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Can CT and MRI features differentiate benign from malignant meningiomas?☆

F. Salah [a,1], A. Tabbarah [b,1], N. ALArab y [a], K. Asmar [a], H. Tamim [c], M. Makki [c], A. Sibahi [d], R. Hourani [a,*]

[a] Department of Diagnostic Radiology, American University of Beirut Medical Center, Beirut, Lebanon
[b] Department of Pathology and Laboratory Medicine, American University of Beirut Medical Center, Beirut, Lebanon
[c] Biostatistics Unit, Clinical Research Institute, American University of Beirut Medical Center, Beirut, Lebanon
[d] Department of Biomedical Engineering, American University of Beirut, Beirut, Lebanon

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AIM: To highlight magnetic resonance imaging (MRI) and computed tomography (CT) characteristics in distinguishing benign from high-grade meningiomas (World Health Organization [WHO] grade II and III) preoperatively.

MATERIALS AND METHODS: Seventy-one patient who underwent surgical resection of intracranial meningiomas at American University of Beirut Medical Center between 2008 and 2017 were evaluated for various CT and MRI features. The correlation between imaging findings, histopathological grading, and operative reports was analysed via univariate and multivariate logistic regression analysis. MRI specificity and sensitivity in detecting meningioma brain invasion as compared to operative reports post-resection was detected.

RESULTS: Univariate analysis results showed a significant correlation between high-grade meningiomas and several MRI features including tumour size and volume (p=0.002,0.02), heterogeneous enhancement (p<0.0001), presence of intra-tumoural necrosis (p<0.0001), ill-defined margin (p=0.003), bone erosion (p=0.004), brain invasion (p=0.001), and a higher rate of recurrence (p=0.007) Only brain invasion and presence of intra-tumoural necrosis were significantly correlated with the high-grade meningioma in multivariate analysis. Hyperostosis of the adjacent skull was the only significant CT feature predicting the presence of low-grade meningioma. MRI showed 79% specificity and 20% sensitivity, 92% negative predictive value and 7% positive predictive value in detecting meningioma brain invasion.

CONCLUSION: MRI has a promising role in predicting meningioma grade prior to resection, which can directly impact patients' management protocols regarding surgical planning and complications.

Introduction

Meningiomas are the most frequent primary tumours of the central nervous system (CNS). They are tumours arising from the meningothelial cells of the arachnoid layer.[1,2] The World Health Organization (WHO) classification of CNS

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* Guarantor and correspondent: R. Hourani, Department of Diagnostic Radiology, American University of Beirut Medical Center, Riad El Solh 1107 2020, P.O.Box: 11-0236 Beirut, Lebanon. Tel.: + 961 1 350 000; fax: + 961 1 744 464.

E-mail address: rh64@aub.edu.lb (R. Hourani).

[1] These authors contributed equally as first authors of this manuscript.

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tumours stratifies meningiomas into three major groups. WHO grade I meningiomas are typical or benign (88–94%), grade II are atypical (5–7%), and grade III are anaplastic or malignant (1–2%).[1,3]

Although mostly benign, meningiomas still represent a major challenge to neurosurgeons and other medical disciplines involved in their diagnostic and therapeutic management. Neuroimagining features on CT and MRI have been found to differentiate benign from malignant meningiomas. These features include intratumoural cystic change; hyperostosis of the adjacent skull; bony destruction; extracranial tumour extension through the skull base; arterial encasement; and peritumoural brain oedema.[4] The apparent diffusion coefficient (ADC) values of benign and malignant meningiomas have also been compared.[5] Unfortunately, many of these neuroimaging comparative studies had limitations. These limitations included small sample size, subjectivity in assessment of some variables such as the peritumoural oedema, or were based on comparing a single imaging characteristic between benign and malignant meningiomas.[5,6] None of the previous studies had analysed both the quantitative and qualitative CT and MRI features at the same time.

The histological appearance of a meningioma is an important predictor of tumour behavior and is frequently a factor in decisions concerning therapy. As modern techniques have greatly improved the prognosis of meningioma patients, the value of clear grading criteria for meningiomas via brain imaging is important to determine the best management protocol and reduce the risk of complications during and after surgery. One of the most important aggressive behaviours of meningioma that need to be addressed preoperatively is brain invasion. Hence, the primary aim of this study is to differentiate meningioma grade by analysing both quantitative and qualitative imaging features on MRI and CT. The secondary aim is to assess the sensitivity, specificity, and positive and negative predictive values of MRI in detecting brain invasion by meningioma as compared to the operative report findings.

Materials and methods

Patient selection

After the approval of this retrospective study by the institutional review board (IRB), records of all patients who underwent total or partial surgical resection for meningiomas between 2008 and 2017 were reviewed. The study involved patients with intracranial meningioma as determined by both MRI and CT images who then underwent surgical resection with WHO grade I, II, and III meningioma histopathology results. Patients who lacked good-quality imaging prior to resection as well as cases with spinal meningiomas were excluded.

Seventy-one patients were assembled into two groups (benign versus high-grade meningioma). Twenty-five patients with confirmed WHO grade II or III meningioma were detected and grouped as high-grade tumours Group 2 (GP2). A cohort of 46 patients with histologically confirmed WHO grade I (benign) meningiomas were randomly selected from consecutive institutional cohort of 300 patients with meningiomas for comparison using a random number generator. These benign tumours comprised Group 1 (GP1).

