Brainstem glioma: Prediction of histopathologic grade based on conventional MR imaging

Yashar Moharamzad¹, Morteza Sanei Taheri², Farhad Niaghi² and Elham Shobeiri¹

Abstract
Objective: The objective of this article is to investigate the association between specific MR imaging findings and histopathologic grading (low-grade vs. high-grade) of brainstem gliomas (BSGs).

Methods: Sixty-two males and 34 females (mean (standard deviation, SD) age of 24.61 (17.20) years, range = 3 to 70 years) with histologically diagnosed BSG underwent conventional 1.5 T MR imaging, which included T1-weighted (T1W), T2W, and post-contrast T1W sequences. There were 39 children (mean age of 9.38 years) and 57 adults (mean age of 35 years). A binary logistic regression analysis was used to explore associations between MRI features and histopathological grade of the BSG.

Results: Binary logistic regression revealed that necrosis (adjusted odds ratio (OR) = 16.07; 95% confidence interval (CI) = 3.20 to 80.52; p = 0.001) and inhomogeneous contrast enhancement (adjusted OR = 8.04; 95% CI = 1.73 to 37.41; p = 0.008) as significant predictors of high-grade BSG. The equation (Nagelkerke R² = 0.575) is Logit (p high-grade BSG) = (2.77 × necrosis) + (2.08 × heterogeneous contrast enhancement) – 3.13. Sensitivity and specificity values were respectively 66.7% and 96.0% for necrosis and 85.7% and 65.9% for inhomogeneous contrast-enhancing lesions. In the pediatric age group, only inhomogeneous contrast enhancement (adjusted OR = 40; 95% CI = 3.95 to 445.73; p = 0.002) was a significant predictor for high-grade BSG.

Conclusion: Conventional MR imaging features such as necrosis and inhomogeneous contrast enhancement in adults and heterogeneous contrast enhancement in children suggest high-grade BSG.

Keywords
Glioma, tumor, brainstem, central nervous system, magnetic resonance imaging, pathology, adult, pediatrics

Introduction
Brainstem tumors are diagnosed in 10% of children and about 2% of adults with brain tumors.¹ Gliomas are the most prevalent tumors in the brainstem.² Brainstem gliomas (BSGs) usually affect the pons and can be focal (well marginated on imaging) or diffuse (poorly marginated on imaging).³ The latter form constitutes about two-thirds of BSGs in children.⁴ Brainstem tumors encompass a heterogeneous group of tumors and although different grading systems (e.g. based on localization and tumor growth pattern) have been proposed,⁵ historically they are categorized as low-grade (slow-growing) and high-grade (wore prognosis and rapidly progressive) gliomas based on World Health Organization (WHO) classification.⁶

The WHO classification of gliomas is the widely accepted system.⁷ In this classification, grades I (pilocytic astrocytoma that are solid and noninfiltrative with low proliferative potential) and II (astrocytoma, oligodendroglioma, and oligoastrocytoma with low-level proliferative activity) gliomas are considered low-grade tumors. Grades III (anaplastic-astrocytoma/oligodendroglioma) and IV (glioblastoma) gliomas are high-grade tumors with histological evidence of malignancy and rapid pre- and postoperative progression).⁶,⁷ Presence of high-grade BSG in a patient indicates a poor prognosis.⁸ High-grade BSGs in children have been found to be significantly associated with an unfavorable outcome with a hazard ratio of 1.7 in a previous population-based study.¹⁰ This has also been reported in adult BSGs.¹¹

Conventional magnetic resonance imaging (MRI) is undoubtedly a critical and usually the primary imaging
modality in BSG diagnosis both in adult and pediatric patients. On MRI, BSGs are visualized as diffuse enlargement of the brainstem and characterized by low-signal intensity on T1-weighted (T1W) and high-signal intensity on T2W images, and variable contrast enhancement as diffuse BSGs usually do not enhance.\(^5\)\(^1\)\(^2\) Sometimes a ventral exophytic pattern is seen in pontine lesions.\(^2\) BSGs can be confined to the midbrain or extend to adjacent structures such as the hypothalamus and spinal cord.\(^5\) In addition to the diagnostic imaging information that MRI provides, it also assists in stereotactic biopsy of more aggressive component of the tumor, considering the high risk of brainstem sampling, which is necessary to guide subsequent treatment.\(^1\) When stereotactic biopsy of larger supratentorial gliomas was performed under MRI guidance, it accurately represented the grade of glioma and helped in planning further treatment to resect the tumor.\(^1\)\(^4\) The application of MRI-guided stereotactic biopsy for BSGs is less studied owing to biopsy-related complications, but more recent findings reported that biopsy improved diagnostic accuracy of BSG.\(^1\)\(^5\)

