

A Clinical Study of Role of Diffusion Tensor Imaging In Evaluation of Brain Tumors

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Abstract

Original Research Article

Diffusion tensor imaging is an evolving technique with a wide range of applications especially in the diagnosis and characterization of involvement of white matter tracts by brain tumors. DTI has shown promising results for detecting the microscopic differences between the tumors. The present study aimed to study the spatial relationship between major white matter tracts and tumors and to study the role of DTI in differentiating High-grade gliomas from Metastasis, Low-grade gliomas and Meningiomas. Methods: This prospective study of patients with brain neoplasms was conducted in the Department of Radiodiagnosis, Prathima Institute of medical sciences, Karimnagar. According to inclusion criteria, n=30 patients referred to Neurosurgery. Data for the study were collected from patients with clinically suspected cerebral neoplasms or from patients, in whom previous images depicted cerebral neoplasms, undergoing DTI according to the set protocols after obtaining informed consent. All these patients had undergone detailed clinical evaluation by the referring neurosurgery unit. Results: Out of n=30 cases, there were n=6 low-grade gliomas (WHO grade I and II), 13 high-grade gliomas (WHO grade III and IV), n=6 metastasis and 5 meningiomas (WHO grade I). In this study, the maximum percentages of tumors were high-grade gliomas (43.3%), followed by low-grade gliomas (20%), metastasis (20%) and meningiomas (16.7%). out of n=11 benign group tumors, edematous white matter tracts were seen in 1 case, displacement was seen in n=10 cases, infiltration was seen in n=2 cases and disruption was seen in n=1 case. Out of n=13 malignant group tumors, edema was observed in n=6 cases, displacement was seen in n=10 cases, infiltration was observed in n=10 cases and disruption was seen in n=9 cases. Conclusion: DTI is a useful technique to demonstrate complex ultrastructural organization of the white matter tracts of the brain. The three-dimensional properties of water are useful in demonstrating the changes in the white matter tracts by DTI Technique. In this study, it was found that DTI was useful than MRI in the evaluation of cerebral neoplasms. DTI was also useful for differentiation between low and high-grade gliomas as well as the distinction between gliomas and metastasis.

Keywords: Diffusion Tensor Imaging, Brain Tumors, DTI.

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INTRODUCTION

Brain tumors represent a group of neoplasm arising either from the brain structures (primary) or secondary due to metastasis from extracranial tumors. These tumors comprise less than 1.5% of all body tumors but have high morbidity and mortality [1]. They are 85% to 90% of all primary CNS tumors [2]. The glial cell tumors, anaplastic astrocytoma and glioblastoma, accounts for approximately 38% of primary brain tumors whereas meningiomas and other mesenchymal tumors account for approximately 27% of primary brain tumor. The incidence of primary brain tumors is escalating due to the increasing age of the population and better diagnostic techniques [3]. Brain tumors are the second leading cause of death in children

and young adults. Most patients die within 9-12 months and less than 3% survive more than 3 years. Before planning surgery for brain tumors, it requires proper pre and intra-operative mapping of the tumor as well as the definition of its relationship with functional structures, so that such structures can be preserved during surgical resection. There are two main reasons why preoperative localization of important white matter tracts can affect the decision of whether to operate or not. Secondly, preoperative localization of important white matter tracts is essential in surgical planning. Magnetic resonance (MR) imaging and MR spectroscopy play an important role in the detection and evaluation of brain tumors but these modalities do not give precise information about the involvement and integrity of the white matter tracts in the immediate region surrounding

tumors. Diffusion-tensor imaging (DTI) is the only novel imaging technique that can demonstrate white matter tracts and their structural changes related to different brain pathologies [4]. Diffusion tensor describes the 3D diffusion phenomenon of the protons according to their microenvironmental properties allowing a unique description of the space where this molecular movement takes place. DTI provides in vivo demonstration of the complex ultrastructural organization of the white matter as well as structural changes due to tumoral invasion. Diffusion tensor imaging has the potential to establish spatial relationships between eloquent white matter and tumor borders and provide clinically valuable information to assess the progression and regression of white matter tracts as a result of tumor growth or resection [5]. This study aims to evaluate the role of DTI in characterization and preoperative assessment of brain neoplasms.