To note that all cases underwent full resection except for six cases. Three of the latter cases were invading the superior sagittal sinus, two were invading the optic nerve, and one was extending into the left cavernous sinus; thus their total resection was not achieved by the neurosurgeons. None of the cases included were biopsy-confirmed cases. It is estimated that 15% of the total encountered cases between 2008 and 2017 were not removed due to either small size of the meningioma, patient choice, or certain medical issues. This further highlights the need for a non-invasive prediction of meningioma grade for adequate treatment planning for these patients.

Image interpretation

All available preoperative imaging of the selected patients was analysed. About one-third of these patients (22 patients) obtained a limited MRI navigation protocol including axial and coronal thin cuts post-contrast T1-weighted images (WIs) of the brain. The remaining two-thirds underwent complete brain MRI. MRI was performed randomly on a 1.5 or 3 T Philips Ingenia MR System (Philips Healthcare, Best, The Netherlands). For both field strengths, the imaging protocols included: two three-dimensional (3D) T1 turbo echo sequences (repetition time [TR]=8.3 ms, echo time [TE]=3.8ms, flip angle=8°, matrix size=240×222, field of view [FOV]=24×24×17 cm^2, section thickness=1 mm, gap=0 mm) with and without gadolinium injection (0.1mmol/kg).

A 3D fluid-attenuated inversion recovery (FLAIR) sequence (TR=4,800 ms, TE=347 ms, TI=1660, matrix size=224×224, FOV=25×25×17 cm^2, section thickness=1.1 mm, gap=−0.56 mm) of the whole brain with multiplanar reconstruction. Axial T2-weighted fast spin-echo (TR=6,449 ms, TE=100 ms, matrix size=348×240, FOV=24×24 cm^2, section thickness=3 mm, gap=1 mm) and axial diffusion-weighted imaging (DWI) single-shot spin-echo echo-planar DWI sequence was performed with two b-values (b=0 and b=1,000 s/mm^2; TR=2,300 ms; TE=75 ms). CT prior to resection was made available in 18 patients; in four of these, CT was the only source of imaging available. The images were interpreted retrospectively by a senior radiology resident in training and a fellowship trained neuroradiologist (>15 years of experience).

Both MRI and CT images before surgical resection were evaluated and assessed for tumour size, location, margin, degree of enhancement (mild, moderate or strong), as well as presence or absence of intra-tumour cystic change or necrosis, dural tail, hyperostosis in the adjacent skull, bone erosion, extracranial extension through skull, peritumoural oedema, brain or dural venous sinus invasion.

Tumour size was defined as the longest diameter of the mass. Tumour locations were grouped into four sites:

midline (olfactory groove), convexity (including frontal, parietal, temporal, occipital), posterior fossa, and others (intraventricular, suprasellar). The tumour margin was classified as either well defined, when the tumour–brain interface was smooth with no significant lobulations, or ill-defined when the interface was irregular and lobulate. A complete peritumoural rim of cerebrospinal fluid (CSF) was considered present if a T2 hyperintense, T1 hypointense CSF cleft is seen between the tumour and the brain7 Whereas brain invasion was described based on the lack of ability to draw a sharp definite boundary between the tumour and the surrounding brain tissue. The presence of peritumoural oedema was determined based on presence of hyperintense T2 and hypointense T1 signal on MRI or surrounding hypodensity on CT. Philips Intellispace Portal 7.0 software (Philips, Best, the Netherlands) was used for volumetric measurements of both the tumour and the peritumoural oedema. A volume ratio (oedema volume/tumour volume) was also calculated. All volumetric measurements were performed by two operators and verified by a neuroradiologist, using the tumour tracking tool on Intellispace with the integrated volumetric calculator.

Additional features examined on MRI included tumour signal intensity on T2WI, T1WI, and DWI, enhancement pattern on post-contrast T1WI, and ADC values of tumour relative to normal brain tissue. The signal intensity of the tumour was characterised as hyper, iso, or hypointense compared to normal brain grey matter. A uniform equal enhancement pattern was classified as homogeneous, whereas a variable enhancement pattern was classified as heterogeneous. Tumour necrosis was specifically noted if a T2 hyperintense non-enhancing area is present within the tumour. Furthermore, two additional parameters were studied using CT imaging only. Those were the presence of intra-tumour calcifications and tumour density relative to brain parenchyma on pre-contrast images.

Selected patients were followed up annually looking for tumour recurrence just after the first surgical resection up to the closure of this study. Tumour recurrence was defined as interval appearance of a new tumour at same surgical site after documented complete resection by a previous post-operative MRI/CT.

Chart review

The patients' charts were retrieved from the medical records and were reviewed for age, recurrent admissions, and operative and pathology reports. Operative reports were assessed for presence or absence of brain invasion based on whether the tumour breached the arachnoid membrane or pia and inseparable from the brain at the time of surgery.

Histopathology analysis

The pathology specimens were examined by a fellowship-trained board-certified neuropathologist who characterised them according to the 2016 WHO classification of meningioma. Cases were assigned to three histological categories including grade I (benign meningioma), grade II (atypical meningioma), and grade III (anaplastic meningioma).

A diagnosis of atypical meningioma was established in tumours with elevated mitotic activity ($\geq$4 mitoses/10 high-power fields) or brain invasion. Alternatively, the diagnosis was also established in the presence of three of the following parameters: increased cellularity, sheeting, small cell change, prominent nucleoli, presence of spontaneous necrosis. On the other hand, a diagnosis of anaplastic meningioma was reported in tumours exhibiting markedly elevated mitotic activity reaching $\geq$20 mitoses/10 high-power fields and/or the presence of overtly malignant cytology. Most anaplastic meningiomas usually show extensive necrosis, but necrosis itself is not considered a grading criterion. Furthermore, chordoid and clear cell histological variants are considered WHO grade II while papillary and rhabdoid variants are considered WHO grade III.

