Original Research Article

Application of diffusion tensor imaging in deciding surgical management of brain tumours

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Abstract

Background: A good evaluation of the patient with a suspected brain tumor needs a complete history, exact physical examinations especially neurologic ones, and suitable diagnostic neuroimaging studies. Tumour resection has an effect on eloquent functions related to motor, sensory, speech and visual pathways. The integration of preoperative anatomical and functional imaging and functional studies allows for a functional resection that significantly widens the extent of resection in lesions in relevant eloquent areas. **Aim and objective:** To study the application of diffusion tensor imaging in deciding surgical management of brain tumours **Methodology:** Present study was a study conducted at Indraprastha Apollo hospital, New Delhi on 50 patients with brain tumour.
Key Word: brain tumours.

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INTRODUCTION

A brain tumor is a collection of abnormal cells that grows in or around the brain. It poses a risk to the healthy brain by either invading or destroying normal brain tissue or by compressing and displacing the brain. According to the Population Based Cancer Registry data for Delhi between 2003-2007, the incidence rates of primary brain and central nervous system tumors in Delhi for males was 3.9 per 100000 whereas for females it was 2.4 per 100000 females. Glioma was the most frequently reported histology in both males and females[1]. In the united states, incidence rates for primary brain and nervous system tumors in adults (aged 20 or older) was estimated to be 24.6 per 100,000 persons (data from 46 cancer registries, 2004 to 2007), among which 33% were malignant. Tumors of neuroepithelial tissue were the most common histological group of malignant brain tumors with glioblastoma being the most common subtype. In contrast, incidence of the tumors that arise in younger population (aged 0 to 19 years) was much lower (48.6 per 1,000,000 persons). However 65% of these were malignant. Metastatic lesions comprise about 30% of all CNS neoplasms among the adults; however it is rare in children.[2] Intracranial tumours are classified according to the World Health Organization (WHO) classification of tumours of the central nervous system (CNS). [3] The WHO classification of tumours of the CNS also includes a grading system that describes a malignancy scale across a wide variety of neoplasms. WHO grading of neoplasms consists of four levels, from grade I to grade IV. Grade I lesions have low proliferative potential. Grade II neoplasms are generally infiltrative in nature, but have low-level proliferative activity. Some grade II tumours tend to progress to higher grades of malignancy. For example, low-grade diffuse astrocytomas can transform

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into anaplastic astrocytoma and glioblastoma. Grade III tumours are lesions with histological evidence of malignancy, including nuclear atypia and brisk mitotic activity. Grade IV tumours are cytologically malignant, mitotically active and necrosis-prone. [3] The history of brain tumor surgery is central to the development of neurosurgery as a specialty and how imaging became integral part of management of brain tumors. William McEwen is considered to have performed the first successful brain tumor removal in 1879 in a young woman. The surgical management of patients suffering from brain tumour involving eloquent brain cortex and brainstem poses three main challenges 1. Adequate excision of tumour. 2. Preserving anatomical and functional integrity of viable neural structures. 3. Prognostic evaluation. The eloquent brain consists of areas of brain that allow us to perceive, interpret, communicate and have movement. These areas of brain regulate our senses, speech and movement, damage to which can cause loss of function.

Aim and objective: To study the application of diffusion tensor imaging in deciding surgical management of brain tumors

MATERIAL AND METHODS

Present study was a study conducted at Indraprastha Apollo hospital, New Delhi during May 2011 to January 2013. Study population was 50 patients with brain tumour. Study was approved by ethical committee of the institute. A valid written consent was taken from patients or guardians after explaining study to them. All patients underwent conventional MRI supplanted by diffusion tensor imaging in Philips Achieva 3T scanner. 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 find out best possible surgical approach and management for the space occupying lesion. Later we evaluated these patients using diffusion tensor imaging and fiber tractography complimentary to the conventional MRI. We evaluated relevant white matter fiber tracts 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. After detailed re-evaluation, we consulted again with the neurosurgical team and documented whether previously chalked out plan needed to be modified or not, in terms of directional approach to the lesion and/or degree of resection of tumor.

