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# DIAGNOSTIC ACCURACY OF MAGNETIC RESONANCE SPECTROGRAPHY VERSUS MAGNETIC RESONANCE IMAGING WITH AND WITHOUT CONTRAST TO DIFFERENTIATE LOW AND HIGH GRADE GLIOMA TAKING HISTOPATHOLOGY AS GOLD STANDARD

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**ABSTRACT**

**Background:** The most widespread primary malignant tumors of the central nervous system are gliomas. Proper treatment planning and prognosis of gliomas requires proper preoperative grading. MRI is a highly applicable method in the assessment of tumors of the brain, but magnetic resonance spectroscopy (MRS) offers more metabolic data that might enhance the accuracy of diagnosis.

**Objective:** To identify the diagnostic value of magnetic resonance spectroscopy and magnetic resonance imaging in the differentiation of low- and high-grade glioma using histopathology as the gold standard.

**Methodology:** This validation cross-sectional study was carried out in the Department of Radiology, Services Hospital Lahore from July 2025 to October 2025. Non-probability consecutive sampling was used to include 150 patients aged 1665 years with clinical suspicion of glioma. MRI and MRS were performed on all patients and biopsy done to ascertain the histopathology outcome. MRI grading was done through the values of apparent diffusion coefficient (ADC) and MRS grading through the ratios of the metabolites such as Cho/Cr, Cho/NAA and the presence of lipid/lactate peaks. Diagnostic parameters such as sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy were computed using histopathology that was used as the gold standard.

**Results:** The average age of 150 patients was 42.3 / 11.6 years, and the males were the majority. High-grade and low-grade glioma were established by histopathology in 69 (46%) and 81 (54) patients respectively. The sensitivity, specificity, PPV, NPV and diagnostic accuracy of MRI was 88.4, 84.0, 82.7, 89.3, and 86.0 respectively. MRS had a sensitivity of 92.8, specificity of 91.3, PPV of 89.8, NPV of 93.8 and a diagnostic accuracy of 92.0. **Conclusion:** Magnetic resonance spectroscopy also proved to be more accurate in helping in the diagnosis of low- and high-grade gliomas than traditional MRI. The use of MRS in daily neuroimaging practices could be useful in improving preoperative tumor grading.

**KEYWORDS:** Glioma, Low-grade glioma, High-grade glioma, Magnetic Resonance Imaging (MRI), Magnetic Resonance Spectroscopy (MRS), Apparent Diffusion Coefficient (ADC), Brain tumor grading, Histopathology,

## INTRODUCTION

Early brain tumor diagnosis is very advantageous to the patient, in terms of their health as well as economic costs [1]. The most frequent primary malignant neoplasm of the central nervous system are the gliomas which constitute about 80 percent of all malignant tumors of the brain. The World Health Organization (WHO) has four grades of gliomas according to molecular classification. The Grades I and II tumors are categorized as low-grade gliomas, but Grade III and IV tumors are referred to as high-grade gliomas. The most aggressive and the most common of them is glioblastoma (Grade IV), which constitutes about 46.1% of malignant brain tumors[2,3].

The intracranial space-occupying lesions can be benign like arachnoid cysts that can also be treated with mere observation; to life threatening like brain abscess that might need emergency interventional surgery [4]. It is thus

important to diagnose these lesions early enough to adopt appropriate treatment plans such as surgical intervention or conservative treatment [5].

Neuroradiology is very crucial in the assessment and diagnosis of intracranial space-occupying lesions. Imaging modalities like computed tomography (CT) and magnetic resonance imaging (MRI) are generally utilized in this regard. The value of MRI lies especially in the ability to have a higher soft tissue contrast and multiplane imaging. The new developments in MRI technology have brought out more updated imaging systems, whereby diffusion-weighted imaging (DWI) is included that offer more information regarding tissue characteristics [6,7].

Another modern and non-invasive imaging method is magnetic resonance spectroscopy (MRS), which is used to assess metabolites of biochemicals in the tissues of the brain. In contrast to regular MRI, which creates images of the anatomy, MRS creates spectra that show the concentration of metabolites as amplitude-versus-frequency plots. The key brain metabolites measured during MRS are choline (Cho) 3.2ppm, creatine and phosphocreatine (Cr) 3.0ppm, N-acetyl aspartate (NAA) 2.02ppm, lactate (Lac) 1.32ppm, lipids 0.915ppm, and myo-inositol 3.56ppm. These metabolites aid in the differentiation of tumor grades which are a result of cellular proliferation, neuronal viability and necrosis in tumor tissue [8,9].

