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Comparative Evaluation of Diffusion Weighted Imaging and Magnetic Resonance Spectroscopy in the Diagnosis and Grading of Brain Tumors: A Prospective Clinical Study

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A B S T R A C T

Background*:** Accurate diagnosis and grading of brain tumors are critical for effective treatment. This study evaluated the diagnostic accuracy of Diffusion Weighted Imaging (DWI) and Magnetic Resonance Spectroscopy (MRS) compared to conventional MRI, with histopathology as the gold standard.Methods*:** This prospective study included 60 patients undergoing MRI for suspected brain tumors. Each patient was assessed using conventional MRI, DWI, and MRS. Apparent Diffusion Coefficient (ADC) values and metabolic ratios were analyzed, and diagnostic performance was compared to histopathological results. Statistical analysis was performed using SPSS, with p-values < 0.05 considered significant. ***Results*:**Glioblastomamultiforme was the most common tumor, comprising 26.7% of cases. MRS demonstrated a diagnostic accuracy of 82.5%, outperforming DWI (72.5%). MRS had a sensitivity of 75% and specificity of 90.9% for glioblastomamultiforme, while DWI had a sensitivity of 68.75% and specificity of 86.36%. The mean ADC values for high-grade gliomas ($0.65 \pm 0.13 \times 10^{-3}$ mm²/s) were significantly lower than for low-grade gliomas ($1.02 \pm 0.16 \times 10^{-3}$ mm²/s; $p < 0.001$).***Conclusion*:** MRS is a reliable tool for non-invasive brain tumor grading, showing higher diagnostic accuracy than DWI. Combining DWI and MRS with conventional MRI could enhance diagnostic precision, guiding better treatment planning. Future research should explore integrated imaging approaches for improved tumor diagnosis and monitoring.

Keywords: Brain tumors, Diffusion Weighted Imaging, Magnetic Resonance Spectroscopy, Diagnosis, ADC values, Glioma grading.

INTRODUCTION

Central nervous system (CNS) tumors constitute approximately 2% of all malignancies, yet they pose a significant public health burden due to associated morbidity and mortality, particularly affecting young and middle-aged individuals, leading to high death-adjusted life years compared to other cancers [1]. In India, the incidence of CNS tumors ranges from 5 to 10 per 100,000 population [2]. CNS tumors encompass a broad spectrum of histological types, clinical manifestations, and prognostic outcomes. Astrocytomas are the most common primary CNS tumors in adults, with high-grade gliomas comprising a significant portion. In the pediatric population, astrocytomas also lead, followed by medulloblastomas [3].

Clinical presentation of brain tumors can be varied, ranging from generalized symptoms like headaches and cognitive dysfunction to more specific symptoms such as seizures, motor deficits, and personality changes [4]. The variability in presentation is often due to differences in tumor size, location, and growth rate [5]. Despite advances in treatment, the prognosis of CNS tumors largely depends on accurate diagnosis and classification, which guide therapeutic strategies.

Conventional magnetic resonance imaging (MRI) remains a fundamental tool for initial diagnosis, providing essential information on tumor size, location, and effects on adjacent brain structures. MRI's ability to offer superior soft

tissue contrast makes it preferable over computed tomography (CT) [6]. However, conventional MRI has limitations, particularly in differentiating tumor types and assessing malignancy grades, which are crucial for planning treatment strategies.

Recent advancements in neuroimaging, particularly Diffusion Weighted Imaging (DWI) and Magnetic Resonance Spectroscopy (MRS), have enhanced the diagnostic accuracy of CNS tumor assessment. DWI measures the diffusion of water molecules in tissues, providing insights into tumor cellularity. Tumors with higher cellularity restrict water diffusion, leading to lower apparent diffusion coefficient (ADC) values, which are commonly associated with higher-grade malignancies [7]. MRS, on the other hand, assesses the biochemical profile of brain tissue by analyzing metabolite concentrations, such as choline (Cho), creatinine (Cr), and N-acetyl aspartate (NAA). Variations in these metabolites help distinguish between tumor types and grades, enabling better diagnostic precision [8].

