

## A Cross-Sectional, Prospective Assessment of the Utilizing Diffusion Tensor Imaging to Accurately Map the White Matter Tracts in Relation To Brain Malignancies

Anshupriya<sup>1</sup>, Vinayak Gautam<sup>2</sup>

<sup>1</sup>Assistant Professor, Department of Radio-diagnosis, Madhubani Medical College and Hospital, Madhubani, Bihar, India

<sup>2</sup>Professor and HOD, Department of Radio-diagnosis, SKMCH, Muzaffarpur, Bihar, India

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Corresponding Author: Dr. Vinayak Gautam

Conflict of interest: Nil

### Abstract

**Aim:** Utilizing diffusion tensor imaging to accurately map the white matter tracts in relation to brain malignancies.

**Materials and Methods:** This cross-sectional, prospective, hospital-based study was conducted in the Department of Radio-diagnosis, Madhubani Medical College and Hospital, Madhubani, Bihar, India from Feb 2022 to January 2023. A total of 50 patients with brain tumours were evaluated. 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.

**Results:** 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.

**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.

**Keywords:** Diffusion tensor imaging, White matter, Brain malignancies

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### Introduction

Diffusion tensor imaging (DTI) has emerged as a powerful neuroimaging technique, providing detailed visualization and mapping of white matter tracts in the brain. This method is particularly valuable in the context of brain tumors, where precise delineation of white matter pathways is crucial for both preoperative planning and postoperative evaluation. DTI exploits the anisotropic diffusion of water molecules along axonal fibers, allowing for the characterization of fiber orientation and integrity. This capability is essential in assessing the impact of brain tumors on surrounding white matter and in guiding neurosurgical interventions to maximize tumor resection while preserving vital neural structures.

[1,2] The integration of DTI in the management of brain tumors has gained significant attention due to its ability to reveal subtle changes in white matter architecture that are not detectable with conventional MRI. The technique provides quantitative measures such as fractional anisotropy (FA) and mean diffusivity (MD), which can be used to assess white matter integrity. Lower FA values and higher MD values typically indicate disrupted white matter tracts, which are common in the vicinity of brain tumors. This information is crucial for understanding the extent of tumor infiltration and for predicting potential neurological deficits. Recent studies have demonstrated the clinical utility of DTI in preoperative planning for brain tumor surgeries.

By mapping the white matter tracts, neurosurgeons can identify and preserve critical pathways, such as the corticospinal tract and the arcuate fasciculus, thereby reducing the risk of postoperative motor and language deficits. For instance, in glioma surgery, DTI has been shown to improve the accuracy of tumor resection while minimizing damage to eloquent areas of the brain. This has led to better functional outcomes and quality of life for patients. [3,4] Moreover, DTI plays a vital role in differentiating between tumor recurrence and treatment-related changes, such as radiation necrosis. Conventional MRI often fails to distinguish these entities due to their similar appearances. However, DTI can provide additional information about the microstructural integrity of white matter, aiding in accurate diagnosis and appropriate management. This is particularly important in the follow-up of patients with high-grade gliomas, where early detection of recurrence can significantly impact treatment decisions and prognosis. In addition to its diagnostic and surgical planning applications, DTI is being explored for its potential in prognostication. Changes in DTI metrics have been correlated with patient outcomes in various brain tumor types. For example, reduced FA in peritumoral regions has been associated with shorter progression-free survival in glioblastoma patients. These findings suggest that DTI could serve as a valuable biomarker for predicting disease course and tailoring individualized treatment strategies. Recent advancements in DTI technology, such as high-angular resolution diffusion imaging (HARDI) and multi-shell diffusion imaging, have further enhanced its capability to resolve complex fiber configurations and improve the accuracy of white matter tractography. These developments are paving the way for more detailed and reliable mapping of brain connectivity, which is essential for advancing our understanding of brain tumor biology and improving patient care. [5-8]

#### Materials and Methods:

This cross-sectional, prospective, hospital-based study was conducted in the Department of Radiodiagnosis, Madhubani Medical College and Hospital, Madhubani, Bihar, India from Feb 2022 to January 2023. A total of 50 patients with brain tumours were evaluated. 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 / mm<sup>2</sup>, 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).

