VOLUME - 10, ISSUE - 08, AUGUST- 2021 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

Radiodiagnosis

DIFFUSION TENSOR IMAGING (DTI) AND MAGNETIC RESONANCE TRACTOGRAPHY IN SUPRATENTORIAL BRAIN TUMOURS: SIMPLIFIED APPROACH TO DIFFERENTIATE BENIGN AND MALIGNANT TUMOURS

Dr. Aarti Anand	MD, Professor And Head, Department Of Radiodiagnosis, Government Medical College, Nagpur.
Parvathy Suresh K.*	MD, Assistant Professor, Department Of Radiodiagnosis, Government Medical College, Nagpur. *Corresponding Author
Amit G Disawal	M.D, Associate Professor, Department Of Radiodiagnosis, Government Medical College, Nagpur.
Ashwini M Bakade	M.D, Associate Professor, Department Of Radiodiagnosis, Government Medical College, Nagpur.

KEYWORDS :

BACKGROUND:
When conventional MR techniques could not give information regarding the involvement of separate white matter tracts and its relation to tumors, Tractography emerged as a promising tool that could visualize the white matter tracts (WM) in the brain in three-dimensional format (1). Diffusion-tensor MR imaging allows visualization of the anisotropy (directionality) of water movement caused by the presence of axons, axonal sheaths, glia cells, and vasculature. The alteration of the anisotropy in the peritumoral white matter is governed by multiple factors like cellularity, infiltration, vascular tortuosity, etc. Tumors like metastasis and meningiomas are associated with pure vasogenic edema whereas high-grade glial neoplasms are associated with mixed edema which also includes cellular infiltration by the malignant cells altering the extracellular cellular environment(2)(3). By evaluating the type of involvement of white matter tracts by tractography as well as DTI metrics like mean diffusivity and fractional anisotropy, we can attempt at differentiating the lesions, at least in broader categories of benign and malignant groups. Many previous studies using DTI metrics show conflicting findings. The study aimed to delineate white matter tracts in the brain using tractography to evaluate its relation to various brain lesions and study the pattern of involvement of peritumoral white matter tracts. The study also aimed at measuring the DTI metrics in peritumoral white matter and their role in differentiating the lesions into malignant and benign groups (4)(5)

METHODS:
The study was conducted in a tertiary care center after approval from the ethical committee from December 2015 to October 2017. All patients who were diagnosed with supratentorial brain tumors or found to have supratentorial brain tumors during an MRI scan were included in the study. Patients who had a prior history of intracranial surgery, radiation, and contraindications for undergoing MRI were excluded from the study. Non-cooperative patients were imaged under sedation given by anaesthesiologists.

The study was performed on 1.5 Tesla Philips Achieva scanner. In addition to routine brain tumor protocol sequences including pre and post contrast multiplanar images, DTI sequence was obtained with diffusion gradients applied along 16 axes, using a b value of 0 and 1000s/mm2 (FOV=224mm, 60 slices, thickness 2mm, TR=8190,TE=0. 83 MATRIX 112/128r. Scan time =7 minutes)

The study was conducted in a sample size of 40 patients. Post-processing was done on Philips's workstation using standard DTI atlas as reference. Co-registration of the FA maps to contrast T1-weighted images was performed for accurate placement of regions of interest (ROIs). 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.

Algorithm for fiber tracking -Minimum FA value was taken as 0.15, maximum angle change =27, minimum fiber length =10. The following white matter tracts were studied in all the 40 cases – Corticospinal tract, corticopontine tract, corpus callosum, superior longitudinal fasciculus, inferior longitudinal fasciculus, thalamic radiation, fornix, and Cingulum.