As MRI findings are a cornerstone in biopsy decisions and treatment plans of BSG patients, limited studies have been conducted to find potential correlations between various MRI findings with histologic grading.\(^1\)\(^6\)\(^1\)\(^8\) Focal lesions were correlated with more favorable histologic tumors.\(^1\)\(^6\) Another study showed that focal and contrast enhancement correlated with diagnoses other than diffuse BSGs in adults.\(^1\)\(^7\) However, evidence suggests that owing to heterogeneity of MRI findings in BSG, MRI appearance may not necessarily predict pathologic findings and further studies are required to elucidate the role of MRI findings in predicting histologic grading of BSGs.\(^1\)\(^2\)

As biopsy of BSGs is not always readily feasible and most often further treatment plans rely mainly on radiologic findings, it is essential to have more details about the significance of various MRI findings seen in BSGs. MRI findings found to be correlated with histologically higher-grade BSGs enable clinicians to employ better decisions in further management of patients with more appropriate treatments. Therefore, we undertook this study to explore associations between conventional MRI findings and histopathologic grading of BSGs in a sample of adult and pediatric patients.

**Materials and methods**

**Study design**

This was an observational analytic retrospective study.

**Study setting**

This study was conducted in our university hospital, which is a general tertiary medical center.

**Samples**

The study population consisted of histologically confirmed primary BSGs of either gender and at any age. All patients who were diagnosed by this tumor in a five-year period at our referral center, which covers a population of about 5 million people, were included. Histopathology reports indicating metastases, lymphoma, vascular abnormalities, inflammatory and infectious processes, and receiving radiotherapy before performing MRI were not included. The pathologic samples consisted of stereotactic biopsies archived in the Department of Pathology in a five-year period. In this time period, 96 pathologically proved BSG cases were included in the study. Then, the MR images and clinical records were reviewed.

**Variables**

The histopathologic grading reports were categorized as low-grade or high-grade glioma. Low-grade gliomas that are slow-growing tumors consisted of WHO grade I (pilocytic astrocytoma and ganglioglioma) and grade II category (astrocytoma and oligodendroglioma). High-grade tumors consisted of anaplastic glioma (WHO grade III) and glioblastoma (WHO grade IV).\(^6\)

The MRI findings included the location of the tumor (midbrain, pons, or medulla), its size, and extension to adjacent structures, and other features such as necrosis, peritumoral edema, T1W and T2W signal intensity changes, and contrast enhancement were recorded in a checklist.

**MRI**

MRI protocol consisted of T1W sequence with repetition time (TR) of 370 to 630 ms, echo time (TE) of 9 to 15 ms, field of view (FOV) of 270 mm, and flip angle of 90/180. For T2W images, TR was 3000 to 3500 ms, TE was 91 to 120 ms, FOV was 230 mm, and flip angle was 90/160 or 90/180. Slice thickness varied from 5 mm to 6 mm. Sagittal, axial and coronal planes were acquired.

A board-certified radiologist (MST, 14 years of experience) reviewed the conventional brain MRI. He was blinded to the histopathologic reports. The image series included T1W, T2W, and post-contrast (intra-venous gadolinium) T1W sequences (Avanto\(^8\)\(^1\)\(^,\) 1.5 Tesla, Siemens Healthcare, Erlangen, Germany). Hypo-, iso-, and hyper-signal intensity of the lesions were determined in relation to the intensity of the gray matter.

**Statistical analyses**

Categorical variables were expressed by frequency and percentage. For quantitative variables, the normal distribution was determined by performing the Kolmogorov-Smirnov test as well as evaluating skewness, kurtosis, and histogram of the particular variable. Tumor size had a normal distribution and mean...
(standard deviation, SD) was used to describe it, and the Student's t test was applied to compare mean values of tumor size between low- and high-grade tumor groups. However, age had a non-normal distribution and median (interquartile range, IQR) was used to report it, and the Mann–Whitney U test was used in two-by-two comparison. In order to compare the nominal variables between low- and high-grade groups, the Chi-squared test or the Fisher's exact test was used.