MATERIAL AND METHODS

This prospective study of patients with brain neoplasms was conducted in the Department of Radiodiagnosis, Prathima Institute of medical sciences, Karimnagar. Institutional Ethical committee permission was obtained for the study. According to inclusion criteria, n=30 patients referred to Neurosurgery. Data for the study were collected from patients with clinically suspected cerebral neoplasms or from patients, in whom previous images depicted cerebral neoplasms, undergoing DTI according to the set protocols after obtaining informed consent. All these patients had undergone detailed clinical evaluation by the referring neurosurgery unit.

INCLUSION CRITERIA

- Patients with clinical suspicion of cerebral neoplasms, irrespective of age and sex.
- Patients already diagnosed with having cerebral neoplasms, requiring MR Imaging evaluation before surgery.
- Patients with known primary, presenting with symptoms of raised intracranial pressure.

EXCLUSION CRITERIA

- Patients were excluded if contraindications to MR imaging (claustrophobia, pacemaker, potentially magnetic implants, etc.) were present.
- Patients not giving informed consent.
- Patients who were pregnant.

MR Imaging Protocol

MRI examinations were performed with a 16 channel 1.5T whole-body imager (Achieva 1.5 Tesla, Philips Medical System, Netherlands) equipped with a high-performance gradient system. A commercially available 16 channel head and neck coils were used for imaging all the patients. Patients were positioned supine

on a scanner table and head immobilization was achieved. The following sequences were acquired: T2-weighted sequences, Fluid Attenuated Inversion Recovery (FLAIR), T1-weighted sequences before and after intravenous administration of paramagnetic contrast material.

DTI Protocol

DT imaging data were acquired by using a single-shot echo-planar imaging sequence with the sensitivity-encoding, or SENSE, parallel-imaging scheme (reduction factor, 2). The imaging Matrix was 128 X 128, with a Field of view of 224mm. Transverse sections of 2.0 mm thickness were acquired parallel to the anterior commissural–posterior commissural line. A total of 65 sections covered the entire hemisphere and brainstem without gaps with a scan duration of 4 minutes 51 seconds. Diffusion weighting was encoded along 15 independent orientations, and the b value was 700 mm²/sec. Other imaging parameters were as follows: echo time = 67 ms, repetition time = 8825ms, number of acquisitions = two.

Post Processing and Image Analysis

All images were transferred to a workstation (Philips Medical System) and post-processed with standard commercial software which is based on the Fiber Assignment by Continuous Tracking (FACT) method. 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 as red (x, element, left-right), green (y, anterior-posterior), and blue (z, superior-inferior) with a proportional intensity scale according to the FA. Three dimensional FT was then achieved by connecting voxel to voxel with the FACT algorithm. The threshold values for the termination of the fiber tracks were less than 0.3 for FA and greater than 45L for the trajectory angles between the ellipsoids.

Three-Dimensional Tract Reconstruction

Tracking was performed from all pixels inside the brain (“brute force” approach), and that. When multiple ROIs were used for a tract of interest, three types of operations, AND, OR, and NOT (the choice of which depended on the characteristic trajectory of each tract) were used.

RESULTS

The study population consisted of 14 males (46.7 %) and 16 females (53.3 %). The age of the patients with benign tumors ranged from 5 – 72 yrs, with a mean age of 39.6 yrs and the age of patients with malignant tumors ranged between 15-77 yrs, with a mean age of 49.5 yrs.

Table-1: Distribution of Study Population according to age

Age (years)	Male	Female	Total (%)
0-10	1	0	01 (3.33%)
11-20	2	0	02 (6.66%)
21-30	1	0	01 (3.33%)
31-40	2	6	08 (26.66%)
41-50	2	4	06 (20.0%)
51-60	4	2	02 (6.66%)
61-70	1	2	03 (10.0%)
71-80	1	2	03 (10.0%)
Total	14	16	30 (100%)

In the present study, the most common presenting symptom was seizures (46.7%), followed by headache and hemiparesis (20%), altered sensorium (10%) and visual complaints (3.3%).