Involvement of fibers was categorized into (figure 1)
I- DISPLACED - spaced apart and the value of the anisotropy in the tumor is normal or slightly reduced, on a colorful map FA color fiber unchanged, only the brightness changed.
II-EDEMA- fibers displaced, FA reduced, on a colorful FA map fibers color partially changed.
III-INFILTRATED, numerous crossing fibers, spurious fibers, increased or decreased FA values.
IV- DESTROYED, anisotropy of about 0[1]

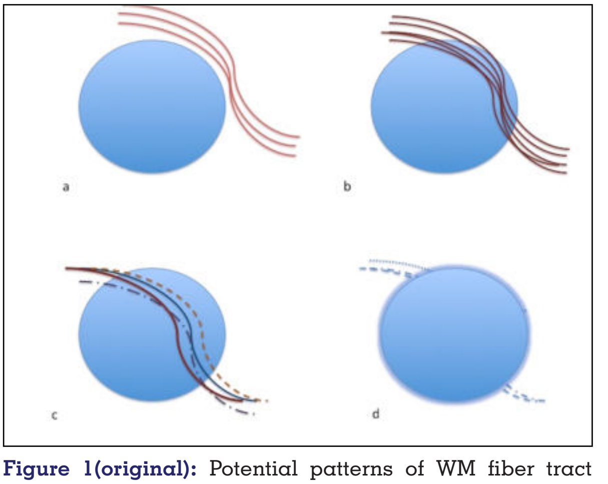

Figure 1(original): Potential patterns of WM fiber tract alteration by cerebral neoplasms. (a) Displaced but intact white matter tracts resulting in a normal to slightly decreased FA in tumor boundaries. (b) Normally located white matter tracts in edematous white matter with decreased FA (c) Tumor-infiltrated, but identifiable white matter tracts with decreased FA in tumor boundaries (d) Disrupted non-identifiable white matter tracts with decreased FA in tumor boundaries.

Patients were divided into benign and malignant groups for comparison with benign group comprising of low-grade gliomas, meningiomas, and epidermoid. The malignant group comprised of high-grade gliomas and lymphoma.

Data were subjected to statistical analysis using paired T-test and chi-square test using STATA VERSION 14.0.

Method of tracking for different fibers (adapted from Role of diffusion tensor imaging in characterization and preoperative planning of brain neoplasms by Ibrahim et al). (6):

• Corticospinal tract: Three ROIs were placed on the transverse color-coded DT images, the first was placed in the pons anteriorly, the second in the posterior limb of the internal capsule, and the third at the motor cortex.
•Thalamic radiation - The entire thalamus was defined as the first ROI. The second ROI for the anterior and posterior thalamic radiations was placed on coronal sections to define the frontal lobe at the section level where the frontal and temporal lobes were separated and to define the occipital lobe at the section level of the posterior tip of the putamen, respectively. For superior thalamic radiation, the second ROI was defined on a transverse section above the corpus callosum, and it occupied the entire hemisphere.
• Superior longitudinal fasciculus - ROIs were placed in the cerebral deep white matter on a coronal directional color-coded map. An anterior ROI was placed in the plane passing through the reconstructed corticospinal tract, and a posterior ROI was placed in the plane passing through the rostral surface of the splenium of the corpus callosum.
• Corpus callosum - ROI was placed in the corpus callosum in the midsagittal plane.
• Inferior longitudinal fasciculus - ROI at the parieto-occipital sulcus, which was identified at the middle of the coronal section along the superior-inferior axis. A second ROI was defined on a coronal section at the mid temporal lobe at the section level of the posterior tip of the putamen.
• Fornix -The body of the fornix was best found in the midsagittal plane. Then, the full fornix can be delineated on the corresponding coronal slice.
• The Cingulum was traced in the midsagittal plane using single fiber tracking using color-coded maps.
• The fronto-pontine tract can be selected by placing a relatively large ROI in the frontal lobe. The temporo-parietooccipito-pontine tract can be selected by placing a relatively large ROI in the parieto-occipital area. The second ROI was placed in the pons anteriorly.

Calculation of FA, ADC, and MD values were done using region of interest placed in the peritumoral white matter. Simultaneously ROI was placed on the contralateral white matter for comparison with normal white matter.