A binary logistic regression analysis with forward approach was performed to determine significant MRI predictors of high-grade BSGs. The variables that had significant/marginally significant difference (defined as p values of less than 0.1) in two-group comparisons (low-grade vs. high-grade tumor groups) were included in the model. The high-grade tumor was coded as 1 and low-grade as 0. The significance level for each variable's entry to or removal from the model was set at 0.05 and 0.1, respectively.

Sensitivity [true positive/(true positive + false negative)] and specificity [true negative/(true negative + false positive)] values for the MRI findings found by the regression analysis to be significant predictor for high-grade BSGs were calculated using cross-tabulations. In the cross-tabulations, the distribution of each significant MRI finding was placed at the rows and BSG grade (low-grade and high-grade) was placed at the columns. True positive (sensitivity) was defined as number of patients with the particular MRI finding whose BSG was of high grade. True negative (specificity) was defined as number of patients without the particular MRI finding whose BSG was of low grade.

The data were analyzed using SPSS software (ver. 18.0, IBM, US). p values of less than 5% were considered statistically significant.

Ethics

The study protocol was approved by the ethics committee of our medical university. The study was in conformity with the Declaration of Helsinki.

Results

Demographic and histopathologic findings

Of 96 studied patients, 62 (64.6%) were male and 34 (35.4%) were female. The mean (SD) age of the sample was 24.61 (17.20) years (range, 3 to 70 years). There were 39 children (defined as age < 18 years) with a mean (SD) age of 9.38 (3.84) years and 57 adults (≥18 years) with a mean (SD) age of 35 (14.20) years. Cranial nerve involvement (44 patients, 45.8%) followed by dizziness (40 cases (41.6%), headache (36 patients, 37.5%) and hemiparesis (32 cases, 33.3%) were respectively the most common signs and symptoms. Seventy-five patients (78.1%) had low-grade BSGs and 21 cases (21.9%) had high-grade BSGs. High-grade BSG was documented in seven children (17.9%) and 14 adults (24.6%). Of 62 males, 49 patients (79%) had low-grade BSG and 13 patients (21%) had high-grade tumors (p = 0.7). Median (IQR) age values in low- and high-grade groups were respectively 19 (24) and 21 (45) years (p = 0.37).

MRI findings

Pons (84 patients, 87.5%), midbrain (67 patients, 69.8%), and medulla (17 cases, 17.7%) were respectively the most common locations of BSGs. Tumoral extension was seen in thalamus (nine cases, 9.4%), spinal cord (five cases, 5.2%), and other locations (cerebellar peduncles and cerebellum). Exophytic growth was seen in 21 cases (21.9%). No statistically significant difference was seen between low- and high-grade groups regarding tumor location or its extension pattern (Table 1).

Table 2 compares MR image patterns between low- and high-grade BSG. As observed, asymmetrical lesions, necrosis, and prominent peritumoral edema were significantly more common in high-grade tumors. On the other hand, homogenous expansion of the tumors was more prevalent among low-grade BSGs. None of the tumors showed calcification.
Intra-tumoral hemorrhage was observed in only one patient, who was a 59-year-old male with high-grade BSG. Mean (±SD) tumor size was comparable between low-grade (3.64 ± 1.56 cm) and high-grade (3.86 ± 1.27 cm) groups (p = 0.56).

Table 3 summarizes T1W and T2W signal intensities and contrast enhancement in the studied groups. As observed, all high-grade tumors had high-signal intensity on T2W images and all enhanced after gadolinium injection, which showed significant difference with low-grade tumors. Among tumors that showed enhancement, heterogeneous enhancement was seen in 18 cases of high-grade tumor (85.7%), which was significantly higher than in the low-grade group (15 cases, 54.9%; p = 0.07). On the other hand, homogenous expansion was considerably more frequent in the low-grade (23 cases, 71.9%) compared to the high-grade (just one patient, 14.3%) group; p = 0.008.

**Table 3.** Comparison of magnetic resonance imaging T1-weighted (T1W), T2-weighted (T2W) signal intensities, and contrast enhancement among 96 patients with histologically confirmed brainstem glioma between low-grade and high-grade tumors.