Statistical analysis

The Statistical Package for Social Sciences (SPSS), version 24.0 was used for data cleaning, management, and analyses. Results were reported as mean and standard deviation (SD) for continuous variables and number and percentage for categorical variables. The association between the categorical variables was carried out by using the chi-square test. Student's *t*-test was used for the association with continuous variables. Multivariate regression analysis was used to adjust for potentially confounding variables. Goodness of fit of the obtained logistic regression model was measured by Hosmer and Lemeshow. The sensitivity, specificity, and positive and negative predictive values (PPV and NPV) of MRI in detecting brain invasion of the meningioma as compared to the peri-operative report findings were calculated. The results were presented as odds ratios (ORs) with 95% confidence intervals (CIs). A p-value of <0.05 was considered statistically significant.

Results

A total of 71 patients with meningioma were included in the present study. According to the pathological grading after surgical resection, 46 were considered WHO grade I (GP1; Fig 1a) whereas 21 were classified as WHO grades II and only four cases were WHO grade III (GP 2; Fig 1b; Table 1). Twenty-four cases were men (33.8%). GP1 included 17 men (37%) and 29 women (63%) with a mean age of 51.8±13.8 years. GP2 included seven men (28%) and 18 women (72%) with a mean age of 56.92±14.04 years (Table 1). Among the 71 cases, 67 underwent MRI whereas only 18 patients underwent CT.

As for the patients who underwent MRI, the presence of the heterogeneous pattern of enhancement ($p<0.001$), intratumoural cyst or necrosis ($p<0.0001$; Fig 2a and b), ill-defined tumoural margin ($p=0.003$), invasion of brain ($p=0.001$; Fig 3), bone erosion ($p=0.004$), and dural sinus invasion ($p=0.03$) were found to be significantly more

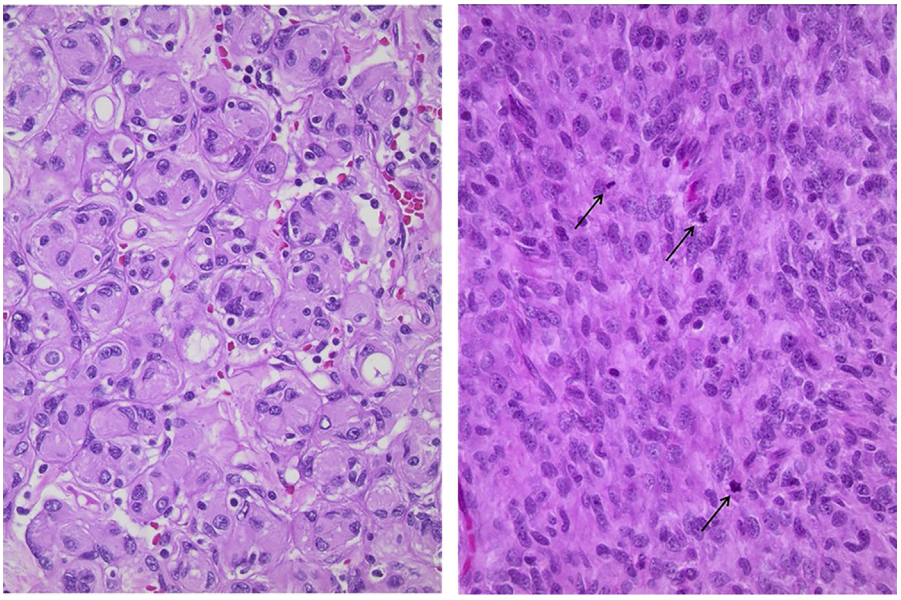

Figure 1 (a) Transitional meningioma, WHO grade I, with prominent whorl formation and inconspicuous mitotic activity. (b) Atypical meningioma, WHO grade II, with elevated mitotic activity (arrows) reaching 13 mitoses per 10 high-power fields. H&E stain, total magnification ×400.

frequent in high-grade meningioma (GP 2; Table 1). Interestingly, the presence of complete peritumoural rim of CSF on MRI was weekly significant (p=0.05) as 32 out of 46 cases in GP1 showed a complete rim (76.2%) compared to 50% of the cases in GP 2 (Table 1). Tumour size measured on MRI was also predictive of a higher grade (p=0.002). The mean size of meningioma in GP1 was 4±1.53 cm compared to 5.57±2.02 cm in GP2 (Table 1).

The mean tumour volume measured by MRI was 34.51±40.42 cm^3 in GP1 compared to approximately double the value in GP2 (64.88±53.88 cm^3), which suggests the volume of meningioma on MRI to be predictive of a higher grade (p=0.02; Table 1). Eleven cases (44%) of WHO grade II and III were recurrent meningiomas compared to only six (13%) in GP1 (Table 1). GP2 patients had a higher risk of recurrence (p=0.007). Pathology reports after surgical resection showed brain invasion in four cases (16%) in GP2 whereas none of the cases in GP1 showed any brain invasion (Table 1) with a statistically significant difference (p=0.01) between the two groups. All the other variables were not significantly different between cases in GP1 and GP2 with a p-value of >0.05 (Table 1).

The only CT feature that significantly correlated with the grade of the meningioma on the univariate analysis was hyperostosis of the adjacent skull (p=0.01). All of GP1 (nine patient) had hyperostosis compared to three patients (37.5%) in GP2. The other variables studied on CT show no significant statistical difference.

