

# Correlation between magnetic resonance imaging grading and pathological grading in meningioma

## Clinical article

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**Object.** This study investigated the specific preoperative MRI features of patients with intracranial meningiomas that correlate with pathological grade and provide appropriate preoperative planning.

**Methods.** From 2006 to 2012, 120 patients (36 men and 84 women, age range 20–89 years) with newly diagnosed symptomatic intracranial meningiomas undergoing resection were retrospectively analyzed in terms of radiological features of preoperative MRI. There were 90 WHO Grade I and 30 WHO Grade II or III meningiomas. The relationships between MRI features and WHO histopathological grade were analyzed and scored quantitatively.

**Results.** According to the results of multivariate logistic regression analysis, age  $\geq 75$  years, indistinct tumor-brain interface, positive capsular enhancement, and heterogeneous tumor enhancement were identified factors in the prediction of advanced histopathological grade. The prediction model was quantified as a scoring scale:  $2 \times (\text{age}) + 5 \times (\text{tumor-brain interface}) + 3 \times (\text{capsular enhancement}) + 2 \times (\text{tumor enhancement})$ . The calculated score correlated positively with the probability of high-grade meningioma.

**Conclusions.** This scoring approach may be useful for clinicians in determining therapeutic strategy and in surgical planning for patients with intracranial meningiomas.

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**KEY WORDS** • meningioma • magnetic resonance imaging •  
radiological prediction • histopathological • WHO grade • oncology

**M**ENINGIOMAS are the most common primary intracranial tumors, with an incidence of 13%–26%.<sup>2</sup> In the 2007 WHO classification system, Grade I meningiomas are defined as slow-growing and well-circumscribed with benign histopathological features. In contrast, Grade II and III meningiomas have more aggressive biological features, malignant behavior, and clinical recurrence. The difference between WHO Grade II and Grade III meningiomas is based on degrees of histological anaplasia, with WHO Grade III meningiomas having histopathological characteristics of metastasis.<sup>19</sup>

Magnetic resonance imaging is a well-established, essential tool in the diagnosis of CNS neoplasms. Its role for neurosurgeons in the management of intracranial meningi-

omas is mainly for differential diagnosis and for planning surgical intervention.<sup>11</sup> The extent of resection and WHO histopathological grade are the most important factors in determining clinical outcome.<sup>6,29</sup> Identifying meningiomas with advanced histopathological grade using preoperative MRI is important. This maneuver could achieve more appropriate tumor resection and even underlying dura substitution in treating advanced meningiomas.

Some specific MRI features of meningiomas have been identified to be associated with high proliferative potential or aggressive biological behavior.<sup>9,13,17,18,28</sup> In clinical practice, various combinations of radiological features usually appear within one meningioma. Thus, it is reasonable to make an exclusive and comprehensive assessment of all related clinical and radiological features

Abbreviations used in this paper: ADC = apparent diffusion coefficient; DWI = diffusion-weighted imaging; FLAIR = fluid-attenuated inversion recovery; OR = odds ratio.

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for each patient. The purpose of this study was to investigate specific preoperative MRI features to build a model that could predict meningiomas with advanced histopathological grades.

## Methods

### Patient Population

The patient population in this retrospective study was collected from our institution, a single tertiary medical care center. From January 2006 to December 2012, 120 patients were screened from 141 patients with newly diagnosed symptomatic intracranial meningiomas undergoing resection. The diagnosis and histopathological grade of meningioma for each patient was confirmed by pathologists (including W.C.T.). The exclusion criteria were previous radiotherapy or radiosurgery, preoperative transarterial embolization, and incomplete or uninterpretable preoperative MRI studies. Our institutional review board approved this study.

A total of 120 patients were enrolled, including 90 (75%) with Grade I meningiomas and 30 (25%) with high-grade (Grade II or III) meningiomas. The mean age of the study population at the time of surgery was 58.6 years (range 20–89 years).

### MRI Acquisition

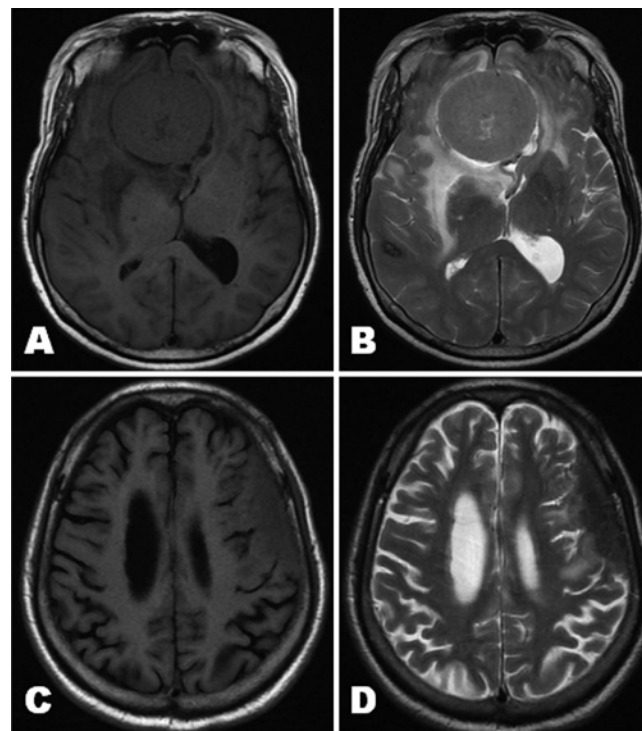
Preoperative MRI was available for each patient and was performed using a 1.5-T MR unit (Vision Plus, Siemens). The MRI protocol was TR 2140 msec, TE 30 msec, TI 420 msec, matrix size  $256 \times 256$ , section thickness 3 mm, and intersection gap 0.21 mm. Routine images of the whole brain, including spin echo T1-weighted images, spin echo T2-weighted images, and fluid-attenuated inversion recovery (FLAIR) images were obtained. Spin echo contrast-enhanced T1-weighted images were obtained in the coronal, sagittal, and axial planes after intravenous Gd administration (0.1 mmol/kg body weight). Diffusion-weighted imaging (DWI) was acquired in the axial plane using a single-shot, spin echo, echo planar imaging sequence.