<table>
<thead>
<tr>
<th></th>
<th>Low-grade (N = 75)</th>
<th>High-grade (N = 21)</th>
<th>p value</th>
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<tbody>
<tr>
<td>T1W</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyposignal</td>
<td>72 (96.0%)</td>
<td>19 (90.5%)</td>
<td>0.14a</td>
</tr>
<tr>
<td>Iso signal</td>
<td>3 (4.0%)</td>
<td>1 (4.8%)</td>
<td></td>
</tr>
<tr>
<td>Hypersignal</td>
<td>0</td>
<td>1 (4.8%)</td>
<td></td>
</tr>
<tr>
<td>T2W</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyposignal</td>
<td>1 (1.3%)</td>
<td>0</td>
<td>0.006a</td>
</tr>
<tr>
<td>Iso signal</td>
<td>21 (28.0%)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Hypersignal</td>
<td>53 (70.7%)</td>
<td>21 (100.0%)</td>
<td></td>
</tr>
<tr>
<td>Contrast enhancement</td>
<td>44 (58.7%)</td>
<td>21 (100.0%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Homogenous</td>
<td>29 (65.9%)</td>
<td>3 (14.3%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Heterogeneous</td>
<td>15 (34.1%)</td>
<td>18 (85.7%)</td>
<td></td>
</tr>
</tbody>
</table>


**MRI findings in adults**

Similar to children, tumor size, location, and extension as well as well-defined margins, cystic component, and T1W signal intensity were comparable between the low- and high-grade groups. Asymmetrical lesions, necrosis, prominent peritumoral edema, high-signal intensity on T2W, and contrast enhancement were more common in the high-grade group. Homogenous expansion was more prevalent in the low-grade tumor (results not shown).

**Binary logistic regression analysis**

Based on the two-by-two comparisons (i.e. comparison of MRI findings in two independent samples, namely low-grade BSGs vs. high-grade BSGs) in the whole sample and those conducted separately in adults and pediatric patients, the following seven MRI variables were selected as input variables to be entered into the regression model: necrosis, homogenous expansion, enhancement pattern, prominent peritumoral edema, contrast enhancement, asymmetrical morphology, and well-defined margins. Since “homogenous expansion” and “well-defined margins” were significantly more common in low-grade tumors, presence of these features was recorded as 0 and their absence was recorded as 1. Table 4 shows the binary logistic regression results. Necrosis (adjusted odds ratio (OR) = 16.07, p = 0.001) and inhomogeneous contrast enhancement (adjusted OR = 8.04, p = 0.008) were significant predictors of high-grade BSG (Figures 1 and 2). The following equation can be used to predict high-grade BSG (Nagelkerke R² = 0.575):

\[
\text{Logit} (p_{\text{high-grade BSG}}) = (2.77 \times \text{necrosis}) + (2.08 \times \text{heterogeneous contrast enhancement}) - 3.13
\]
Nagelkerke $R^2$ of 0.575 indicated a moderately significant relationship between predictors and BSG histopathologic grade. Adjusted OR values showed that the odds of high-grade BSGs were respectively 2.77 and 2.08 times greater for those MRIs with necrosis and inhomogeneous contrast enhancement.

**Significant MRI findings in children and adults**

In the pediatric age group, only inhomogeneous contrast enhancement ($B = 3.73, p = 0.002$) with adjusted OR of 40 (95% CI = 3.95 to 445.73) was recognized as the prognostic factor for high-grade BSG. In the adult age group, similar to the whole population, necrosis ($B = 3.64; p = 0.003$) with adjusted OR of 38.34 (95% CI = 3.54 to 415.11) and heterogeneous contrast enhancement ($B = 2.08, p = 0.03$) with adjusted OR of 8.03 (95% CI = 1.18 to 54.36) were predictors of high-grade BSG.

**Sensitivity and specificity**

Sensitivity and specificity values of significant predictors for high-grade tumors were respectively 66.7% (14/21) and 96.0% (72/75) for necrosis and 85.7% (18/21) and 65.9% (29/44) for inhomogeneous contrast-enhancing lesions. Table 5 presents sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of the MRI findings.

