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Prediction of meningioma subtypes using qualitative assessment of fractional anisotropy maps

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AIM: In this study, we explore the role of FA maps in predicting the histopathological subtypes of meningioma using a qualitative ordinal scale and quantitative histogram features.

MATERIAL & METHODS: Retrospective analysis of grey-scale FA maps of 96 cases of meningioma was done by two observers blinded to the histopathological diagnosis. An ordinal scale of 1–4 was used to grade the degree of FA in each lesion. Histogram features were calculated from the region of interest and statistical analysis was carried out for discriminating between the above-mentioned qualitative gradings.

RESULTS: Out of 98 cases, there were 9 meningothelial/15 transitional/14 chordoid/8 angiomatous/15 microcystic/17 fibroblastic/18 atypical meningiomas. Interobserver reliability had intraclass correlation coefficient of 0.92. The intergroup comparison revealed significantly low FA grade in microcystic/angiomatous/transitional meningioma compared to meningothelial/chordoid/ fibroblastic/ atypical meningioma with transitional being a relatively heterogenous subgroup compared to the former two. While all fibroblastic meningiomas showed high FA grade, it is relatively non-specific since several grade 3 and 4 meningiomas were also seen among meningothelial/chordoid/ atypical subtypes. All quantitative median FA values were found to be significantly correlated with qualitative FA grades as assigned by the interpreting radiologist (Spearman's Rho for mean is 0.502 ($P < 0.001$), for 75th percentile is 0.505 ($P < 0.001$). However, the strength of correlation for all metrics was moderate and positive.

CONCLUSION: Qualitative grading of FA maps is useful in predicting the meningioma subtype. Low FA is characteristically seen in microcystic and angiomatous variants. High FA within tumour although a consistent feature of Fibroblastic variant, is nonspecific.

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Introduction

Meningiomas are the most common extra-axial brain tumours that originate from the meningeal layers of the brain and spinal cord. They account for 30% of all intracranial brain tumours.[1] Although most meningiomas are grade I tumours, up to 20% are atypical (grade 2) or anaplastic (grade 3).[2,3] Certain histological subtypes are associated with a higher risk of recurrence, even after seemingly complete resection.[4] Most of meningiomas have signature imaging characteristics of a well-circumscribed, dural-based avidly enhancing mass lesion. However, conventional imaging does not allow the distinction of meningioma subtypes. Preoperative determination of meningioma subtypes aids in surgical planning. Surgical management and prognosis of meningioma depend on their histopathological subtype and grade which can be predicted from tumour consistency and intratumoural diffusion of water.

The previous studies have explored the potential of various magnetic resonance imaging characteristics in grading meningiomas and differentiating histopathological subtypes. A study based on 120 meningiomas revealed that loss of tumour-brain interface, presence of capsular enhancement and heterogenous enhancement of the lesion on preoperative MR imaging in addition to age more than 75 years was predictive of a higher grade of meningioma. They also devised a scoring system incorporating these features.[5] Another study showed an inverse relation between lesional apparent diffusion coefficient (ADC) values and grade of meningioma measured using high b value imaging at 3 Tesla.[6] Suzuki *et al.*[7] showed that the consistency of meningiomas can be predicted from the T2 signal intensity characteristics, which is beneficial for preoperative planning. However, no correlation was observed between the degree of enhancement and histopathology in a study by Chen *et al.*[8]

Diffusion tensor imaging (DTI) can detect water diffusivity characteristics in different tissues and the degree of anisotropy. Fractional anisotropy (FA), a component of DTI, represents the directional asymmetry of diffusion and is affected by microstructural changes. FA measures the degree of deviation from isotropic diffusion.[9–11] It is influenced by the content of tissue, its consistency and geometry.[12] Diffusion-weighted imaging (DWI) has been extensively employed earlier to characterise meningiomas;[13–15] however, the emphasis has largely revolved on ADC.[16–19] While it seems reasonable that FA and ADC can inversely correlate, the relationship is relatively complex and nonlinear.[20] Tumours with compact tissue and higher consistency are likely to have higher FA values. Given the diverse spectrum of histopathological variants of meningioma each with its own histoarchitecture,[21] it is a compelling proposition to study them from another facet of diffusion property, viz FA. There are very few studies in the literature regarding the imaging correlates of histopathological meningioma subtypes and FA maps.[22,23] Quantitative measurements have been used which might be difficult to implement in daily clinical practice. In this study, we explore the role of FA maps in differentiating histopathological subtypes of meningioma using a qualitative ordinal scale and quantitative histogram features.

Material and methods

It is a single-centre, retrospective observational study. It was a retrospective study, for which institutional ethics approval was obtained. The patients who underwent MRI as a part of regular preoperative imaging workup were included in this study.

Subjects

All histologically proven cases of meningioma, irrespective of age and gender, who underwent preoperative MRI between 2015 and 2019 for whom FA maps were available were included in the study.