The utility of DWI and MRS has been demonstrated in differentiating high-grade from low-grade gliomas, guiding treatment planning and prognosis [9]. However, the sensitivity and specificity of these techniques can vary, and their integration into routine clinical practice remains under evaluation [10]. This study aims to evaluate the diagnostic performance of DWI and MRS in comparison to conventional MRI, with histopathological findings serving as the gold standard, to establish their role in the non-invasive diagnosis and grading of brain tumors.

Aims and Objectives

The primary aim of this study was to evaluate the diagnostic role of Diffusion Weighted Imaging (DWI) with Apparent Diffusion Coefficient (ADC) correlation and Magnetic Resonance Spectroscopy (MRS) in the grading and differentiation of brain tumors. The study also aimed to assess the sensitivity and specificity of these advanced imaging techniques in comparison to conventional MRI, using histopathological findings as the gold standard. Additionally, the study sought to determine the effectiveness of DWI and MRS in guiding treatment planning and monitoring therapeutic response, wherever applicable.

Materials and Methods

This hospital-based prospective clinical study was conducted over a period of two years, from September 2022 to September 2024, at the Department of Radio-diagnosis, SSIMS & RC, Davangere, India. The study included a total of 60 patients who were referred to the radiology department with a history of headache, focal neurological deficits, or known brain tumors. The study was approved by the Institutional Ethics Committee, and informed consent was obtained from all participants before the commencement of the study.

The sample size was determined based on data obtained from medical records, which indicated an approximate number of 53 cases of brain tumors diagnosed in the preceding year. To account for variability and to ensure sufficient data for statistical analysis, an additional 10% was added to the estimated sample size, resulting in a total of 60 participants. This sample size was considered adequate to perform a comprehensive analysis of the diagnostic capabilities of DWI and MRS in differentiating between various brain tumors.

Patients were selected based on specific inclusion and exclusion criteria. The inclusion criteria comprised individuals of all age groups, genders, and ethnic backgrounds who presented with clinical symptoms suggestive of brain tumors, such as headache, motor and sensory impairments, aphasia, hemianopia, diplopia, dysphagia, apraxia, ataxia, and perception deficits. Additionally, patients with known risk factors, including hypertension, diabetes mellitus, smoking, and ischemic heart disease, were documented and included. The study aimed to provide a comprehensive analysis across a diverse demographic to ensure the generalizability of the findings.

Exclusion criteria were clearly defined to ensure the accuracy and safety of the imaging procedures. Patients who were claustrophobic or had metallic implants, such as cardiac pacemakers or cochlear implants, were excluded from the study due to the contraindications for MRI. Additionally, patients who were unwilling to undergo imaging or had conditions unrelated to the clinical suspicion of brain tumors, such as other known pathological conditions or those lacking sufficient clinical information, were excluded. Cases in which the diagnosis could not be confirmed due to the absence of histopathological evaluation, or where necropsy was unavailable, were also excluded.

Upon selection, each patient underwent a detailed clinical evaluation followed by imaging using a GE 1.5 Tesla MRI scanner at SSIMS & RC, Davangere. The imaging protocol included conventional spin echo sequences, such as axial T1, T2, and FLAIR, coronal T2 FLAIR, sagittal T1, and axial SWAN sequences. Diffusion Weighted Imaging was performed using a b-value of 1000, with a subset of cases using a b-value of 2000 to further evaluate tumor characteristics. Additionally, post-contrast sequences in axial, coronal, and sagittal planes were acquired to enhance the imaging details. Magnetic Resonance Spectroscopy was performed using a multivoxel approach with TR values of 144

and 35 ms.The voxel was strategically positioned to cover the maximum area of the lesion, ensuring accurate metabolic analysis. Care was taken to avoid small lesions situated close to bone structures, where spectroscopy could yield unreliable results due to technical limitations.

The study meticulously recorded data on tumor location, margin characteristics, post-contrast enhancement patterns, and diffusion restriction grades. The metabolic profiles obtained through MRS, including choline (Cho), creatinine (Cr), and N-acetyl aspartate (NAA) ratios, were analyzed to evaluate tumor differentiation. The collected imaging data were then compared to histopathological findings, which served as the definitive diagnostic benchmark. Histopathological examination was performed following biopsy or surgical resection, and tissue samples were analyzed to confirm the type and grade of the tumor.

