

# Investigation of the Correlation Between Preoperative Diffusion Tensor Imaging Parameters and Histopathological Findings in Patients with Meningioma

Enes Oğuzhan Alkan<sup>1</sup>, Lutfullah Sarı<sup>2</sup>, Serdar Balsak<sup>2</sup>, Fatma Çelik Yabul<sup>2</sup>, Fazılhan Altıntaş<sup>2</sup>,  
Ganime Çoban<sup>3</sup>

<sup>1</sup>Medical Student, Bezmialem Vakıf University, Faculty of Medicine, İstanbul, Turkey

<sup>2</sup>Department of Radiology, Bezmialem Vakıf University, Faculty of Medicine, İstanbul, Turkey

<sup>3</sup>Department of Pathology, Bezmialem Vakıf University, Faculty of Medicine, İstanbul, Turkey

**Cite this article as:** Alkan EO, Sarı L, Balsak S, Çelik Yabul F, Altıntaş F, Çoban G. Investigation of the correlation between preoperative diffusion tensor imaging parameters and histopathological findings in patients with meningioma. *Current Research in MRI*. 2022; 1(1): 15-17.

**Corresponding author:** Lutfullah Sarı, e-mail: drlutfullahsari@gmail.com

**Received:** April 30, 2022 **Accepted:** August 1, 2022

DOI: 10.5152/CurrResMRI.2022.220813



Content of this journal is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License.

## Abstract

**Objective:** Our study aimed to investigate whether the tumor differs in terms of apparent diffusion coefficient and fractional anisotropy values, mitotic index, and Ki-67 proliferation index in cases with transitional and atypical meningioma.

**Methods:** Forty-five patients (14 male and 31 female; 57±13.98 years old) were assessed using magnetic resonance imaging and diffusion tensor imaging before surgery. Apparent diffusion coefficient and fractional anisotropy values of the tumor were determined. Patients with atypical meningioma were classified as group 1 and those with transitional meningioma were considered group 2. The relationship between fractional anisotropy, apparent diffusion coefficient, Ki-67 proliferation index, and mitotic index was evaluated. Fractional anisotropy and apparent diffusion coefficient values of atypical meningiomas and transitional meningiomas were compared. Mann–Whitney U-test was used to compare the groups.

**Results:** Significant differences were found between group 1 and group 2 in terms of mitotic index and Ki-67 proliferation index (respectively,  $P = .001$  and  $P = .000$ ). There was no statistically significant difference between group 1 and group 2 in terms of fractional anisotropy and apparent diffusion coefficient values. In group 1, there was a positive correlation between fractional anisotropy values and mitotic index ( $P = .02$ ,  $r = 0.421$ ). Also, a negative correlation was found between apparent diffusion coefficient values and mitotic index ( $P = .04$ ,  $r = -0.374$ ). A negative correlation was found between apparent diffusion coefficient values and Ki-67 proliferation index in group 2 ( $P = .009$ ,  $r = -0.614$ ).

**Conclusions:** In preoperative imaging, adding diffusion tensor imaging to conventional magnetic resonance imaging and measuring fractional anisotropy and apparent diffusion coefficient values to predict the grade of meningiomas can be a guide for treatment planning.

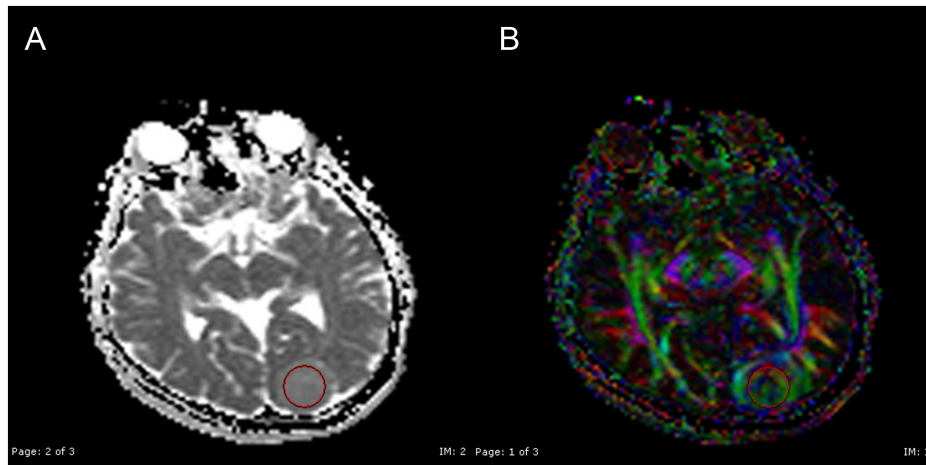
**Keywords:** Atypical meningioma, apparent diffusion coefficient, diffusion tensor imaging, fractional anisotropy, meningioma, transitional meningioma

## INTRODUCTION

Among primary intracranial tumors, meningiomas account for 13–26% of all cases.<sup>1</sup> Arachnoid cap cells are known to be the origin of meningiomas. Parasagittal area, convexity, falx, skull base, as well as the ridge of the sphenoid bone are some of the most common localizations for these lesions. There are several treatment options available such as stereotactic radiosurgery, conformal radiotherapy, surgery, or their combinations<sup>2</sup> although passive check out is usually advised in case of asymptomatic lesions of lesser caliber or when the patient is elderly. If the tumor shows significant size growth or invades important structures and starts to become symptomatic, treatment is indicated.

