

# Grading Meningiomas by Used Imaging Features on Magnetic Resonance Imaging

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## Abstract

**Background:** Meningioma's are by far the most frequent primary tumors occurring inside the cranium. Prognostic wise, the problem with grade II and grade III neoplasms is the high recurrence rate following surgical resection. Surgical goal is to offer complete resection of the tumor to avoid future recurrence; however, such complete resection is limited by a number of factors such as the tumor location with the central nervous system, invasion of underlying vital brain tissue, involvement of cranial nerves and invasion of dural sinuses. Therefore, pre-operative imaging assessment of meningioma is necessary and the ability to grade these tumors on sole imaging background is an essential step in order to select the optimum surgical and or radiation based therapy.

**Aim of the study:** In the current systemic review we collected information about radiological features detected by MRI techniques and analyzed these futures statically with respect to accuracy, sensitivity and specificity aiming at providing an MRI criteria predicting atypical grade II and III meningiomas prior to surgical intervention.

**Materials and methods:** The current systematic review was based on the preferred reporting items for systematic reviews and meta-analysis guidelines. The primary objective of the current review was to evaluate the currently published data on the potential role of the technique such as Diffusion Weighted Imaging (DWI), and Apparent Diffusion Coefficient (ADC) for the assessment of meningioma grade. The principal research questions were: 1. What is the sensitivity of magnetic resonance imaging in Grading meningioma for brain?. 2. What is the specificity of magnetic resonance imaging in Grading meningioma for brain?.

**Results:** We found that peritumoral edema, tumor necrosis, apparent diffusion coefficient, diffusion weighted trace, tumor enhancement, dural tail, tumor margin and tumor brain interface are all associated with significant prediction potential with respect to meningioma grade ( $p < 0.05$ ). On the other hand, capsular enhancement, T1-weighted imaging, T2-weighted imaging and tumor location are all insignificant predictors of high grade tumor ( $p > 0.05$ ). Highest sensitivity was seen in association with peritumoral edema (73.0 %). Highest specific level was seen in association with Apparent Diffusion Coefficient (ADC) (90.4 %). Tumor necrosis was associated with highest PPV (61.9 %). Highest negative predictive value was seen in association with shape of tumor margin (85.7 %) and highest level of accuracy was observed in association with tumor brain interface (78.2 %).

**Conclusion:** A number of imaging characteristics in MRI can predict the grade of meningioma prior to surgical intervention including peritumoral edema, tumor necrosis, apparent diffusion coefficient, diffusion weighted trace, tumor enhancement, dural tail, tumor margin and tumor brain interface and the presence of any combination of these characteristics will make the decision even more precise.

**Keywords:** Meningioma • Grade • MRI • Benign • Atypical

## Introduction

The development of a tool with the ability to predict prognosis, complications and outcomes for a particular health issue has become increasingly essential throughout medical literature [1]. To be more precise, the discrimination between binary outcomes in a particular disease state is often critical and such binary characteristics may be in the form of benign versus malignant or death versus survival [2,3]. Indeed, the use of imaging techniques in the pre-operative evaluation and characterization of certain disease state such as neoplastic conditions offer a number of advantages with respect to surgical approach and helps the surgeon to take the decision to operate sooner or to treat conservatively and also to determine how to be aggressive when resecting such a neoplastic condition [1].

One such neoplastic condition in the field of neurosurgery is meningioma. In most patients, meningioma follows a benign course; however, in a minority of patients, the tumor may be atypical or anaplastic in its biological behavior [4]. Meningiomas are by far the most frequent primary tumors occurring inside the cranium. These neoplasms account for 36.6 % of all primary tumors of central nervous system and 53.2 % of primary non-malignant central nervous system tumors in the USA. The annual incidence

rate of these neoplasms is estimated to be 8.3 per 100,000 individual. The incidence of meningioma is relatively low during childhood and becomes increasingly higher with increasing age and the disease is more common in females than in males with an approximate male to female ratio of 1:2.27 [5]. The most consistent risk factor among medical literature is exposure of head to ionizing radiation [6].