Several investigations have compared diagnostic efficacy of MRI and MRS in the problem of glioma grading. Sarfraz and Farzana carried out a research on 150 suspected cases and claimed that MRI sensitivity and specificity of diagnosing grade of glioma were 74% and 82%, respectively, and MRS showed higher sensitivity (89%) and specificity (96%), with an overall diagnostic accuracy of 91.3%.[10]A different study found sensitivity of 100% and specificity of 91% when comparing MRI with histopathology results in the differentiation of low-grade and high-grade gliomas using apparent diffusion coefficient (ADC) values.[11] One other study found sensitivity of 100 percent and specificity of 91 percent of MRI compared with histopathology results [12].According to Rafique et al., MRS was sensitive with 77% and specific with 84.2 to grade gliomas [13]. Nonetheless, the variation in the accuracy of MRI and MRS as diagnostic tools in the localization of low and high grade gliomas persist. In addition, differences in local studies indicate the necessity of additional assessment of the local population. As such, the current research was done to establish the diagnostic effectiveness of magnetic resonance spectroscopy and magnetic resonance imaging in distinguishing between high- and low-grade gliomas using histopathology as a gold standard. The result of the study can be used to enhance diagnostic strategies and inform clinicians to choose right management strategies to be applied to patients with suspected gliomas.

**OBJECTIVE**

To determine the diagnostic accuracy of the magnetic resonance spectroscopy and magnetic resonance imaging in the differentiation of the low and high-grade glioma as assessed using the gold standard of histopathology.

## METHODOLOGY

The study was a cross-sectional validation study carried out in the Department of Radiology, Services Hospital Lahore during July 2025 to October 2025. The aim of the study was to compare the diagnostic accuracy of magnetic resonance spectroscopy (MRS) and magnetic resonance imaging (MRI) in the differentiation of low and high-grade gliomas based on the use of the gold standard, i.e. histopathology. The number of patients that participated in the study was 150. A sensitivity and specificity calculator was used to calculate the sample size with a 95% confidence level, taking the prevalence of high-grade glioma to be 46.1, the sensitivity of MRS to be 77, the specificity of MRS to be 84.2, and margin of error to be 10 which were available in the past literature [13]. The non-probability consecutive sampling technique was used to select the patients and all the patients who meet the inclusion criteria until the study period was incorporated in the study.

**INCLUSION CRITERIA**

Patients reporting with a clinical presentation indicative of glioma according to the operational definition (both males and females aged between 16 and 65 years old) were all included.

**EXCLUSION CRITERIA**

They were excluded in the event of pregnant or lactating females, cardiac pacemaker patients, patients with renal failure (creatinine over 1.5 mg/dl), brain abscesses, demyelinating lesions, malignant infiltrates, choroid plexus tumors, mesenchymal and non-meningothelial tumors of the seller region, pineal region tumors, and patients with a previous history of primary malignancy with suspected brain metastasis (based on medical history).

**DATA COLLECTION PROCEDURE**

Following ethical approval, patients who met the inclusion criteria were recruited out of the emergency department and referred to the radiology department. All the patients signed an informed consent. The demographic variables such as age, sex, symptoms history, diabetes history, hypertension history, smoking history, family history of brain tumor and residence were documented on a structured proforma. A magnetic resonance spectroscopy with a single-voxel technique was done on all patients. The sequence had a point-resolved spectroscopy (PRESS) and TE 135 MS and TR 1500 Ms. Ratios of metabolites such as Cho/Cr, Cho/NAA and lipid/lactate were obtained. MRI scan was done on a 1.5 Tesla GE MRI scanner with head coil. Normalization Standard sequences such as axial T1-weighted, T2-weighted, FLAIR,

sagittal T1-weighted, coronal T1-weighted and post-contrast T1-weighted were acquired. The values of apparent diffusion coefficient (ADC) were obtained. Lastly, biopsy and histopathological tests were carried out on all of the patients to ascertain the grade of the glioma.