Post- operative evaluation is done in terms of following parameters-

Gross total tumor resection was defined as 100% macroscopic removal of the tumor mass, no gross total resection as less than 100% tumor removal. No gross total tumor resection included subtotal (<100%, but ≥90%) and partial (<90%) resection, as well as an open or stereotactic biopsy without tumor debulking. The estimation of the extent of tumor removal was primarily the responsibility of the local neurosurgeons, but was also validated by post-surgical MRI scan review whenever possible. Extent of resection was defined as gross-total resection ([GTR], no residual enhancement), near-total resection ([NTR], thin rim of enhancement in resection cavity only) or sub-total resection ([STR], residual nodular enhancement) based on immediate postoperative MRI findings.

Clinical examination of patients was done pre-operatively and post-operatively at end of 1st and 3rd week. Observed parameters were as follows-

The motor system- Weakness, Hyper-reflexia, Babinski's sign, Grasp reflex, increased muscle tone/Spasticity

0 Zero -No active muscle contraction; flaccid

1. Trace -A flicker of muscle contraction, but no movement
2. Poor -Muscle contraction with movement in non-gravity plane (abduction of leg)
3. Fair -Muscle movement against gravity without resistance (lifting leg or arm up)
4. Good -Muscle movement against gravity with mild to moderate resistance (placing hand against lifted leg)
5. Normal -Movement through full joint range of motion with maximum resistance (straightening and lifting leg against maximum resistance of examiner)

The Sensory Examination: Primary Modalities to Be Tested- Light touch, Vibration, Pain, Temperature Position sense,

Cortical Discrimination Testing: Two-point discrimination, Stereognosis, Sensory extinction\ Double simultaneous stimulation. Lesions of the cerebral cortex cause diminution of all sensory modalities on the contralateral side of the body. In addition, higher integrative sensory functions are impaired causing defects in stereognosis, two-point discrimination, double simultaneous stimulation. Visual field testing- It assesses the integrity of the optic pathways as it comes from the retina, optic nerves, optic chiasm, optic tracts, and optic radiations to the primary visual cortex. It is most commonly performed by confrontation test. Lack of vision in quadrants can then be detected and mapped out to various types of field defect. If the patient is uncooperative, visual field examination may be grossly tested by asserting a threatening hand to half of a visual field (while cautiously avoiding movement of air that can result in a corneal blink reflex) and observing for a blink to threat.

Evaluation of Speech and Language: Aphasia/Dysphasia-

- Wernicke's aphasia (sensory aphasia, receptive aphasia, fluent aphasia.).
- Broca's aphasia (motor aphasia, expressive aphasia, nonfluent aphasia).
- Conduction aphasia.

Data was analysed with appropriate statistical tests.

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. (fig 1) 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. 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 found that, in 14 out of 50 patients, neurosurgical management had to be modified after DTI-FT evaluation compared to management decided on conventional MRI. It stands out significantly at 28%. In 36 patients (i.e.72%) management remained unchanged. (table 1) Post-operative assessment of patients was done for neurological deficit involving motor and sensory function, vision and speech. We correlated nature and degree of post-operative neurological deficit in these eloquent functions, with preoperative neurological status of patient, and our own imaging prediction of postoperative outcome of affected eloquent function. DTI-FT showed sensitivity of 87% in predicting postoperative neurological outcome. Table 2 showed comparison of accurate preoperative prediction of neurological status involving motor, speech, vision and sensory functions(unchanged), with the altered neurological status other than what was predicted on preoperative imaging(changed), as confirmed on postoperative evaluation. Post operative evaluation in motor function showed 76.6% prediction was unchanged. In speech function the prediction was 93.7% unchanged. prediction about vision was 96.3% unchanged. Sensory function prediction remained unchanged in 85.2% patients. Figure 2 showed sensitivity of radiological evaluation using DTI-FT, in predicting the neurological prognosis in patients with intracranial tumors affecting brainstem and eloquent brain cortex. 87 % diagnosis was correct prediction and 13% had altered diagnosis.