The clinical presentation of these tumors depends largely on its location in the central nervous system. The tumor can potentially involve any dural surface surrounding the brain or spinal cord and rarely can be identified inside ventricles. The tumor is often slowly growing with insidious onset and many of these lesions are discovered accidentally during routine imaging. Headache due to raised intracranial pressure, focal neurological deficit and seizures are among frequent non pathognomonic clinical features of meningioma [7,8].

Pathologically speaking, meningiomas are composed of neoplastic tissue of proliferating meningotheial cells in the form of whorls and are classified according to WHO classification into three grades. Grade I meningiomas account for approximately 80 to 85% of cases and are characterized by low mitotic activity ( $< 4/10$  high power fields), no brain invasion and various histological subtypes. Grade II meningiomas (atypical

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meningiomas) account for approximately 15% to 20% of cases and are characterized by a mitotic rate of 4 to 15/10 high power fields, brain invasion, necrosis, high nucleus to cytoplasmic ratio, prominent nucleoli and high cellularity. Grade III meningiomas (anaplastic meningiomas) are responsible for 1% to 2% of cases and are characterized by high mitotic rate (>20/10 high power fields) and specific histopathological features such as papillary or rhabdoid configurations [4,9].

Prognostic wise, the problem with grade II and grade III neoplasms is the high recurrence rate following surgical resection. The recurrence rate of grade II tumors is estimated to be approximately 50% within 5 years and that for grade III tumors is estimated to be approximately 90 % within 5 years [4]. Surgical goal is to offer complete resection of the tumor to avoid future recurrence; however, such complete resection is limited by a number of factors such as the tumor location with the central nervous system, invasion of underlying vital brain tissue, involvement of cranial nerves and invasion of dural sinuses. Therefore, pre-operative imaging assessment of meningioma is necessary and the ability to grade these tumors on sole imaging background is an essential step in order to select the optimum surgical and or radiation based therapy [10]. If the grade of meningioma is identified before treatment, it will be of profound clinical benefit. Basically, tumors detected by radiographic assessment are either removed surgically or being observed and surgical treatment is indicated when there is cerebral edema, large tumors and in symptomatic cases; however, early resection of grade II and III tumors may be more beneficial for patents even when clinical features of such tumors are initially absent [1].

Previous research work failed to identify a single unique criterion with the ability to predict atypical or anaplastic meningioma, in spite of thorough analysis of clinical, radiological and even immunohistochemical

features. Furthermore, the statistical power of most of these studies has been challenged by the significant overlap in features among, benign, atypical and anaplastic meningiomas and by the relatively small sample size [11]. The characterization of meningiomas based on classic Magnetic Resonance Imaging (MRI) relies on features such as high signal on T2, low signal on T1 and dural tail, but these are seen in almost all cases of meningioma and are poor tools for the prediction of a particular WHO grade of meningioma [12,13].

In the current systemic review we collected information about radiological features detected by MRI techniques and analyzed these futures statically with respect to accuracy, sensitivity and specificity aiming at providing an MRI criteria predicting atypical grade II and III meningiomas prior to surgical intervention.

## Materials and Methods

### Study design

The current systematic review was based on the Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines, as shown in Figure 1. The primary objective of the current review was to evaluate the currently published data on the potential role of the technique such as Diffusion Weighted Imaging (DWI), aperient diffusion coefficient for the assessment of meningioma grade. The principal research questions were: 1.What is the sensitivity of magnetic resonance imaging in grading meningioma for brain? 2. What is the specificity of magnetic resonance imaging in grading meningioma for brain?