The collected data were compiled into a master chart for analysis. Continuous data, such as age and ADC values, were expressed as means and standard deviations, while categorical data, including gender distribution and diagnostic accuracy, were represented as frequencies and proportions. Statistical analysis was conducted using IBM SPSS Statistics Version 22. Appropriate tests of significance were applied based on the type of data, and a p-value of less than 0.05 was considered statistically significant. Sensitivity, specificity, and accuracy were calculated to assess the diagnostic performance of DWI and MRS, comparing them against conventional MRI and histopathological results.

This methodological approach ensured a comprehensive evaluation of the role of DWI and MRS in the non-invasive diagnosis and grading of brain tumors, highlighting their potential as effective diagnostic tools in routine clinical practice. The study's rigorous design and adherence to ethical standards provided robust and reliable results, contributing valuable insights into the application of advanced neuroimaging techniques.

RESULTS

A total of 60 patients were included in the study, with a wide range of age, gender, and clinical backgrounds. The results were categorized based on demographic characteristics, histopathological diagnosis, and comparative analysis of the diagnostic accuracy of Diffusion Weighted Imaging (DWI), Magnetic Resonance Spectroscopy (MRS), and conventional MRI.

Demographic Characteristics

The study population had a mean age of 56.22 years (±10.21), with participants ranging from 28 to 74 years. The majority of patients (40%) were within the 51-60 years age group, indicating a higher prevalence of brain tumors among older adults. The demographic data are summarized in Table 1.

Table 1: Age Distribution of Study Participants

Age Group (years)	Frequency (N)	Percentage (%)
≤30	1	1.7
31-40	3	5.0
41-50	13	21.7
51-60	24	40.0
>60	19	31.7
Total	**60**	**100.0**

Histopathological Diagnosis

Histopathological examination was performed on all participants, providing a definitive diagnosis. Glioblastomamultiforme was the most prevalent tumor type, accounting for 26.7% of the cases, followed by metastasis (23.3%) and high-grade glioma (18.3%). The distribution of diagnoses is shown in Table 2.

Table 2: Histopathological Diagnosis of Study Participants

Diagnosis	Frequency (N)	Percentage (%)
GlioblastomaMultiforme	16	26.7
High-Grade Glioma	11	18.3
Low-Grade Glioma	5	8.3
Lymphoma	7	11.7
Meningioma	7	11.7
Metastasis	14	23.3
Total	**60**	**100.0**

Association Between Diagnosis and Age

The mean age varied significantly across different diagnoses. Patients with glioblastomamultiforme and metastasis were predominantly older, with a mean age of over 60 years, suggesting a higher prevalence in the elderly population. This association was statistically significant ($p < 0.001$), as detailed in Table 3.

Table 3: Association Between Diagnosis and Age

Diagnosis	Mean Age (years)	Standard Deviation	Minimum Age	Maximum Age	p-value
GlioblastomaMultiforme	63.25	6.51	52	74	<0.001
High-Grade Glioma	48.45	7.19	35	59	
Low-Grade Glioma	49.80	8.79	40	60	
Lymphoma	47.14	11.07	28	62	
Meningioma	51.00	4.40	45	58	
Metastasis	63.71	6.96	52	74	
Total	**56.22**	**10.21**	**28**	**74**	**<0.001**

Diagnostic Performance of DWI and MRS

The sensitivity and specificity of DWI and MRS in diagnosing different tumor types were evaluated. DWI had a sensitivity of 68.75% and specificity of 86.36% for diagnosing glioblastomamultiforme, while MRS showed superior performance with 75.00% sensitivity and 90.90% specificity. This trend was observed across various tumor types, indicating that MRS was generally more accurate. Detailed sensitivity and specificity data are presented in Table 4.

Table 4: Sensitivity and Specificity of DWI and MRS in Diagnosing GlioblastomaMultiforme

Diagnostic Modality	Sensitivity (%)	Specificity (%)	Positive Cases (N)	Negative Cases (N)
DWI	68.75	86.36	11	6
MRS	75.00	90.90	12	4

Comparison of ADC Values AcrossTumor Types

The study utilized ADC values obtained from DWI to distinguish between different grades of tumors. The mean ADC value was significantly lower in high-grade gliomas compared to low-grade gliomas, indicating higher cellularity and restricted diffusion. This differentiation is crucial for accurate tumor grading and has implications for treatment planning. The mean ADC values for each diagnosis are summarized in Table 5.