RESULTS:
In the study, the majority of patients belonged to the age group 41-50 years with the mean age being 42.5 yrs. The mean age for malignant tumors was found to be 44.3 and of benign was 40 years. On the correlation of the age distribution with the type of tumor (i.e. Benign or malignant) using the chi-square test, no statistical significance was found. In our study, the majority of the patients were males (60%).

On the correlation of the sex distribution with the type of tumor (i.e. Benign or malignant), out of 24 male patients, 14 had a malignant tumor and ten patients had benign tumors and out of the 16 female patients, six had a malignant tumor and ten had benign tumors. Again, no statistical significance was found for sex as well. The most common location of the tumor was found to be in the frontal region (35%) followed by parasagittal location (20 %). Out of 40 patients, 28 patients had a lesion on the right side while eight patients had a left-sided lesion, four patients had midline lesions.

High-grade gliomas were the most common type of tumor encountered in the study with 18 patients having it, followed by low-grade glioma which was present in eight patients. Meningiomas comprised of ten cases in which four cases were atypical meningiomas and six were classical meningiomas.

Destructed and displaced pattern was most commonly found in the corticospinal, corticopontine, and thalamic radiation, each found in 14 patients. Edema pattern was most commonly found in the corticospinal, corticopontine, corpus callosum, and thalamic radiation. Infiltration was most frequently found in corticospinal, corticopontine tracts.

Out of 80 tracts, which were destructed, 66 tracts were involved in malignant tumors, whereas 14 tracts were involved in benign tumors. There was statistically proven significance between the destruction of fibers and histology of tumors (p-value <0.0001, HS). Hence, the destructive pattern was more commonly seen in malignant tumors. (Figure 2)

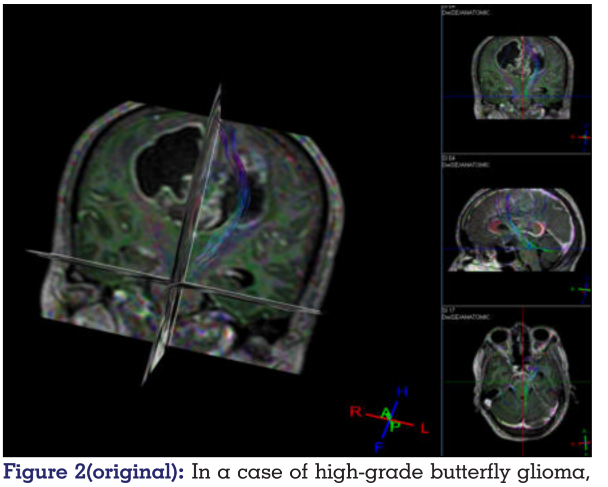

Figure 2(original): In a case of high-grade butterfly glioma, there is complete destruction of corticospinal tracts on right side at tumor location and partial destruction with infiltration on left side.

In case of displacement, out of the 56 tracts that were displaced, 44 were caused by benign tumors and 12 were caused by malignant tumors. There was found to be a statistically proven significance between the displacement of fibers and the type of tumor (p-value <0.0001, HS). Hence, displacement was a more common pattern in benign tumors. (Figure 3)

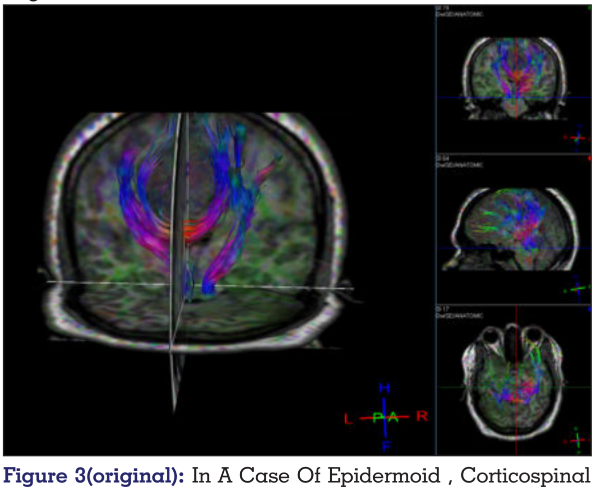

Figure 3(original): In A Case Of Epidermoid , Corticospinal Tracts Shows Displaced Pattern Without Any Change In Colour.