The number of mitoses, signs of necrosis as well as parenchymal invasion are the main components of histopathological meningiomas grading. Grade 1 transitional meningiomas, also known as mixed meningiomas, are known to have features of both meningothelial and fibrous meningioma. Grade 2 atypical meningiomas make up about 8% of all meningiomas.<sup>3</sup> Atypical meningiomas, on the other hand, constitute 20–25% of recurring meningiomas.<sup>4</sup>

Diffusion tensor imaging (DTI) provides information regarding the direction of diffusion as well as tissue microstructural integrity. The most widespread parameters for DTI evaluation are apparent diffusion coefficient (ADC) and fractional anisotropy (FA). The significance of FA values in meningioma follow-up and diagnosis remains a controversial issue.<sup>1</sup> Several different studies reported variable FA values about meningioma grade.<sup>1,5</sup> It is known that ADC values correlate with tumor cellularity and the Ki-67 proliferation index.<sup>1,6</sup> As far as we know, the number of studies evaluating the radiation effects on meningioma patients who underwent Gamma Knife radiosurgery (GKR) with respect to volume changes and DTI parameters is few.<sup>4</sup> Our study aimed to investigate whether the tumor differs in terms of ADC and FA values, proliferation index, and mitotic index in cases with transitional and atypical meningioma.



**Figure 1.** A 37-year-old woman with left occipital atypical meningioma. Apparent diffusion coefficient (A) and fractional anisotropy (FA) (B) values were calculated by placing region of interest that covers the tumor completely in FA maps.

## METHODS

The institutional ethics committee has approved our study (Date: 19 May, 2021, Decision No: 2021-16601). The data of the patients who were operated on with meningioma diagnosis between 2014 and 2020 at the Bezmialem University Hospital have been retrospectively gathered. Forty-five patients (14 male and 31 female;  $57 \pm 13.98$  years old) with meningioma treated with surgery were assessed using MRI and DTI preoperative. Fractional anisotropy and ADC values of the tumor were determined. Brain tissue invasion and the presence of 4 or greater mitoses have been accepted as the threshold for atypical meningioma diagnosis. Twenty-eight patients with atypical meningioma were classified as group 1 and 17 patients with transitional meningioma were considered group 2.

### Magnetic Resonance Imaging

Assessment of GKR treatment planning of the meningioma patients was done by a 1.5T MRI system (Avanto, Siemens, Erlangen, Germany). Following sequences of MRI were encompassed: coronal and axial fluid-attenuated inversion recovery (repetition time [TR]: 8000 ms, time echo [TE]: 90 ms, inversion time [TI]: 2500 ms), axial T1 (TR: 550, TE: 14 ms)-weighted images, axial and sagittal T2 TSE (TR: 4500, TE: 90 ms). Contrast (IV gadolinium-diethylenetriamine penta-acetic acid [Gd-DTPA]) T1 images in coronal, sagittal as well as axial planes were acquired. Three-dimensional T1 MPRAGE sequences with or without contrast were also included.

Following DTI parameters were used in the evaluation of the patients: single-shot SE echo-planar, TR/TE: 6000/89 ms; matrix,  $128 \times 256$ ;

FOV, 230 mm; spatial resolution, 1.54; and slice thickness, 5 mm. Diffusion-encoding in 30 separate aspects were obtained at  $b = 0 \text{ s/mm}^2$  and  $b = 1000 \text{ s/mm}^2$ . Obtained DTI information has been processed and FA maps were created on the workstation (Leonardo, Siemens, Erlangen, Germany). Fractional anisotropy and ADC values were quantified by manually positioning the elliptical regions of interest (ROI) within the tumor (Figure 1). Volumetric contrast 3D T1 MPRAGE images were taken as a reference when placing the ROI on the tumor. The dimensions of all ROIs were  $27.75 \pm 17.83 \text{ cm}^3$  (median,  $24 \text{ cm}^3$ ). The adaptation of the size and place of all ROIs within the tumor was implemented simultaneously by 2 radiologists. The association between FA, Ki-67 values, ADC proliferation index, and mitotic index was evaluated. Apparent diffusion coefficient and FA values of atypical meningiomas and transitional meningiomas were equated.