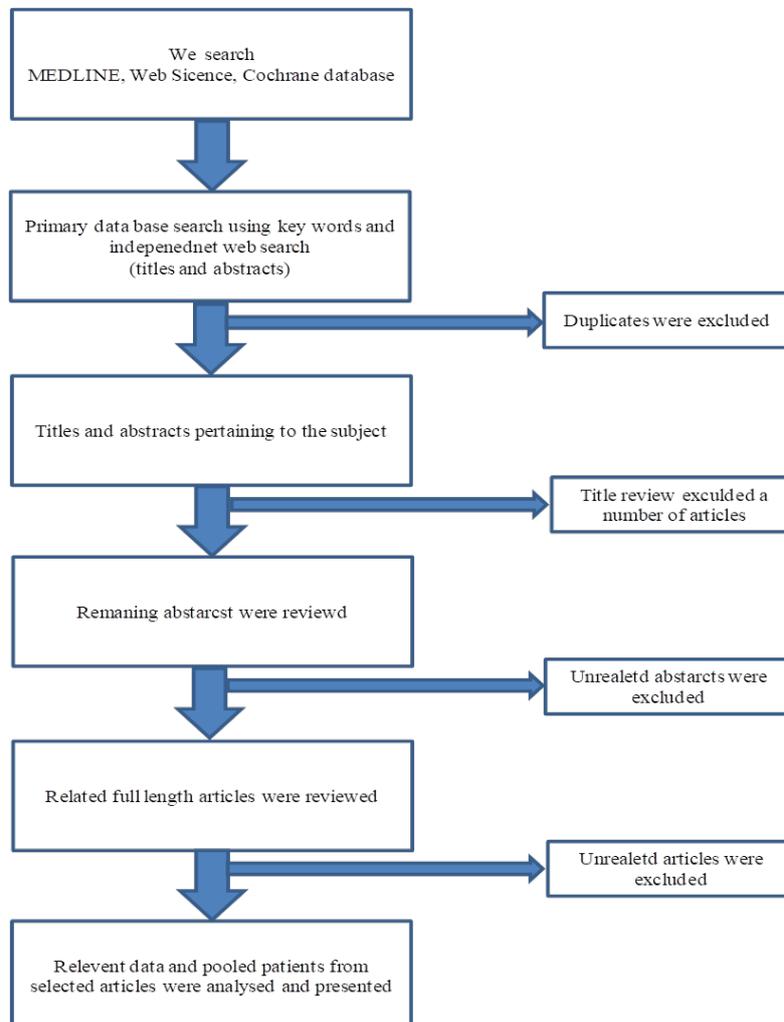


Figure 1. Preferred reporting items for systematic reviews and meta-analysis for identification of final articles.

In this study, two independent reviewers have carried out a thorough search of available electronic literatures including the MEDLINE, Web of Science and Cochrane database to identify eligible studies. The following key words constituted the search query: "meningioma" "MRI" and "grade" "benign" "atypical". In order to include all possible missed eligible records, the reference lists of the primarily included articles were checked manually. The articles printed in the last 10 years were included in the study.

**Inclusion and exclusion criteria**

**Studies had to meet the following criteria:** (1) Patients with histopathologically confirmed meningiomas. (2) High-Grade Meningiomas (HGMs) from Low-Grade Meningiomas (LGMs) were differentiated by advance techniques. (3) The number of HGMs and LGMs could be retrieved from the reported data in order to generate 2 x 2 tables. The values of True Positive (TP), False Positive (FP), False Negative (FN), True Negative (TN) will be used to calculate sensitivity and specificity. (4) Published as original articles. From each study, the optimal, diffusion and aperiient diffusion coefficient that provided the highest diagnostic accuracy was included in the statistical analysis.

**The exclusion criteria were as follow:** (1) Any non-English or other species articles were excluded, (2) case reports/case series and reviews, (3) overlapping patient population (single-published study included in a larger multicenter analysis), (4) other imaging techniques (Fractal Analysis, Conventional MRI) due to insufficient sample to pool data, (5) insufficient data for obtaining 2 x 2 tables, (6) studies reporting on specific subtypes of meningiomas (i.e., cystic).

**Data extraction and quality assessment**

The quality and risk of bias of the included studies were evaluated using the quality assessment of diagnostic accuracy studies by two independent reviewers and all emerging conflicts resolved with consensus.