As shown in Table 2, a stepwise multivariate regression analysis was used to ascertain the association of confounding factors in predicting the grade of the meningioma. The multivariate regression included gender, age, and some variables on MRI including tumour volume, peri-tumoural oedema volume, presence of intratumoural necrosis, as well as detection of brain invasion by meningioma. Meningioma volume could be included in future studies to investigate the effect of other variables on it, after it was significantly higher in GP2 patients in the univariate analysis. The results showed that the presence of intratumoural necrosis and brain invasion were the only positive predictors of grade when controlling for other variables inserted in the model and the tumour volume was no longer considered a predictor for grade (p=0.82; Table 2). The presence of intratumoural necrosis was the strongest predictor of higher grade with a high OR (OR=12.22). Brain invasion was seven times more likely in high-grade meningiomas as compared to benign tumours. The goodness of fit for this model was tested showing a p-value of 0.242.

Furthermore, ability to detect the presence of brain invasion by meningioma at MRI was studied. MRI findings were compared to the operative report results. Table 3 shows 20% (15–71) sensitivity and 79% (67–88) specificity. The positive predictive value of MRI was 7% (0.3–36) and its negative predictive value was 92% (81–98).

Discussion

Multiple studies have tackled the correlation of specific imaging appearances with the grade of meningiomas after surgical resection. Such findings can go beyond providing a simple diagnosis of meningioma to predicting the tumour grade preoperatively, which offers helpful information to the clinicians and neurosurgeons working to determine the best management protocol.[8,9] For example, a tumour with imaging features favouring a benign meningioma can safely

Table 1
Association between demographics, magnetic resonance imaging (MRI) findings in grade I versus grade II and III.

Demographics *(N=71)*	Grade I *n* (±SD or%)	Grade II & III *n* (±SD or%)	*p*-Value
	n=46	*n=25*	
Age	51.80±13.80	56.92±14.04	0.19
Sex (male)	17 (37)	7 (28)	0.60
Recurrent tumour, *yes*	6 (13)	11 (44)	0.007[a]
Operative report brain invasion, *yes*	3 (6.5)	3 (12)	0.66
Pathology report brain invasion, *yes*	0 (0.00)	4 (16)	0.01[a]
MRI features (*N*=67)	*n=44*	*n=23*	
Tumour location			0.52
Midline	12 (27.3)	5 (21.7)	
Posterior fossa	5 (11.4)	1 (4.3)	
Convexity	26 (59.1)	15 (65.2)	
Others	1 (2.3)	2 (8.7)	
Tumour size	4.00±1.53	5.57±2.02	0.002[a]
T2 signal intensity			0.16
Isointense	7 (22.6)	0 (0)	
Hyperintense	24 (77.4)	12 (100)	
T1 signal intensity			0.09
Hypointense	9 (29)	7 (58.3)	
Isointense	22 (71)	5 (41.7)	
Enhancement pattern			<0.0001[b]
Homogeneous	34 (79.1)	6 (26.1)	
Heterogeneous	9 (20.9)	17 (73.9)	
Enhancement intensity			0.28
Mild/moderate	1 (2.3)	2 (8.7)	
Strong	42 (97.7)	21 (91.3)	
Dural tail, *yes*	36 (83.7)	19 (82.6)	1.00
Intratumoural necrosis, *yes*	9 (20.9)	18 (78.3)	<0.0001[b]
Complete peritumoural rim of CSF, yes	32 (76.2)	11 (50)	0.05[c]
Tumour margin			
Ill defined	0 (0)	5 (21.7)	0.003[a]
Well defined	44 (100)	18 (78.3)	
Bone erosion, *yes*	4 (9.8)	8 (44.4)	0.004[a]
Hyperostosis, yes	20 (45)	10 (40)	0.78
Extracranial tumour extension through the skull, *yes*	6 (13.6)	0 (0)	0.09
Peritumoural oedema, *yes*	27 (61.4)	19 (82.6)	0.10
Brain invasion, *yes*	3 (6.8)	11 (47.8)	0.001[a]
Dural sinus invasion, *yes*	9 (20.5)	11 (47.8)	0.03[c]
Diffusion signal			0.07
Isointense	13 (41.9)	1 (8.3)	
Hyperintense	18 (58.1)	11 (91.7)	
ADC value of tumour	851.90±148.94	888.42±458.69	0.32
ADC ratio	0.81±0.56	0.58±0.75	0.06
Tumour volume	34.51±40.42	61.52±67.52	0.02[c]
Oedema volume	52.75±55.41	64.88±53.88	0.33
Volume (oedema/tumour) ratio	1.11±1.70	1.36±1.42	0.17

[a] $p<0.01$.
[b] $p<0.001$.
[c] $p<0.05$.

undergo conservative measures such as interim observation. On the contrary, an atypical or malignant tumour prompts more aggressive measures including complete surgical resection or even radiation therapy.[10]

The results of the present study showed that the most significant findings to differentiate between the two groups included a heterogeneous pattern of enhancement (Fig 2b–d), as well as the presence of intra-tumoural cystic change or necrosis; both more described in GP2 meningiomas. This can further explain that both imaging features are correlated. Heterogeneous enhancement seen in meningiomas at MRI may be due to the presence of necrosis. Interestingly, these two features were reported as significantly associated with grade by the study of Coroller *et al.* as part of a total of four qualitative (semantic) predictors of meningioma grade.[11] In addition, intratumoural necrosis as well as cystic changes were found to be one of the main texture features obtained by radiomics feature-based machine classifiers, which play an important role in predicting high-grade tumours.[12]

Tumour necrosis was found to be present in 78% of patients in GP2. The most common mechanism for the described necrosis in meningioma is said to be hypoxia.[13] Necrosis originates from cellular nutritional insufficiency and hypoxia due to high metabolic demands suggesting that it may be related to a more aggressive progression.[14]