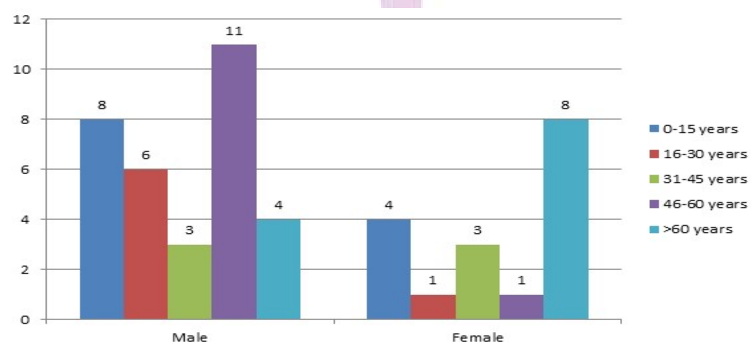

Figure 1: Age-wise distribution of observed cases in different age groups

Table 1: Plan on conventional imaging VS Procedure performed after DTI-FT evaluation

Planned on conventional imaging		Performed after DTI-FT evaluation	
Approach	**No. of cases**	**Unchanged (%)**	**Changed**
Supracerebellar infratentorial GTR	3	3 (100%)	
Trans-cisternal biopsy+conservative palliation	1	1 (100%)	
Bifrontal interhemisheric GTR	2	2 (100%)	
Bilateral subfrontal STR	1		1 (100%)
Interhemispheric transcallosal biopsy+follow up	1		1 (100%)
Interhemispheric transcallosal STR	1		1 (100%)
Lt parieto-temporal craniotomy+GTR	2	1 (50%)	1 (50%)
Lt frontoparietal craniotomy+ GTR	1		1 (100%)
Lt fronto-parieto-temporal craniotomy+ GTR	2	1 (50%)	1 (50%)
Lt parietal craniotomy+GTR	3	3 (100%)	
Lt pterional middle temoral NTR	2	2 (100%)	
Lt pterional+GTR	1	1 (100%)	
Lt subfrontal GTR	1	1 (100%)	
Midline suboccipital craniotomy+ PR	1		1 (100%)
Rt extended pterional craniotomy+GTR	3	3 (100%)	
Rt fronto parietal craniotomy+ GTR	1	1 (100%)	
Rt fronto-parieto-temporal craniotomy+GTR	1	1 (100%)	
Rt parieto temporal craniotomy+GTR	3	3 (100%)	
Rt parieto-temporal craniotomy+ NTR	1	1 (100%)	
Rt parieto-occipital craniotomy+ NTR	1	1 (100%)	
Rt pterional craniotomy+GTR	1	1 (100%)	
Rt pterional craniotomy+STR	1		1 (100%)
Rt pterional trans-sylvian+GTR	1	1 (100%)	
Rt temporal trans-sylvian STR	1	1 (100%)	
Stereotactic biopsy+radiotherapy	1	1 (100%)	
Supracerebellar infratentorial GTR	1		1 (100%)
Supracerebellar infratentorial NTR	1	1 (100%)	
Supracerebellar infratentorial PR	1	1 (100%)	
Supracerebellar transtentorial biopsy+PR	2	2 (100%)	
Supracerebellar transtentorial biopsy+STR	2		2 (100%)
Supracerebellar transtentorial GTR	2	2 (100%)	
Transcisternal STR	1		1 (100%)
Trans-spenoidal biopsy+chemo, radiotx	1		1 (100%)
Trans-sphenoidal GTR	1		1 (100%)
Trans-sphenoidal PR	1	1 (100%)	
Total		**36 (72%)**	**14 (28%)**

Table 2: Prediction of eloquent function on Imaging VS Post-op evaluation

Function	**Affected**	**Prediction on Imaging**			**Post-Op. Evaluation**	
		Status-quo	**Improvement**	**Down-grading**	**Unchanged (%)**	**Changed (%)**
Motor	30	4	18	8	23 (76.6)	7 (23.3)
Speech	16	4	12	0	15 (93.7)	1 (6.2)
Vision	27	8	18	1	26 (96.3)	1 (3.7)
Sensory	27	15	11	1	23 (85.2)	4 (14.8)
Total	**100**	**31**	**59**	**10**	**87 (87)**	**13 (13)**

