Original Research Article

# Diffusion-tensor imaging of white matter tracts in patients with brain tumours

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## Abstract

**Background:** Brain tumours have high mortality rate. Surgeries for brain tumour are associated with higher complication rates. Proper diagnosis and preoperative knowledge of fibre tract involvement is helpful for surgeries with less complications. Diffusion tensor imaging is new technique used for knowing malignancy potential of the tumour. **Aim and objective:** To study the diffusion tensor imaging of white matter tracts in patients with brain tumours **Methodology:** A total of 50 patients with brain tumours were evaluated at Indraprastha Apollo hospital, New Delhi. All patients underwent conventional MRI supplanted by diffusion tensor imaging in Philips Achieva 3T scanner. DTI was performed. Anisotropy was calculated by using orientation-independent fractional anisotropy (FA), and diffusion-tensor MR imaging– based color maps were created from the FA values. **Results:** The FA values of displaced WMFT ranged between 0.413-0.511. The FA values of edematous WMFT ranged between 0.370-0.458. The FA values of infiltrated WMFT ranged between 0.337-0.427. The FA values of displaced WMFT ranged between 0.235-0.345. The ADC values (× 10-3 mm2/s) of displaced WM fibers ranged from 0.609 to 0.833. The ADC values (× 10-3 mm2/s) of edematous WM fibers ranged from 1.221 to 1.457. The ADC values (×10-3 mm2/s) of infiltrated WM fibers ranged from 0.938 to 1.114. The ADC values (× 10-3 mm2/s) of disrupted WM fibers ranged from 0.940 to 1.110.

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## INTRODUCTION

According to the Population Based Cancer Registry of India, crude incidence of primary brain tumour in India between 1999-2007 was 3.4 per 100,000 populations for males and 1.2 per 100,000 populations for females. It represents < 1% of new cancer cases detected every year in the country. However, there has been a steady increase in the incidence of primary brain tumours over the last decade or so primarily due to higher detection rates due to more widespread availability of diagnostic imaging.[1] Intracranial tumours are classified according to the World Health Organization (WHO) classification of tumours of the central nervous system (CNS) [2]. The WHO classification is based on the cellular origin of the tumours and describes seven different groups: tumours originating from neuroepithelial cells, cranial and spinal nerves, the meninges, lymphatic and haematopoietic tissue, germ cells and the sellar region, and tumours of metastatic origin [2]. This classification was revised in 2007. The presenting symptoms of an intracranial tumour are related to infiltration of brain parenchyma by the mass lesion, tissue destruction and mass effect. The most common symptom is a headache, which occurs in approximately 35% of patients. A new onset of headaches in a patient with no previous history of headaches is most characteristic. This is the case especially if the headaches are more severe in the morning and are associated with nausea, vomiting or focal neurologic deficits. In patients with a previous history of headaches, a change in the characteristics of the headaches or an increase in their frequency and/or intensity

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can also indicate the presence of an intracranial tumour. Seizures occur in approximately 33% of patients with gliomas, especially in patients with low-grade tumours. However, seizures may be associated with any CNS tumour. Focal neurologic deficits are related to the location of the tumour. [3] Altered mental status may develop in 15–20% of patients with gliomas. [4] and cognitive impairment has been observed in 65% of patients with brain metastases, usually across multiple domains. [5] Surgery is the initial therapy for nearly all patients with brain tumours and can be curative for most low grade tumours. The goal of surgery is to remove as much of the tumour as possible while minimizing damage to healthy tissue. Initially X rays were used for diagnosis of brain tumor. After innovation of computed tomography and magnetic resonance imaging, radiology has grown by leaps and bounds and found its place as integral facet of brain tumor management. [6] Pioneering work by Stejskal and Tanner [7] showed that random motion of water molecule in all the directions in a particular environment, also termed as Brownian motion, could be the basis of diffusion weighted imaging. They proposed that MRI can make it possible to estimate the diffusivity of water molecules. To sensitize MRI images to diffusion, instead of a homogeneous magnetic field, the homogeneity is varied linearly by a pulsed field gradient. Present study was aimed to study the diffusion sensor imaging of white matter tracts in patients with brain tumour.

