffected	Lt OR displaced	No residual symptoms
11.	50/M	Rt hemiparesis, headache	2 days	Lt BG haematoma	Unaffected	Lt CST displaced, but preserved	Partial recovery of motor symptoms at 4 wks.

Key: ACA: anterior cerebral artery; ADC: apparent diffusion coefficient; AMI: acute myocardial infarction; BG: basal ganglia; CST: corticospinal tract; F: female; FA: fractional anisotropy; GCS: Glasgow coma scale; LL: lower limb; Lt: left; M: Male; MCA: middle cerebral artery; MRI: magnetic resonance imaging; MRT: MR tractography; mths: months; OR: optic radiation; PCA: posterior cerebral artery; Rt: right; TIA: transient ischaemic attack; wks: weeks; WMT: white matter tract; +: increase; -: decrease.

METHODS

The study included both retrospective and prospective data. We applied DTI to image 11 patients with stroke (Table I). The time of imaging varied from under one week to more than eight weeks after the onset of acute symptoms. Conventional MR images (T1 and T2 weighted images, isotropic diffusion weighted images) were obtained on a clinical 3T unit (Gyroscan Intera, Philips Medical System, Einthoven, The Netherlands) using a quadrature head coil. Diffusion tensor images were obtained using echo planar single shot technique with TR/TE/flip angle of 6000/88/90 and six motion probing gradient orientations. A b value of 800 s/mm^2 was used, and six averages were gathered to increase SNR. The data were recorded on a 128 x 96 matrix, and were zero filled for a final resolution of 128 x 128. Thirty-six slices were obtained with three mm slice thickness without any interslice gap. The total imaging time was five minutes and ten seconds.

The FA values were measured in the involved white matter tracts at the region of abnormality and were compared with the normal values on the unaffected contralateral side. MR tractography of the white matter tracts was performed offline on a PC-based workstation (PRIDE, Philips Medical System, Einthoven, The Netherlands) using the methodology and FACT (fibre assignment by continuous tracking) algorithm described by Mori et al[7]. Based on known anatomy, regions of interest (ROI) were drawn as seeds in the uninvolved portions of the white matter tracts (multi-ROI technique), and the software algorithm tracked the white matter tracts that passed through these ROIs. A threshold value of FA = 0.2 or more was assigned for fibre tracking. Three-dimensional DTI-based colour maps were later generated with the standard colour coding system as described in the literature[7].

DTI data and MR tractography of the involved white matter tracts (corticospinal tract [CST] in

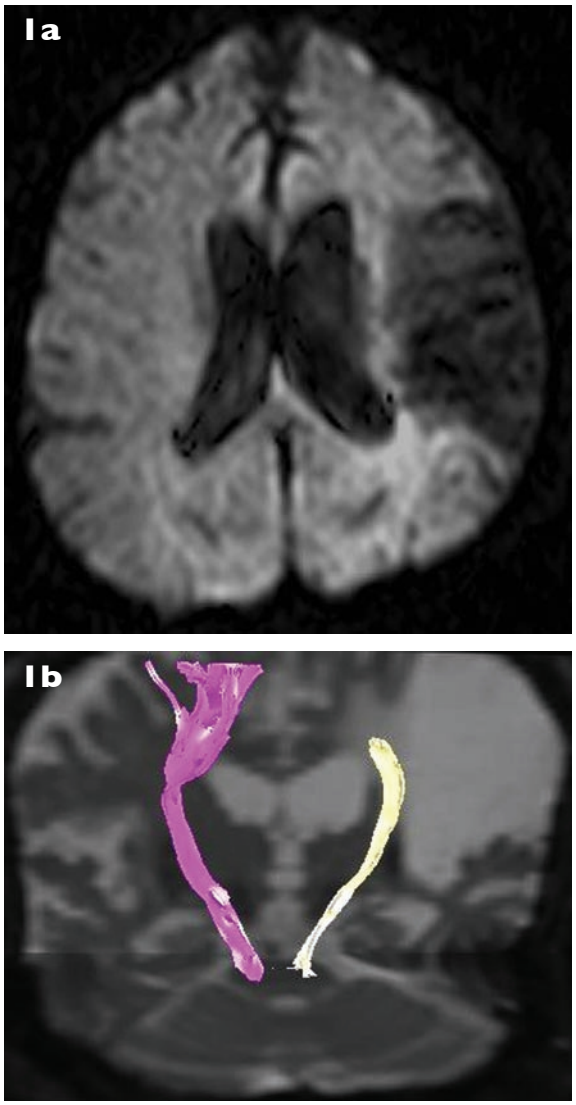


Fig. 1 Case 1. (a) DWI shows a large chronic infarction in the left middle cerebral artery distribution. (b) MR tractography shows complete disruption of left corticospinal tract at the level of infarction with small calibre of the rest of the tract.