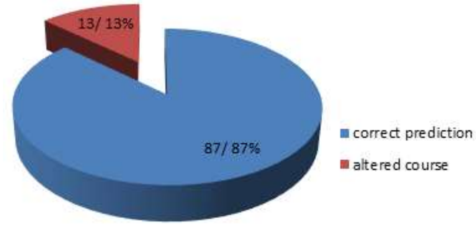

Figure 2: Sensitivity of radiological evaluation using DTI-FT, in predicting the neurological prognosis in patients with intracranial tumors affecting brainstem and eloquent brain cortex.

Table 3: Classification of affected WM fiber tracts

	Displaced	Edematous	Infiltrated	Disrupted	NA	No. of Affected Individuals
SOFF-RT						
Affected Fibre Type	1	16	2	-		19
Intraoperative Finding	-	9	2	-	8	
SOFF-LT						
Affected Fibre Type	3	13	1	-		17
Intraoperative Finding	3	4	3	-	7	
IOFF-RT						
Affected Fibre Type	3	8	-	8		19
Intraoperative Finding	-	7	1	8	3	
IOFF-LT						
Affected Fibre Type	2	4	5	2		13
Intraoperative Finding	-	4	2	2	5	
SLF-RT						
Affected Fibre Type	-	3	7	4		14
Intraoperative Finding	-	6	5	3	-	
SLF-LT						
Affected Fibre Type	-	-	5	1		6
Intraoperative Finding	-	4	1	1	-	
ILF-RT						
Affected Fibre Type	3	4	1	8		16
Intraoperative Finding	-	3	2	8	3	
ILF-LT						
Affected Fibre Type	1	1	3	2		7
Intraoperative Finding	-	4	-	2	1	
UF-RT						
Affected Fibre Type	6	1	1	8		16
Intraoperative Finding	3	1	2	7	3	
UF-LT						
Affected Fibre Type	5	2	3	-		10
Intraoperative Finding	-	2	2	-	6	
Cingulum-RT						
Affected Fibre Type	3	12	-	1	-	16
Intraoperative Finding	-	6	1	1	8	
Cingulum-LT						
Affected Fibre Type	-	11	-	-		11
Intraoperative Finding	-	7	-	-	4	
CS-RT						
Affected Fibre Type	12	12	9	1		34
Intraoperative Finding	7	15	5	1	6	
CS-LT						
Affected Fibre Type	18	8	4	-		30
Intraoperative Finding	9	6	4	-	11	
MLSL-RT						
Affected Fibre Type	7	13	8	1		29
Intraoperative Finding	7	14	8	-	-	
MLSL-LT						

Affected Fibre Type	14	6	6	1		27
Intraoperative Finding	10	6	7	-	4	
OR-RT						
Affected Fibre Type	-	6	4	5		15
Intraoperative Finding	-	9	1	5	-	
OR-LT						
Affected Fibre Type	-	6	1	1		8
Intraoperative Finding	-	6	1	1	-	
CC						
Affected Fibre Type	-	17	4	7		28
Intraoperative Finding	-	11	7	7	3	
AC						
Affected Fibre Type	19	-	-	-		19
Intraoperative Finding	8	-	-	-	11	
TP						
Affected Fibre Type	5	7	4	-		16
Intraoperative Finding	4	7	3	1	1	
Grand Total						
Affected Fibre Type	102	150	68	50		
Intraoperative Finding	51	131	57	47	84	