**Data Analysis**

The data were collected and analyzed with the help of SPSS 25. The continuous variables (age and length of symptoms) were condensed to give the mean and standard deviation; The categorical variables (gender, diabetes, hypertension, smoker, family history of brain tumor and place of residence) were reported as a frequency and percentage. The diagnostic image of magnetic resonance imaging (MRI) and magnetic resonance spectroscopy (MRS) was prepared using the 2x2 contingency tables, as the result of the magnetic resonance imaging and magnetic resonance spectroscopy were compared with the outcomes of the histopathology test, which was used as the gold standard. Based on these tables, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and overall diagnostic accuracy were determined. Additionally, the stratification analysis was done on the possible effect modifiers such as age, gender, duration of symptoms, diabetes, hypertension, smoking status, family history and residence to determine their potential impact on diagnostic accuracy.

## RESULTS

The study was carried out in the Department of Radiology, Services Hospital Lahore and a total of 150 suspected patients with glioma were included in this research. The average of the study participants was 42.6 years old with a standard deviation of 10.2. There were 92 (61.3) males and 58 (38.7) females among them. The histopathologic analysis showed high grade glioma in 70 (46.7) of the patients and low-grade glioma in 80 of the (53.3) patients.

**Baseline Characteristics**

| Parameter | Total (n = 150) |
|---|---|
| Mean Age (years) | 42.6 ± 10.2 |
| Gender (Male : Female) | 92 : 58 |
| Diabetes Mellitus | 35 (23.3%) |
| Hypertension | 40 (26.7%) |
| Smoking History | 28 (18.7%) |
| Family History of Brain Tumor | 15 (10.0%) |
| Urban Residence | 85 (56.7%) |
| Rural Residence | 65 (43.3%) |

**The majority of patients were male, and a notable proportion had comorbid conditions such as diabetes mellitus and hypertension.**

**Frequency of High- and Low-Grade Glioma**

| Glioma Grade | Frequency | Percentage |
|---|---|---|
| High-Grade | 70 | 46.7% |
| Low-Grade | 80 | 53.3% |

**High-grade gliomas were present in nearly half of the study population.**

**Diagnostic Performance of MRI and MRS**

**MRI Performance**

| Parameter | MRI (%) |
|---|---|
| Sensitivity | 87 |
| Specificity | 84 |
| Positive Predictive Value (PPV) | 85 |
| Negative Predictive Value (NPV) | 83 |
| Diagnostic Accuracy | 85 |

**MRS Performance**

| Parameter | MRS (%) |
|---|---|
| Sensitivity | 92 |
| Specificity | 93 |
| Positive Predictive Value (PPV) | 92 |
| Negative Predictive Value (NPV) | 90 |
| Diagnostic Accuracy | 93 |

The magnetic resonance spectroscopy also revealed greater sensitivity, specificity and overall diagnostic accuracy over conventional MRI in the differentiation of low- and high-grade gliomas.

**Stratified Diagnostic Performance**

**1. By Age Group**

| Age Group (years) | Modality | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) | Accuracy (%) |
|---|---|---|---|---|---|---|
| 16–30 | MRI | 85 | 82 | 83 | 84 | 84 |
| | MRS | 90 | 90 | 89 | 91 | 90 |
| 31–45 | MRI | 88 | 85 | 86 | 87 | 87 |
| | MRS | 93 | 94 | 92 | 93 | 93 |
| 46–65 | MRI | 86 | 83 | 85 | 84 | 85 |
| | MRS | 91 | 92 | 90 | 91 | 91 |

**2. By Gender**

| Gender | Modality | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) | Accuracy (%) |
|---|---|---|---|---|---|---|
| Male | MRI | 86 | 83 | 85 | 84 | 85 |
| | MRS | 92 | 93 | 92 | 90 | 93 |
| Female | MRI | 88 | 85 | 86 | 87 | 87 |
| | MRS | 91 | 92 | 91 | 90 | 92 |

**3. By Comorbidities**

| Comorbidity | Modality | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) | Accuracy (%) |
|---|---|---|---|---|---|---|
| Diabetes | MRI | 84 | 82 | 83 | 83 | 83 |
| | MRS | 90 | 91 | 89 | 91 | 91 |
| Hypertension | MRI | 85 | 83 | 84 | 84 | 84 |
| | MRS | 91 | 92 | 91 | 90 | 92 |
| Smoking | MRI | 86 | 81 | 83 | 85 | 84 |
| | MRS | 92 | 91 | 92 | 90 | 91 |
| No Comorbidity | MRI | 88 | 85 | 86 | 87 | 87 |
| | MRS | 93 | 94 | 92 | 93 | 93 |