Imaging technique

All patients had undergone MRI in one of the following three scanners: 1.5T Aera Siemens, 3T Skyra Siemens and 3T Philips Achieva scanner. Sagittal, axial and coronal T2-weighted, axial T1-weighted, axial fluid-attenuated inversion recovery (FLAIR) and axial susceptibility weighted imaging, diffusion tensor imaging (DTI) and post-contrast T1-magnetisation prepared rapid gradient echo (MPRAGE)/3D T1 turbo-field echo (TFE) sequences were acquired in all patients as routine protocol for meningioma. DTI was acquired with single shot, spin echo (echo planar imaging) with diffusion gradients applied in 6 directions using b values: 0, 1000. TE: 83 ms, TR: 3800 ms, diffusion weightings: 2, matrix size: 112 × 90 × 30, voxel size: 1.8 × 1.8 × 5mm. Post-contrast MPRAGE/3D T1 TFE sequence was obtained after injecting 0.1mmol/kg of gadolinium-based contrast agent at the rate of 1.5–2 ml per second through an 18 gauge IV cannula placed in a peripheral vein.

Image analysis

Qualitative FA map analysis

Auto-generated, greyscale FA maps of the cases were evaluated by two observers blinded to the histopathological subtype of the tumour. A qualitative ordinal scale of 1–4 was used to grade the degree of fractional anisotropy in

each lesion based on the brightness of the lesion on the FA maps. Both the observers were alloted different workstations for image analysis. The MRI images of all the cases were loaded on the desktop of the reporting monitor. The unique hospital identity numbers and other personal identification details of the patients were removed from the given set of images. MS Excel sheet was used for entry and analysis of the data. Results of these 98 patients were analysed using the following parameters—serial number from 1 to 98, FA grade of the tumour in these 98 cases and tumour location. Another exactly similar Excel sheet containing the same parameters in the same sequence is created as the mother data entry sheet, which also additionally contained the unique hospital identity number of the patients, histopathology type and grade of the tumour. For the second observer, the sequence of the serial number of the cases was changed randomly. Greyscale viewing windows of the images were dynamically adjusted to reference the lesional FA to the subcortical white matter in the uninvolved frontal region. Grade 1 (denoting very low FA) was assigned to those tumours that were appearing dark on FA map and resembling Cerebro Spinal Fluid (CSF) and grade 4 (denoting very high FA) to those which were as bright as or brighter than the subcortical white matter on FA map. Values of 2 and 3 (meaning predominantly low and predominantly high FA, respectively) were assigned to tumours which on FA maps were predominantly dark (more than 50% dark areas) with patchy bright areas and predominantly bright with scattered dark areas (less than 50 % dark), respectively (Fig 1). For the purpose of dichotomisation, grades 1 and 2 were arbitrarily considered as low FA lesions and grades 3 and 4 were categorised as high FA.

Quantitative FA map analysis

Histogram features. Region of interest (ROI) was carefully marked by an experienced neuroradiologist on a single slice (depicting the largest tumour section) of axial T2-weighted image around the tumour boundary. ROIs were placed on T2-weighted image of each subject using 3D slicer[24] and saved as binary masks. FA maps were registered to respective T2W images and ROIs were then transferred to FA maps. Histogram features including 'minimum', 'maximum', 'Mean', 'Median', 'Skewness', 'Kurtosis', '10^{th} percentile', '25^{th} percentile', '75^{th} percentile', '95^{th} percentile', and '99^{th} percentile' were calculated from the ROIs for each FA map using an in-house python-based script.

Statistical analysis

The distributions of the four FA grades in each meningioma subtype were expressed as percentages. Interobserver reliability was assessed using the intraclass correlation coefficient with values less than 0.5, 0.5–0.75, 0.75–0.9 and more than 0.9 indicating poor, moderate, good and excellent reliability, respectively. Intergroup comparison of FA grades between meningioma subtypes was performed using the Kruskall–Wallis test with Bonferroni correction. A P value less than 0.05 was considered as significant. A statistical test was also applied to histogram features to carry out between group analysis with a threshold of P value < 0.05.

Data were analysed using R software version 4.1.2. Interval/ordinal scale variables are described by medians and interquartile ranges and nominal data described as frequencies and percentages. The histopathology types were separated into dummy variables and used as dependent variables for prediction using dichotomised FA grade (low = 1, 2 and high = 3, 4). The models were built using binomial logistic regression and results were presented as odds ratios with 95% confidence intervals. Discriminatory ability of quantitative FA values (min, max, median and mean) for each individual histopathology subtype was assessed using receiver operating characteristic curve analysis and results presented as area under curve values with 95% confidence intervals. The best cutoff thresholds