Table-2: Distribution of Cases according to clinical symptoms

Clinical Symptom	Frequency	Percentage
Headache	6	20
Hemiparesis	6	20
Seizures	14	46.7
Altered Sensorium	3	10
Visual Complaints	1	3.3

Table-3: Classification of Tumors in the Study Population

Category	Frequency	Percentage
Benign Group (LGG and Meningiomas)	11	36.7
Malignant Group (HGG and Metastasis)	19	63.3

Out of n=30 cases, there were n=6 low-grade gliomas (WHO grade I and II), 13 high-grade gliomas (WHO grade III and IV), n=6 metastasis and 5 meningiomas (WHO grade I). In this study, the

maximum percentages of tumors were high-grade gliomas (43.3%), followed by low-grade gliomas (20%), metastasis (20%) and meningiomas (16.7%).

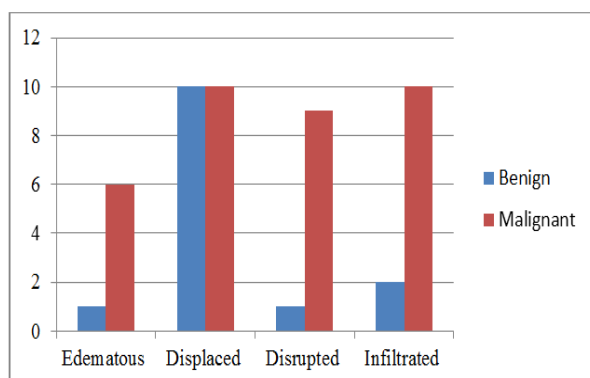
Table-4: Distribution of Tumors in the Study Population

Tumor	Frequency	Percentage
Low-Grade Glioma (WHO grade I & II)	6	20
High-Grade Glioma (WHO grade III & IV)	13	43.3
Metastasis	6	20
Meningiomas (WHO grade I)	5	16.7

In this study, out of n=11 benign group tumors, edematous white matter tracts were seen in 1 case, displacement was seen in n=10 cases, infiltration was seen in n=2 cases and disruption was seen in n=1 case. Out of n=13 malignant group tumors, edema was observed in n=6 cases, displacement was seen in n=10 cases, infiltration was observed in n=10 cases and disruption was seen in n=9 cases.

Table-5: Prevalence of edema, Displacement, Infiltration, and disruption of white matter tracts in both Benign and Malignant groups

	Benign	Malignant	Total
Edema			
Yes	1	6	7
No	10	13	13
Displaced			
Yes	10	10	20
No	1	9	10
Infiltrated			
Yes	2	10	12
No	9	9	18
Disruption			
Yes	1	9	10
No	10	10	20



Graph-1: Pattern of involvement of White matter tracts by tumor

The Table-5 shows that the prevalence of edema was higher among the malignant group in comparison to the benign group. The prevalence of displacement was higher among the benign group in comparison to the malignant group. The prevalence of infiltration was higher among the malignant group in comparison to the benign group. The prevalence of disruption was higher among the malignant group in comparison to the benign group with a significant difference in between by using the chi-square test.

Table-6: Mean Values of DTI Parameters in Peritumoral region

Peritumoral Region			
Tumor	Mean FA	Mean MD (10^{-3} mm ² /s)	P values
HGG	0.26	0.9	0.001*
Metastasis	0.27	1.25	
HGG	0.26	0.9	<0.004*
LGG	0.36	1.3	
HGG	0.26	0.9	0.001*
MENINGIOMA	0.34	1.6	

Table-7: Mean Values of DTI Parameters in Intratumoral region

Intratumoral Region			
Tumor	Mean FA	Mean MD (10^{-3} mm ² /s)	P values
HGG	0.24	1.2	0.002*
Metastasis	0.23	2.3	
HGG	0.24	1.2	0.05
MENINGIOMA	0.33	1	