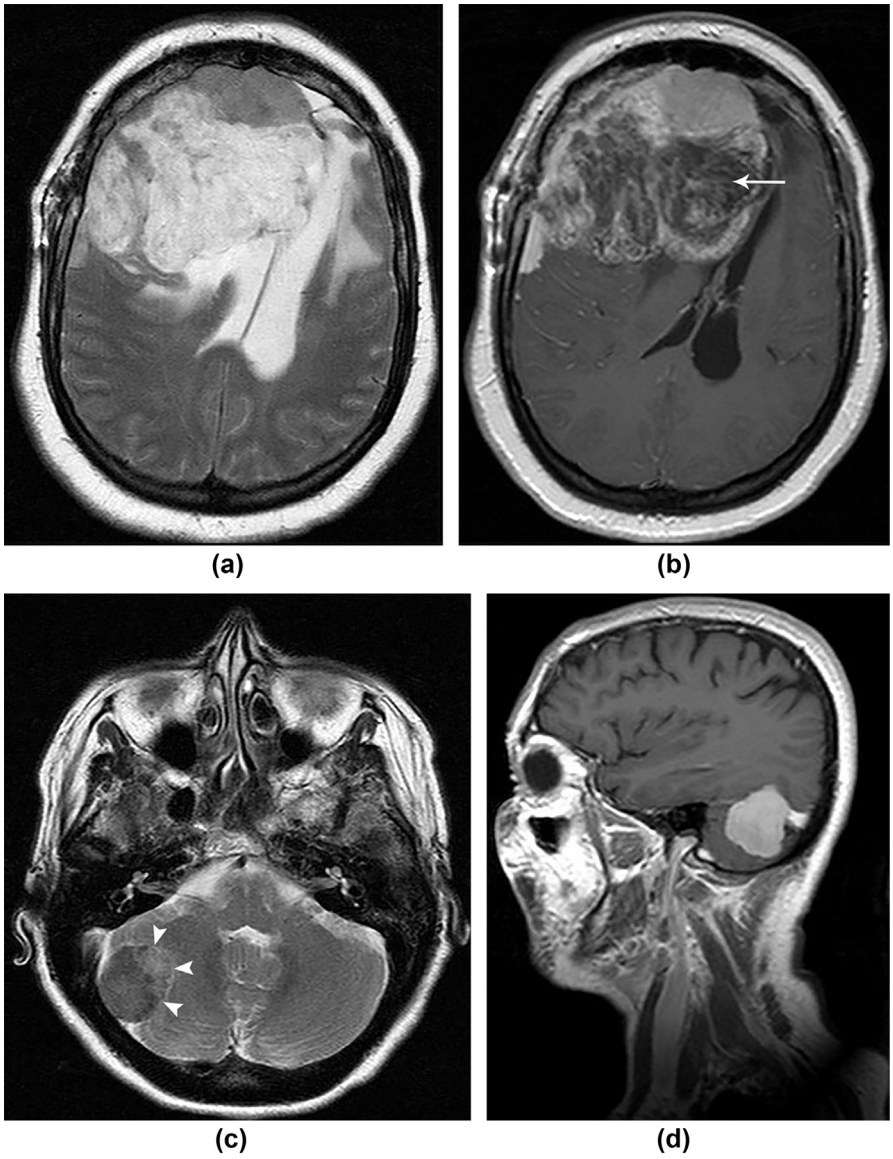

Figure 2 (a,b) Brain MRI of a 46-year-old female patient with grade III anaplastic meningioma. (a) Axial T2WI shows a large heterogeneous right frontal mass with mixed hyper and hypo signal and surrounding vasogenic oedema, mass effect and subfalcine herniation. (b) Axial contrast-enhanced T1WI demonstrates strong heterogeneous enhancement of the mass with areas of necrosis (white arrow). (c,d) Axial T2WI and sagittal enhanced T1WI of a 62-year-old female patient with grade I meningioma in the right aspect of the posterior fossa. The tumour has a well-defined borders, homogeneous signal, and enhancement with no evidence of intra-tumoural necrosis, bone erosion or brain invasion. There is a CSF rim between the mass and the cerebellum (white arrowheads).

Góes *et al.* found that benign meningiomas with atypical features such as necrosis are at a higher risk of progression and recurrence compared to those with benign tumours without atypical features.[15] Such lesions behave more similarly to those currently classified as WHO grade II meningioma.[15] It is worth noting that previous studies addressed primarily the presence of spontaneous necrosis as determined by histopathology; this study was one of the first to analyse gross necrosis evident radiologically rather than microscopically and study its impact on tumour grading.

In addition, larger tumour size and tumour volume were more likely to be observed in higher-grade meningiomas. The mean tumour volume in GP2 was almost double that of GP1, a finding that agreed with the literature.[8,9,11] Furthermore, a higher percentage of GP2 meningiomas were found to demonstrate bone erosion (44.4%), dural sinus invasion (47.8%), and brain tissue invasion (47.8%) on MRI. All of these described findings were similarly reported as significant in the grading of meningiomas in a previous study.[9] Although brain invasion is one of the criteria for diagnosis of high-grade meningiomas, it was observed in three benign cases (Table 1). In fact, the diagnosis of tumour adhesion using conventional MRI has rarely been effective[16] with false-positive results, thus non-invasive techniques have recently been used, such as brain surface motion imaging