**Statistical analysis**

Obtained data were transferred into a spread sheet of the Statistical Package for Social Sciences (SPSS for Windows, Version 16.0. Chicago, SPSS Inc.). The Microsoft Office Excel 2007 was also used to do a number of calculations. Qualitative data were expressed as number and percentage. The sensitivity, specific, Positive Predictive Value (PPV), Negative Predictive Value (NPV) and accuracy were calculated according to the following equations:

$$\text{Sensitivity} = \frac{\text{True Positive Count}}{\text{True Positive Count} + \text{False Negative Count}} \times 100$$

$$\text{Specificity} = \frac{\text{True Negative Count}}{\text{True Negative Count} + \text{False Positive Count}} \times 100$$

$$\text{PPV} = \frac{\text{True Positive Count}}{\text{True Positive Count} + \text{False Positive Count}} \times 100$$

$$\text{NPV} = \frac{\text{True Negative Count}}{\text{True Negative Count} + \text{False Negative Count}} \times 100$$

$$\text{Accuracy} = \frac{\text{True Positive Count} + \text{True Negative Count}}{\text{True Positive Count} + \text{False Positive Count} + \text{True Negative Count} + \text{False Negative Count}} \times 100$$

**Results**

In this systemic review ten studies were included after fulfilling inclusion criteria and these studies are outlined in Table 1. The MRI imaging characteristics included in these studies were highly variable as well as the number of low grade and high grade meningioma cases. These studies were arranged according to date of publication and the most recent one was that carried out [14]. This study included the following imaging characteristics: Enhancement degree, Enhancement homogeneity, Lobulation, Flowing voids and Dural tail [14]. The study of Salah included: T2 signal intensity, T1 signal intensity, Enhancement pattern, Enhancement intensity, Dural

tail, Necrosis, Complete pertitumeral rim of CSF, Tumor margin, Bone erosion, Hyperostosis, Extracranial tumor extension, Pertitumeral edema, Brain invasion, Dural sinus invasion, Difusion signal [15]. The study of Zhang included: Vascularity index, Hemorrhage, Calcification, Peritumeral edma, Tumor border, Tumor location, ADC feature [16]. The studies of Hale included: Draining vein, edema, necrosis, location [1,17]. The study of Yan included: Tumor brain interface, Peritumoral edema, Peritumoral edema, Capsular enhancement, Tumor enhancement, Tumor shape [18]. The study of Lin included T1-weighted imaging, T2-weighted imaging, Tumor brain interface, Tumor enhancement, Capsular enhancement, DWI, Brain edema, Tumor location [19]. The study of Kawahara included: TBI (Tumor Brain Interface), CapE (Capsular enhancement), Heterogeneity, TM (Tumor margin) [20]. The study of Santelli included: DWI signal intensity and the study of Toh included: ADC (Apparent Diffusion Coefficient), DW (Diffusion-Weighted trace), FA (Fractional Anisotropy maps) [21,22].

Variables included in analysis	Author reference
Enhancement degree, Enhancement homogeneity, Lobulation, Flowing voids, dural tail	[14]
T2 signal intensity, T1 signal intensity, Enhancement pattern, Enhancement intensity, Dural tail, Necrosis, Complete pertitumeral rim of CSF, Tumor margin, Bone erosion, Hyperostosis, Extracranial tumor extension, Pertitumeral edema, Brain invasion, Dural sinus invasion, Difusion signal	[15]
Vascularity index, Hemorrhage, Calcification, Peritumeral edma, Tumor border, Tumor location, ADC feature	[16]
Draining vein, edema, necrosis, location	[17]
Draining vein, Edema, Necrosis, Location	[17]
Tumor brain interface, Peritumoral edema, Peritumoral edema, Capsular enhancement, Tumor enhancement, Tumor shape	[18]
T1-weighted imaging, T2-weighted imaging, Tumor brain interface, Tumor enhancement, Capsular enhancement, DWI, Brain edema, Tumor location	[19]
TBI (Tumor Brain Interface), CapE (Capsular Enhancement), Heterogeneity, TM (Tumor Margin)	[20]
DWI signal intensity	[21]
ADC (Apparent Diffusion Coefficient), DW (Diffusion-Weighted trace), FA (Fractional Anisotropy maps)	[22]