### MRI Analysis

**Signal Intensities.** Signal intensities of the meningiomas on T1- and T2-weighted imaging were recorded as hypointense, isointense, or hyperintense relative to the intensity of the gray matter.

**Tumor-Brain Interface.** Meningiomas with distinct peritumoral rims and CSF clefts, which were hypointense on T1-weighted imaging and hyperintense on T2-weighted imaging, were defined as clear tumor-brain interface (Fig. 1A and B). In contrast, tumors without distinct borders were defined as unclear tumor-brain interface (Fig. 1C and D).

**Tumor Enhancement.** The pattern of contrast enhancement after Gd administration was divided into homogeneous (Fig. 2A) or heterogeneous (Fig. 2B). Intratumoral cystic change, defined as an area of hyperintensity



**FIG. 1.** Axial MR images showing clear versus unclear tumor-brain interface. **A and B:** Clear tumor-brain interface shown in 1 representative olfactory meningioma with a distinct peritumoral rim was hypointense on T1-weighted imaging (A) and hyperintense on T2-weighted imaging (B). **C and D:** Unclear tumor-brain interface shown in a representative left frontal convexity meningioma with an indistinct peritumoral rim on T1- (C) and T2-weighted imaging (D).

on T2-weighted imaging and hypointensity on T1-weighted imaging without contrast enhancement, was regarded as heterogeneous enhancement in this study (Fig. 2C and D).

**Capsular Enhancement.** Capsular enhancement was defined as the entire enhanced layer at the tumor-brain interface and was categorized as positive or negative.

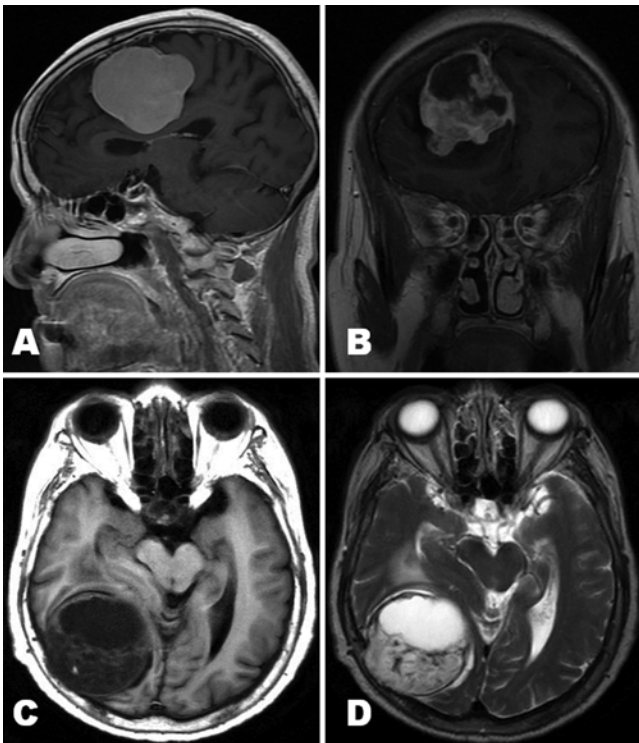
**Brain Edema.** The presence of brain edema was judged as a hyperintense extension adjacent to tumors on T2-weighted imaging and was judged as positive or negative.

**Diffusion-Weighted Imaging.** The DWI was visually inspected and classified as hyperintense, isointense, or hypointense in comparison with normal white matter.

**Tumor Localization.** According to the particular site of origin, the location of each intracranial meningioma was divided into a basal group, a fissural group, or a dorsal group. The image interpretation of each MRI feature was described and confirmed by 2 experienced radiologists.

### Pathological Verification

Hematoxylin and eosin slides were verified from 120 paraffin-embedded tissues from the meningiomas. At least 2 experienced pathologists reviewed the pathological diagnosis. The histopathological differentiation of the brain tumors was determined according to the criteria of



**FIG. 2.** Sagittal (A), coronal (B), and axial (C and D) MR images of tumor enhancement. **A and B:** Falx and parasagittal meningiomas showing homogeneous (A) and heterogeneous enhancement (B), respectively, on T1-weighted imaging after Gd administration. **C and D:** One convexity meningioma with an intratumoral cyst was hypointense (C) on T1-weighted imaging and hyperintense (D) on T2-weighted imaging.