DISCUSSION

The extent of involvement of white matter tracts by malignant cells is an important step towards the successful management of tumors. Tumor cells tend to invade the white matter fibers by widening, displacing or sometimes disrupting fiber bundles. Surgical management is aimed at the removal of tumor cells with minimal damage to neurological bundles. The pre-operative and intraoperative mapping of tumor cells and its relationship with functional structures can be preserved during surgical resection [6]. DTI is a non-invasive imaging technique that provides information about tissue microstructure and architecture by measuring the average and directional variation of water diffusivity for a given voxel in terms of MD and FA, respectively. In normal neuronal tissues, the diffusion anisotropy is related to the extent of myelination of white matter. Hence, the DTI is sensitive in detecting alterations in the integrity of white matter tracts and allows accurate characterization of intrinsic tissue damage [7]. In the current study out of n=30 patients included out of which we found n=6(20%) low-grade gliomas, n=3 (10%) WHO Grade III gliomas, n=10(16.7%) Glioblastoma multiforme WHO grade IV gliomas, n=6 (20%) metastasis and n=5 (16.7 %) WHO grade I meningiomas. In the present study, out of n=11 benign group tumors, edematous white matter tracts were seen in n=1 case, displacement was seen in n=10 cases, infiltration was seen in n=2 cases and disruption was seen in n=1 case. Out of n=13 malignant group tumors, edema was observed in n=6 cases, displacement was seen in n=10 cases, infiltration was observed in n=10 cases and disruption was seen in n=9 cases. This classification of tract involvement was similar to the studies done by Witwer *et al.*, [8] and Field *et al.*, [9]. However, this was slightly different from the classification done by Yu *et al.*, [10] who divide the relationship between tumor and tracts into three types only; type I: simple displacement, type II: displacement with disruption, and type III: simple disruption

In the present study, the displaced and edematous patterns seen in both malignant and benign tumors, the infiltrating pattern being demonstrated in infiltrating gliomas and the disrupted pattern being observed in both low- and high-grade tumors. All n=6 cases of metastasis showed an edematous pattern but, the edematous pattern was also observed in low-grade glioma, which makes this pattern nonspecific. In this study, the disrupted pattern was shown in n=9 high-grade gliomas and one case of angioblastic meningioma. There was a statistical difference between these groups, with the prevalence of displacement among the benign group and disruption among the malignant group. This is contrary to the effect of edema and infiltration where there was no significant difference between the two groups. Witwer *et al.*, [8] have studied DTI findings in nine patients with brain tumors, applying the previously mentioned DTI classification. They evaluated six cases of low-grade gliomas, two of high-grade gliomas and one case of metastasis. The authors found the displaced pattern only in patients with low-grade gliomas. The edematous pattern was shown in one case of high-grade glioma and the patient with metastasis. The infiltrated and the disrupted patterns were found in one case of high and in one of the low-grade gliomas, respectively.

In this study, there were significant changes between the MD and FA values of normal-appearing white matter and those of the peritumoral T2 signal intensity abnormality. Surrounding both gliomas and metastatic lesions, there was an increase in MD and a decrease in FA, which are best explained by increased extracellular bulk water [11]. In the present study, the changes in peritumoral FA don't differ significantly between high-grade gliomas and metastatic tumors. However, the peritumoral MD surrounding metastatic lesions proved to be significantly greater than that of surrounding high-grade gliomas. This was attributed to the fact that MD is primarily determined by increased extracellular water and therefore, metastasis-related

vasogenic edema reflects greater increased water content of the surrounding tissue.

KS. Holly *et al.*, [12] compared both intratumoral and peritumoral fractional anisotropy (FA), mean diffusivity (MD) and fluid-attenuated inversion recovery (FLAIR) measurements between high-grade gliomas and metastases. They found was that there was no significant difference in age, gender, or race between the two patient groups. The high-grade gliomas had a significantly higher tumor-to-brain area ratio compared to the metastases. The present study indicates that there are statistically significant differences between the FA values of meningiomas and high-grade gliomas. The higher FA and lower MD values found in meningiomas reflect their higher level of fibrous organization as compared to intra-axial high-grade gliomas which present a more anarchic microstructure. Therefore, the conclusion was that DTI can contribute to quantitatively differentiate between meningiomas and high-grade gliomas.

CONCLUSION

DTI is a useful technique to demonstrate complex ultrastructural organization of the white matter tracts of the brain. The three-dimensional properties of water are useful in demonstrating the changes in the white matter tracts by DTI Technique. In this study, it was found that DTI was useful than MRI in the evaluation of cerebral neoplasms. DTI was also useful for differentiation between low and high-grade gliomas as well as the distinction between gliomas and metastasis.

Conflict of Interest: None

Source of support: Nil

Ethical Permission: Obtained

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