**Table 1.** Studies included in the current systematic review and meta-analysis.

MRI characteristics that are significantly associated with high grade meningioma are shown in Table 2. Peritumoral edema was significantly associated with high grade meningioma (p<0.001) and it was described by 5 authors [1, 15,16,18,19]. Tumor necrosis was also significantly associated with high grade meningioma (p<0.001) and it was mentioned by two previous authors [1,15]. Apparent Diffusion Coefficient (ADC) was also significantly associated with high grade meningioma (p=0.006) and it was mentioned by two previous authors [16,22]. Diffusion-Weighted trace (DW) was in addition significantly associated with high grade meningioma (p=0.004) and it was mentioned by 4 previous authors [15,16,19,21].

Tumor enhancement was in addition significantly associated with high grade meningioma (p<0.001) and it was mentioned by 5 previous authors [14,15,18-20]. Dural Tail was in addition significantly associated with high grade meningioma (p=0.022) and it was mentioned by 2 previous authors [14,15]. Tumor margin was in addition significantly associated with high grade meningioma (p<0.001) and it was mentioned by 3 previous authors [16,18,20]. Tumor brain interface was in addition significantly associated with high grade meningioma (p<0.001) and it was mentioned by 3 previous authors [18-20].

Total (Grade II and III Vs Grade I) count	Characteristic	Grade II and III	Grade I	p	Included studies
		n=148	n=432		
580 (148 vs 432)	Peritumoral edema				[15-19]
	Positive	108 (73.0 %)	206 (47.7 %)	<0.001 C	
	Negative	40 (27.0 %)	226 (52.3 %)	**	
195 (57 vs 138)	Necrosis				[15,17]
	Yes	26 (45.6 %)	16 (11.6 %)	<0.001 C	
	No	31 (54.4 %)	122 (88.4 %)	**	
153 (49 vs 104)	Apparent diffusion coefficient (ADC)				[16,22]
	Hypointense	13 (26.5 %)	10 (9.6 %)	0.006 C	
	Isointense/hyperintense	36 (73.5 %)	94 (90.4 %)	**	
253 (76 vs 177)	Diffusion-weighted trace (DW)			0.004 C	[15,19,21,22]
	Hyeprintense	45 (59.2 %)	70 (39.5 %)	**	
	Isointense	31 (40.8 %)	107 (60.5 %)		
509 (137 vs 372)	Tumor enhancement				[14,15,18-20]
	Heterogenous	91 (66.4 %)	105 (28.2 %)	<0.001 C	
	Homogenous	46 (33.6 %)	267 (71.8 %)	**	
194 (60 vs 134)	Dural Tail				[14,15]
	No	15 (25.0 %)	16 (11.9 %)	0.022 C	
	Yes	45 (75.0 %)	118 (88.1%)	*	
325 (84 vs 241)	Tumor margin				[16,18,20]
	Irregular	51 (60.7 %)	44 (18.3 %)	<0.001 C	
	Regular	33 39.3 (%)	197 (81.7 %)	**	
316 (77 vs 239)	Tumor brain interface				[18-20]
	Unclear	41 (53.2 %)	33 (13.8 %)	<0.001 C	
	Clear	36 (46.8 %)	206 (86.2 %)	**	

C: Chi-square test; \*: significant at p ≤ 0.01; \*\*: significant at p ≤ 0.05

**Table 2.** MRI characteristics those are significantly associated with high grade meningioma

Sensitivity, specificity, positive predictive value, negative predictive value and accuracy associated with MRI characteristics that are significantly associated with high grade meningioma were shown in Table 3. Highest sensitivity was seen in association with peritumoral edema (73.0%). Highest specific level was seen in association with Apparent Diffusion Coefficient