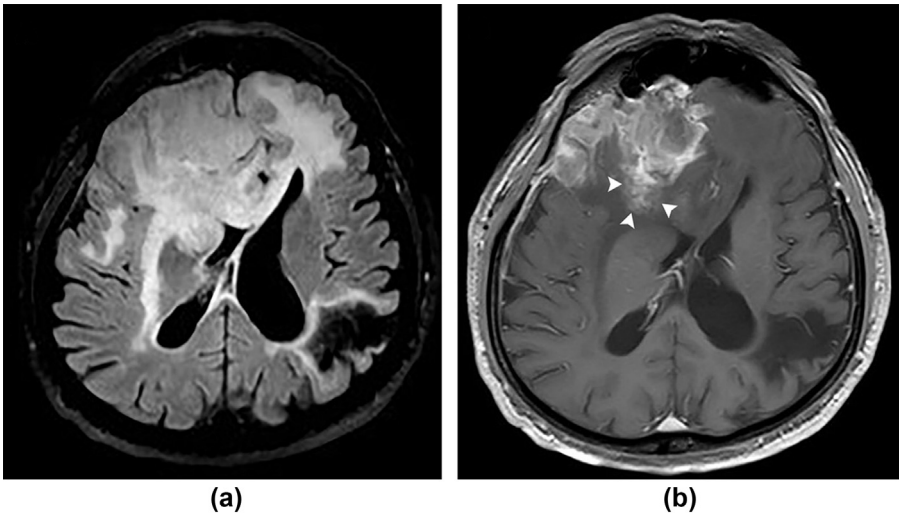

Figure 3 Brain MRI of a 75-year-old man with a recurrent grade II atypical meningioma. (a) Axial FLAIR and (b) enhanced T1WI showing a large right frontal ill-defined heterogeneous mass. There is no sharp definite boundary between the tumour and the surrounding brain tissue (white arrowheads).

(BSMI), which showed higher-accuracy prior to the surgery.[17]

Similarly, ill-defined margins were more often associated with high-grade meningiomas (Fig 3). The absence of a CSF rim separating the meningioma from brain parenchyma was suggested to represent a sign of higher-grade tumour due to the possibility of invasion of the adjacent brain parenchyma.[18] In the present study, the absence of a complete rim of CSF around the tumour, which suggests brain invasion, was found to be a weak predictor of high grade (p=0.05). In fact, the absence of a complete CSF rim is not a specific feature of brain invasion in high-grade meningioma unless ill-defined margins and an obvious insinuation of the tumour border into the brain parenchyma was seen on contrast-enhanced images.

Although peritumoural oedema has been repeatedly described in the literature as an important discriminating feature of atypical or malignant meningiomas, it was not found to be of significance in the present univariate or multivariate analysis. In fact, this study depended on quantitative volume measurements of the oedema rather than previously used subjective grading. Several studies have similarly suggested a rather weak relation between peritumoural oedema and grading.[9,19] This could be explained by the presence of moderate or severe oedema, a finding commonly described in grade II and III meningiomas, but also found in angiomatous and meningothelial meningiomas (two subtypes of grade I meningiomas)[20,21] (Fig 4). Although oedema may be the result of the invasive potential of meningioma, there are additional biological mechanisms involved in this phenomenon such as venous congestion and ischaemia from tumour mass effect.

The results revealed no significant differences in either the ADC value or the ADC ratio between the different grades of meningiomas. As a matter of fact, the use of ADC in meningioma is widely discussed in the literature showing different results.[9,22,23] The discrepant outcomes concluded from analysing ADC values in meningiomas advocate caution before application to real-life clinical scenarios.

In the present stepwise multivariate analysis, meningioma volume was not a valuable predictor after controlling for other variables shown in Table 2 although it was considered a striking predictor in a previous study.[8] Thus, if measured alone, tumour volume could not be considered a strong predictor for detecting meningioma grade. The presence of intratumoural necrosis and brain invasion on MRI was still a strong predictor for high-grade meningioma (p=0.003 and 0.02 respectively).

CT features studied showed no significant results except for presence of hyperostosis, which was seen in 100% of benign meningioma cases compared to 37.5% of those in GP2 (Electronic Supplementary Material Table. S1; Fig 5). On the other hand, Shaporaitis *et al.* mentioned that osseous changes, such as hyperostosis, are due to the osteoblastic activity associated with certain meningiomas, which may be related to the more rapid tumour growth. He added that thickening of the inner table of the skull has not been associated with tumour invasion but rather is a reactive change.[18] This finding was seen in further studies, which concluded that hyperostosis associated with meningiomas

Table 2
Stepwise multivariate analysis for the predictors of meningioma grading: grade II/III versus grade I.

Grade (reference: grade I)		
Variables	OR (95% CI)	p-Value
Volume of tumour	0.99 (0.87–1.12)	0.82
MRI brain invasion	7.71 (1.36–43.60)	0.02
MRI intra-tumoural necrosis	12.22 (2.311–64.58)	0.003

Variables included in the model were: imposed: volume of tumour (increase by 10 units); stepwise regression with the following covariates: age; gender (reference: male); volume of oedema (increase by 10 units); MRI intra-tumoural necrosis (reference: no); MRI brain invasion (reference: no).
MRI, magnetic resonance imaging; OR, odds ratio; CI, confidence interval.

Table 3
Results and comparison of brain invasion between magnetic resonance imaging (MRI) and the operative report.