#### 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. 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. 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 1: Demographic and Age Distribution of Patients**

Age Group (Years)	Number of Male Patients	Number of Female Patients	Total Patients
0-15	8	4	12
16-30	6	1	7
31-45	3	3	6
46-60	11	1	12
>60	4	8	12
<b>Total</b>	<b>33</b>	<b>17</b>	<b>50</b>

**Table 2: Handedness of Patients**

Handedness	Number of Male Patients	Number of Female Patients	Total Patients
Right-handed	29	14	43
Left-handed	4	3	7
<b>Total</b>	<b>33</b>	<b>17</b>	<b>50</b>

**Table 3: Lesion Location Distribution**

Lesion Location	Number of Male Patients	Number of Female Patients	Total Patients
Supratentorial	25	14	39
Infratentorial	8	3	11
<b>Total</b>	<b>33</b>	<b>17</b>	<b>50</b>

**Table 4: Classification of White Matter Fiber Tracts (WMFT) by FA and ADC Values**

WMFT Class	Mean FA Value	Standard Deviation (FA)	Mean ADC Value	Standard Deviation (ADC)
Displaced	0.462	0.049	0.721	0.112
Edematous	0.414	0.044	1.339	0.118
Infiltrated	0.382	0.045	1.026	0.088
Disrupted	0.290	0.055	1.025	0.085

**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 peritumoral 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 aaron 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 ( $\times 10^{-3}$  mm<sup>2</sup>/s) of displaced WM fibers ranged from 0.609 to 0.833. The ADC values ( $\times 10^{-3}$  mm<sup>2</sup>/s) of edematous WM fibers ranged from 1.221 to 1.457. The ADC values ( $\times 10^{-3}$  mm<sup>2</sup>/s) of infiltrated WM fibers ranged from 0.938 to 1.114. The ADC values ( $\times 10^{-3}$  mm<sup>2</sup>/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 enhancing tumor margins. Anisotropy is reduced in cerebral lesions due to the loss of structural organization in studies by Wieshmann et al. [13] and Mascacchi 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 Gossel et al. [18]), infiltrated, or disrupted by the tumor (Witwer et al.<sup>10</sup>). 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.

### References

1. Aboian MS, Tong E, Grossman R, et al. Diffusion tensor imaging in glioblastoma: exploring the relationship between fractional anisotropy, tumor infiltration, and patient survival. *J Neurooncol.* 2020;146(1):151-160. doi:10.1007/s11060-019-03326-2.
2. Essayed WI, Unadkat P, Cosgrove GR, Golby AJ, Ozduman K. An overview of diffusion tensor imaging and tractography in neurosurgery. *Neurosurg Focus.* 2021;50(5). doi:10.3171/2021.2.FOCUS20947.
3. Leclercq D, Delingette H, Baudracco I, et al. Connectivity-based parcellation of the cortical mantle using DTI: application to the human brain. *Neuroimage.* 2020;218:116937. doi:10.1016/j.neuroimage.2020.116937.
4. Price SJ, Jena R, Burnet NG, et al. Improved delineation of glioma margins and regions of infiltration with the use of diffusion tensor imaging: an image-guided biopsy study. *AJNR Am J Neuroradiol.* 2021;42(1):125-133. doi:10.3174/ajnr.A6986.
5. Guo R, Liu Y, Zhou Y, et al. Diffusion tensor imaging of glioblastomas: predicting IDH1 mutation status and survival using histogram analysis. *Eur Radiol.* 2022;32(3):1778-1787. doi:10.1007/s00330-021-08269-5.
6. Yeh FC, Panesar S, Fernandes D, et al. Population-averaged atlas of the macroscale human structural connectome and its network topology. *Neuroimage.* 2021;178:57-68. doi:10.1016/j.neuroimage.2018.05.027.
7. Stejskal EO, Tanner JE. Spin diffusion measurements: spin echoes in the presence of a time-dependent field gradient. *J Chem Phys* 1965;42:288-292.
8. Field AS, Wu YC, Alexander AL. Principal diffusion direction in peritumoral fiber tracts: Color map patterns and directional statistics *Ann N Y Acad Sci.* 2005 Dec;1064:193-201.

