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The Role of MR Spectroscopy in Differentiating Intraaxial Brain Tumors: A Non-invasive Diagnostic Approach

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Abstract

Background: Intraaxial brain tumors present significant diagnostic challenges due to their varied histopathological types and overlapping imaging characteristics. Accurate differentiation among gliomas, metastases, and medulloblastomas is essential for effective treatment planning and improved patient outcomes.

Objective: This study aims to evaluate the diagnostic utility of Magnetic Resonance Spectroscopy (MRS) in differentiating various types of intraaxial brain tumors by correlating metabolic findings with clinical and histopathological diagnoses.

Methods: A prospective, observational study was conducted at a tertiary care center, involving 30 patients with clinically suspected intraaxial brain tumors. MRS was performed alongside conventional MRI, and metabolite ratios, including choline (Cho), N-acetyl aspartate (NAA), and creatine (Cr), were calculated. Histopathological diagnosis served as the gold standard for comparison.

Results: High-grade gliomas demonstrated significantly elevated Cho/NAA ratios (2.8 ± 0.5) compared to low-grade gliomas (1.4 ± 0.3) and other tumor types. The optimal cutoff for the Cho/NAA ratio to differentiate high-grade from low-grade gliomas was found to be 2.0, with

a sensitivity of 85% and specificity of 88%. A strong correlation (Pearson's r = 0.75, p < 0.001) was observed between MRS findings and histopathological grade.

Conclusion: MRS is a valuable non-invasive diagnostic tool for differentiating intraaxial brain tumors, providing critical metabolic information that enhances tumor characterization and supports clinical decision-making. Further studies are warranted to validate these findings and standardize MRS applications in clinical practice.

Keywords: Magnetic Resonance Spectroscopy, intraaxial brain tumors, gliomas, tumor differentiation, non-invasive diagnosis, metabolite ratios.

Introduction

Intraaxial brain tumors, which originate within the brain parenchyma, present complex diagnostic challenges due to their diverse histopathological types and overlapping imaging features. Accurate differentiation of these tumors, including gliomas, metastases, and medulloblastomas, is critical for establishing the appropriate treatment approach and improving patient outcomes【1】. Conventional imaging techniques, such as Magnetic Resonance Imaging (MRI), primarily offer anatomical details but often lack the specificity needed to differentiate between tumor types, particularly in cases where tumor borders are indistinct or when edema or necrosis is present【2】. Magnetic Resonance Spectroscopy (MRS) has emerged as a non-invasive imaging modality that supplements MRI by providing crucial metabolic information【3】. By analyzing the levels of metabolites such as choline, N-acetyl aspartate (NAA), creatine, and lactate, MRS detects the biochemical environment of brain tissues, allowing for improved tumor characterization【4】. The unique metabolic signatures of different intraaxial tumors offer insights that assist in distinguishing between neoplastic and non-neoplastic lesions, as well as between high-grade and low-grade tumors【

5】. The increasing use of MRS in clinical practice highlights its potential to refine diagnostic accuracy without the need for invasive procedures like biopsy【6】. Despite these advances, there is still a lack of clear, standardized metabolic markers for differentiating certain tumor types, and the potential of MRS remains underutilized【7】. This study is justified by the need to address these gaps in knowledge, aiming to validate the role of MRS in improving diagnostic accuracy and aiding in non-invasive tumor differentiation【8】.

Aim of the Study

The aim of this study is to assess the diagnostic utility of Magnetic Resonance Spectroscopy (MRS) in differentiating various types of intraaxial brain tumors, by correlating metabolic findings with clinical and histopathological diagnoses, and to evaluate its potential as a non-invasive diagnostic tool to improve tumor classification and treatment planning.

Materials and Methods

Study Design and Setting

This is a prospective, observational study conducted at Department of Radiodiagnosis in Basaveshwara medical college and Hospital, Chitradurga., involving patients with clinically suspected intraaxial brain tumors.

Patient Selection

A total of 30 patients, aged 18–70 years, who were referred for MRI evaluation of suspected intraaxial brain tumors were included in the study. Patients with known primary brain tumors or newly detected intraaxial masses on conventional MRI were considered eligible. The inclusion criteria were:

1. Patients with suspected intraaxial brain tumors based on clinical or radiological findings.
2. Ability to undergo MRI and MRS without contraindications.
3. Willingness to provide informed consent.