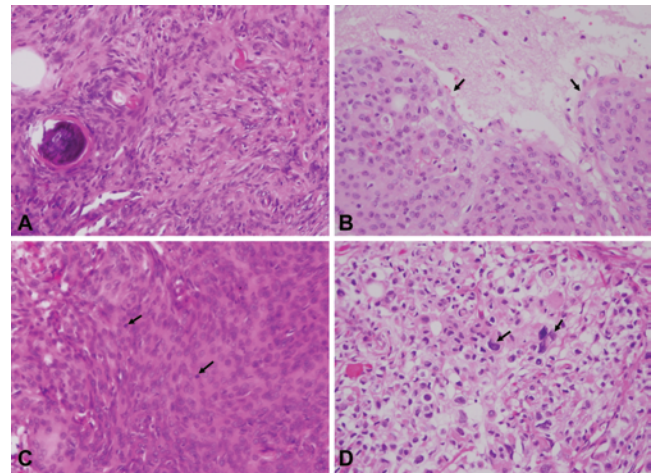
the 2007 WHO classification of meningiomas.<sup>19</sup> Representative photomicrographs are shown in Fig. 3.

#### Statistical Analysis

All data were analyzed using the SPSS statistical program (version 20, IBM), and statistical significance was set at  $p < 0.05$ . The association between radiological features of MRI along with patient age and sex and the histopathological grade of meningiomas were examined by univariate and multivariate analyses. Logistic regression was used to identify significant factors that were predictive of high-grade meningiomas. Each variable in logistic regression was converted to the binary variable. All of the odds ratios (ORs) in analyses reflected the odds of a meningioma being a high-grade meningioma.

Multiple logistic regression analyses with variable selection in a stepwise fashion were used to develop the multivariate models for prediction of high-grade meningiomas. While building the most parsimonious model to explain the data, we preferred to seek one with maximized confidence and minimized number of variables. Likelihood ratio and Akaike information criterion for each model were presented to judge the merit. Choice between models was made on the basis of clinical availability and statistical significance.

According to the final model, the risk of high-grade meningioma was quantitated by a scoring system consist-



**FIG. 3.** Photomicrographs demonstrating the histopathology of meningioma. **A:** Meningotheliomatous meningioma, WHO Grade I, with psammoma bodies. **B:** Meningioma with benign histopathology and focal brain invasion, WHO Grade II. The arrows indicate the site of tumor invasion into the brain parenchyma (budding appearance). **C:** Atypical meningioma, WHO Grade II, showed hypercellular tumor cells with a few mitoses (arrows). **D:** Anaplastic meningioma, WHO Grade III, with bizarre nuclei (arrows). H & E, original magnification  $\times 400$ .

ing of regression coefficients of identified variables. The minimum coefficient of identified predictive factors was converted to X score (an integer), and the scores of identified variables were expressed as the following equation:

$$\text{Score}_{\text{specific predictive factor}} = (\text{coefficient of specific predictive factor} / \text{the minimum coefficient of all identified predictive factors}) \times X.$$

#### Results

Of 120 patients in this study, 90 (75%) had benign meningiomas and 30 (25%) had high-grade meningiomas. Their demographic data and radiological features are summarized in Table 1. Age, tumor-brain interface, tumor enhancement, brain edema, and tumor location were significantly different between patients with benign meningiomas and those with high-grade meningiomas. According to the results of multivariate logistic regression analysis, age  $\geq 75$  years, unclear tumor-brain interface, and heterogeneous tumor enhancement were strong independent predictive factors, with ORs of 4.28 (95% confidence interval [CI] 1.14–16.10;  $p = 0.0314$ ), 16.55 (95% CI 2.23–122.85;  $p = 0.0061$ ), and 4.39 (95% CI 1.26–15.33;  $p = 0.0204$ ), respectively (Table 2). There was a negative correlation between unclear tumor-brain interface and positive capsular enhancement (OR 0.1;  $p = 0.001$ , data not shown). Thus, unclear tumor-brain interface was a negative confounder in the association between positive capsular enhancement and high-grade meningioma.

#### Model Development

In building the prediction model, each variable was transformed into dichotomous data. The regression coefficients for the variables and statistics for goodness of fit in different prediction models are shown in Table 3. Model 1 had 3 degrees of freedom, including age, tumor-



TABLE 1: Results of clinicoradiological characteristics

| Characteristics       | Benign (%) | High-Grade (%) | p Value |
|-----------------------|------------|----------------|---------|
| no. of patients       | 90 (75)    | 30 (25)        |         |
| demographics          |            |                |         |
| sex                   |            |                |         |
| women                 | 66 (73.3)  | 18 (60.0)      | 0.176   |
| men                   | 24 (26.7)  | 12 (40.0)      |         |
| age in yrs            |            |                |         |
| <75                   | 80 (88.9)  | 19 (63.3)      | 0.004   |
| ≥75                   | 10 (11.1)  | 11 (36.7)      |         |
| radiological findings |            |                |         |
| T1-weighted imaging   |            |                |         |
| hypointense           | 26 (28.9)  | 10 (33.3)      | 0.652   |
| isointense            | 64 (71.1)  | 20 (66.7)      |         |
| hyperintense          | 0 (00.0)   | 0 (00.0)       |         |
| T2-weighted imaging   |            |                |         |
| hypointense           | 5 (5.5)    | 2 (6.7)        | 0.945   |
| isointense            | 37 (41.1)  | 13 (43.3)      |         |
| hyperintense          | 48 (53.4)  | 15 (50.0)      |         |
| tumor-brain interface |            |                |         |
| clear                 | 85 (94.4)  | 20 (66.7)      | <0.001  |
| unclear               | 5 (5.6)    | 10 (33.3)      |         |
| tumor enhancement     |            |                |         |
| homogenous            | 74 (82.2)  | 17 (56.7)      | 0.007   |
| heterogeneous         | 16 (17.8)  | 13 (43.3)      |         |
| capsular enhancement  |            |                |         |
| negative              | 34 (37.8)  | 9 (30.0)       | 0.514   |
| positive              | 56 (62.2)  | 21 (70.0)      |         |
| DWI                   |            |                |         |
| hypo/isointense       | 63 (70.0)  | 23 (76.7)      | 0.641   |
| hyperintense          | 27 (30.0)  | 7 (23.3)       |         |
| brain edema           |            |                |         |
| negative              | 35 (38.9)  | 5 (16.7)       | 0.027   |
| positive              | 55 (61.1)  | 25 (83.3)      |         |
| tumor location        |            |                |         |
| basal                 | 34 (37.8)  | 6 (20.0)       | 0.043   |
| fissural              | 23 (25.5)  | 5 (16.7)       |         |
| dorsal                | 33 (36.7)  | 19 (63.3)      |         |