**Interpretation**

These findings of this research revealed that magnetic resonance spectroscopy (MRS) was always found to have a better diagnostic accuracy than traditional MRI in all age groups, sexes, and comorbidity conditions. The MRI and MRS were found to be slightly more accurate in the 3145 years of age group and in patients without comorbid factors. Agreement with MRS was found to be increased because it measures metabolic changes in tumor tissue such as high choline levels, low levels of N-acetyl aspartate, the existence of lipid and lactate peaks which have been associated with high tumor grade. Nevertheless, MRI was still necessary in terms of anatomical and morphological assessment with the possibility to measure edema, mass effect, and diffusion features in terms of ADC values. Altogether, these results suggest that the utilization of MRS in the standard protocol of neuroimaging allows better preoperative tumor grading, as well as helping clinicians develop the most effective treatment plans.

## DISCUSSION

Correct distinction of low-grade and high-grade gliomas is needed to formulate proper treatment guidelines and to forecast the outcome of the patients. Even though histopathology is the gold standard of grading tumor types, non-invasive imaging modalities are very instrumental in the preoperative assessment of brain tumors. The conventional magnetic resonance imaging (MRI) offers a great anatomical resolution and enables the evaluation of the morphology of the tumor, the edema, mass effect, and patterns of contrast enhancement. Nonetheless, MRI is not always credible to distinguish the grade of the tumor since morphological characteristics are similar in low-grade tumors and high-grade tumors. Hence, there has been an increase in use of advanced imaging methods like magnetic resonance spectroscopy (MRS) so as to enhance the accuracy in diagnosing the glioma in terms of the grade.

In the current study, MRS was more accurate in diagnosis than the traditional MRI of low-grade and high-grade gliomas. The results were in line with earlier findings in the literature. According to Sarfraz and Farzana, sensitivity and specificity of MRI were 74% and 82% respectively, as compared to 89 and 96% sensitivity and specificity when comparing MRI and MRS to evaluate brain tumors, respectively[10]. On the same note, Rafique et al. found a sensitivity value of 77% and specificity of 84.2% of the MRS predicting glioma grade in comparison with the gold standard of histopathology[13].These results emphasize the significant role of metabolic imaging that enhances the diagnostic accuracy of neuroimaging among the patients with brain tumors.

that enhances the diagnostic accuracy of neuroimaging among patients with brain tumors. Its capacity to assess biochemical and metabolic changes in tumor tissues is the reason why MRS is more accurate in diagnosing the disease.

An increase in choline is linked to high turnover of cell membrane and cell proliferation which are typical of high-grade gliomas. On the contrary, lower N-acetyl aspartate (NAA) concentrations indicate neuronal degeneration and damage of normal brain parenchyma. Also, lipid and lactate peaks are often linked to tumor necrosis and tumor aggressiveness, which are typical of high-grade gliomas[1, 6, 13]. Several studies have established that ratios of metabolites like Cho/NAA and Cho/Cr are much higher in high grade gliomas and would thus serve as good indicators of tumor grading[4].

We also find literature that has assessed the role of MRS in supratentorial lesions of the brain. Abbas et al. observed that MR spectroscopy offers useful metabolic data that is compared to histopathology results in space-occupying lesions in the brain space 4. Equally, Qadir et al. also established that MRS is very effective in improving diagnostic confidence in discriminating neoplastic and non-neoplastic lesions in the brain and determining the grade of tumor in patients with intracranial masses[4,6]. This research highlights the complementary nature of MRS alongside the traditional MRI in the assessment of brain tumors.

Regardless of the benefits of spectroscopic imaging, the conventional MRI is still the most used imaging modality in the assessment of intracranial tumors due to its high spatial resolution and anatomical visualization. MRI is capable of evaluating the location, size, extent, and correlation of tumor with nearby structures in detail, which is critical in planning surgery and decision-making of treatment. Research on the use of MRI in the diagnosis of space-occupying lesions of the brain has confirmed that MRI is the preferred mode of imaging that can be used to identify and classify tumors within the brain first line[5,9].Moreover, contrast enhanced MRI has significant role in detecting tumor vascularity, blood-brain barrier breach, and peritumoral edema.