		Operative report: brain invasion	
		No	Yes
MRI brain invasion	No	49 (73.1)	4 (6)
	Yes	13 (19.4)	1 (1.5)
Sensitivity and specificity		0.2 (0.15–0.71)	0.79 (0.67–0.88)
Positive and negative predictive value		0.07 (0.003–0.36)	0.92 (0.81–0.98)

involving the cranial base are caused by tumour invasion of the bone histologically.[24]

Adhesion or invasion of adjacent brain parenchyma by meningioma is a critical factor in surgical planning and the ability of MRI to detect invasion preoperatively is important for estimating difficulties and predicting complications at surgery.[17]

In the present study, MRI was found to have low sensitivity estimated to 20% with only one out of five cases of brain invasion detected preoperatively by MRI. Nevertheless, when indeed described on MRI, invasion was mostly specific of true infiltration of brain tissue intraoperatively with specificity of 79%. This implies that whenever a clear picture of brain invasion is seen at MRI, this finding is most likely present. On the contrary, if brain invasion was not detected, a physician cannot assert its absence. This was further emphasised by the fact that MRI showed a 92% negative predictive value; thus a high rate of patients not showing brain invasion on MRI will mean that surgeons will not encounter evidence of brain invasion intraoperatively. The 13 false-positive cases seen at MRI may be because those meningiomas were adherent to the arachnoid and leptomeninges rather than invading the brain itself.

Both a small sample size and the significant overlap in presenting features of benign and atypical meningioma were limitations of the present study. Additionally, the study was restricted to recruiting patients from one medical institution rather than multiple centres. The variability of the cohort was increased by increasing the age range and subtypes of meningioma. In addition, counting mitotic figures required for WHO histological grading is a process that is subject to considerable human error.

A strength of the present study was the variety of both CT and MRI features, which are seldom recognised in previously published papers. An additional strength was quantifying the volume of oedema rather than grading it subjectively, rendering the present results more accurate and objective. It would be interesting to use radiomics feature-based machine learning classifiers in tumour grading involving more advanced techniques in a multicentric study; however, its use is not available to all radiologists worldwide considering consideration the financial support, advanced software and machines, as well as the experience in artificial intelligence techniques that many institutions and centres lack. In the future, the plan is to collaborate with regional centres to increase the power of the study and implement new and advanced techniques, such as diffusion tensor imaging and radiomics.

In conclusion, large tumour size and volume along with heterogeneous enhancement on MRI, the presence of intratumoural necrosis, ill-defined margin, invasion of the brain and dural sinuses, as well as high recurrence rates

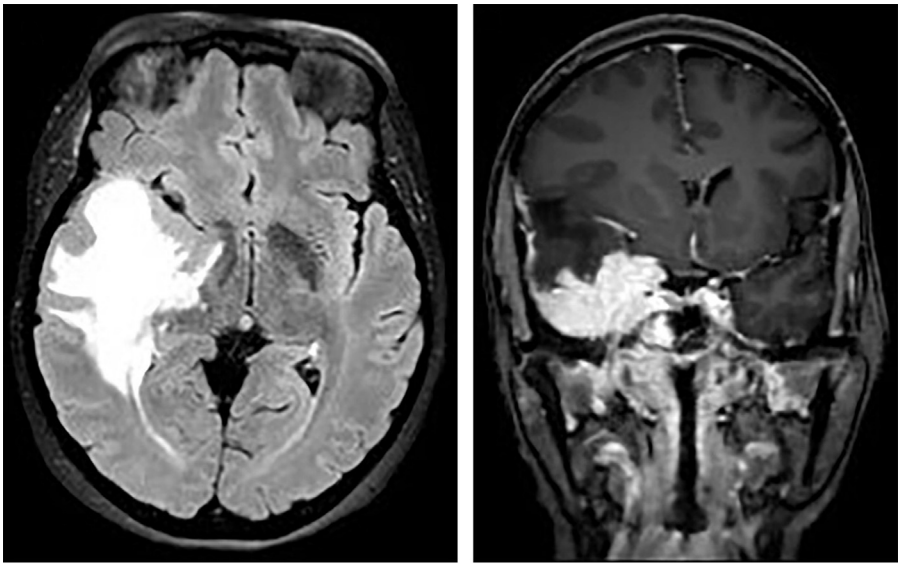

Figure 4 (a) Axial FLAIR and (b) coronal contrast-enhanced T1WI of the brain of a 58-year-old woman showing a lobulate well-defined right temporal mass with homogeneous enhancement. There is extensive peri-tumoural oedema with secondary mass effect on the right cerebral hemisphere and mild midline shift to the left. This tumour was categorised as a grade I meningioma (meningothelial subtype recognised for causing substantial vasogenic oedema despite its benign nature).

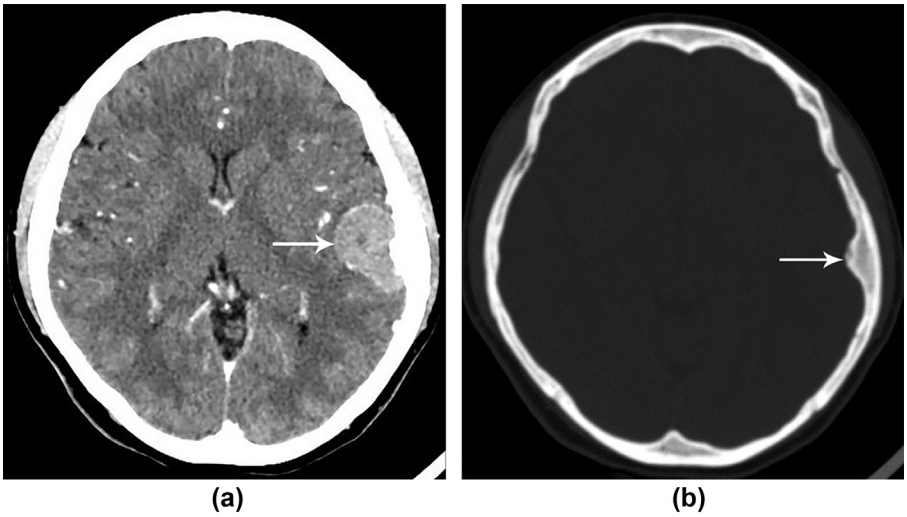

Figure 5 CT image of the brain of a 33-year-old man with grade I meningioma. (a) Axial enhanced CT (soft-tissue window) image showing left frontal extra-axial mass strongly enhancing (white arrow). (b) Bone window image at the same level showing underlying bony hyperostosis and thickening of the inner table of the skull (white arrow).

were all predictors for high-grade meningioma. MRI has a promising role in predicting meningioma grade prior to resection, which can directly impact future management protocols regarding surgical planning and complications.