**Aim and objective:** To study the diffusion tensor imaging of white matter tracts in patients with brain tumours.

## MATERIAL AND METHODS

A total of 50 patients with brain tumours were evaluated between May 2011 to January 2013 at Indraprastha Apollo hospital, New Delhi. Informed consent was received from all patients or the participant's parents or legal guardian and the studies were approved by the hospital's Research Ethics Committee. They underwent conventional MRI supplanted by diffusion tensor imaging in Philips Achieva 3T scanner. DTI was performed using dual spin echo, a single shot, a pulsed gradient and an echo-planar imaging (EPI) sequences, single-shot spin echo, echo-planar imaging (EPI) and parallel imaging techniques to achieve motion-free and higher signal-to-noise ratio (SNR) DTI. The total imaging time for DTI and FT was 7–9 minutes according to the section numbers, which was added to the routine MR imaging examinations. (TR- 6.6s, TE – 70ms, voxel size 2 x 2 x 2mm, FOV – 224x224x120mm, B value 800s / mm2, SAR mode- high). Anisotropy was calculated by using orientation-independent fractional anisotropy (FA), and diffusion-tensor MR imaging– based color maps were created from the FA values and the three vector elements. The vector maps were assigned to red (x element, left-right), green (y, anterior-posterior), and blue (z, superior- inferior) with a proportional intensity scale according to the FA. The threshold values for the termination of the fiber tracking were less than 0.2 for FA and greater than 25° for the trajectory angles between the ellipsoids. For tracking of the white matter fibers, the region of interest (ROI) method was applied. We placed the single or multiple ROIs on the color maps. The plane of the ROI was varied according to the running direction of the white matter fibers (e.g., corticospinal tract on the axial views, corpus callosum on the sagittal views).

White matter fibre tracts were evaluated and classified as:-

1. Normal: maintained normal anisotropy relative to the normal contralateral tract in the corresponding location and normally oriented and located in a normal T2-weighed signal intensity area.
2. Displaced: maintained normal anisotropy relative to the normal contralateral tract in the corresponding location but situated in an abnormal T2-weighted signal intensity area or presenting in an abnormal orientation.
3. Infiltrated: reduced anisotropy relative to the normal contralateral tract in the corresponding location but remaining identifiable on orientation maps.
4. Disrupted: marked reduced anisotropy relative to the normal contralateral tract in the corresponding location and unidentifiable on orientation maps.
5. Edematous: maintained normal anisotropy relative to the normal contralateral tract in the corresponding location and normally oriented but located in an abnormal T2-weighed signal intensity area.

## RESULTS

Among 50 patients in our study 33 were male and 17 female patients. Youngest among these was 3 years old male and oldest patient was 77 years old female. Mean age was 41.1 year. These patients were classified into age groups of 0- 15 years, 16 -30 years, 31- 45 years, 46 – 60years and > 60 years of age. In the first group that is 0-15 years, we observed 8 male patients and 4 female patients. In 16 – 30 years age group, we observed 6 male patients and 1 female patient. In 31- 45 years age group, we observed 3 male and female patients. In 46- 60 years age group, we observed 11 male patients and 1 female patient. In > 60 year age group, we observed 4 male patients and 8 female patients. We included handedness of patient locate dominant hemisphere, as it is the simplest way of doing so. 43 patients were right handed and 7 patients were left handed. Among these, 29 male and 14 female patients were right handed, while 4 male and 3 female patients were left handed. (table1) Among 50

patients in our study, 39 had lesion in supratentorial location with 25 male and 14 female patients in this category. Infratentorial lesion was seen in 8 male and 3 female patients. Space occupying lesions are described according to their location and broader morphological characteristics on conventional MRI.

We examined all the patients for neurological deficit and documented affection of motor and sensory function, speech and vision in them. After reaching the radiological diagnosis of lesion (evaluated by senior consultant radiologists), we collaborated with neurosurgical team to chalk out best possible surgical approach and management for the space occupying lesion. (table 2) Later we evaluated these patients using diffusion tensor imaging and fiber tractography complimentary to the conventional MRI. We evaluated relevant white matter fiber tracts (WMFT) in supra- and infratentorial compartments and documented their FA and ADC values. We classified them into four classes i. e. displaced, edematous, infiltrated and disrupted; according to altered FA and ADC values and whether they lie in normal or abnormal MRI signal intensity area on conventional images. We also considered anatomical location and orientation of fiber tracts, their density or clustering compared to contralateral side. Our imaging findings were later correlated with intraoperative findings. We found that mean FA value for displaced WMFT was 0.462 with standard deviation of 0.049 while mean ADC value was 0.721 with standard deviation of 0.112. In case of edematous fibers, we found that mean FA value was 0.414 with standard deviation of 0.044 while mean ADC value was 1.339 with standard deviation of 0.118. Infiltrated fibres showed mean FA value of 0.382 with standard deviation of 0.045. Mean ADC value for infiltrated fibers was 1.026 with standard deviation of 0.088. In case of disrupted fibers, we observed significant drop in FA value compared to normal contralateral side. Mean FA value for disrupted fibers was 0.290 with standard deviation of 0.055. However, ADC values for disrupted fibers were not strikingly different from that for infiltrated fibres. Mean ADC value for disrupted fibers was 1.025 with standard deviation of 0.085. (Table no.3)