Table 5: ADC Values Across Different Tumor Types

Diagnosis	Mean ADC ($\times 10^{-3}$ mm²/s)	Standard Deviation	Range ($\times 10^{-3}$ mm²/s)
GlioblastomaMultiforme	0.69	0.08	0.6 - 0.8
High-Grade Glioma	0.65	0.13	0.5 - 0.9
Low-Grade Glioma	1.02	0.16	0.8 - 1.3
Lymphoma	0.68	0.08	0.6 - 0.8
Meningioma	1.21	0.11	1.1 - 1.4
Metastasis	0.82	0.09	0.7 - 0.9
Total	**0.81**	**0.22**	**0.5 - 1.4**

Overall Diagnostic Accuracy of DWI and MRS

The overall diagnostic accuracy of DWI and MRS was evaluated by comparing imaging findings with histopathological results. MRS demonstrated a higher diagnostic accuracy across all tumor types, particularly in differentiating between high-grade and low-grade gliomas. This supports the utility of MRS as a non-invasive tool for accurate diagnosis and grading. The overall accuracy of both imaging modalities is detailed in Table 6.

Table 6: Overall Diagnostic Accuracy of DWI and MRS Compared to Histopathology

Diagnostic Modality	Diagnostic Accuracy (%)
DWI	72.5
MRS	82.5

The findings of this study highlight the importance of using advanced neuroimaging techniques, such as DWI and MRS, in conjunction with conventional MRI. While DWI provides valuable insights into tumor cellularity, MRS adds another layer of diagnostic precision by offering metabolic information that aids in accurate tumor differentiation and grading. The results consistently showed that MRS was superior in sensitivity and specificity across various tumor types, making it a more reliable tool in the non-invasive diagnosis of brain tumors.

DISCUSSION

The present study evaluated the diagnostic performance of Diffusion Weighted Imaging (DWI) and Magnetic Resonance Spectroscopy (MRS) in the grading and differentiation of brain tumors, comparing their accuracy against conventional MRI with histopathological findings as the gold standard. Our results indicate that MRS showed superior diagnostic accuracy compared to DWI, a finding consistent with other studies in the literature.

Our study found that the sensitivity of MRS for diagnosing glioblastomamultiforme was 75%, with a specificity of 90.9%. Similar findings were reported by Gupta *et al*., who demonstrated that MRS had a sensitivity of 78% and a specificity of 92% in distinguishing high-grade gliomas from low-grade ones, underscoring its reliability in clinical settings [11]. Furthermore, our study observed that DWI was less sensitive (68.75%) compared to MRS, although it maintained a comparable specificity of 86.36%. This is consistent with the findings of Lee *et al*., who reported that DWI, while effective, often had reduced sensitivity for lower-grade gliomas due to overlapping ADC values between tumor grades [12].

Our study's ADC values further demonstrated the utility of DWI in providing information about tumor cellularity, with high-grade gliomas showing significantly lower mean ADC values ($0.65 \pm 0.13 \times 10^{-3}$ mm²/s) compared to low-grade gliomas ($1.02 \pm 0.16 \times 10^{-3}$ mm²/s). These findings align with those of Murakami *et al*., who reported mean ADC values of 0.69×10^{-3} mm²/s for high-grade tumors and 1.05×10^{-3} mm²/s for low-grade tumors, indicating that lower ADC values are indicative of higher cellularity and grade [13]. The use of ADC as a distinguishing factor has been extensively validated, as lower ADC values correlate with increased cell density, a characteristic feature of high-grade tumors [14].

Comparatively, the use of MRS provided metabolic insights that were crucial for accurate tumor grading. The study showed elevated choline (Cho) and reduced N-acetyl aspartate (NAA) ratios in high-grade gliomas, with a Cho/NAA ratio mean of 2.93 (± 1.72) in glioblastomamultiforme cases. Previous studies, such as that by Kim *et al*., reported similar metabolic patterns, where the Cho/NAA ratio in high-grade gliomas was significantly higher (mean ratio 3.01 ± 0.89) compared to low-grade gliomas, supporting the premise that increased choline levels are reflective of higher cell membrane turnover and tumor aggressiveness [15].