The pattern of edema was observed in 16 malignant tumors and 24 benign tumors (Figure 4). Pattern of infiltration was found in 18 malignant and 12 benign tumors(Figure 5). Both these cases, we didn't find any statistically significant association.

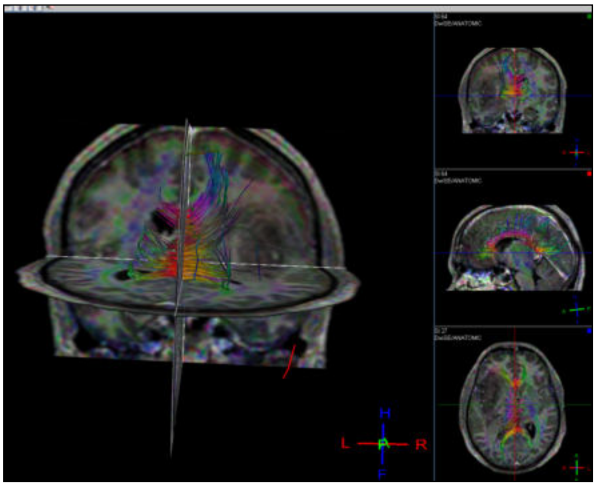

Figure 4(original): In a case of low grade glioma, there is decreased brightness of corpus callosum on right side with maintained primary colour coding s/o oedema.

Comparing ADC values in benign and malignant tumors, the mean value in malignant was found to be 1.61 and in benign it was found to be 1.2, on applying t-test, there was a significant statistical difference between the two groups (p-value 0.0016). Comparing the FA values in malignant and benign tumors, the mean FA value in malignant tumors was found to be 0.18 and in benign tumors was 0.29, again there was a statistically significant difference(p value=0.0033). Comparing the MD, the mean MD value in malignant tumors was found to be 1.58 and in benign tumors, it was found to be 1.35, a marginal level of significance was found here. (p-value 0.0419).

A sensitivity of 90 % and a specificity of 70% obtained for ADC when the cut-off value of 1.37 is used (area under the ROC curve=0.75; 95% CI=0.58 to 0.91) . A sensitivity of 90 % and a specificity of 50% obtained for FA when cut-off value of 0.17 is used (area under the ROC curve=0.72; 95% CI=0.56 to 0.88). A sensitivity of 70 % and a specificity of 60% obtained for MD when the cut-off value of 1.41 is used (area under the ROC curve=0.68; 95% CI=0.51-0.85)

DISCUSSION:

MR Tractography is one of the analytical methods used in diffusion tensor imaging that is gaining popularity in everyday reporting because of its varied applications. In the evaluation of brain tumors, tractography is an indispensable tool for preoperative surgical planning as it can help in assessing the involvement of the major white matter tracts and their salvageability(7)(8). In this study, the involvement of white matter tracts was categorized into four categories, i.e. displacement, edema, infiltration, and destruction(6). We have found that benign tumors like meningioma tend to displace the tracts and high-grade neoplasms cause more destruction of the adjacent tracts. Differentiating between edema and infiltration is more difficult and in this scenario, the DTI metrics come to the rescue.

There are numerous studies which prove the role of tractography in preoperative planning and how it had helped in the prediction of clinical improvement post-surgery, especially in lesions involving eloquent fibers (9)(10)(5)(8)(11)(12). In our study, we had categorized the cases into two groups, i.e. Benign (low-grade gliomas, meningiomas, epidermoid) and malignant (high-grade glioma, lymphoma) similar to another study by Ahmed S. Ibrahim et al(6). Similar to his study, our study showed a significant association between the destructive pattern and malignant tumors (p-value <0.0001, HS). Also, there was found to be a significant association that displacement of the white matter tracts is more commonly seen in benign lesions(p-value <0.0001, HS). Even though edema of white matter tracts was seen more in benign tumors and infiltration was found more commonly in malignant tumors, no statistical significance was found in these categories. This result was also similar to what was observed in the study by Ahmed S. Ibrahim et al(6).