Patients were excluded if they had extraaxial brain tumors, significant comorbidities affecting MRI outcomes (e.g., severe claustrophobia, metallic implants, or unstable cardiovascular conditions), or prior brain surgery. Additionally, patients with benign intracranial lesions were excluded from the study.

Imaging Protocol

Magnetic Resonance Spectroscopy (MRS) was performed as an adjunct to conventional MRI, using a 1.5T MRI system with an 8-channel head coil. The imaging protocol included standard sequences such as T1-weighted, T2-weighted, and fluid-attenuated inversion recovery (FLAIR) sequences to identify anatomical details of the tumors. Single-voxel proton MRS was employed to evaluate the metabolic profile of the tumor and adjacent brain tissue.

MRS Acquisition Parameters:

- Voxel size: 2 x 2 x 2 cm^3, placed at the center of the tumor mass.
- TR (Repetition Time): 2000 ms
- TE (Echo Time): 144 ms
- Acquisition mode: Point Resolved Spectroscopy (PRESS)

Spectra were acquired from both the tumor core and peritumoral regions to assess metabolic heterogeneity. The key metabolites assessed included choline (Cho), creatine (Cr), N-acetyl

aspartate (NAA), lactate, and lipids. Water suppression techniques were applied to minimize interference from water signals.

Data Interpretation and Analysis

Spectral analysis was conducted using the manufacturer's software, and metabolite peaks were quantified in terms of signal intensities. Ratios of Cho/Cr, NAA/Cr, and Cho/NAA were calculated for each region of interest. The MRS findings were compared with the histopathological diagnosis to determine the diagnostic accuracy of MRS in differentiating between tumor types and grades.

Tumor Classification:

- Tumors were classified as low-grade or high-grade based on MRS metabolite ratios. A Cho/NAA ratio greater than 2.0 was considered suggestive of high-grade tumors, whereas a ratio below 1.5 was indicative of low-grade tumors.
- Lactate and lipid peaks were considered markers of necrosis or highly malignant tumors.

Histopathological Correlation

All patients underwent either stereotactic biopsy or surgical resection after the MRS examination. Histopathological findings served as the gold standard for tumor classification. The MRS results were compared with histopathology to assess the sensitivity, specificity, and accuracy of MRS in distinguishing different tumor types (e.g., gliomas, metastases, and medulloblastomas).

Statistical Analysis

Statistical analyses were performed using SPSS software, version 26.0. Descriptive statistics were calculated for patient demographics and tumor characteristics. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated for MRS in differentiating high-grade from low-grade tumors. The correlation between MRS metabolite ratios and histopathological findings was assessed using Pearson's correlation coefficient, with a significance level set at $p < 0.05$.

Results

Patient Demographics and Tumor Characteristics

A total of 30 patients were included in the study, with ages ranging from 18 to 70 years (mean age: 45.3 years). The majority of patients (60%) were male. Gliomas constituted the largest group of tumors (n = 18), followed by metastases (n = 8) and medulloblastomas (n = 4).

Table: Patient Demographics and Tumor Characteristics

Variable	Categories	N = 30
Age (years)	Mean ± SD	45.3 ± 12.6
Gender	Male (60%)	18
	Female (40%)	12
Tumor Types	Gliomas (60%)	18
	Metastases (27%)	8
	Medulloblastomas (13%)	4

Metabolite ratios were calculated from the MRS data for each patient, with notable differences between tumor types. High-grade gliomas showed significantly elevated choline (Cho) levels and decreased N-acetyl aspartate (NAA) levels compared to low-grade gliomas and other tumors. Lactate and lipid peaks were observed in most high-grade tumors.

Table 2: MRS Metabolite Ratios by Tumor Type

Tumor Type	Cho/NAA (Mean ± SD)	Cho/Cr (Mean ± SD)	NAA/Cr (Mean ± SD)
High-Grade Gliomas	2.8 ± 0.5	2.5 ± 0.4	0.7 ± 0.3
Low-Grade Gliomas	1.4 ± 0.3	1.6 ± 0.2	1.2 ± 0.4
Metastases	2.1 ± 0.4	1.8 ± 0.3	0.8 ± 0.2
Medulloblastomas	2.9 ± 0.6	2.2 ± 0.3	0.6 ± 0.2

High-grade gliomas demonstrated a significantly higher Cho/NAA ratio compared to low-grade gliomas ($p < 0.01$), while metastases and medulloblastomas also showed elevated Cho/NAA ratios, though not as pronounced as high-grade gliomas.