DISCUSSION

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.*[4] Tummala *et al.*[5] Henry *et al.*[6] The patients with large intra-axial mass lesion had one feature in common: they all had oedema formation around the tumour. It appears that when the tumour is resected, the pressure on the brain and specifically on the affected eloquent cortices decreases; it could be that an eloquent function in preserved cortex would improve as a result of decreased oedema. Resection of a glioma surrounded by oedema and in contact with the eloquent cortex causes improvement in the neurological response**.** Previous studies observed that complete resection is thought to be the best initial treatment for glial tumors, although there is no scientific evidence that a greater extent of resection is associated with a better prognosis. [7-11] according to Claes *et al.* [12] The infiltrative growth pattern of glial tumors is the reason for surgical treatment not being curative and therefore the majority of patients will suffer a relapse or local progression of the disease sometime after surgery. The known molecular mechanisms that drive this pattern of cellular migration have been deeply studied by Giese *et al.*,[13]. Although until new treatments for glial tumors are developed, the cytoreduction provided by surgery will maintain its value, because it offers material for diagnosis and research, alleviates both the focal and clinical symptoms of intracranial hypertension, and contributes to a greater efficacy of oncological treatments. Following this line of reasoning, there is a large number of modern series supporting the idea of resecting the largest possible volume of tumor.[14] Our experience with DT imaging indicates that anatomically intact fibers may be present in abnormal appearing areas of the brain. Careful preoperative planning has to be complemented by intraoperative mapping and monitoring of eloquent cortical areas in order to insure a good neurological outcome of the surgery and valid functional prognostic. We support maximal resection of tumor if it significantly improves survival and reduces chances of residual tumor mass being left. It will also reduce the chances of recurrence. But we caution against deliberate gross total resection without knowing peritumoral viable WM fibers. Thereby DTI-FT helps to balance between these contrasting still essential components of management of intracranial tumors. We propose that it is no longer necessary to compare different methods of pre-operative brain mapping because of their intrinsically different functioning; rather, we propose that now it would be most desirable to share preoperative (fMR, DTI, and neuropsychology) and postoperative protocols in order to accumulate a major cohort of patients in multicentre studies. At the same time, results of intraoperative stimulations should be well documented and standardized together with preoperative imaging and postoperative outcome to create a common comprehensive database of long term results. According to the studies by Jacobs *et al.* [15] and Rao *et al.* [16] It has been recommended that early postoperative conventional MRI should be performed no later than three days after the operation and imaging within 24 hours has been suggested by Vidiri *et al.*. [17] Due to postoperative changes, it might indeed have been more favourable to perform the early postoperative DTI to all of the patients within three days – or even 24 hours – postoperatively. However, for logistical reasons this was not possible in our study. It is also likely that at least some of the patients would not have been alert and co-operative enough for DTI so soon after a major operation. Previous studies done by various authors [18-20] support our finding that DTI-FT gives significant benefit among patients undergoing DTI-aided resection in maximal resection with minimal damage to eloquent brain areas. Also, detailed imaging provides insight into probable neurological prognosis post-operatively. The extent of resection was greater with less chances of damage to eloquent brain, in patients who had undergone DTI incorporated neuronavigation. The assessment of surgical trajectories by DTI-FT close to the tumour resulted in a modification of the surgical approach to corticotomy or definition of the resection margins during surgery was 28%(14 out of 50 cases). This finding supports previous work done by Romano et. al. [21] however the overall impact percentage on the surgical procedure was much higher in their study (82%). Some authors studied use of fluorescence guided resection with 5 –aminolevulinic acid. This technique allows the visualization of malignant tissue during surgery for malignant glioma (grades III and IV WHO). Tumor resection guided by fluorescence involves giving the patient a natural precursor, 5-aminolevulinic acid (5-ALA HCl), which is taken up by cells of malignant gliomas and, when summed, becomes a fluorescent substance. Thus, by applying a special light during surgery, the malignant cells are stained red offering the surgeon a clear distinction between the healthy and which are not, letting increasing the extent of tumor resection, minimizing brain damage. [22]. In future these newer techniques can be used to optimize the management if combined with preoperative mapping by DTI-FT and fMRI.

CONCLUSION

Diffusion Tensor Imaging and Tractography provided neurosurgeons useful information to decide on the surgical approach to the tumour, extend of tumour resection and on the option to use intra-operative cortical stimulation and also provided insight into expected neurological outcomes.

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