brain interface, and tumor enhancement, and the likelihood ratio was 23.8. Adding additional variables, capsular enhancement resulted in a significant increase in the likelihood ratio in Model 2 ( $p = 0.023$ ). The Akaike information criterion was lower for Model 2 than for Model 1 (115.9 vs 119.1, respectively). From Model 3 to Model 8, inclusion of another identified variable besides those in Model 2 did not significantly increase the likelihood ratio but elevated the degrees of freedom and Akaike information criterion. This effect also occurred after inclusion of all variables, as noted in Model 9. This result meant that the difference in explanatory power between Model 2 and those models with more than 4 degrees of freedom was not statistically significant. Therefore, Model 2 was the

most suitable for prediction of high-grade meningioma based on our strategy of model selection.

#### Score Evaluation

According to the selected prediction model, patient age, tumor-brain interface, tumor enhancement, and capsular enhancement were the most significant predictors of high-grade meningioma. A scoring scale was then created as positive integers proportionate to the parameter estimate (Table 4):

$$\text{score} = 2 \times (\text{age}) + 5 \times (\text{tumor-brain interface}) + 2 \times (\text{tumor enhancement}) + 3 \times (\text{capsular enhancement}).$$

Parameters obtained from the logistic regression model were used to obtain a score as follows: patient age ( $\geq 75$  years = 1,  $< 75$  years = 0), tumor-brain interface (unclear = 1, clear = 0), tumor enhancement (heterogeneous = 1, homogeneous = 0), and capsular enhancement (positive = 1, negative = 0). Then the meningiomas were classified into several groups based on the calculated score (Table 5). An increased probability of a high-grade meningioma was accompanied by a higher score. A total score  $\geq 2$  had an 80.0% sensitivity and 45.6% specificity, and a total score  $\geq 4$  had a 40.0% sensitivity and 85.6% specificity for predicting high-grade meningiomas.

#### Discussion

Correct prediction of the histopathological grade of meningioma before surgery is helpful to guide optimal treatment, and the association between specific radiological features and aggressive biological behavior has been studied separately by other investigators.<sup>9,13,17,18,28</sup> In clinical practice, the coexistence of several radiological features within 1 meningioma is not uncommon. Confusion frequently occurs because we do not know which finding is important and which is not. This study attempts to incorporate various radiological findings to develop 1 exclusive and comprehensive prediction model in forecasting high-grade meningioma. According to the results of multivariate logistic regression analyses, it is evident that age, tumor-brain interface, tumor enhancement, and capsular enhancement are the most powerful identified variables in our prediction model. The scoring scale was developed after weighting each parameter in accordance with their regression coefficients in the multivariate logistic regression analysis.

The finding that age was a risk factor for high-grade meningiomas is controversial. It has been reported that age is an independent variable in predicting tumor recurrence and degree of differentiation according to previous reports.<sup>22,24</sup> However, this statement is not supported by other studies.<sup>13,16,17</sup> This problem occurs because different years were used as the dividing line in different reports. In this study, we use different years as the dividing line including 65, 70, and 75 years old. Not surprisingly, the difference between benign and high-grade meningiomas increases with advanced years of age. According to the results of the multivariate logistic regression analysis, age  $\geq 75$  years is a factor in the prediction of high-grade meningioma.