**Table 1:** General characteristics of study population

| | |
|---|---|
| **Gender** | |
| Male | 33 |
| Female | 17 |
| **Age** | |
| Mean | 41.1 years |
| SD | 23.4 |
| **Handedness** | |
| Right | 43 |
| Left | 7 |

**Table 2:** Location and gross morphology of tumour

| Tumour Location | N |
|---|---|
| 3rd and 4th ventricular mass causing hydrocephalus | 1 |
| 4th ventricular mass | 3 |
| Antero-lataral pontine mass on Rt side | 1 |
| Diffuse pontine mass | 1 |
| Exophytic medullary mass | 1 |
| Exophytic posterior midbrain mass | 1 |
| Focal anterior pontine mass | 1 |
| Focal midbrain mass | 1 |
| Lt basifrontal mass | 1 |
| Lt frontal lobe mass | 1 |
| Lt lateral ventricular obstructive mass | 2 |
| Lt medial temporal mass | 1 |
| Lt parietal lobe mass | 3 |
| Lt parieto-occipito-temporal mass | 1 |
| Lt temporal lobe mass | 3 |
| Lt temporal mass, intraventricular extension | 1 |
| Midbrain cystic mass with mural nodule | 3 |
| Midline corpus callosum mass | 2 |
| Pontine cystic mass with mural nodule | 1 |
| Ponto-medullary cystic mass | 1 |

| | |
|---|---|
| Posterior ponto-medullary mass | 1 |
| Rt basifrontal intraventricular mass | 2 |
| Rt frontal region | 1 |
| Rt fronto-temporal mass | 3 |
| Rt fronto-parietal mass | 1 |
| Rt fronto-parietal -temporal mass | 1 |
| Rt parietal mass | 2 |
| Rt parieto-occipital mass | 1 |
| Rt parieto-temporal mass involving internal capsule | 1 |
| Rt temporal infrasylvian mass | 2 |
| Rt temporo-parietal mass | 1 |
| Rt thalamo-ganglionic mass | 1 |
| Suprasellar mass | 3 |
| **Total** | **50** |

**Table 3:** Range of FA and ADC values for nature of pathology involving WM fiber tracts

| Fibre Type | FA value | | | | ADC value | | | |
|---|---|---|---|---|---|---|---|---|
| | Mean | SD | Median | Mode | Mean | SD | Median | Mode |
| **Displaced** | 0.462 | 0.049 | 0.465 | 0.484 | 0.721 | 0.112 | 0.710 | 0.703 |
| **Edematous** | 0.414 | 0.044 | 0.407 | 0.410 | 1.339 | 0.118 | 1.311 | 1.293, 1.311, |
| **Infiltrated** | 0.382 | 0.045 | 0.383 | 0.382, 0.388 | 1.026 | 0.088 | 1.005 | 0.973 |
| **Disrupted** | 0.290 | 0.055 | 0.286 | 0.382 | 1.025 | 0.085 | 1.012 | 1.009 |

**Table 3:** Range of FA and ADC values for nature of pathology involving WM fiber tracts

| Fibre Type | FA value | | | | ADC value | | | |
|---|---|---|---|---|---|---|---|---|
| | Mean | SD | Median | Mode | Mean | SD | Median | Mode |
| **Displaced** | 0.462 | 0.049 | 0.465 | 0.484 | 0.721 | 0.112 | 0.710 | 0.703 |
| **Edematous** | 0.414 | 0.044 | 0.407 | 0.410 | 1.339 | 0.118 | 1.311 | 1.293, 1.311, |
| **Infiltrated** | 0.382 | 0.045 | 0.383 | 0.382, 0.388 | 1.026 | 0.088 | 1.005 | 0.973 |
| **Disrupted** | 0.290 | 0.055 | 0.286 | 0.382 | 1.025 | 0.085 | 1.012 | 1.009 |