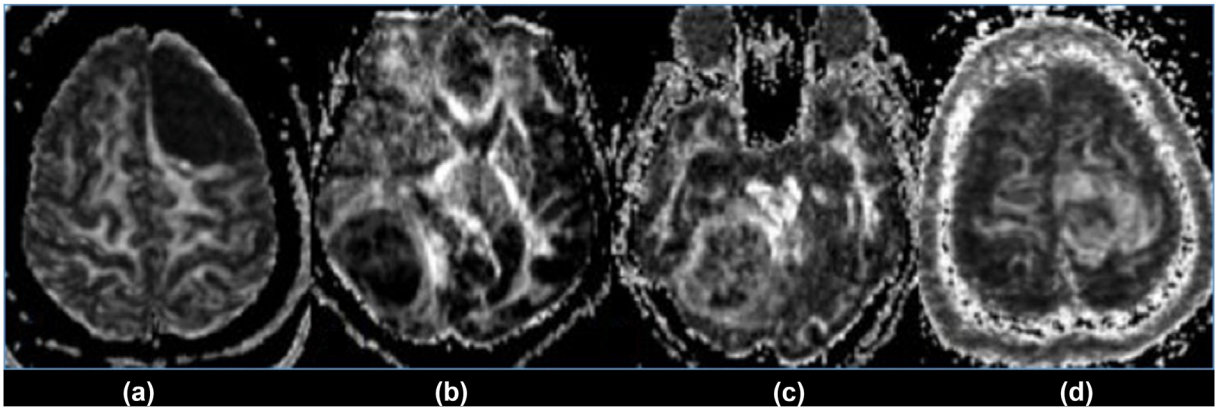


Figure 1 Representative images of the four different FA grades of meningioma on grayscale as indicated by the yellow arrows. FA maps (a) shows the lesion in the left frontal convexity to be completely dark, representative of FA grade 1, (b) shows right parietal convexity tumour which is predominantly dark as that of CSF with few scattered areas approaching the subcortical white matter in brightness depicting FA grade 2, (c) shows predominantly bright lesion like that of the subcortical white matter in the right cerebellopontine angle with few dark areas like those of CSF corresponding to FA grade of 3 and (d) shows nearly the entire lesion in the left frontal convexity to be bright representing FA grade 4 lesion. FA, ractional anisotropy.

were determined using Youden's method. Correlation of each FA value metric with qualitative FA grade was conducted using Spearman's correlation.

Results

Patient characteristics

A total of 98 cases of meningioma were reviewed. There were 30 males and 68 females with a male female ratio of 2.3:1. The mean age along with the standard deviation was 48.2 ± 14.8 years with a range of 14–78 years.

Meningioma subtypes

There were 9 meningothelial (grade 1), 15 transitional (grade 1), 14 chordoid (grade 2), 8 angiomatous (grade 1), 15 microcystic (grade 1), 17 fibroblastic (grade 1) and 18 atypical (grade 2) meningiomas. Overall, there were 64 grade 1 and 32 grade 2 meningiomas.

Interobserver reliability for qualitative FA grading

The average measured intraclass correlation coefficient was 0.924 (95% confidence interval (CI) : 0.886 to 0.949) indicating excellent interobserver reliability.

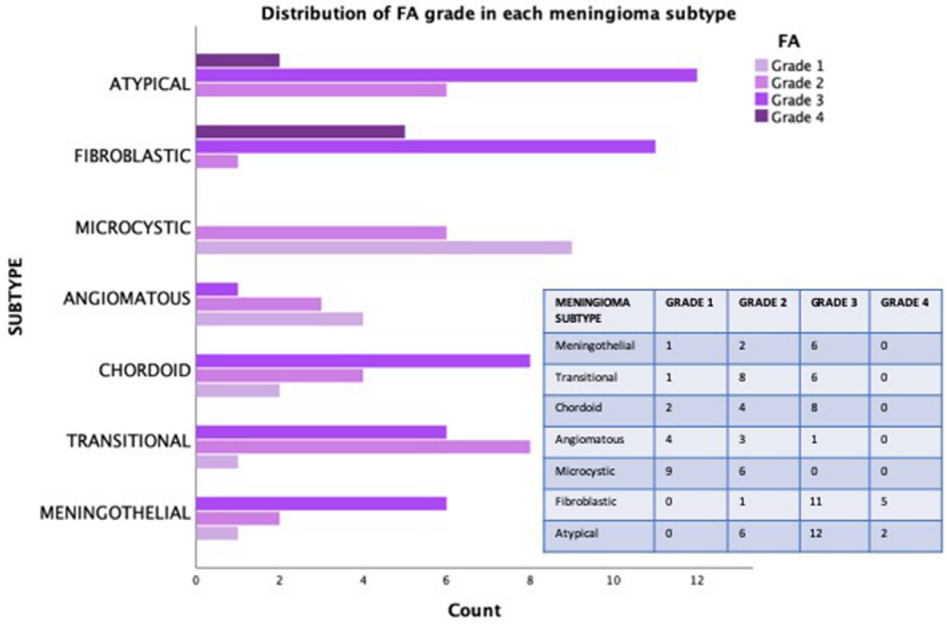
Distribution of FA grades in each meningioma variant

The distribution of qualitative FA grades in each meningioma subtype are shown in Fig 2. There were 3 low FA lesions versus 6 high FA lesions in the meningothelial subtype (ratio-1:2) (Supplementary Fig 1); 9 low FA versus 6 high FA among transitional meningiomas (ratio-1.5:1); 6 low FA versus 8 high FA in chordoid (ratio-1:1.3); 7 low FA versus 1 high FA in the angiomatous variant (ratio-7:1); 1 low FA versus 16 high FA in fibroblastic (1:16) (Supplementary Fig 2) and 6 low FA versus 14 high FA among atypical meningiomas (1:2.6) (Supplementary Fig 3). All 15 microcystic meningiomas belonged to the low FA category (Supplementary Fig 4). An unequivocal predominance of low FA lesions was seen in the angiomatous and microcystic variants, while all lesions of the fibroblastic category were of the high FA type. All other subgroups showed a heterogenous distribution of FA grades.