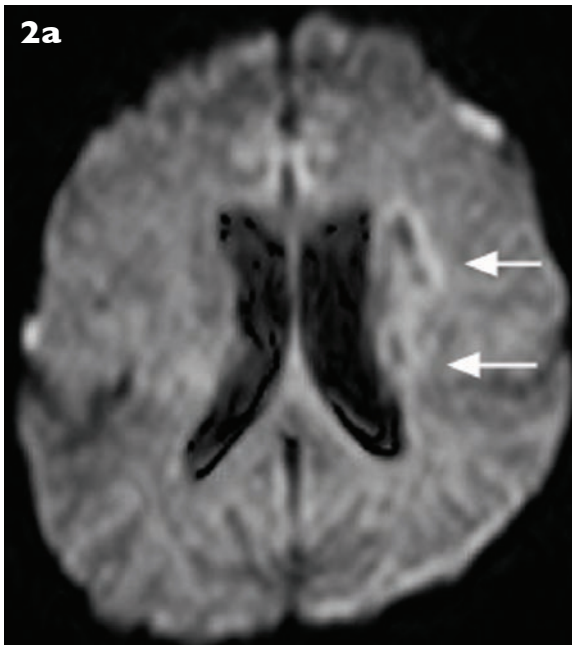
nine, optic radiation in two) were compared with the corresponding tracts of the contralateral normal hemisphere. The tracts were visually inspected for changes in size and orientation, and compared to those in the contralateral hemisphere. The tracts were characterised as either displaced or disrupted, based on the system proposed by Witwer et al[10]. They were considered displaced if they maintained normal anisotropy relative to the corresponding tract in the contralateral hemisphere but had abnormal location or orientation; disrupted if anisotropy was markedly reduced such that the tract could not be identified on the DTI based maps and/or by the failure of the fibre tracking algorithm. The DTI and MR tractography data were analysed by two neuroradiologists by consensus, both of whom were blinded to the patient's clinical details. All patients were followed-up clinically (period lasting from six weeks till twelve months) for residual neurological deficits. Follow-up imaging was not performed.

RESULTS

DTI and MR tractography were successful in all patients. We were able to delineate the involved white matter tract reliably and repeatedly in all patients and these were consistent with known anatomy. There were seven male and four female patients, with ages ranging from 47 to 75 years (mean 63.8 years). There were seven patients with ischaemic infarctions (three acute: imaged within the first week, four chronic: imaged after one week of symptom onset). In these seven cases, there were a total of nine infarcts: six in the middle cerebral artery (MCA), one in the posterior cerebral artery (PCA), one in the anterior cerebral artery (ACA) distribution, while one patient had a small infarction of the anterior brainstem. Two patients (both imaged within two weeks) had haemorrhagic conversion of their infarcts, both in the MCA distribution. Two patients had primary intracranial haemorrhage (ICH), one in the basal ganglia and one in the temporal lobe (Table I).

Conventional MR imaging, comprising T1- and T2-weighted images, as well as isotropic diffusion weighted imaging (DWI), were abnormal in all patients. In five patients with ischaemic infarcts and one with haemorrhagic infarct, FA values in the involved white matter tracts were reduced by 6%-42%, compared to the corresponding tracts in the contralateral hemisphere (Table I). MR tractography showed disruption of the CSTs in the region of infarction in a total of three patients (cases one, five and eight) with ischaemic MCA/ACA infarcts (Fig. 1). The calibre of the rest of the ipsilateral CST was small compared to the opposite side. One patient (case two) showed decrease in the size of the CST, but it was intact throughout its extent. We attributed this to wallerian degeneration (Fig. 2). The patient with PCA territory infarction (case three) showed disruption with loss of continuity of the terminal fibres of the involved optic radiation (Fig. 3).