We had also compared the pattern of white matter involvement in high grade and low-grade gliomas, where a association of high-grade gliomas to cause destruction of the fibers as compared to low-grade counterparts was found (p-value <0.0001). Displacement, edema, and infiltration did not show any statistically significant difference between the high grade and low-grade gliomas.

Another study with similar observations was by Corie W. Wei, Gang Guo et al (2007) which had shown that tumor disruption of WM tracts was observed in glioblastoma multiforme and site of origin of anaplastic astrocytoma, whereas in meningioma, tractography illustrated bulk displacement of the tract. They had concluded that fiber tracking results correlated with the clinical and histopathological features of the tumor (4).

Considering the use of DTI metrics for differentiating vasogenic edema and infiltration, studies show mixed results. The two types of edema have commonly increased water accumulation in the extracellular spaces. In pure vasogenic edema, as seen with low-grade gliomas, metastases, or meningiomas, water accumulates in spaces in the intact extracellular matrix. In mixed vasogenic edema, the edema associated with high-grade gliomas, the breakdown of the extracellular matrix by infiltrating tumor cells occurs. This results in higher diffusivity of mixed vasogenic edema that is associated with high-grade glioma(13).

This was also seen in our study with the mean MD value in malignant tumors was significantly higher than benign tumors. This result is in agreement with most of the previous similar studies differentiating infiltrative high-grade glioma with tumors associated with vasogenic perilesional edema like metastasis and meningiomas. However, there are other studies which have found increased MD in the peritumoral white matter of metastasis as compared to HGG, which may be attributed to different degrees of vasogenic edema (14)(15)(16) (17)In a similar study comparing neoplastic and non-neoplastic lesions, the mean MD values were significantly higher in the non-neoplastic group (P = 0.015) compared to the neoplastic group(18). A meta-analysis revealed a moderate diagnostic performance in 6 studies that used perienhancing ADC or MD as a parameter to determine optimal cutoff values, with a pooled sensitivity of 84.7% (95% CI, 73.6%–91.6%) and a pooled specificity of 84.0% (95% CI, 71.8%–91.6%). (19)

Our study showed a significantly lower mean FA value in malignant tumors as compared to benign tumors (p value=0.0033). Studies comparing the FA values in HGG and metastasis were done by many authors but again with conflicting findings. A disruption of the glial structure of the white matter fibre will increase the anisotropy and hence decrease FA compared to normal white matter. But in case of infiltrative edema other factors come into play. Glioma cells tend to produce large amounts of extracellular matrix components(20). This extracellular matrix serves as a substrate for adhesion and subsequent migration of the tumor cells along the enlarged extracellular space. These molecules are concentrated and are oriented in the extracellular matrix, which results in high FA(21) Also another postulation is that increased cellularity in the infiltrated edema may result restriction of movement of extracellular water molecules and result in increased FA(22). 3 studies demonstrated that high-grade glioma showed higher FA values in enhancing tumor than brain metastases with a statistically significant difference in 2 of these studies (9)(19)(24) (15) (25). A recent systematic review also documented no significant changes in the FA of enhancing tumor between high-grade glioma and brain metastasis(26)(16). However, few other studies decreased FA in high grade gliomas compared to metastasis and meningiomas (27)(28). The fact that metastatic lesions show high expression of vascular endothelial growth factor, may be responsible for the increased vasogenic edema comparable to high grade glioma(29)

In one study which aimed at differentiating IDH -1 mutant and IDH-1 wild type counterpart, even though did not find any significant correlation between the grade of glioma and DTI metrics, found that DTI metrics can be used to differentiate IDH 1 wild type and IDH 1 mutants, with significantly higher FA values and significant lower MD values in IDH 1 wildtype patients(30).