## MRI features and histopathological grade in meningioma

**TABLE 2: Univariate and multivariate analyses of potential predictors for high-grade meningiomas**

| Predictor                            | Univariate Analysis |           |         | Multivariate Analysis |             |         |
|--------------------------------------|---------------------|-----------|---------|-----------------------|-------------|---------|
|                                      | OR                  | 95% CI    | p Value | OR                    | 95% CI      | p Value |
| male sex                             | 1.83                | 0.77–4.36 | 0.1707  | 1.74                  | 0.56–5.39   | 0.3372  |
| age ≥75 yrs                          | 4.63                | 1.72–12.4 | 0.0025  | 4.28                  | 1.14–16.10  | 0.0314  |
| T1-weighted imaging iso/hyperintense | 0.81                | 0.34–1.97 | 0.6459  | 2.09                  | 0.53–8.31   | 0.2934  |
| T2-weighted imaging iso/hypointense  | 1.14                | 0.50–2.61 | 0.7517  | 1.70                  | 0.56–5.18   | 0.3501  |
| unclear tumor-brain interface        | 8.50                | 2.61–27.6 | 0.0004  | 16.55                 | 2.23–122.85 | 0.0061  |
| heterogeneous tumor enhancement      | 3.54                | 1.44–8.72 | 0.0061  | 4.39                  | 1.26–15.33  | 0.0204  |
| positive capsular enhancement        | 1.42                | 0.58–3.45 | 0.4429  | 4.35                  | 0.80–23.60  | 0.0889  |
| DWI iso/hypointense                  | 1.41                | 0.54–3.67 | 0.4840  | 1.37                  | 0.37–5.12   | 0.6372  |
| positive brain edema                 | 3.18                | 1.11–9.09 | 0.0307  | 1.24                  | 0.36–4.21   | 0.7322  |
| location dorsal/fissural*            | 2.43                | 0.90–6.54 | 0.0793  | 2.18                  | 0.71–6.66   | 0.1709  |

\* Non-skull base groups.

Heterogeneous MRI enhancement after Gd injection is associated with uneven distribution of tumor cells or even ischemic necrosis, the biological features of malignant tumors.<sup>1,10</sup> Intratumoral cystic change, defined as areas of hyperintensity on T2-weighted imaging and hypointensity on T1-weighted imaging without contrast enhancement, was regarded as heterogeneous enhancement in the present study. The real cause of cyst formation within the meningioma is uncertain. Ischemic necrosis, hemorrhage, cystic degeneration, accumulation of tumor cell secretion, and evidence of rapid tumor expansion have been suspected as underlying causes.<sup>3,8</sup> Several re-

ports have stated that Grade II and III meningiomas have significantly more intratumoral cystic changes compared with Grade I meningiomas.<sup>5,14</sup> In the present study, heterogeneous enhancement, as well as the presence of an intratumoral cyst, was an independent factor predictive of high-grade meningioma, consistent with previous studies.

The interface between the tumor and the brain is determined by the expression of a peritumoral rim. A clear peritumoral rim indicates the presence of a physiological barrier between the meningioma and brain parenchyma and an unclear peritumoral rim suggests tumor adhesion and invasion of the surrounding brain tissue, the patho-

**TABLE 3: Regression coefficients and statistics for sequential models in the prediction of high-grade meningiomas\***

| Variable                             | Model |       |       |       |       |       |       |       |       |
|--------------------------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
|                                      | 1     | 2     | 3     | 4     | 5     | 6     | 7     | 8     | 9     |
| <b>predictors</b>                    |       |       |       |       |       |       |       |       |       |
| male sex                             |       |       | 0.73† |       |       |       |       |       | 0.55† |
| age ≥75 yrs                          | 1.24  | 1.16  | 1.16  | 1.21  | 1.40  | 1.18  | 1.08† | 1.19  | 1.45  |
| T1-weighted imaging iso/hyperintense |       |       |       | 0.86† |       |       |       |       | 0.74† |
| T2-weighted imaging iso/hypointense  |       |       |       |       | 0.67† |       |       |       | 0.53† |
| unclear tumor-brain interface        | 1.73  | 2.78  | 2.85  | 3.03  | 2.82  | 2.74  | 2.70  | 2.67  | 2.81  |
| heterogeneous tumor enhancement      | 1.21  | 1.07  | 1.14  | 1.46  | 1.12  | 1.12  | 1.04  | 1.07  | 1.48  |
| positive capsular enhancement        |       | 1.55  | 1.66  | 1.65  | 1.63  | 1.48† | 1.51† | 1.44† | 1.47† |
| DWI iso/hypointense                  |       |       |       |       |       | 0.37† |       |       | 0.32† |
| positive brain edema                 |       |       |       |       |       |       | 0.33† |       | 0.21† |
| location dorsal/fissural‡            |       |       |       |       |       |       |       | 0.53† | 0.78† |
| <b>model information</b>             |       |       |       |       |       |       |       |       |       |
| Akaike information criterion§        | 119.1 | 115.9 | 116.0 | 115.9 | 116.3 | 117.5 | 117.6 | 117.1 | 120.6 |
| likelihood ratio§                    | 23.8  | 29.0  | 30.7  | 31.1  | 30.7  | 29.5  | 29.3  | 31.4  | 36.6  |
| degrees of freedom                   | 3     | 4     | 5     | 5     | 5     | 5     | 5     | 5     | 10    |
| p value (vs Model 2)                 | 0.023 | —     | 0.202 | 0.150 | 0.199 | 0.502 | 0.578 | 0.128 | 0.888 |

\* Data are presented as regression coefficients unless otherwise specified; p values are for comparison of likelihood ratios between different models versus Model 2.

† Regression coefficients with  $p > 0.05$ ; all other regression coefficients are significant ( $p < 0.05$ ).

‡ Non-skull base groups.

§ Lower values for Akaike information criterion and higher values for likelihood ratio indicate better models.