(ADC) (90.4%). Tumor necrosis was associated with highest PPV (61.9 %). Highest negative predictive value was seen in association with shape of tumor margin (85.7%) and highest level of accuracy was observed in association with tumor brain interface (78.2%).

v	Sensitivity%	Specificity%	PPV%	NPV%	Accuracy%
Peritumoral edema	73	52.3	34.4	85	57.6
Necrosi	45.6	88.4	61.9	79.7	75.9
Apparent Diffusion Coefficient (ADC)	26.5	90.4	56.5	72.3	69.9
Diffusion-Weighted trace(DW)	59.2	60.5	39.1	77.5	60.1
Tumor enhancement	66.4	71.8	46.4	85.3	70.3
Dural tail	25	88.1	9.2	38.6	68.6
Tumor margin	60.7	81.7	53.7	85.7	76.3
Tumor brain interface	53.2	86.2	55.4	85.1	78.2

PPV: Positive predictive Value; NPV: Negative Predictive Value

**Table 3.** Sensitivity, specificity, positive predictive value, negative predictive value and accuracy associated with MRI characteristics that are significantly associated with high grade meningioma.

MRI characteristics that are not significantly associated with high grade meningioma were outlined in Table 4 and included Capsular enhancement,

T1-weighted imaging, T2-weighted imaging and tumor location.

Total (Grade II and III Vs Grade I) count	Characteristic	Grade II and III	Grade I	p	Included studies
		n = 148	n = 432		
316 (166 vs 150)	Capsular enhancement				[18-20]
	Negative	54(32.5 %)	50(33.3%)	0.879 C	
	Positive	112(67.5%)	100(66.7%)	NS	
163 (42 vs 121)	T1-weighted imaging				[15,19]
	Hypointense	17(40.5 %)	35(28.9 %)	0.166 c	
	Isointense/ hyperintense	25(59.5 %)	86(71.1 %)	NS	
	T2-weighted imaging				
	Isointense	25(59.5 %)	61(50.4 %)	0.308 C	
	Hypointense/ Hyperintense	17(40.5 %)	60(49.6 %)	NS	
377 (101 vs 276)	Location				[16,17,19]
	Convexity	59(58.4 %)	115(41.7%)	0.124 C	
				NS	
	Skull base	17(16.8 %)	86(31.2 %)	0.135 C	
				NS	
	Others	25(24.8 %)	75(27.2 %)	Reference	

C: Chi-square test; NS: Not Significant at p>0.05

**Table 4.** MRI characteristics those are not significantly associated with high grade meningioma.

## Discussion

In a nearly all previous studies, which tried to figure out MRI characteristics in line with WHO high grade meningioma, the sample size was an important limiting criterion from statistical perspective. Therefore, in the current study, a systematic reviews and meta-analysis approach was carried aiming at increasing the sample size to as much as possible so that minor differences in particular MRI features may result in significant and more accurate identification of WHO high grade lesions. After thorough search in the available published articles dealing with the dilemma of imaging characterization and identification of high grade meningioma, we succeeded to collect information about 10 studies that fulfilled the inclusion criteria suggested by the authors of the current study [1,14-22]. The oldest of these articles has analyzed 24 cases of meningioma, 12 benign and 12 atypical and they made use of Apparent Diffusion Coefficient (ADC), Diffusion-Weighted (DW) and Fractional Anisotropy (FA) MRI imaging characteristics and they described significant contribution for ADC in discriminating between WHO low grade and high grade meningioma [22]. In the next study by Santelli, the authors tested the reliability of Diffusion Weighted Imaging (DWI) in the discrimination between high grade and low grade meningioma and they found that this parameter do not provide significant association with high grade meningioma on the contrary to the finding of Toh and this is probably because of the small sample size or the relatively larger sample size included in the study of Santelli (n=102) [21,22]. In an another study, Kawahara and colleagues in 2012 analyzed the potential role of a number of MRI features (tumor brain interface, capsular enhancement, tumor enhancement and tumor margin) in segregation between WHO high grade and low grade meningioma tumors and they described highly significant role for all these factors in univariate analysis; however, the sample size was 65 (26 high grade and low grade 39) [20]. In a further study, Lin and colleagues in 2014 studied the reliability of T1-weighted imaging, T2-weighted imaging, tumor brain interface, tumor enhancement, capsular enhancement, DWI, brain edema and tumor