Conflict of interest

The authors declare that they have no conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.crad.2019.07.020.

References

1. Louis DN, Perry A, Reifenberger G, *et al*. The 2016 world Health organization classification of tumours of the central nervous system: a summary. *Acta Neuropathol* 2016;**131**(6):803–20.
2. Mehdorn HM. Intracranial meningiomas: a 30-year experience and literature review. *Adv Tech Stand Neurosurg* 2016;**43**:139–84.
3. Strassner C, Buhl R, Mehdorn HM. Recurrence of intracranial meningiomas: did better methods of diagnosis and surgical treatment change the outcome in the last 30 years? *Neurol Res* 2009;**31**(5):478–82.
4. Hanft S, Canoll P, Bruce JN. A review of malignant meningiomas: diagnosis, characteristics, and treatment. *J Neurooncol* 2010;**99**(3):433–43.
5. Todua F, Chedia S. Differentiation between benign and malignant meningiomas using diffusion and perfusion MR imaging. *Georgian Med News* 2012;**206**:16–22.
6. Tanaka M, Imhof HG, Schucknecht B, *et al*. Correlation between the efferent venous drainage of the tumour and peritumoural oedema in intracranial meningiomas: superselective angiographic analysis of 25 cases. *J Neurosurg* 2006;**104**(3):382–8.
7. Nakano T, Asano K, Miura H, *et al*. Meningiomas with brain oedema: radiological characteristics on MRI and review of the literature. *Clin Imaging* 2002;**26**(4):243–9.
8. Hale AT, Wang L, Strother MK, *et al*. Differentiating meningioma grade by imaging features on magnetic resonance imaging. *J Clin Neurosci* 2018;**48**:71–5.
9. Lu Y, Liu L, Luan S, *et al*. The diagnostic value of texture analysis in predicting WHO grades of meningiomas based on ADC maps: an attempt using decision tree and decision forest. *Eur Radiol Eur Radiol.* 2019 Mar;**29**(3):1318–28.
10. Nabors LB, Portnow J, Ammirati M, *et al*. NCCN guidelines insights: central nervous system cancers, version 1.2017. *J Natl Compr Canc Netw* 2017;**15**(11):1331–45.
11. Coroller TP, Bi WL, Huynh E, *et al*. Radiographic prediction of meningioma grade by semantic and radiomic features. *PloS One* 2017;**12**(11):e0187908.
12. Yip SS, Aerts HJ. Applications and limitations of radiomics. *Phys Med Biol* 2016;**61**(13):R150.
13. Kano T, Kobayashi M, Yoshida K, *et al*. Central tumour necrosis of a large meningioma following acute anemia caused by hysterectomy. *Neurol Med Chir (Tokyo)* 2009;**49**(9):424–6.
14. Perry A, Stafford SL, Scheithauer BW, *et al*. Meningioma grading: an analysis of histologic parameters. *Am J Surg Pathol* 1997;**21**(12):1455–65.
15. Góes P, Santos BFO, Suzuki FS, *et al*. Necrosis is a consistent factor to recurrence of meningiomas: should it be a stand-alone grading criterion for grade II meningioma? *J NeuroOncol* 2018;**137**(2):331–6.
16. Takashi Takeguchi HM, Teruhiko Shimizu, Keiichi Kikuchi, *et al*. V.I. Gavrilov. *Acta Virol.* 1975;**19**(6):510.
17. Rezaei S, Faeghi F, Samadian M, *et al*. Preoperative evaluation of tumour adhesion to adjacent brain tissue in patients with meningioma with BSMI method and its comparison with the width of oedema around tumour. *Asian Pac J Cancer Prev* 2018;**19**(7):2007–12.
18. Sheporaitis LA, Osborn AG, Smirniotopoulos JG, *et al*. Intracranial meningioma. *AJNR Am J Neuroradiol* 1992;**13**(1):29–37.
19. de Vries J, Wakhloo AK. Cerebral oedema associated with WHO-I, WHO-II, and WHO-III-meningiomas: correlation of clinical, computed tomographic, operative and histological findings. *Acta Neurochir* 1993;**125**(1):34–40.
20. Elster AD, Challa VR, Gilbert TH, *et al*. Meningiomas: MR and histopathologic features. *Radiology* 1989;**170**(3):857–62.
21. Zhang T, Yu JM, Wang YQ, *et al*. WHO grade I meningioma subtypes: MRI features and pathological analysis. *Life Sci* 2018;**213**:50–6.
22. 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**(7):2047981613512484.
23. Phuttharak W, Boonrod A, Thammaroj J, *et al*. Preoperative MRI evaluation of meningioma consistency: a focus on detailed architectures. *Clin Neurol Neurosurg* 2018;**169**:178–84.
24. Pieper DR, Al-Mefty O, Hanada Y, *et al*. Hyperostosis associated with meningioma of the cranial base: secondary changes or tumour invasion. *Neurosurgery* 1999;**44**(4):742–6.