Peri tumoral ADC values were significantly found to be higher in our study in the malignant group compared to the benign group. Two studies reported that the mean minimum perienhancing ADC values in high-grade glioma were significantly higher than those in brain metastases(31) (32)whereas 1 study reported lower mean minimum perienhancing ADC values in high-grade glioma.(33) (19)

The mixed results in different studies reflect the limitations of DTI metrics in differentiation vasogenic edema from mixed infiltrative edema. The infiltration in high-grade tumors essentially is not an all or none phenomenon but a continuous spectrum with variable degrees of infiltration and numerous other factors influencing the diffusivity. It also depends on the temporal progression of the disease and whether the tumor was primary or secondary glioblastoma, as primary Glioblastoma Multiforme (GBM) shows minimal infiltration. (21)One of the main limitation in the study and numerous other studies is the subjective nature of placemnet of ROIs and interpretaion of the color map of tractography. This is a problem that could benefit from upcoming advances especially A.I bases techniques. Further studies with more objective analysis and involvement of A.I could help in overcoming these discrepancies in the future.

CONCLUSION:

Incorporating MR tractography in the preoperative assessment of patients with brain tumors may provide additional information on the course of important white matter tracts and their relationship to the tumor. Though tractography could give a wide perspective about the aggressiveness of the lesion differentiating between pure vasogenic edema and mixed edema is still a challenge and needs more objective techniques.

ABBREVIATIONS

DTI - Diffusion tensor imaging
WM- white matter
TR- repetition time
TE – Echo time
FLAIR – Fluid attenuated inversion recovery
FFE- Fast field echo
TSE- Turbo spin echo
EPI- Echo Planar Imaging
FOV – Field of view
FA – Fractional anisotropy
ROI – Region of interest
HS- Highly significant
ADC – Apparent diffusion coefficient
MD- Mean Diffusivity
ROC- Reciever operating characteristic curve
CC- Corpus Callosum
PT- Pyramidal Tract

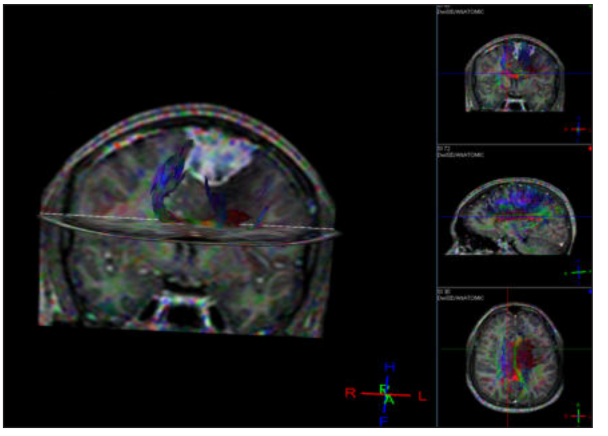

Figure5(original): Corpus callosum shows decreased brightness of tract with abnormal hues, s/o infiltrative pattern.

REFERENCES:

1. He G, Shen T, Chen X. [Diffusion tensor tracking of cerebral white matter fibers: a preliminary study]. Zhonghua Yi Xue Za Zhi. 2005 Oct 19;85(39):2775–9.
2. Yoshioka H, Hama S, Taniguchi E, Sugiyama K, Arita K, Kurisu K. Peritumoral brain edema associated with meningioma. Cancer. 1999;85(4):936–44.
3. Yamahara T, Numa Y, Oishi T, Kawaguchi T, Seno T, Asai A, et al. Morphological and flow cytometric analysis of cell infiltration in glioblastoma: a comparison of autopsy brain and neuroimaging. Brain Tumor Pathol. 2010 Oct;27(2):81–7.
4. Wei CW, Guo G, Mikulis DJ. Tumor effects on cerebral white matter as characterized by diffusion tensor tractography. Can J Neurol Sci J Can Sci Neurol. 2007 Feb;34(1):62–8.
5. Chen X, Weigel D, Ganslandt O, Buchfelder M, Nimsky C. Diffusion tensor imaging and white matter tractography in patients with brainstem lesions. Acta Neurochir (Wien). 2007 Nov;149(11):1117–31; discussion 1131.
6. Ibrahim AS, Gomaa M, Sakr H, Elzaher YA. Role of diffusion tensor imaging in characterization and preoperative planning of brain neoplasms. Egypt J Radiol Nucl Med. 2013 Jun 1;44(2):297–307.
7. Bagadia A, Purandare H, Misra BK, Gupta S. Application of magnetic resonance tractography in the perioperative planning of patients with eloquent region intra-axial brain lesions. J Clin Neurosci. 2011 May 1;18(5):633–9.
8. Castellano A, Bello L, Michelozzi C, Gallucci M, Fava E, Iadanza A, et al. Role of diffusion tensor magnetic resonance tractography in predicting the extent of resection in glioma surgery. Neuro-Oncol. 2012 Feb;14(2):192–202.
9. M S, B S, Hk H, J R, O K, Ho P. Detection of tumour infiltration in axonal fibre bundles using diffusion tensor imaging. Int J Med Robot Comput Assist Surg MRCAS. 2005 Sep 1;1(3):80–6.
10. Laundre BJ, Jellison BJ, Badie B, Alexander AL, Field AS. Diffusion Tensor Imaging of the Corticospinal Tract before and after Mass Resection as Correlated with Clinical Motor Findings: Preliminary Data. Am J Neuroradiol. 2005 Apr 1;26(4):791–6.
11. Bonney PA, Conner AK, Boettcher LB, Cheema AA, Glenn CA, Smitherman AD, et al. A Simplified Method of Accurate Postprocessing of Diffusion Tensor Imaging for Use in Brain Tumor Resection. Oper Neurosurg. 2017 Feb 1;13(1):47–59.
12. Yu CS, Li KC, Xuan Y, Ji XM, Qin W. Diffusion tensor tractography in patients with cerebral tumors: a helpful technique for neurosurgical planning and postoperative assessment. Eur J Radiol. 2005 Nov;56(2):197–204.
13. Morita K, Matsuzawa H, Fujii Y, Tanaka R, Kwee IL, Nakada T. Diffusion tensor analysis of peritumoral edema using lambda chart analysis indicative of the heterogeneity of the microstructure within edema. J Neurosurg. 2005 Feb;102(2):336–41.
14. Byrnes TJD, Barrick TR, Bell BA, Clark CA. Diffusion tensor imaging discriminates between glioblastoma and cerebral metastases in vivo. NMR Biomed. 2011 Jan;24(1):54–60.
15. Bauer AH, Erly W, Moser FG, Maya M, Nael K. Differentiation of solitary brain metastasis from glioblastoma multiforme: a predictive multiparametric approach using combined MR diffusion and perfusion. Neuroradiology. 2015 Jul;57(7):697–703.
16. Tan Y, Wang X-C, Zhang H, Wang J, Qin J-B, Wu X-F, et al. Differentiation of high-grade-astrocytomas from solitary-brain-metastases: Comparing diffusion kurtosis imaging and diffusion tensor imaging. Eur J Radiol. 2015 Dec;84(12):2618–24.
17. Abdel Razek AAK, Talaat M, El-Serougy L, Abdelsalam M, Gaballa G. Differentiating Glioblastomas from Solitary Brain Metastases Using Arterial Spin Labeling Perfusion- and Diffusion Tensor Imaging-Derived Metrics. World Neurosurg. 2019 Jul;127:e593–8.
18. Soni N, Srindharan K, Kumar S, Bhaisora KS, Kalita J, Mehrotra A, et al. Application of diffusion tensor imaging in brain lesions: A comparative study of neoplastic and non-neoplastic brain lesions. Neurol India. 2018 Dec;66(6):1667–71.