One of the two patients (cases four and seven) with haemorrhagic anterior MCA infarct showed no observable decrease in the FA values in the ipsilateral CST. In this patient (case four), the CST was distorted due to the mass effect and tissue oedema from the adjacent infarct, but was otherwise preserved (Fig. 4). One patient (case seven) however had disruption of the CST at the level of the infarcted area. Both cases with primary ICH (cases ten, eleven) had displacement of the



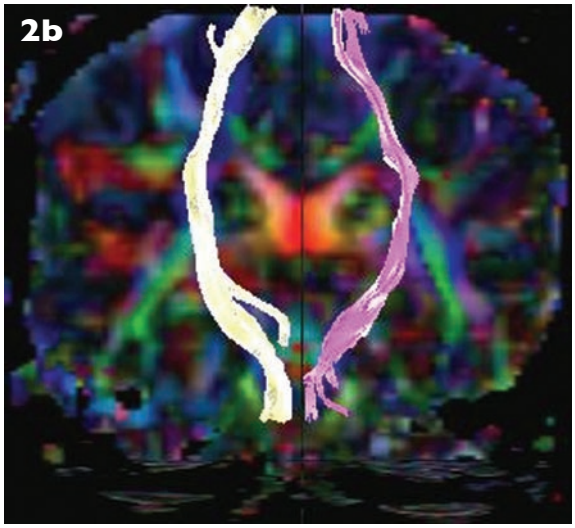
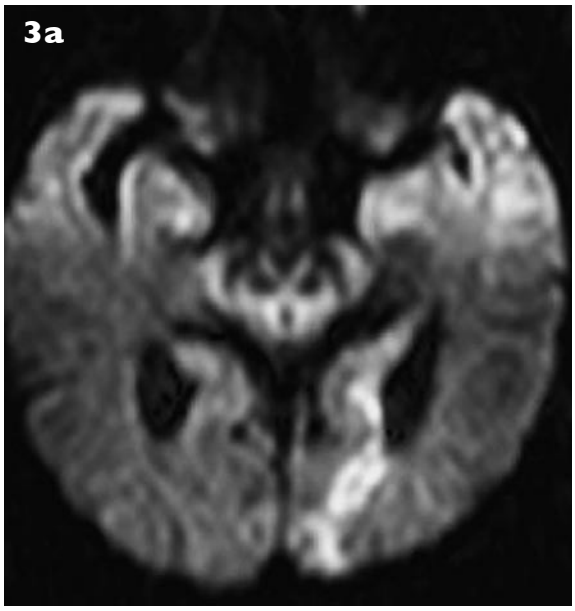


Fig. 2 Case 2. (a) DWI shows left cortical and subcortical chronic infarction (arrows). (b) MR tractography shows the full extent of the left corticospinal tract, which shows decrease in calibre compared to the right side, due to wallerian degeneration.