Comparison of qualitative FA grades between meningioma subtypes

Kruskall–Wallis test with Bonferroni correction for intergroup comparison revealed significantly lower qualitative FA grades (*P* value: .000-.026) in microcystic meningioma compared with all other subtypes except for transitional and angiomatous variants (Table 1). Fibroblastic, meningothelial and atypical meningiomas showed a trend towards high FA grades with statistically significant difference between fibroblastic meningioma and that of microcystic, transitional and angiomatous variants. The largest proportion of high FA grade was seen in fibroblastic meningioma—94% versus 70%, 66.67% and 57% in atypical, meningothelial and chordoid meningiomas, respectively; however, there was no statistically significant difference in FA grades among these subtypes.

The results of predictive ability of FA grade values for individual histopathological subtypes have been presented in odds ratio (Table 3). A higher FA grade (grades 3, 4) has



MENINGIOMA SUBTYPE	GRADE 1	GRADE 2	GRADE 3	GRADE 4
Meningothelial	1	2	6	0
Transitional	1	8	6	0
Chordoid	2	4	8	0
Angiomatous	4	3	1	0
Microcystic	9	6	0	0
Fibroblastic	0	1	11	5
Atypical	0	6	12	2

Figure 2 A bar graph showing the distribution of FA grades among meningioma subtypes: Note consistently low FA grades (1 and 2) in microcystic and angiomatous meningioma and high FA grades (3 and 4) in fibroblastic meningioma. Inset table on the right shows the exact number of FA grades in each meningioma subtype. FA, fractional anisotropy.

Table 1
Intergroup comparison of qualitative FA grades in meningioma subtypes using the Kruskall-–Wallis test with Bonferroni correction.

	Adjusted *P* value						
Subtype	Meningothelial	Transitional	Microcystic	Chordoid	Angiomatous	Fibroblastic	Atypical
Meningothelial	-	1.000	**0.028**	1.000	0.521	1.000	1.000
Transitional	1.000	-	0.107	1.000	1.000	**0.045**	1.000
Microcystic	***0.028**	0.107	-	**0.028**	1.000	**0.000**	**0.000**
Chordoid	1.000	1.000	**0.028**	-	0.749	0.230	1.000
Angiomatous	0.521	1.000	1.000	0.749	-	0.000	**0.026**
Fibroblastic	1.000	**0.045**	**0.000**	0.230	**0.000**	-	1.000
Atypical	1.000	1.000	**0.000**	1.000	**0.026**	1.000	-

Significant p *P* alues are highlighted in bold.
FA, ractional anisotropy

5.76 times higher odds of having atypical morphology and 15.78 times higher odds of having a fibroblastic morphology compared with those with lower FA grades (grades 1, 2).

Other histopathological subtypes were not found to have a statistically significant association with dichotomised FA grade. Microcystic morphology could not be tested due to the absence of the same in samples with low FA grades.

Histogram analysis

Table 2 shows the descriptive values of quantitative FA metrics for each histopathological subtype. The typical features of representation of any given histogram analysis of pixel intensities of an image, viz, minimum, maximum, mean pixel intensities of the FA maps is depicted. Also the gradient of pixel intensity distribution across the various percentiles, viz, 10, 25, 50, 75, 95 and 99 has been highlighted to represent the kurtosis. The median FA grade which was subjectively visually/manually estimated by the readers is presented for a reference, to compare it with PC50 that was estimated by the radiomic analysis. Discriminatory ability of quantitative FA values (min, max, mean and median) for all histopathological subtypes using area under ROC (AUC) has been summarised in Table 4. For fibroblastic morphology, min, mean and median FA values showed statistically significant AUCs. For microcystic morphology, all FA metrics showed significant AUCs. None of the other morphologies were reliably discriminated by quantitative FA metrics.

The threshold values for median FA to discriminate fibroblastic morphology (against all other morphologies) was found to be 0.239 (sensitivity = 0.75 and specificity = 0.68). The same for microcystic morphology was found to be 0.16 (sensitivity = 0.83 and specificity = 0.77).

All quantitative FA values were found to be significantly correlated with qualitative FA grades as assigned by the interpreting radiologist (Table 5). However, the strength of correlation for all metrics was moderate and positive.

Discussion

The grade and histopathological subtype determine the management strategy and recurrence rates of meningioma.[13] Besides a role in surgical planning, recommendation of conservative management with observation for incidentally detected, asymptomatic meningiomas[14] makes it pertinent to identify various imaging correlates of the histopathological subtype and avoid unnecessary surgical intervention. In the current study, we devised a qualitative scale for grading the degree of fractional anisotropy in meningiomas which showed good interobserver reproducibility. We validated the qualitative scale of assessment with quantitative histogram analysis of FA matrices. We emphasise on the utility of qualitative visual grading scale in routine clinical practice since it can be promptly be done on visual inspection without sophisticated computational analysis and gives a fairly consistent representation of the quantitative FA characteristics. Low FA grade was observed in all cases of microcystic meningioma,

Table 2
Table showing summary of the mean histogram features of quantitative FA metrics for various histopathological subtypes of meningioma, with feature ranges indicated in parentheses.