9. Brian J. Jellison, Aaron S. Field, Joshua Medow, Mariana Lazar, M. Shariar Salamat, and Andrew L. Alexander. Diffusion Tensor Imaging of Cerebral White Matter: A Pictorial Review of Physics, Fiber Tract Anatomy, and Tumor Imaging Patterns. *AJNR Am J Neuroradiol* 25:356–369, March 2004.
10. Witwer BP, Moftakhar R, Hasan KM, Deshmukh P, Haughton V, Field A, Arfanakis K, Noyes J, Moritz CH, Meyerand ME, Rowley HA, Alexander AL and Badie B (20 02) Diffusion-tensor imaging of white matter tracts in patients with cerebral neoplasm. *J Neurosurg* 97(3): 568–75.
11. Sinha, S., Bastin, M.E., Whittle, I.R. and Wardlaw, J.M. (2002). Diffusion tensor MR Imaging of high-grade cerebral gliomas. *American Journal of Neuroradiology* Vol. 23: 520-7.
12. Lu S, Ahn D, Johnson G, Cha S. Peritumoral diffusion tensor imaging of high-grade gliomas and metastatic brain tumors. *AJNR Am J Neuroradiol.* 2003 May;24(5):937-41.
13. Wieshmann, U.C., Clark, C.A., Symms, M.R., Franconi, F., Barker, G.J. and Shorvon, S.D. (1999). Reduced anisotropy of water diffusion in structural cerebral abnormalities demonstrated with diffusion tensor imaging. *Magnetic Resonance Imaging* Vol. 17:1269-74.
14. Mascalchi, M., Filippi, M., Floris, R., Fonda, C., Gasparotti, R. and Villari, N. (2005). Diffusion weighted MR of the brain: methodology and clinical application. *Radiologia Medica* Vol. 109(3):155-97.
15. Beppu, T., Inoue, T., Shibata, Y., Kurose, A., Arai, H., Ogasawara, K., Ogawa, A., Nakamura, S. and Kabasawa, H. (2003). Measurement of fractional anisotropy using diffusion tensor MRI in supratentorial astrocytic tumors. *Journal of Neurooncology* Vol. 63: 109-16.
16. Price SJ, Burnet NG, Donovan T, Green HA, Peña A, Antoun NM, Pickard JD, Carpenter TA, Gillard JH Diffusion tensor imaging of brain tumours at 3T: a potential tool for assessing white matter tract invasion *Clin Radiol.* 2003 Jun;58(6):455-62.
17. Wieshmann UC, Symms MR, Parker, G.J., Clark, C.A., Lemieux, L., Barker, G.J. and Shorvon, S.D. (2000). Diffusion tensor imaging demonstrates deviation of fibres in normal appearing white matter adjacent to a brain tumour. *Journal of Neurology, Neurosurgery and Psychiatry* Vol. 68: 501-3.
18. Gossel, C., Fahrmeir, L., Putz, B., Auer, L.M. and Auer, D.P. (2002). Fiber tracking from DTI using linear state space models: detectability of the pyramidal tract. *Neuroimage* Vol. 16: 378-88.
19. Holodny, A.I. and Ollenschleger, M. (2002). Diffusion imaging in brain tumors. *Neuroimaging Clinic of North America* Vol. 12: 107-24.
20. Tummala, R.P., Chu, R.M., Liu, H. and Hall, W.A. (2003). Application of diffusion tensor imaging to magnetic-resonance-guided brain tumor resection. *Paediatric Neurosurgery* Vol. 39: 39-43.
21. Henry, R.G., Berman, J.I., Nagarajan, S., Mukherjee, P. and Berger, M.S. (2004). Subcortical pathways serving cortical language sites: initial experience with diffusion tensor imaging fiber tracking combined with intraoperative language mapping. *Neuroimage* Vol. 21:616–622.