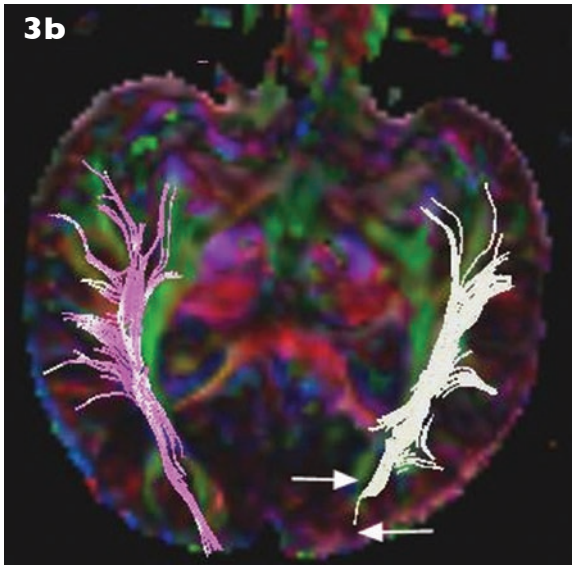


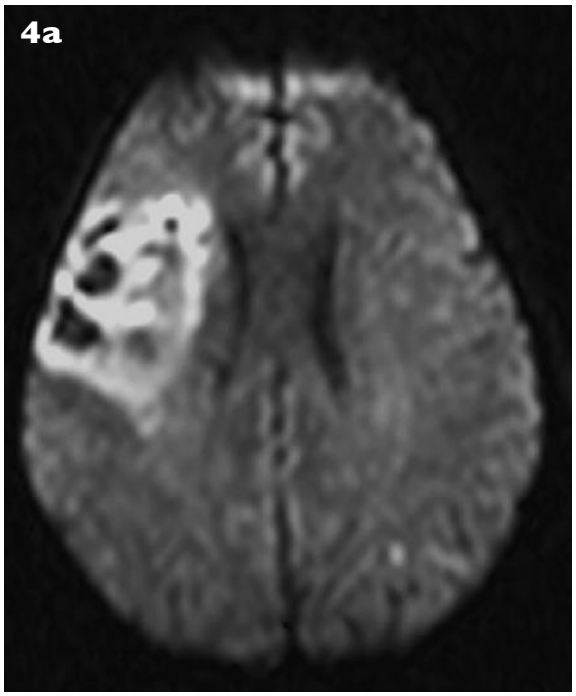
Fig. 3 Case 3. (a) DWI shows acute infarction in the left occipital lobe with sparing of occipital pole cortex due to left posterior artery occlusion. (b) MR tractography shows disruption of terminal fibres of the left optic radiation (arrow).

white matter tracts adjacent to the haematomas (Fig. 5). The tracts were not disrupted.

On clinical follow-up, the patients with disrupted white matter tracts (three with ischaemic infarcts and one with haemorrhagic infarct) continued to have residual neurological deficits. These were in the form of motor deficits or homonymous hemianopia (case three). The patient with wallerian degeneration (case two) also continued to show residual motor deficits. One patient with ischaemic infarction and tract disruption (case eight) had no follow-up as he died due to an unrelated cause. All the patients with displacement rather than disruption of the white matter tracts showed complete to near complete recovery in their presenting symptoms.

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 of tissue oedema and mass effect associated with infarction and haemorrhage[3]. However, for long-term recovery, relative preservation of the integrity and anisotropy of the white matter tracts (CSTs particularly) plays an important role and indicates a better clinical outcome[3-5]. Conventional imaging however does not give data about the microstructural organisation of the white matter fibre tracts, which can be obtained from DTI and MR tractography. The information so obtained may prove more sensitive



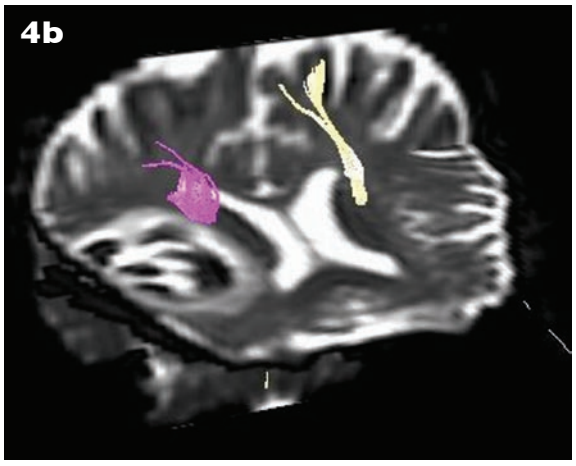
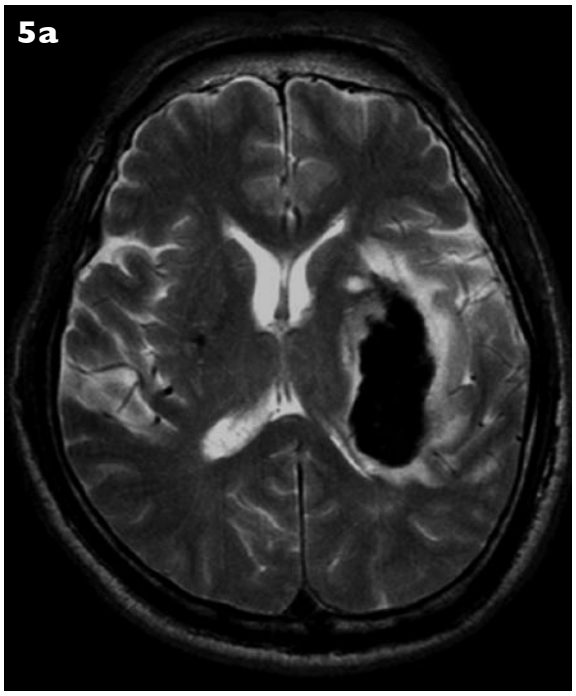


Fig. 4 Case 4. (a) DWI shows right middle cerebral artery infarction with haemorrhagic conversion. (b) MR tractography shows displacement of right corticospinal tract due to mass effect and tissue oedema. The tract is otherwise preserved.