### Statistical Analysis

Shapiro–Wilk and Kolmogorov–Smirnov tests were used to determine if there is a normal distribution present. Fractional anisotropy and ADC points of atypical meningiomas and transitional meningiomas were equated. Mann–Whitney U-test was used to check our null hypothesis because of the total number one of the patient groups were smaller than 30 patients. The relationship between FA and ADC values, mitotic index, and Ki-67 was investigated by the Pearson correlation test. Statistical Package for the Social Sciences version 22.0. (IBM SPSS Corp.; Armonk, NY, USA) was used throughout the entire statistical analysis process.

## RESULTS

Both groups were compared in terms of the Ki-67 proliferation index and mitotic index, and significant differences were found (respectively,  $P = .000$  and  $P = .001$ ). There was no statistically meaningful disparity between atypical meningioma and transitional meningioma about ADC ( $P = .256$ ) and FA ( $P = .361$ ) values.

In group 1, a positive correlation was detected between mitotic index and FA values ( $P = .02$ ,  $r = 0.421$ ). As well, a negative correlation was detected between ADC values and mitotic index ( $P = .04$ ,  $r = -0.374$ ). A negative correlation was detected between Ki-67 proliferation index and ADC values in group 2 ( $P = .009$ ,  $r = -0.614$ ).

### MAIN POINTS

- Among primary intracranial tumors, meningiomas account for 13–26% of all cases.
- There are several treatment options available such as stereotactic radiosurgery, conformal radiotherapy, surgery, or their combinations.
- In preoperative imaging, adding diffusion tensor imaging to conventional magnetic resonance imaging and measuring fractional anisotropy and apparent diffusion coefficient values to predict the grade of meningiomas can be a guide for treatment planning.

## DISCUSSION

Diffusion tensor imaging provides useful information that can help us detect the abnormalities that meningiomas can have both before and after treatments such as radiosurgery.<sup>7-9</sup> Diffusion tensor imaging parameters provide important data on the level of microstructural damage and the behavior and organization of tumors according to their histological subtypes.<sup>6</sup> Fractional anisotropy quantifies anisotropic water diffusion and reveals its versatility and texture integrity. Fractional anisotropy gives salient details regarding the microorganization of fiber density, myelination, axon diameter, and white matter. Apparent diffusion coefficient separately quantifies the aspect of total water diffusion in textures and gives principal data regarding nucleus–cytoplasm ratio and tissue cellularity.<sup>1</sup> Despite the high sensitivity of FA and ADC in the differential diagnosis of high- and low-grade meningiomas, they do not furnish important details in the evaluation of microstructural texture alterations.<sup>1</sup> Compared to other types of meningiomas, fibroblastic meningiomas have been described as having relatively high FA and low ADC values.<sup>1</sup>

The evaluation of meningioma consistency could be navigated by FA values.<sup>10,11</sup> Due to the solid consistency of meningiomas, it is thought that isointensity in ADC maps and hyperintensity in FA maps are observed.<sup>10</sup> Apparent diffusion coefficient measurements contribute to determining the degree of meningioma.<sup>5,11,12</sup> There is a relationship between decreased tumor cellularity and increased ADC values.<sup>6</sup> It is thought that there may be a relationship between increased ADC values and decreased tumor cellularity.<sup>5,12</sup> Compared with fiber-rich fibroblastic meningiomas, meningiomas with a high proliferation index are more successfully treated with radiotherapy.<sup>6</sup> Long spindle-shaped tumor cells in meningiomas rich in fibrous tissue are predicted to own low ADC and high FA values because of their fascicular arrangement and increased content of interfascicular fibers.<sup>5,13-15</sup> It is speculated that fibroblastic meningiomas have a solid density may be due to their intracellular reticulin and collagen ingredient.

Due to the grade difference between atypical meningioma and transitional meningioma, significant differences were found when atypical meningioma and transitional meningioma were compared regarding the mitotic index and Ki-67 proliferation index. When comparing atypical meningioma and transitional meningioma regarding FA and ADC values, no substantial differences were seen between them. The number of patients is low and for this reason, it was thought that no statistically significant difference was detected. In group 1, a positive correlation was found between the mitotic index and FA values. Also, a negative correlation was found between the mitotic index and ADC values. In group 2, there was a negative correlation between the Ki-67 proliferation index and ADC values. The findings were thought to be compatible with the grade difference.

There are several limitations to our study. One of them is our study is a retrospective study. The other is the limited number of patients. Another major limitation is ROI placement, which is caused by the partial volume effect as a result of ROIs being placed in different locations. Diffusion tensor imaging values can be influenced by tumor heterogeneity.