Histogram features	Angiomatous	Atypical	Chordoid	Fibroblastic	Microcystic	Others	Transitional
Minimum	0.05 (0.03–0.05)	0.09 (0.04–0.16)	0.03 (0.02–0.06)	0.06 (0.05–0.07)	0.02 (0.02–0.05)	0.06 (0.05–0.07)	0.04 (0.04–0.07)
Maximum	0.44 (0.32–0.55)	0.60 (0.31–0.65)	0.34 (0.25–0.41)	0.41 (0.35–0.46)	0.21 (0.19–0.26)	0.43 (0.38–0.6)	0.42 (0.36–0.59)
Mean	0.24 (0.16–0.30)	0.38 (0.16–0.43)	0.19 (0.13–0.26)	0.26 (0.23–0.30)	0.09 (0.08–0.15)	0.25 (0.21–0.27)	0.20 (0.18–0.24)
PC10	0.15 (0.08–0.18)	0.25 (0.10–0.32)	0.11 (0.06–0.15)	0.15 (0.13–0.18)	0.06 (0.04–0.08)	0.13 (0.12–0.15)	0.11 (0.09–0.13)
PC25	0.18 (0.11–0.23)	0.31 (0.13–0.38)	0.14 (0.09–0.19)	0.20 (0.18–0.24)	0.07 (0.06–0.11)	0.17 (0.15–0.21)	0.15 (0.13–0.17)
PC50	0.24 (0.15–0.30)	0.38 (0.16–0.43)	0.19 (0.13–0.25)	0.26 (0.23–0.30)	0.09 (0.08–0.14)	0.23 (0.20–0.27)	0.20 (0.18–0.22)
PC75	0.29 (0.20–0.37)	0.46 (0.20–0.49)	0.23 (0.17–0.31)	0.33 (0.30–0.36)	0.12 (0.10–0.17)	0.31 (0.25–0.33)	0.25 (0.22–0.29)
PC95	0.39 (0.29–0.47)	0.51 (0.26–0.56)	0.29 (0.22–0.39)	0.39 (0.34–0.43)	0.17 (0.15–0.24)	0.41 (0.35–0.45)	0.34 (0.31–0.42)
PC99	0.42 (0.31–0.52)	0.55 (0.29–0.61)	0.32 (0.24–0.40)	0.41 (0.35–0.46)	0.20 (0.17–0.26)	0.43 (0.38–0.53)	0.40 (0.35–0.50)
Median FA Grade	1.00 (1.00–2.50)	3.00 (3.00–4.00)	2.50 (2.00–3.75)	4.00 (3.00–4.00)	1.00 (1.00–2.00)	3.00 (2.00–3.00)	2.00 (2.00–3.00)

PC: Percentile; FA, ractional anisotropy.

Table 3
Table showing the odds ratio of the individual histopathological subtypes against the rest of the histopathological subtypes based on the FA grade.

Histopathology	OR (95% CI)	*P* value
Angiomatous	0.36 (0.05–1.82)	0.246
Atypical	5.76 (1.34–40.06)	0.034
Chordoid	1.00 (0.25–3.95)	1.000
Fibroblastic	15.78 (2.78–298.62)	0.011
Others	1.55 (0.24–12.36)	0.644
Transitional	0.51 (0.12–1.90)	0.329

CI, confidence interval; FA, ractional anisotropy; OR: odds ratio. The table represents the effects derived from binary logistic regression models with each histopathology of meningioma (relative to all other histopathologies) being predicted by a higher FA grade (grade 3/4). The results are presented as odds ratios with 95% confidence intervals. For example, a higher FA grade increases the chances of the meningioma having a atypical histopathology 5.76 times higher than any other subtype.

Table 5
Table showing Spearman's rho for correlation of quantitative FA values with qualitative FA grades.

	Rho	*P* value
Min	0.473	<0.001
Max	0.411	<0.001
Mean	0.502	<0.001
PC10	0.497	<0.001
PC25	0.500	<0.001
PC50	0.498	<0.001
PC75	0.505	<0.001
PC95	0.446	<0.001
PC99	0.423	<0.001

FA, ractional anisotropy; PC: Percentile.

angiomatous subtypes and in few cases of transitional variants. Although there was a predominance of low FA lesions among transitional meningiomas, it is a relatively heterogenous subgroup compared with microcystic and angiomatous variants. Both fibroblastic and atypical meningioma showed high FA grades with few showing grade 2 and no grade 1 patterns. More than half of the cases of meningothelial and chordoid meningiomas showed FA grades higher than 2 with no significant difference when compared with the fibroblastic and atypical meningiomas.

The findings from our study can partly be explained by differences in tissue architecture at the microscopic level which leads to changes in fractional anisotropy. Fractional anisotropy represents the directional asymmetry of diffusion of water molecules in a given tissue. It depends on the number, density and arrangement of cells and thus varies with cellularity and tissue architecture. Besides the cellular component, the extracellular matrix and its arrangement also plays a major role in determining the pattern of diffusion in various directions and thus the degree of fractional anisotropy. FA is thus sensitive to changes in tissue structure at the microscopic level.[25] The correlation of FA and ADC is relatively obscure. In gliomas, where FA has been extensively studied, other histologic characteristics apart from cellularity, vascularity, cell density, neuronal/axonal structures influence FA.[26]

Due to different cellular structures and organisation of the extracellular matrix in various meningioma subtypes, it is plausible that these microstructural differences will reflect as different imaging signatures. Earlier studies showed a correlation between the T2 signal intensity and consistency of meningiomas.[8,27,28] All these studies have unanimously shown that higher the signal intensity on T2, softer is the meningioma. T2 hypointense lesions are usually fibroblastic, while those with high T2 signal intensity are usually angiomatous or meningothelial variants. Transitional meningiomas tend to be isointense and of a harder consistency than meningothelial and angiomatous subtypes.