TABLE 4: Results of multivariate logistic regression in the prediction model and the scoring scale

| Predictor             | Definition                         | $\beta$ Coefficient | SEM  | OR   | 95% CI     | p Value | Score |
|-----------------------|------------------------------------|---------------------|------|------|------------|---------|-------|
| age                   | <75 yrs: 0<br>≥75 yrs: 1           | 1.16                | 0.57 | 3.20 | 1.04–9.83  | 0.0404  | 2     |
| tumor-brain interface | clear: 0<br>unclear: 1             | 2.78                | 0.90 | 16.1 | 2.76–94.35 | 0.0020  | 5     |
| tumor enhancement     | homogeneous: 0<br>heterogeneous: 1 | 1.07                | 0.52 | 2.92 | 1.06–8.07  | 0.0388  | 2     |
| capsular enhancement  | negative: 0<br>positive: 1         | 1.55                | 0.79 | 4.69 | 1.00–21.91 | 0.0493  | 3     |

logical feature of aggressive biological behavior.<sup>27,34</sup> As in previous reports, an unclear tumor-brain interface was a significant indicative factor in predicting high-grade meningiomas in both univariate and multivariate analyses in our study.

Positive capsular enhancement, defined as the enhanced layer at the tumor-brain interface, was another identified predictor in our study. This result was not reported by previous studies. The interesting finding is the existence of a negative association between an unclear tumor-brain interface and positive capsular enhancement according to the result of the correlation matrix of each predictor (data not shown). Because all meningiomas with unclear tumor-brain interface result in negative capsular enhancement, it means that unclear tumor-brain interface is a negative confounder in determining the association between positive capsular enhancement and high-grade meningioma. This effect could be observed by the difference between prediction Model 1 and Model 2. An elevated regression coefficient of unclear tumor-brain interface with increased weight is noted after adding positive capsular enhancement as another identified predictor in Model 2.

The development of meningioma-related brain edema is attributed to an interruption of the physiological

barrier, the combination of an arachnoid membrane and a CSF cleft, between the tumor and the adjacent brain parenchyma.<sup>7,15,23,31</sup> Nakano et al.<sup>26</sup> reported that the invasive pattern of tumor-brain interface—including irregular tumor margins, disappearance of the peritumoral rim, and hyperintensity of the tumor on T2-weighted imaging—was associated with meningioma-related brain edema. However, several studies showed no significant correlation between histological subtypes of meningiomas and peritumoral brain edema.<sup>1,17</sup> In the present study, there was no statistically significant difference between benign and high-grade meningiomas related to brain edema.

Some studies have reported that meningiomas with skull base locations were associated with a decreased risk of being high grade.<sup>16,20,21,30</sup> We also observed a similar finding in our study, that non-skull base meningiomas were more likely to be high-grade. Tumors locations are significantly different between patients with benign and those with high-grade meningiomas. However, this relationship disappears after controlling for confounders by multivariate logistic regression. In addition, we demonstrated no improvement in model performance with the addition of tumor location as a variable. Male sex is reported to be associated with a higher risk of high-grade meningioma than female sex according to a few

TABLE 5: Predicted probability of high-grade meningiomas using the proposed prediction model

| Score* | No. of Meningiomas† | High-Grade Meningiomas‡ | Parameter§ | SEM  | Probability (%)¶ | 95% CI    | Sensitivity (%) | Specificity (%) |
|--------|---------------------|-------------------------|------------|------|------------------|-----------|-----------------|-----------------|
| 0      | 47                  | 6                       | −1.76      | 0.32 | 14.6             | 8.40–24.1 | 100.0           | 0.0             |
| 2      | 23                  | 10                      | −1.31      | 0.24 | 21.2             | 14.5–30.1 | 80.0            | 45.6            |
| 3      | 25                  | 2                       | −1.08      | 0.22 | 25.3             | 18.0–34.4 | 46.7            | 60.0            |
| 4      | 4                   | 2                       | −0.86      | 0.23 | 29.8             | 21.3–40.0 | 40.0            | 85.6            |
| 5      | 7                   | 1                       | −0.63      | 0.26 | 34.8             | 24.4–46.9 | 33.3            | 87.8            |
| 7      | 1                   | 1                       | −0.17      | 0.35 | 45.7             | 29.8–62.5 | 30.0            | 94.4            |
| 8      | 3                   | 1                       | 0.05       | 0.40 | 51.4             | 32.3–70.0 | 26.7            | 94.4            |
| 9      | 1                   | 1                       | 0.28       | 0.47 | 57.0             | 34.7–76.7 | 23.3            | 96.7            |
| 10     | 8                   | 5                       | 0.51       | 0.53 | 62.5             | 37.1–82.4 | 20.0            | 96.7            |
| 12     | 1                   | 1                       | 0.96       | 0.66 | 72.4             | 41.9–90.5 | 3.3             | 100.0           |

\* Score =  $2 \times (\text{age}) + 5 \times (\text{tumor-brain interface}) + 3 \times (\text{capsular enhancement}) + 2 \times (\text{tumor enhancement})$ .

† The number of meningiomas with a specific calculated score using the prediction model.

‡ The number of high-grade meningiomas with a specific calculated score using the prediction model.

§ Parameter =  $-1.765 + \text{score} \times 0.227$ .

¶ Probability =  $e^{\text{Parameter}} / (1 + e^{\text{Parameter}})$ .

# MRI features and histopathological grade in meningioma

reports.<sup>16,17</sup> Although male sex was more likely to be a predictor of high-grade meningioma in our study (OR 1.83, 95% CI 0.77–4.36), there was not a statistically significant difference. Also, adding this variable did not improve the model's explanatory power.