**Discussion**

Based on the obtained findings, necrosis and inhomogeneous contrast enhancement were the MRI variables found to have significant association with high-grade gliomas of the brainstem. Differentiating between

<table>
<thead>
<tr>
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<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Necrosis</td>
<td>66.7% (57.1% to 76.3%)</td>
<td>96.0% (92.0% to 100.0%)</td>
<td>82.3% (74.5% to 90.1%)</td>
<td>91.1% (85.3% to 96.9%)</td>
</tr>
<tr>
<td>Inhomogeneous contrast enhancement</td>
<td>85.7% (78.6% to 92.8%)</td>
<td>65.9% (56.3% to 75.5%)</td>
<td>54.5% (44.4% to 64.6%)</td>
<td>90.6% (84.7% to 96.5%)</td>
</tr>
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</table>
low- and high-grade gliomas is a critical step in management of glioma. Tumor grade directly influences treatment aggressiveness.\textsuperscript{18} MRI is usually the first noninvasive imaging tool in pre-treatment assessment of patients with intracranial tumors and is considered the most sensitive technique in diagnosing posterior fossa lesions.\textsuperscript{19} Hence, studies have been conducted to define those MRI features that can predict tumor aggressiveness and prognosis.\textsuperscript{16,17,20–22} Determination of prognosis in BSG is somewhat difficult owing to varying degrees of aggressiveness of these tumors.\textsuperscript{11} Some experts agree that in childhood BSG, without pathologic confirmation and solely based on MRI features, chemotherapy or radiotherapy could be initiated.\textsuperscript{5}

The pons was the most common location in our sample, which is in agreement with earlier reports.\textsuperscript{23,24} We did not find any association between tumor location and histology type. However, a previous study of 51 adult BSG patients showed that low-grade tumor was associated with pontine involvement.\textsuperscript{5}

Our results are consistent with some previous reports that indicate intra-tumoral necrosis (due to elevated level of lactate metabolite in tumor tissue) is associated with higher-grade tumors and/or worse prognosis.\textsuperscript{12,21} In 48 diffuse BSGs in adults, necrosis on MRI, histologic grading, and duration of symptoms were determined as significant predictors for unfavorable outcome. Those with contrast enhancement (representing anaplastic transformation) and necrosis were resistant to treatment and had a median survival of less than one year.\textsuperscript{23} Another study analyzing 48 BSGs reported that all 15 patients with malignant BSG had necrosis, but most low-grade BSGs did not show necrosis. The authors also found that using multivariate analyses, necrosis on conventional MRI and longer (>3 months) duration of symptoms prior to diagnosis were the two significant prognostic factors for shorter survival.\textsuperscript{23} The finding of necrosis and its association with histologic grading and prognosis is also documented in supratentorial gliomas. In a study of 36 cases with supratentorial gliomas, mass effect and necrosis/cyst formation were reported to be the main conventional MRI predictors for anaplastic astrocytoma and glioblastoma multiforme.\textsuperscript{26} In contrast to the mentioned findings, a former series of 86 BSGs conducted to determine factors that predict late (survival > 1 year) vs. early progressors (survival < 1 year) did not report necrosis or contrast enhancement as significant predictors; only duration of symptoms lasting < 3 months was a significant variable.\textsuperscript{24}

In intrinsic diffuse BSGs, absence of contrast enhancement has been mentioned to indicate a lower-grade histopathologic examination.\textsuperscript{16} Contrast enhancement (indicating blood-brain barrier breakdown related to neovascularization) is one of the imaging features noted to be associated with decreased survival and a progressive course of gliomas.\textsuperscript{11,13,23,27} Here, all patients with high-grade BSGs had contrast-enhancing lesions and consequently in two-by-two comparisons, the difference in distribution between groups was highly significant. But, inhomogeneous contrast enhancement, not contrast enhancement alone, reached a statistically significant level. This finding is comparable with previous evidence that contrast material enhancement per se may not necessarily be an accurate indicator of tumor grade.\textsuperscript{13,21} The MRI findings of necrosis and heterogeneous contrast enhancement are related as small necrosis areas may merge to form central necrosis, which is responsible for intrinsic areas of necrosis and the inhomogeneous nature of contrast-enhancing appearance of higher-grade gliomas.\textsuperscript{20} In diffuse intrinsic pontine gliomas, which constitute 60%–80% of BSGs in children and usually have a poor prognosis,\textsuperscript{9} contrast enhancement may not occur at all. But, in cases of contrast enhancement, a heterogeneous pattern of enhancement (focal ring, spotty, or focal patchy) on T2W images is usually seen.\textsuperscript{20} This supports our findings that the pattern of enhancement, rather than presence or absence of enhancement, should be considered by radiologists when trying to correlate with aggressive behavior of BSGs. Focal or diffuse extension of the BSG as well as enhancing vs. non-enhancing appearance, albeit considered by some clinicians as characteristic findings for BSGs, did not differentiate low-grade from high-grade BSGs.\textsuperscript{17} The heterogeneous contrast-enhancement pattern may be independent of focal or diffuse extension of BSG as focal malignant BSGs often exhibit ring-like or heterogeneous contrast enhancement.\textsuperscript{13} Interestingly, analysis of 96 patients with brainstem lesions reported that contrast enhancement and focal appearance of the lesions were in favor of non-tumor diagnoses.\textsuperscript{17}