19. Suh CH, Kim HS, Jung SC, Kim SJ. Diffusion-Weighted Imaging and Diffusion Tensor Imaging for Differentiating High-Grade Glioma from Solitary Brain Metastasis: A Systematic Review and Meta-Analysis. Am J Neuroradiol. 2018 Jul 1;39(7):1208–14.
20. Zamecnik J. The extracellular space and matrix of gliomas. Acta Neuropathol (Berl). 2005 Nov;110(5):435–42.
21. Pope WB, Mirsadraei L, Lai A, Eskin A, Qiao J, Kim HJ, et al. Differential Gene Expression in Glioblastoma Defined by ADC Histogram Analysis: Relationship to Extracellular Matrix Molecules and Survival. Am J Neuroradiol. 2012 Jun 1;33(6):1059–64.
22. Sinha S, Bastin ME, Whittle IR, Wardlaw JM. Diffusion Tensor MR Imaging of High-Grade Cerebral Gliomas. Am J Neuroradiol. 2002 Apr 1;23(4):520–7.
23. Bette S, Huber T, Wiestler B, Boeckh-Behrens T, Gempt J, Ringel F, et al. Analysis of fractional anisotropy facilitates differentiation of glioblastoma and brain metastases in a clinical setting. Eur J Radiol. 2016 Dec;85(12):2182–7.
24. Wang S, Kim SJ, Poptani H, Woo JH, Mohan S, Jin R, et al. Diagnostic Utility of Diffusion Tensor Imaging in Differentiating Glioblastomas from Brain Metastases. Am J Neuroradiol. 2014 May 1;35(5):928–34.
25. Holly KS, Barker BJ, Murcia D, Bennett R, Kalakoti P, Ledbetter C, et al. High-grade Gliomas Exhibit Higher Peritumoral Fractional Anisotropy and Lower Mean Diffusivity than Intracranial Metastases. Front Surg. 2017;4:18.
26. Jiang R, Du F-Z, He C, Gu M, Ke Z-W, Li J-H. The value of diffusion tensor imaging in differentiating high-grade gliomas from brain metastases: a systematic review and meta-analysis. PloS One. 2014;9(11):e112550.
27. Min Z, Niu C, Rana N, Ji H, Zhang M. Differentiation of pure vasogenic edema and tumor-infiltrated edema in patients with peritumoral edema by analyzing the relationship of axial and radial diffusivities on 3.0T MRI. Clin Neurol Neurosurg. 2013 Aug 1;115(8):1366–70.
28. De Belder FE, Oot AR, Van Hecke W, Venstermans C, Menovsky T, Van Marck V, et al. Diffusion tensor imaging provides an insight into the microstructure of meningiomas, high-grade gliomas, and peritumoral edema. J Comput Assist Tomogr. 2012 Oct;36(5):577–82.
29. Wang S, Kim S, Chawla S, Wolf RL, Knipp DE, Vossough A, et al. Differentiation between Glioblastomas, Solitary Brain Metastases, and Primary Cerebral Lymphomas Using Diffusion Tensor and Dynamic Susceptibility Contrast-Enhanced MR Imaging. Am J Neuroradiol. 2011 Mar 1;32(3):507–14.
30. Zhao J, Wang Y-L, Li X-B, Hu M-S, Li Z-H, Song Y-K, et al. Comparative analysis of the diffusion kurtosis imaging and diffusion tensor imaging in grading gliomas, predicting tumour cell proliferation and IDH-1 gene mutation status. J Neurooncol. 2019 Jan;141(1):195–203.
31. Caravan I, Ciortea CA, Contis A, Lebovici A. Diagnostic value of apparent diffusion coefficient in differentiating between high-grade gliomas and brain metastases. Acta Radiol Stockh Swed 1987. 2018 May;59(5):599–605.
32. Han C, Huang S, Guo J, Zhuang X, Han H. Use of a high b-value for diffusion weighted imaging of peritumoral regions to differentiate high-grade gliomas and solitary metastases. J Magn Reson Imaging JMRI. 2015 Jul;42(1):80–6.
33. Lee EJ, terBrugge K, Mikulis D, Choi DS, Bae JM, Lee SK, et al. Diagnostic Value of Peritumoral Minimum Apparent Diffusion Coefficient for Differentiation of Glioblastoma Multiforme From Solitary Metastatic Lesions. Am J Roentgenol. 2011 Jan 1;196(1):71–6.