The lack of linear or whorl-like arrangement of meningothelial cells, vacuolation and loose myxoid matrix with extracellular microcysts may be responsible for the near isotropic diffusion seen in microcystic meningioma.[29] It is to be noted that prior work has categorically stated that diffusion restriction is a striking finding in microcystic meningioma, despite it being a grade I tumour. In this context, the results of the current work assume importance, in that, despite a diffusion restriction (low ADC), a characteristic low FA that we describe may be a unique imaging feature of this lesion. Also, this observation is an exception to the general axiom that low ADC roughly scales with high FA, underscoring the influence of tissue architecture to FA.[30] In angiomatous meningioma, although the cells are arranged in whorls around blood vessels, high vascularity of the lesion with more than half of the tumour volume occupied by vessels[29] may lead to reduced anisotropy. The low FA in microcystic and angiomatous meningioma acquires even more significance because the presence of extensive peritumoural edema in these lesions[31] may lead to suspicion of a high-grade lesion. Microcystic and angiomatous subtypes show similarity in features at the micro as

Table 4
Table showing area under receiver operating characteristic curves and 95% confidence levels for discriminatory ability of quantitative FA values for individual morphologies.

	Min	Max	Mean	Median
Angiomatous	0.45 (0.21–0.68)	0.58 (0.35–0.80)	0.55 (0.30–0.79)	0.55 (0.30–0.79)
Atypical	0.67 (0.45–0.88)	0.63 (0.42–0.84)	0.68 (0.49–0.87)	0.69 (0.49–0.88)
Chordoid	0.60 (0.38–0.82)	0.59 (0.41–0.77)	0.58 (0.38–0.78)	0.59 (0.40–0.79)
Fibroblastic	0.64 (0.51–0.78)	0.53 (0.40–0.67)	0.65 (0.51–0.78)	0.66 (0.52–0.79)
Others	0.66 (0.48–0.83)	0.63 (0.38–0.89)	0.57 (0.34–0.81)	0.56 (0.31–0.8)
Microcystic	0.76 (0.62–0.90)	0.80 (0.61–1.00)	0.80 (0.61–0.99)	0.79 (0.60–0.98)
Transitional	0.49 (0.32–0.66)	0.62 (0.46–0.78)	0.51 (0.35–0.67)	0.51 (0.35–0.67)

FA, ractional anisotropy.

well as macroscopic levels and the two components may coexist in a single lesion. The degree of peritumoural edema in a microcystic meningioma correlates with the extent of the angiomatous component.[30] Low FA in an otherwise aggressive looking meningioma with extensive edema and even diffusion restriction should suggest a grade I lesion especially the microcystic and angiomatous variants.

The histopathological features of transitional meningioma resemble those of meningothelial and fibroblastic subtypes with the presence of whorls and clusters of cells. A previous study also showed transitional meningioma to have a relatively hard consistency compared with other variants, although softer than fibroblastic meningioma.[28] In our study, although, transitional subgroup did trend towards low FA, it was a relatively heterogenous group compared with microcystic and angiomatous variants. The presence of spindle-shaped cells arranged in sheets with thick bundles of collagen in fibroblastic meningioma is likely responsible for the anisotropic pattern of diffusion.[1,29,32] Increased FA in atypical meningioma may be attributed to high cellular density with loss of lobular pattern and sheet-like random arrangement of cells.[29]

In a previous study, there was no significant difference in the mean ADC values and ADC ratio in relation to the normally appearing white matter between typical and atypical meningiomas. Meningothelial, fibroblastic and transitional meningiomas were the common histopathological subtypes in the benign category. There was no significant difference in these values within the benign subtypes as well. Qualitative grading of DWI signal intensity as hypointense, isointense and hyperintense to grey matter also did not show any correlation with meningioma grading.[33] In contrast to this, a multicenter study in which 389 patients were collected, showed significantly higher ADC values in grade 1 compared with grade 2/3 meningiomas.[34] Another study revealed an inverse correlation between ADC values and meningioma grade only at high b values of 4000 s/mm^2 performed at 3 Tesla.[6]

The results from our study suggest that fractional anisotropy is useful in predicting the grade and histopathological type of meningioma. One of the earliest studies based on FA showed that high FA values were associated with hard tumours. The FA values were significantly higher in fibroblastic meningioma compared with the meningothelial variant.[15] Another study showed that diffusion tensor imaging-derived metrics are unique in fibroblastic meningioma in view of fascicular arrangement of spindle-shaped cells leading to anisotropic diffusion.[22] Fibroblastic meningioma had high FA values with non-spherical tensors. Atypical meningioma showed higher linear anisotropy than fibroblastic meningioma; however, the difference did not reach statistical significance. Other subtypes including meningothelial meningioma showed predominantly isotropic diffusion in view of whorled arrangement of cells. Despite significant differences in FA, there was no significant difference in the mean diffusivity among various subtypes of meningioma. Although, our study also showed high FA grades in fibroblastic meningioma, there was considerable overlap with atypical meningiomas which showed predominantly high FA grades and transitional, meningothelial and chordoid meningiomas which were more heterogenous showing a mix of high as well as low FA lesions. On the other hand, microcystic and angiomatous variants almost entirely consisted of low FA grade lesions. This may be on account of the fact that the earlier study only included WHO grade 1 lesions comparing fibroblastic meningioma with all other benign variants grouped either into meningothelial or mixed lesions. In contrast, our study compared different types of grade 1 meningioma with each other as well as atypical meningiomas. Our results show that lesions with low FA are suggestive of a microcystic or angiomatous meningioma in spite of other aggressive features like extensive edema, while high FA grade is nonspecific and seen across several subtypes and grades of meningiomas.