Another consideration concerning evolution of diffuse intrinsic BSGs in children is that it is not uncommon for this tumor to progress from no enhancement at earlier stages to focal enhancement, and finally to diffuse enhancement.\textsuperscript{7} However, inhomogeneous contrast enhancement is not a specific finding and here its specificity was only 65.9%. About one-third of gliomas that do not exhibit enhancement may be malignant. On the other hand, some low-grade gliomas (in particular gangliogliomas and pilocytic astrocytomas) may show enhancement.\textsuperscript{13}

Usually, BSGs are hyperintense on T2W images.\textsuperscript{20} In the presented sample, about two-thirds of the low-grade BSG group also had high-signal intensity on T2W sequences. On the other hand, all high-grade tumors had this finding. But this is not a specific finding. T2W hyperintensity, especially in children, cannot discriminate acute vs. chronic lesions of various etiologies.\textsuperscript{19} For instance, in a study by Delaret et al. of 96 brainstem lesions (both tumor and non-tumor) in adults, all of them were hyperintense on T2W images.\textsuperscript{17} Likewise, all T2W images of 33 children’s brainstem tumors showed hyperintense lesions on MRI.\textsuperscript{4} So, it is apparent that T2W hyperintensity should not be described alone in differentiating
high- vs. low-grade BSGs, and even in discriminating tumor from non-tumor etiologies.

When contrast enhancement, prominent edema, and necrosis are not seen on conventional MRI, a high-grade tumor may be mistaken for a low-grade one. The reverse situation can also occur and such findings can be present in low-grade tumors. Therefore, we think that each of these findings has its own diagnostic importance. Although more advanced MRI techniques have been introduced in recent years that unquestionably have advantages over conventional MRI in delineating cellularity, angiogenesis, and metabolic features of tumors, conventional MRI still has widespread use in many centers. Therefore, we think that the presented findings here are of sufficient value to help manage BSG.

**Limitations and strengths**

We faced some limitations in this study. First, we included only BSG tumors. Adding supratentorial gliomas can add valuable information to compare between these two distinct locations for intracranial tumors. Second, only conventional MRI was studied. Although conventional MRI does not yield information about biological details of gliomas, it provides essential high-resolution structural information. There is evidence that more advanced sequences such as diffusion-weighted imaging (DWI), perfusion-weighted imaging (PWI), diffusion tensor imaging, and protein transfer imaging and fluid-attenuated inversion-recovery (FLAIR), can assist in preoperative grading of gliomas, and proton MR spectroscopic imaging in nonenhancing gliomas may have added value in preoperative grading of gliomas. In particular, FLAIR sequences were reported to be superior to post-contrast TIW images postoperatively in providing more accurate information about tumor volume and treatment response. Furthermore, perfusion MRI has been shown as a reliable method in detecting progression of high-grade intracranial gliomas compared to standard MRI. As a third limitation, we were not able to follow the patients to determine an association of the MRI features with overall survival and prognosis of the BSGs. Despite these shortcomings, we presented the findings in a relatively larger sample compared to previous BSG reports in the literature. Hence, a significant statistical prediction model was developed that about 50% of the variability in BSG histologic grading was accounted for by the model. Undoubtedly, there are other factors such as angiogenesis, mitotic activity, and metabolism that may have significant effect on the aggressive behavior of BSGs that were not investigated here.

**Conclusion**

Conventional MRI features such as necrosis and inhomogeneous contrast-enhancing lesion in adults and heterogeneous contrast enhancement in children are highly associated with high-grade BSGs.

**Conflict of interest**

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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