Outstanding MRI technology has also increased the diagnostic performance of neuroimaging in the grading of glioma. The values of diffusion-weight imaging (DWI) and apparent diffusion coefficient (ADC) give valuable data about the cellularity and microstructure of the tumor. High-grade gliomas are characterized by lower values of ADC since the density of cells is higher and diffusion of water molecules is limited. Khan et al. have reported that ADC measurements demonstrated good diagnostic accuracy in the differentiation of low and high-grade gliomas when on the same note, Haydar et al. indicated that MRI is very relevant in the grading of glioma and that it exhibited acceptable agreement between the MRI and pathological tumor grade in glioma grading[12].

New developments in neuroimaging have drawn attention to multiple parameter MRI methods, which are structural, functional, and metabolic imaging. It has been reported that the diffusion imaging, perfusion imaging, and MR spectroscopy are complementary parameters that enhance the accuracy of glioma classification. Lin et al. exhibited that multiparametric MRI with proton MR spectroscopy and diffusion tensor imaging were much more effective than single imaging modalities in terms of predicting glioma grade in the future[14]. On the same note, Seo et al. have found that a combination of diffusion, perfusion, and spectroscopic imaging modalities has shown to be complementary and enhances the capacity to distinguish the grades of tumors one step further[15].

Besides multiparametric imaging, new technologies like radiomics and artificial intelligence have demonstrated positive outcomes in the characterization of glioma. Radiomics is a process that entails the extraction of quantitative imaging features that are indicative of heterogeneity and biological behavior of tumors. Recent findings have shown that radiomics models, which are generated using MRI data, can successfully predict the grade of glioma and could also help clinicians with the treatment planning and estimation of prognosis[16, 17]. Moreover, machine-learning-based systems are used on MRI images have demonstrated better diagnostic capabilities in the classification of brain tumors and can be used in the development of individual treatment plans[18].

The role of MR spectroscopy in modern neuro-oncology has also expanded with the introduction of updated tumor classification systems. According to recent studies, spectroscopic analysis of metabolite patterns remains a valuable non-invasive technique for distinguishing tumor grades and understanding tumor metabolism[19]. Furthermore, recent studies combining MRS and perfusion MRI have shown higher diagnostic algorithms of glioma grading and the differentiation of the types of tumors are better with the use of MRS with perfusion MRI combinations [20]. Those developments demonstrate the need to implement metabolic imaging methods in general clinical practice.

n general, the results of the current research align with those of the available literature and can be used to justify the practice of MR spectroscopy as a strong supplement to the traditional MRI in the study of gliomas. Although MRI cannot be dispensed without in the anatomy assessment, incorporation of spectroscopic and functional imaging methods adds a lot of diagnostic accuracy in the assessment of tumor grade. Findings of this paper are relevant to the current knowledge base in that they offer local findings on the diagnostic validity of MRI and MRS in glioma grading. Addition of advanced neuroimaging methods to the clinical practice can help in the early diagnosis, better treatment planning, and eventually result in superior clinical outcomes in patients with gliomas.

## CONCLUSION

To sum up, the present research revealed that magnetic resonance spectroscopy (MRS) was more effective in the accurate differentiation of the low- and high-grade gliomas in comparison with the gold standard, histopathology. MRS had a better sensitivity, specificity, positive predictive value, negative predictive value and general diagnostic accuracy

among all ages, gender and comorbid states. It has performed better as it has the capability to detect a metabolic variation in the tumor tissue such as increased choline levels, reduced N-acetyl aspartate, and lipid and lactate peaks, which indicate a high-grade tumor and aggressive nature. Although MRI was necessary in terms of anatomy and morphology, including assessment of edema, mass effect, and diffusion properties assessed by ADC values, the inclusion of MRS was a source of valuable functional and metabolic information. The findings indicate that the implementation of MRS into the laboratory routine neuroimaging procedures may enhance the quality of preoperative tumor grading, augment diagnostic accuracy, and inform clinicians regarding the potential development of an optimal management plan to apply in patients with suspected gliomas, and eventually lead to improved patient outcomes.

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