In a study by Jolapara *et al.*,[26] significantly higher FA values and low spherical anisotropy were seen in atypical and fibroblastic meningioma compared with other benign subtypes with no differences in mean diffusivity. Another study comparing atypical meningioma with various grade 1 meningiomas using DTI revealed no difference between the groups on qualitative analysis. However, the mean FA values as well as the mean FA ratio with that of the contralateral normal white matter was significantly lower in the enhancing part of benign meningiomas compared with atypical meningioma.[35] The findings from our study are comparable with these studies showing overlap in qualitative FA grades between atypical and fibroblastic meningioma.

Previous studies as described have used complex quantitative metrics from diffusion tensor imaging and machine learning algorithms to distinguish subtypes of meningioma.[15,22,23,25] In this study, we devised a simplified qualitative scale for grading of FA in meningioma variants and evaluated its utility in distinguishing the histopathological subtypes of meningioma. This study shows that a simple, qualitative scale for grading fractional anisotropy is useful for distinguishing various meningioma subtypes. A qualitative scale is easy to implement with good interobserver reliability. It overcomes extensive post-processing and computational analysis. Since lesions are often heterogenous, proper measurement of DTI metrics like FA must ideally involve segmentation of the lesion. An ROI-based analysis from the region of highest FA alone may blur the distinction between meningioma subtypes by ignoring larger areas of low FA. A grading system based on overall appearance of the lesion is likely to overcome this limitation of an intralesional ROI-based analysis. Such a qualitative scale can easily be implemented in routine clinical practice even by a novice radiologist across several centres.

Our study had certain limitations. Firstly, it was a retrospective study with a small sample size in each meningioma subtype. Secondly, we did not have an adequate number of grade 3 meningiomas for comparison. Thirdly, fractional anisotropy is also affected by tumour vascularity in addition to cellular architecture, which was not considered in this study. The evaluation of brightness of the lesion on FA map, although qualitative, argues for applicability in a routine

clinical practice without the requirement for sophisticated tools for quantitation.

In conclusion, qualitative grading of FA maps is useful in predicting the meningioma subtype. Low FA is characteristically seen in microcystic and angiomatous variants, while high FA grades are noted in fibroblastic and atypical meningiomas. Although other meningioma subtypes are heterogenous, low FA (grade 1 and 2) is essentially suggestive of a grade 1 meningioma even in the presence of otherwise aggressive features like extensive peritumoural edema. High FA within the tumour, although a consistent feature of fibroblastic variant, is nonspecific.

Author contribution

1. JS contributed as guarantor of integrity of the entire study.
2. JS, ShJ and KK contributed to study concepts and design.
3. PPB, ShJ, KK contributed to literature research.
4. PPB, KK, JS, SR, NBN and SKK contributed to clinical studies.
5. AI, JS contributed to experimental studies/data analysis.
6. AI and DC contributed to statistical analysis.
7. PPB, ShJ and KK contributed to manuscript preparation.
8. PPB, ShJ, KK, JS, AI, DC, SR, NBN and SKK contributed to manuscript editing.

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Conflict of interest

The authors declare no conflict of interest.

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Appendix A. Supplementary data