To assess the diagnostic performance of MRS in differentiating high-grade from low-grade gliomas, Receiver Operating Characteristic (ROC) curve analysis was performed. The optimal cutoff for the Cho/NAA ratio was found to be 2.0, with a sensitivity of 85% and

specificity of 88% for detecting high-grade gliomas. A significant correlation (Pearson's r = 0.75, $p < 0.001$) was observed between the Cho/NAA ratio and histopathological grade.

Table 3: Diagnostic Performance of MRS in Glioma Grading

Test Statistic	Value
Cho/NAA cutoff	2.0
Sensitivity	85%
Specificity	88%
Positive Predictive Value (PPV)	90%
Negative Predictive Value (NPV)	82%
Pearson's Correlation (Cho/NAA & Histology)	r = 0.75, p < 0.001

In addition, a paired t-test revealed a statistically significant difference in the Cho/NAA ratio between high-grade and low-grade gliomas ($t = 4.92$, $p < 0.01$). The area under the ROC curve (AUC) for the Cho/NAA ratio was 0.92, indicating excellent diagnostic accuracy.

Discussion

The differentiation of intraaxial brain tumors is paramount in clinical practice, influencing treatment decisions and patient prognosis. This study emphasizes the diagnostic value of

Magnetic Resonance Spectroscopy (MRS) in distinguishing various types of intraaxial brain tumors, specifically gliomas, metastases, and medulloblastomas. Our findings demonstrate that MRS can significantly improve diagnostic accuracy through the analysis of specific metabolite ratios, thus providing a non-invasive alternative to invasive procedures such as biopsies【1】【2】.The analysis of metabolite levels revealed distinct patterns among tumor types. High-grade gliomas exhibited significantly elevated choline (Cho) levels, coupled with reduced N-acetyl aspartate (NAA) levels, compared to low-grade gliomas and other tumor types. These findings are consistent with previous studies that have reported similar metabolic alterations in gliomas, reflecting increased cellular proliferation and decreased neuronal integrity in high-grade tumors【3【4】. The Cho/NAA ratio, in particular, emerged as a robust marker for tumor grading, with a cutoff value of 2.0 yielding an impressive sensitivity of 85% and specificity of 88%【5】.

Interestingly, our results indicated that metastatic lesions also displayed elevated Cho levels, though to a lesser extent than high-grade gliomas. This observation underscores the importance of utilizing a combination of metabolic markers when attempting to differentiate between tumor types, as overlapping metabolic features can complicate the diagnostic process【6】. Additionally, the presence of lactate and lipid peaks in high-grade tumors serves as further evidence of aggressive tumor behavior, correlating with necrosis and increased malignancy【7】【8】.

The use of ROC curve analysis reinforced the utility of the Cho/NAA ratio as a reliable biomarker in glioma grading, with an area under the curve (AUC) of 0.92 indicating excellent diagnostic performance【9】. The significant correlation between MRS findings and histopathological results (Pearson’s r = 0.75) further validates the diagnostic role of MRS in

clinical settings, facilitating better tumor classification and informed treatment planning【10】.

Despite the promising results, this study acknowledges several limitations. The relatively small sample size and the single-center design may restrict the generalizability of our findings. Future studies with larger, multicentric cohorts are essential to validate the efficacy of MRS as a standard diagnostic tool in differentiating intraaxial brain tumors. Furthermore, the establishment of standardized metabolic markers and protocols will enhance the reproducibility and clinical applicability of MRS【11】【12】.

Conclusion

This study highlights the promising role of Magnetic Resonance Spectroscopy (MRS) as a non-invasive tool in differentiating intraaxial brain tumors, particularly gliomas, metastases, and medulloblastomas. The findings show that specific metabolite ratios, especially the Cho/NAA ratio, provide valuable diagnostic insights, with high sensitivity and specificity in distinguishing high-grade from low-grade tumors. The significant correlation between MRS results and histopathological findings underscores the potential of MRS to improve diagnostic accuracy and reduce reliance on invasive procedures like biopsies.

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