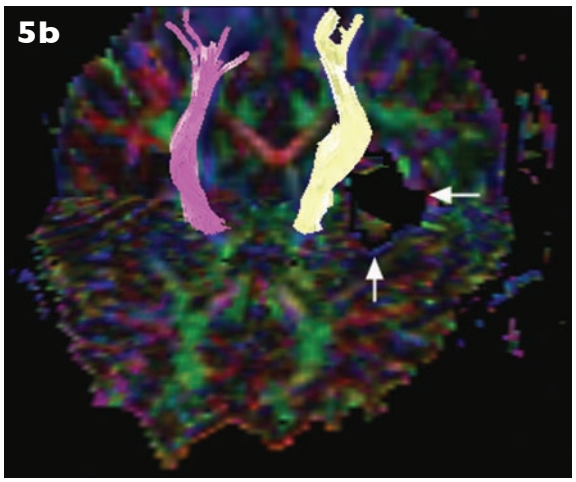


Fig. 5 Case 11 (a) Axial T2-W image shows a large parenchymal haematoma at the level of left basal ganglia. (b): DTI-based colour map with MR tractography shows preservation of the left corticospinal tract which is displaced by mass effect from the haematoma (arrows).

to assess tract damage than the volume estimation of signal abnormality on conventional imaging.

Some recent studies using only axial FA maps have shown quantitatively reduced FA values corresponding to the involved white matter tracts to indicate poor recovery[3-5]. Direct involvement of the CST and other long fibre tracts by infarction/ haemorrhage results in their disintegration. In cases with cortical infarcts, there is neuronal death and resultant wallerian degeneration of the subcortical white matter tract[5]. In both these conditions, the final pathway, i.e. the white matter tract, is involved resulting in poorer clinical outcome with residual neurological deficits[13]. This correlates well with our data where significant decreases in FA to less than 0.2 at the site of infarction corresponded to disruption of the relevant white matter tracts. In addition, the FA values in the affected white matter tracts inferior to the infarct were decreased to a lesser extent. In these patients, there was poor functional recovery with residual deficits. DTI and MR tractography exquisitely depicts these changes in the involved white matter tracts. 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 MR tractography lies in the

fact that it gives direct and superior visualisation of the involved white matter tracts in-vivo, which is currently not possible by conventional imaging. By using a high field scanner for our study, we were able to improve upon the resolution and the SNR in all cases, thus allowing better depiction of the white matter tracts, especially of the peripheral fibres[8]. For example, in patient three, conventional T2 and diffusion WI showed infarction in the subcortical white matter with relative sparing of the cortex. MR tractography, however, showed clear disruption of the terminal fibres of the optic radiation, thus explaining his permanent homonymous hemianopia. With the advent of parallel imaging techniques, the total imaging time will be even shorter, facilitating routine clinical imaging in stroke[8]. The parallel imaging technique allows image reconstruction with only a portion of the encoding steps, thereby reducing scan time, and it also reduces geometric image distortion due to echo-planar imaging, especially at the skull base[14].

We obtained DTI data in a full clinical spectrum of stroke patients comprising small and large territorial infarctions, as would be encountered in a busy clinical setting. We were also able to successfully perform DTI and MR tractography in patients with haemorrhagic infarcts and intracranial haemorrhage. Small haematomas with the presence of blood products does not necessarily imply failure of DTI acquisition and MR tractography, and should not be a constraint to performing such studies in these groups of patients. Our DTI and tractography results showed good correlation with the clinical outcome. The predictability of our MR tractography results compares favourably with the recent reports by Yamada et al[11] and Kunimatsu et al[12], where MR tractography was used to evaluate the involvement of the corticospinal tract in small acute ischaemic infarcts involving the internal capsules.

There are however a few limitations in our study. First is the relatively small and heterogeneous group of patients studied by this novel technique. We did not longitudinally study these cases, and hence are unable to comment upon the exact time course of changes that occurred and how it affected the FA values of the involved white matter tracts. Additionally, our current MR 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 fibre 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 standardised tractography maps in normative space, such as a Talaraich atlas, should allow direct comparison of results between groups.

In conclusion, our preliminary findings suggest that DTI and MR tractography can be performed clinically within a relatively short time. With DTI, we can visualise and quantify the changes in the integrity and orientation of the white matter tracts that are transected by focal ischaemic/haemorrhagic lesions, which are otherwise not shown on conventional MR imaging or even conventional DWI scans. MR tractography can visualise the white matter tracts as being either displaced or disrupted due to oedema or infarction, and offers a potential tool for clinical-imaging correlation of the involved white matter tracts and patient's clinical recovery.

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