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References

1. 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**:584–92.
2. Louis DN, Ohgaki H, Wiestler OD, *et al*. The 2007 WHO classification of tumours of the central nervous system. *Acta Neuropathol* 2007;**114**:97–109.
3. Willis J, Smith C, Ironside JW, *et al*. The accuracy of meningioma grading: a 10-year retrospective audit. *Neuropathol Appl Neurobiol* 2005;**31**:141–9.
4. Riemenschneider MJ, Perry A, Reifenberger G. Histological classification and molecular genetics of meningiomas. *Lancet Neurol* 2006;**5**:1045–54.
5. Lin BJ, Chou KN, Kao HW, *et al*. Correlation between magnetic resonance imaging grading and pathological grading in meningioma. *J Neurosurg* 2014;**121**:1201–8.
6. Watanabe Y, Yamasaki F, Kajiwara Y, *et al*. Preoperative histological grading of meningiomas using apparent diffusion coefficient at 3T MRI. *Eur J Radiol* 2013;**82**:658–63.
7. Suzuki Y, Sugimoto T, Shibuya M, *et al*. Meningiomas: correlation between MRI characteristics and operative findings including consistency. *Acta Neurochir (Wien)* 1994;**129**:39–46.
8. Chen TC, Zee CS, Miller CA, *et al*. Magnetic resonance imaging and pathological correlates of meningiomas. *Neurosurgery* 1992;**31**:1015–21. discussion 1021-1012.
9. Basser PJ, Pierpaoli C. Microstructural and physiological features of tissues elucidated by quantitative-diffusion-tensor MRI. *J Magn Reson B* 1996;**111**:209–19.
10. Beppu T, Inoue T, Shibata Y, *et al*. Measurement of fractional anisotropy using diffusion tensor MRI in supratentorial astrocytic tumors. *J Neurooncol* 2003;**63**:109–16.
11. Beppu T, Inoue T, Shibata Y, *et al*. Fractional anisotropy value by diffusion tensor magnetic resonance imaging as a predictor of cell density and proliferation activity of glioblastomas. *Surg Neurol* 2005;**63**:56–61. discussion 61.
12. Lu S, Ahn D, Johnson G, *et al*. Peritumoral diffusion tensor imaging of high-grade gliomas and metastatic brain tumors. *AJNR Am J Neuroradiol* 2003;**24**:937–41.
13. Modha A, Gutin PH. Diagnosis and treatment of atypical and anaplastic meningiomas: a review. *Neurosurgery* 2005;**57**:538–50. discussion 538-550.
14. Goldbrunner R, Minniti G, Preusser M, *et al*. EANO guidelines for the diagnosis and treatment of meningiomas. *Lancet Oncol* 2016;**17**:e383–91.
15. 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**:784–7.
16. Surov A, Gottschling S, Mawrin C, *et al*. Diffusion-weighted imaging in meningioma: prediction of tumor grade and association with histopathological parameters. *Transl Oncol* 2015;**8**:517–23.
17. Bano S, Waraich MM, Khan MA, *et al*. Diagnostic value of apparent diffusion coefficient for the accurate assessment and differentiation of intracranial meningiomas. *Acta Radiol Short Rep* 2013;**2**. 2047981613512484.
18. Nagar VA, Ye JR, Ng WH, *et al*. Diffusion-weighted MR imaging: diagnosing atypical or malignant meningiomas and detecting tumor dedifferentiation. *AJNR Am J Neuroradiol* 2008;**29**:1147–52.
19. Abdel-Kerim A, Shehata M, El Sabaa B, *et al*. Differentiation between benign and atypical cranial Meningiomas. Can ADC Mmeasurement help? MRI findings with hystopathologial correlation. *Egypt J Radiol Nucl Med* 2018;**49**:172–5.
20. Provenzale JM, Isaacson J, Chen S, *et al*. Correlation of apparent diffusion coefficient and fractional anisotropy values in the developing infant brain. *AJR Am J Roentgenol* 2010;**195**:W456–62.
21. Ahrendsen JT, Alexandrescu S. WHO grading of meningiomas. In: Morris ME, Cai C, editors. *2002-2023, PathologyOutlines.com*. Inc.; 2023.
22. White ML, Zhang Y, Yu F, *et al*. Diffusion tensor MR imaging of cerebral gliomas: evaluating fractional anisotropy characteristics. *AJNR Am J Neuroradiol* 2011;**32**:374–81.
23. 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**:1630–5.
24. Fedorov A, Beichel R, Kalpathy-Cramer J, *et al*. 3D slicer as an image computing platform for the quantitative imaging network. *Magn Reson Imaging* 2012;**30**:1323–41.
25. Tropine A, Dellani PD, Glaser M, *et al*. Differentiation of fibroblastic meningiomas from other benign subtypes using diffusion tensor imaging. *J Magn Reson Imag* 2007;**25**:703–8.
26. Jolapara M, Kesavadas C, Radhakrishnan VV, *et al*. Role of diffusion tensor imaging in differentiating subtypes of meningiomas. *J Neuroradiol* 2010;**37**:277–83.

27. Park YW, Oh J, You SC, *et al*. Radiomics and machine learning may accurately predict the grade and histological subtype in meningiomas using conventional and diffusion tensor imaging. *Eur Radiol* 2019;**29**:4068–76.
28. Alexander AL, Lee JE, Lazar M, *et al*. Diffusion tensor imaging of the brain. *Neurotherapeutics* 2007;**4**:316–29.
29. Carpeggiani P, Crisi G, Trevisan C. MRI of intracranial meningiomas: correlations with histology and physical consistency. *Neuroradiology* 1993;**35**:532–6.
30. Maiuri F, Iaconetta G, de Divitiis O, *et al*. Intracranial meningiomas: correlations between MR imaging and histology. *Eur J Radiol* 1999;**31**:69–75.
31. Cai C. Meningioma. In: Martinez-Lage M, editor. *2002-2023, PathologyOutlines.com*. Inc.; 2023.
32. Azizyan A, Eboli P, Drazin D, *et al*. Differentiation of benign angiomatous and microcystic meningiomas with extensive peritumoral edema from high grade meningiomas with aid of diffusion weighted MRI. *Biomed Res Int* 2014;**2014**:650939.
33. Kleihues P, Cavenee WK. *Pathology and genetics of tumours of the nervous system*. 3 ed. Lyon: International Agency for Research on Cancer; 2000.
34. Santelli L, Ramondo G, Della Puppa A, *et al*. Diffusion-weighted imaging does not predict histological grading in meningiomas. *Acta Neurochir (Wien)* 2010;**152**:1315–9. discussion 1319.
35. Surov A, Ginat DT, Sanverdi E, *et al*. Use of diffusion weighted imaging in differentiating between maligant and benign meningiomas. A multicenter analysis. *World Neurosurg* 2016;**88**:598–602.