## DISCUSSION

In our study we observed mainly four patterns of involvement white matter fibre tracts. Pattern 1 consisted of normal or only slightly decreased FA with abnormal location and/or direction resulting from bulk mass displacement. This is the most clinically useful pattern in preoperative planning because it confirms the presence of an intact peri tumoral tract that can potentially be preserved during resection. Pattern 2 was substantially decreased FA with normal location and direction (i.e, normal hues on directional colour maps). This is frequently observed pattern in regions of vasogenic edema, although the specificity of this pattern is not yet known especially in case of high-grade gliomas. Pattern 3 was substantially decreased FA with abnormal hues on directional color maps. This pattern is identified in a small number of infiltrating gliomas in which the bulk mass effect appeared to be insufficient to account for the abnormal hues on directional maps. It is speculated that infiltrating tumour disrupts the directional organization of fibre tracts to cause altered colour patterns on directional maps, but this phenomenon requires further study. Pattern 4 consisted of isotropic (or near isotropic) diffusion such that the tract cannot be identified on directional color maps. This pattern is observed when some portion of a tract is completely disrupted by tumor. Here FA values were significantly low. This pattern can be useful in preoperative planning in the sense that no special care need be taken during resection to preserve a tract that is shown by DTI to be destroyed. It should be noted that combinations of the above patterns may occur; for example, a combination of patterns 1 and 2 may be observed in a tract that is both displaced and edematous. These findings were in concordance with previous studies done by aoron field *et al.*[8], jellison *et al.*[9] and witwer *et al.*[10] In our study The FA values of displaced WMFT ranged between 0.413-0.511. The FA values of edematous WMFT ranged between 0.370-0.458. The FA values of infiltrated WMFT ranged between 0.337-0.427. The FA values of displaced WMFT ranged between 0.235-0.345. The ADC values (× 10-3 mm2/s) of displaced WM fibers ranged from 0.609 to 0.833. The ADC values (× 10-3 mm2/s) of edematous WM

fibers ranged from 1.221 to 1.457. The ADC values (× 10-3 mm2/s) of infiltrated WM fibers ranged from 0.938 to 1.114. The ADC values (× 10-3 mm2/s) of disrupted WM fibers ranged from 0.940 to 1.110. Various studies like Sinha *et al.*[11] and Lu *et al.*[12] used measures of mean diffusivity and fractional anisotropy to differentiate normal white matter, edematous brain, and en[ha]ncing tumor margins. Anisotropy is reduced in cerebral lesions due to the loss of structural organization in studies by Wieshmann *et al.*.[13] and Mascalchi *et al.*[14] In studies by Beppu *et al.* [15] and Price *et al.*[16] It seems that the abnormalities on DTI are more significant than those seen on T2-weighted images in high grade gliomas. Second, DTI may distinguish if the white matter fibers are displaced (Wieshmann *et al.*.[17] and Gossl *et al.*[18]), infiltrated, or disrupted by the tumor (Witwer *et al*.[10]). Finally, the fiber-tracking technique (DTI-FT) that is able to identify and reconstruct the main white matter connections. This information is very useful for presurgical planning, delineating the spatial relationships of eloquent structures and tumors in order to preserve the functional pathways intraoperatively (Holodny *et al.*[19] Tummala *et al.*[20] Henry *et al*.[21]). Our study support these findings and we recommend routine DTI-FT evaluation of intracranial tumors affecting brainstem and eloquent brain cortex for optimal neurosurgical management and favourable outcome. Diffusion-tensor imaging documented deviation of fibers in normal-appearing white matter in relation to the anterior commissure – posterior commissure line when compared with contralateral side. DTI mapping brings complementary information that helps elucidating the complex relationships between the tumor and its surrounding cerebral tissue. Knowledge of direction of displacement assisted in preoperative planning by informing the surgeon of the tract's shifted location, thus allowing for adaptation of the surgical corridor to avoid destruction of the communicating white matter bundles. In one of our patient the tumor was approached from a temporal posterior direction, allowing for aggressive resection of the tumor while avoiding the anteriorly deviated motor fibers. This resulted in postoperative improvement of the patient's hemiparesis, presumably due to the elimination of pressure on the corticospinal tracts.

## CONCLUSION

The FA and ADC values of white matter fibre tracts affected by tumour and peritumoural oedema can be of assistance when evaluating the malignant potential, extent and operability of the tumour, even though the FA and ADC values cannot be associated with the specific histology of the tumour.

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