Several studies have discussed the utility of DWI with an absolute apparent diffusion coefficient (ADC) in differentiating the histopathological grade of meningiomas.<sup>4,12,25,32,33,35,36</sup> The absolute cutoff and reliability of ADC measurement is controversial, with different b-values, areas of measurement (tumor peduncle, peripheral part of the tumor, and central region of the tumor), and methods of measurement (minimum ADC, mean ADC, maximum ADC, and normalized ADC) used in respective studies. Therefore, the ADC was not used as a possible predictor in our study. Kawahara et al.<sup>18</sup> first demonstrated that it was reasonable to predict the probability of high-grade meningioma based on assessment of a combination of MRI features. Although this study identified 2 independent predictive factors for high-grade meningioma (unclear tumor-brain interface and heterogeneous tumor enhancement), the sampling bias of 26 patients with high-grade meningiomas and 39 patients with benign meningiomas would have influenced the probability calculation. The goal of this study is to build a practical model helpful in the prediction of high-grade meningiomas. All of the identified variables could be collected easily by conventional MRI information. In clinical practice, this prediction model has important implications in forecasting high-grade meningiomas. For meningiomas with a lower probability of advanced histopathological grade, selective resection balanced against the risk of a surgical procedure is recommended. Otherwise, more aggressive resection, and even dura substitution, should be considered for those with a higher probability of a high-grade meningioma.

Our study has a few limitations. First, this is a retrospective study, and further prospective reports are needed to test the validity of our prediction model. Second, the patient population comes from 1 tertiary medical care center, and therefore the generalizability of our findings is not completely representative of the entire population. And third, the description of imaging findings is somewhat subjective, with the possible existence of intraobserver and interobserver variability.

## Conclusions

In this study, patient age  $\geq 75$  years, unclear tumor-brain interface, positive capsular enhancement, and heterogeneous tumor enhancement were identified as factors predictive of advanced histopathological grade of meningiomas. An increase in the calculated score according to our scoring scale was associated with an increased probability of having a high-grade meningioma. This scoring approach is useful for clinicians in determining the treatment strategy and even surgical planning for each patient.

## Disclosure

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Author contributions to the study and manuscript preparation include the following. Conception and design: Hueng, BJ Lin, C Lin, Tsai. Acquisition of data: BJ Lin, Chou, C Lin, Kao, Tsai, Feng. Analysis and interpretation of data: all authors. Drafting the article: Hueng, BJ Lin, C Lin. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Hueng. Statistical analysis: C Lin, Lee. Study supervision: Hueng.

## References

1. Ayerle J, Lobato RD, de la Cruz J, Alday R, Rivas JJ, Gómez PA, et al: Risk factors predicting recurrence in patients operated on for intracranial meningioma. A multivariate analysis. *Acta Neurochir (Wien)* **141**:921–932, 1999
2. Bondy M, Ligon BL: Epidemiology and etiology of intracranial meningiomas: a review. *J Neurooncol* **29**:197–205, 1996
3. Buetow MP, Buetow PC, Smirniotopoulos JG: Typical, atypical, and misleading features in meningioma. *Radiographics* **11**:1087–1106, 1991
4. Cabada T, Caballero MC, Insausti I, Alvarez de Eulate N, Bacaicoa C, Zazpe I, et al: [The role of diffusion-weighted imaging in the evaluation of meningiomas: radio-pathologic correlation.] *Radiologia* **51**:411–419, 2009 (Span)
5. Chen TY, Lai PH, Ho JT, Wang JS, Chen WL, Pan HB, et al: Magnetic resonance imaging and diffusion-weighted images of cystic meningioma: correlating with histopathology. *Clin Imaging* **28**:10–19, 2004
6. Commins DL, Atkinson RD, Burnett ME: Review of meningioma histopathology. *Neurosurg Focus* **23**(4):E3, 2007
7. 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 (Wien)* **125**:34–40, 1993
8. Dell S, Ganti SR, Steinberger A, McMurtry J III: Cystic meningiomas: a clinicoradiological study. *J Neurosurg* **57**:8–13, 1982
9. Demaerel P, Wilms G, Lammens M, Marchal G, Plets C, Goffin J, et al: Intracranial meningiomas: correlation between MR imaging and histology in fifty patients. *J Comput Assist Tomogr* **15**:45–51, 1991
10. Durand A, Labrousse F, Jouvett A, Bauchet L, Kalamarides M, Menei P, et al: WHO grade II and III meningiomas: a study of prognostic factors. *J Neurooncol* **95**:367–375, 2009
11. Essig M, Anzalone N, Combs SE, Dörfner A, Lee SK, Picozzi P, et al: MR imaging of neoplastic central nervous system lesions: review and recommendations for current practice. *AJNR Am J Neuroradiol* **33**:803–817, 2012
12. Filippi CG, Edgar MA, Uluğ AM, Prowda JC, Heier LA, Zimmerman RD: Appearance of meningiomas on diffusion-weighted images: correlating diffusion constants with histopathologic findings. *AJNR Am J Neuroradiol* **22**:65–72, 2001
13. Hashiba T, Hashimoto N, Maruno M, Izumoto S, Suzuki T, Kagawa N, et al: Scoring radiologic characteristics to predict proliferative potential in meningiomas. *Brain Tumor Pathol* **23**:49–54, 2006
14. Hsu CC, Pai CY, Kao HW, Hsueh CJ, Hsu WL, Lo CP: Do aggressive imaging features correlate with advanced histopathological grade in meningiomas? *J Clin Neurosci* **17**:584–587, 2010
15. Inamura T, Nishio S, Takeshita I, Fujiwara S, Fukui M: Peritumoral brain edema in meningiomas—influence of vascular supply on its development. *Neurosurgery* **31**:179–185, 1992
16. Kane AJ, Sughrue ME, Rutkowski MJ, Shangari G, Fang S, McDermott MW, et al: Anatomic location is a risk factor for atypical and malignant meningiomas. *Cancer* **117**:1272–1278, 2011
17. Kasuya H, Kubo O, Tanaka M, Amano K, Kato K, Hori T:



- Clinical and radiological features related to the growth potential of meningioma. **Neurosurg Rev** 29:293–297, 2006
18. Kawahara Y, Nakada M, Hayashi Y, Kai Y, Hayashi Y, Uchiyama N, et al: Prediction of high-grade meningioma by preoperative MRI assessment. **J Neurooncol** 108:147–152, 2012
  19. Louis DN, Ohgaki H, Wiestler OD, Cavenee WK, Burger PC, Jouvet A, et al: The 2007 WHO classification of tumours of the central nervous system. **Acta Neuropathol** 114:97–109, 2007
  20. Mahmood A, Caccamo DV, Tomecek FJ, Malik GM: Atypical and malignant meningiomas: a clinicopathological review. **Neurosurgery** 33:955–963, 1993
  21. Maier H, Ofner D, Hittmair A, Kitz K, Budka H: Classic, atypical, and anaplastic meningioma: three histopathological subtypes of clinical relevance. **J Neurosurg** 77:616–623, 1992
  22. Maillou A, Orfao A, Sayagues JM, Diaz P, Gómez-Moreta JA, Caballero M, et al: New classification scheme for the prognostic stratification of meningioma on the basis of chromosome 14 abnormalities, patient age, and tumor histopathology. **J Clin Oncol** 21:3285–3295, 2003
  23. Mattei TA, Mattei JA, Ramina R, Aguiar PH, Plese JP, Marino R Jr: Edema and malignancy in meningiomas. **Clinics (Sao Paulo)** 60:201–206, 2005
  24. Mermanishvili TL, Dzhorbenadze TA, Chachia GG: [Association of the degree of differentiation and the mitotic activity of intracranial meningiomas with age and gender.] **Arkh Patol** 72:16–18, 2010 (Russian)
  25. Nagar VA, Ye JR, Ng WH, Chan YH, Hui F, Lee CK, et al: Diffusion-weighted MR imaging: diagnosing atypical or malignant meningiomas and detecting tumor dedifferentiation. **AJNR Am J Neuroradiol** 29:1147–1152, 2008
  26. Nakano T, Asano K, Miura H, Itoh S, Suzuki S: Meningiomas with brain edema: radiological characteristics on MRI and review of the literature. **Clin Imaging** 26:243–249, 2002
  27. Nakasu S, Nakajima M, Matsumura K, Nakasu Y, Handa J: Meningioma: proliferating potential and clinicoradiological features. **Neurosurgery** 37:1049–1055, 1995
  28. Nakasu S, Nakasu Y, Nakajima M, Matsuda M, Handa J: Preoperative identification of meningiomas that are highly likely to recur. **J Neurosurg** 90:455–462, 1999
  29. Rockhill J, Mrugala M, Chamberlain MC: Intracranial meningiomas: an overview of diagnosis and treatment. **Neurosurg Focus** 23(4):E1, 2007
  30. Sade B, Chahlavi A, Krishnaney A, Nagel S, Choi E, Lee JH: World Health Organization Grades II and III meningiomas are rare in the cranial base and spine. **Neurosurgery** 61:1194–1198, 2007
  31. Salpietro FM, Alafaci C, Lucerna S, Iacopino DG, Todaro C, Tomasello F: Peritumoral edema in meningiomas: microsurgical observations of different brain tumor interfaces related to computed tomography. **Neurosurgery** 35:638–642, 1994
  32. Santelli L, Ramondo G, Della Puppa A, Ermani M, Scienza R, d'Avella D, et al: Diffusion-weighted imaging does not predict histological grading in meningiomas. **Acta Neurochir (Wien)** 152:1315–1319, 2010
  33. Sanverdi SE, Ozgen B, Oguz KK, Mut M, Dolgun A, Soy-lemezoglu F, et al: Is diffusion-weighted imaging useful in grading and differentiating histopathological subtypes of meningiomas? **Eur J Radiol** 81:2389–2395, 2012
  34. Takeguchi T, Miki H, Shimizu T, Kikuchi K, Mochizuki T, Ohue S, et al: Prediction of tumor-brain adhesion in intracranial meningiomas by MR imaging and DSA. **Magn Reson Med Sci** 2:171–179, 2003
  35. Watanabe Y, Yamasaki F, Kajiwaru Y, Takayasu T, Nosaka R, Akiyama Y, et al: Preoperative histological grading of meningiomas using apparent diffusion coefficient at 3T MRI. **Eur J Radiol** 82:658–663, 2013
  36. Yin B, Liu L, Zhang BY, Li YX, Li Y, Geng DY: Correlating apparent diffusion coefficients with histopathologic findings on meningiomas. **Eur J Radiol** 81:4050–4056, 2012

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