The specificity of DWI and MRS was particularly notable in the differentiation of lymphoma and meningiomas. Our study found DWI's specificity in diagnosing lymphoma to be 100%, highlighting its ability to detect restricted diffusion, a characteristic feature of highly cellular tumors like lymphoma. This finding was consistent with studies by Barajas *et al*., where DWI showed 98% specificity for CNS lymphoma, emphasizing its effectiveness in identifying tumor types characterized by densely packed cells [16]. On the other hand, MRS was found to be more sensitive for detecting metabolic anomalies associated with various tumor types, as demonstrated by Öz*et al*., who confirmed that MRS could accurately identify metabolic profiles even when structural imaging was inconclusive [17].

One of the most critical aspects of our study was the comprehensive comparison of DWI and MRS with histopathology. The overall diagnostic accuracy of MRS was 82.5%, which was higher than DWI's accuracy of 72.5%. These results are in line with those of Caivano*et al*., who found that MRS achieved an accuracy of 80% in differentiating between high and low-grade tumors, while DWI achieved an accuracy of 70%, reinforcing the utility of MRS as a more robust tool for non-invasive tumor grading [18]. The statistical analysis in our study also revealed significant differences in the ADC values between high-grade and low-grade tumors ($p < 0.001$), corroborating the findings by Kang *et al*., who reported p-values of <0.05 in differentiating glioma grades using ADC histogram analysis [19].

Despite these positive findings, some limitations were noted. Although DWI effectively highlighted areas of restricted diffusion, there were cases where overlap in ADC values between high-grade and low-grade tumors led to diagnostic challenges. Similar issues were reported by Darbar*et al*., who noted that while DWI was sensitive, its specificity was occasionally compromised due to ADC value overlaps in different tumor grades [20]. Additionally, the MRS technique, while more accurate, requires longer scanning times and greater expertise in interpretation, which may limit its routine clinical application in settings with limited resources.

Our study demonstrates that while both DWI and MRS are valuable tools for the non-invasive diagnosis of brain tumors, MRS offers superior sensitivity and specificity, making it a more reliable method for tumor grading and differentiation. The integration of these advanced imaging modalities into routine diagnostic protocols can enhance early diagnosis and accurate grading, thus enabling better treatment planning and patient outcomes. Future studies should focus on expanding sample sizes and exploring the combined use of DWI and MRS to improve diagnostic accuracy further.

CONCLUSION

Summary of Findings

This study demonstrated the efficacy of Diffusion Weighted Imaging (DWI) and Magnetic Resonance Spectroscopy (MRS) in the diagnosis and grading of brain tumors, highlighting the strengths and limitations of each modality. DWI was found to be effective in providing insights into tumor cellularity, with high-grade gliomas showing significantly lower mean ADC values ($0.65 \pm 0.13 \times 10^{-3}$ mm²/s) compared to low-grade gliomas ($1.02 \pm 0.16 \times 10^{-3}$ mm²/s; $p < 0.001$). MRS, on the other hand, excelled in metabolic analysis, with a higher diagnostic accuracy of 82.5% compared to 72.5% for DWI. The ability of MRS to differentiate between high-grade and low-grade gliomas based on metabolic ratios, such as an elevated Cho/NAA ratio, provided a reliable, non-invasive method for tumor grading.

Clinical Implications

The findings suggest that MRS should be considered as a routine adjunct to conventional MRI, especially in cases where tumor differentiation and grading are critical for treatment planning. The integration of DWI and MRS could enhance diagnostic precision, guiding therapeutic decisions, and improving patient outcomes. DWI's role in detecting highly cellular tumors, such as lymphoma, was particularly notable, indicating its utility in specific clinical scenarios.

Recommendations for Future Research

Further studies with larger sample sizes and a focus on the integration of DWI and MRS could provide deeper insights into the complementary roles of these modalities. Longitudinal studies assessing treatment response using these imaging techniques would also be valuable, potentially offering non-invasive methods for monitoring tumor progression or regression during therapy.

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