## CONCLUSION

In preoperative imaging, adding DTI to conventional MRI and measuring FA and ADC values to estimate the grade of meningiomas can be a guide for treatment planning.

**Ethics Committee Approval:** Ethics committee approval was received for this study from the ethics committee of Bezmialem Vakıf University (Date: May 19, 2021, Decision No: 16601).

**Informed Consent:** Written informed consent was obtained from all participants who participated in this study.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept – E.O.A., F.A.; Design – L.S.; Supervision – G.Ç., S.B.; Resources – S.B.; Materials – G.Ç., E.O.A.; Data Collection and/or Processing – E.O.A.; Analysis and/or Interpretation – F.C.Y.; Literature Search – F.C.Y.; Writing Manuscript – L.S., F.A.; Critical Review – G.Ç., L.S.; Other – F.A.

**Declaration of Interests:** The authors declare that they have no competing interest.

**Funding:** This study received no funding.

## REFERENCES

- Aslan K, Gunbey HP, Tomak L, Incesu L. The diagnostic value of using combined MR diffusion tensor imaging parameters to differentiate between low- and high-grade meningioma. *Br J Radiol.* 2018;91(1088): 20180088. [\[CrossRef\]](#)
- Nguyen EK, Nguyen TK, Boldt G, Louie AV, Bauman GS. Hypofractionated stereotactic radiotherapy for intracranial meningioma: a systematic review. *Neurooncol Pract.* 2019;6(5):346-353. [\[CrossRef\]](#)
- Louis DN, Perry A, Reifenberger G, et al. The 2016 World Health Organization classification of tumors of the central nervous system: a summary. *Acta neuropathol.* 2016;131(6):803-820. [\[CrossRef\]](#)
- Kim JH, Kim YJ, Kim H, Nam SH, Choi YW. A rare case of transitional meningioma. *Arch Plast Surg.* 2015;42(3):375-377. [\[CrossRef\]](#)
- Wang S, Kim S, Zhang Y, et al. Determination of grade and subtype of meningiomas by using histogram analysis of diffusion-tensor imaging metrics. *Radiology.* 2012;262(2):584-592. [\[CrossRef\]](#)
- Speckter H, Bido J, Hernandez G, et al. Prognostic value of diffusion tensor imaging parameters for gamma knife radiosurgery in meningiomas. *J Neurosurg.* 2016;125(suppl 1):83-88. [\[CrossRef\]](#)
- Fatima N, Meola A, Pollom EL, Soltys SG, Chang SD. Stereotactic radiosurgery versus stereotactic radiotherapy in the management of intracranial meningiomas: a systematic review and meta-analysis. *Neurosurg Focus.* 2019;46(6):E2. [\[CrossRef\]](#)
- Ge Y, Liu D, Zhang Z, et al. Gamma Knife radiosurgery for intracranial benign meningiomas: follow-up outcome in 130 patients. *Neurosurg Focus.* 2019;46(6):E7. [\[CrossRef\]](#)
- Flannery T, Poots J. Gamma knife radiosurgery for meningioma. *Prog Neurol Surg.* 2019;34:91-99. [\[CrossRef\]](#)
- Huang RY, Bi WL, Weller M, et al. Proposed response assessment and endpoints for meningioma clinical trials: report from the Response Assessment in Neuro-Oncology Working Group. *Neuro Oncol.* 2019; 21(1):26-36. [\[CrossRef\]](#)
- Romani R, Tang WJ, Mao Y, et al. Diffusion tensor magnetic resonance imaging for predicting the consistency of intracranial meningiomas. *Acta neurochir.* 2014;156(10):1837-1845. [\[CrossRef\]](#)
- Toh CH, Castillo M, Wong AM, et al. Differentiation between classic and atypical meningiomas with use of diffusion tensor imaging. *AJNR Am J Neuroradiol.* 2008;29(9):1630-1635. [\[CrossRef\]](#)
- Kashimura H, Inoue T, Ogasawara K, et al. Prediction of meningioma consistency using fractional anisotropy value measured by magnetic resonance imaging. *J Neurosurg.* 2007;107(4):784-787. [\[CrossRef\]](#)
- Tropine A, Dellani PD, Glaser M, et al. Differentiation of fibroblastic meningiomas from other benign subtypes using diffusion tensor imaging. *J Magn Reson Imaging.* 2007;25(4):703-708. [\[CrossRef\]](#)
- Speckter H, Bido J, Hernandez G, et al. Pretreatment texture analysis of routine MR images and shape analysis of the diffusion tensor for prediction of volumetric response after radiosurgery for meningioma. *J Neurosurg.* 2018;129(suppl1):31-37. [\[CrossRef\]](#)