location in defining high grade meningioma and they mentioned that tumor brain interface, tumor enhancement, brain edema and tumor location are significant predictors of high grade meningioma; however, enrolled sample size was 120 (90 low grade and 30 high grade) [19]. In a further study, Yan provided information on the use of tumor brain interface, brain edema, tumor enhancement, capsular enhancement and tumor margin in predicting high grade meningioma and they found that tumor brain interface, tumor enhancement and tumor margin can significantly predict high grade meningioma in a sample of 131 patients (110 benign and 21 high grade meningioma) [18].

Yet in another study, Hale and colleagues in 2 different reports in 2018 have analyzed the role of presence of a draining vein, brain edema, tumor necrosis and tumor location in detecting high grade meningioma and they described significant contribution for brain edema, tumor necrosis and tumor location with this regard in a sample of 128 cases (94 grade I and 34 grade II meningioma) [1,17]. In a further study, Zhang studied the significant role of a number of imaging characteristics in diagnosing high grade meningioma and they mentioned that tumor calcification, tumor edema, tumor location and tumor border can play a significant role with this regard [16]. Salah in 2019 have also studied the role of a number of imaging criteria and they found that tumor necrosis, tumor enhancement, tumor margin, bone erosion and brain invasion are all significant predictors of meningioma grade in univariate analysis in a sample of 67 cases (44 low grade and 23 high grade) [15]. Finally, Yu conducted a study in which tumor enhancement, lobulation, flowing voids and dural tail were analyzed in association with meningioma grade including 127 meningioma cases [14].

In the current study, we collected information about each individual MRI characteristic mentioned in the 10 enrolled studies and tried to figure out their significance with respect to diagnosis of high grade meningioma. We included such characteristics that were mentioned in at least two studies and excluded characteristics that were mentioned in a single study in order to increase the sample size and hence the statistical power. We found that

peritumoral edema, tumor necrosis, apparent diffusion coefficient, diffusion weighted trace, tumor enhancement, dural tail, tumor margin and tumor brain interface are all associated with significant prediction potential with respect to meningioma grade. On the other hand, capsular enhancement, T1-weighted imaging, T2 weighted imaging and tumor location are all insignificant predictors of high grade tumor. The point of strength in this study is the sample of enrolled cases so that significant level applied to any of the imaging characteristics carry higher statistical power than that seen in previous studies. Various sensitivity and specificity levels were obtained with various imaging characteristics, in addition, the level of accuracy was also highly variable, but generally speaking finding of more than one criterion will certainly make the accuracy even better. One important limitation of the current study was the inability to perform multivariate analysis because of lack of data necessary to do so.

## Conclusion

A number of imaging characteristics in MRI can predict the grade of meningioma prior to surgical intervention including peritumoral edema, tumor necrosis, apparent diffusion coefficient, diffusion weighted trace, tumor enhancement, dural tail, tumor margin and tumor brain interface and the presence of any combination of these characteristics will make the decision even more precise. The MRI imaging characteristics included in these studies were highly variable as well as the number of low grade and high grade meningioma cases. These studies were arranged according to date of publication and the most recent one was that carried out. MRI characteristic mentioned in the 10 enrolled studies and tried to figure out their significance with respect to diagnosis of high grade meningioma. We included such characteristics that were mentioned in at least two studies and excluded characteristics.

## Acknowledgment

We would like to express our deep thanks and appreciation to all research members enrolled in previous studies searching for imaging criteria on MRI examination to segregate meningioma tumors according to grade before surgical intervention and to all patients enrolled in these previous studies.

## Ethical Consideration

The study was ethically approved by the institutional ethical approval committee.

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