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MAGNETIC RESONANCE SPECTROSCOPY FOR GLIOMA GRADING: ENHANCING NON-INVASIVE IMAGING ACCURACY COMPARED TO HISTOPATHOLOGY

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ABSTRACT

Background: *Gliomas are common primary brain tumours with heterogeneous growth patterns, requiring accurate grading for optimal treatment. While histopathology remains the gold standard, it has limitations like sampling errors. Magnetic Resonance Spectroscopy (MRS) provides metabolic insights, complementing MRI and histopathology in glioma classification.*

Materials and Methods: *This retrospective study included 50 patients undergoing MRI and MRS at VMKVMCH, Salem, using a 1.5T Philips INGENIA scanner. Metabolites such as N-acetyl aspartate (NAA), choline (Cho), creatinine (Cr), lactate (Lac), and lipids (Lip) were analysed. Glioma grades were classified per WHO 2021 and correlated with histopathology using Pearson's correlation coefficient.*

Results: *Among 50 cases, 27 were low-grade and 33 high-grade gliomas. High-grade gliomas showed decreased NAA, elevated Cho and Cr, and increased Lac and Lip peaks, reflecting high cellular turnover and necrosis. A strong correlation ($r = 0.7365$, $p < 0.05$) was found between MRS profiles and histopathological grading.*

Conclusion: *MRS is a valuable, non-invasive tool for glioma grading, improving diagnostic accuracy and treatment planning. Its integration with conventional imaging enhances neuro-oncology decision-making.*

Keywords: *Glioma, MRS, Histopathology, Metabolic Profiling, Neuroimaging.*

INTRODUCTION

Magnetic Resonance Spectroscopy (MRS) has emerged as a critical tool in the grading and management of gliomas, offering detailed insights into the biochemical composition of these brain tumours. Gliomas, which are heterogeneous in nature, vary widely in terms of their aggressiveness and prognosis, making precise grading essential for determining appropriate treatment strategies and predicting patient outcomes. The traditional methods of diagnosis, such as MRI and histopathological analysis, while informative, are enhanced by the integration of MRS, providing a non-invasive approach to assess the metabolic profile of gliomas and offering a clearer understanding of their biological behaviour.

MRS works by detecting and quantifying various metabolites in the tumor tissue, such as N-acetyl aspartate (NAA), choline (Cho), creatinine (Cr), lactate (Lac), and lipids (Lip). These metabolites are key indicators of cellular activity and metabolic processes. Low-grade gliomas (grades I and II) generally exhibit a distinctive metabolic pattern, with high levels of NAA, a marker of neuronal integrity, and low levels of lactate and lipids, reflecting less aggressive behaviour. In contrast, high-grade gliomas (grades III and IV) display significant changes in their metabolic profile, including reduced NAA levels, increased choline, and the presence of lactate and lipids, which indicate elevated cellular turnover, necrosis, and anaerobic metabolism. These metabolic differences can be detected using MRS, allowing clinicians to distinguish between low and high-grade gliomas with greater accuracy.

The use of MRS is particularly valuable in the context of glioma grading because it provides real-time, in vivo data without the need for invasive procedures. When combined with conventional MRI and histopathological analysis, MRS enhances the diagnostic accuracy of gliomas, refining the classification and enabling more tailored treatment planning. By correlating MRS findings with histological features such as cellularity, mitotic activity, and microvascular proliferation, clinicians can make more informed decisions about the tumor grade, its aggressiveness, and the likelihood of recurrence or progression.

One of the most significant advantages of MRS is its ability to guide biopsy procedures. By identifying metabolically active regions of the tumor, MRS allows for more precise targeting of tissue samples, minimizing the risk of sampling errors and ensuring that the tissue obtained for histopathological analysis is representative of the tumour's true nature. This targeted approach is crucial in gliomas, which often infiltrate surrounding brain tissue, making it difficult to identify the most aggressive areas without advanced imaging techniques.

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Gliomas themselves arise from glial cells, which are supportive cells in the brain and spinal cord. They can take many forms, with varying degrees of malignancy, and their classification, as per the World Health Organization (WHO), is based on histological features and molecular characteristics. These tumours are graded from I to IV, with grade IV gliomas, such as glioblastoma, being the most aggressive and lethal. MRS plays a key role in distinguishing these grades, providing a deeper understanding of the metabolic processes that differentiate slow-growing, low-grade tumours from fast-growing, high-grade tumours.

MRS is a powerful, non-invasive imaging tool that significantly enhances the diagnosis, grading, and management of gliomas. By providing detailed metabolic information, MRS aids in the precise classification of gliomas, guides biopsy procedures, and helps tailor treatment plans, ultimately improving patient outcomes. Its integration with conventional imaging and histopathological analysis marks a significant advancement in the management of these challenging brain tumours.

MATERIALS AND METHODS:

Study Design: Retrospective

Study Approach: Quantitative

Study Population: All patients referred to radiology department for evaluation of brain tumours

Study Area: VMKVMCH, Salem.

Sampling Technique: All consecutive study participant satisfying the inclusion/exclusion criteria will be recruited for the study until the sample size is obtained.

Sample Size Calculation: 50 patients fulfilling the inclusion criteria.

Inclusion Criteria: Patient referred to the department of radiodiagnosis for MRI evaluation of brain tumours. Patients from all ages and both sexes were taken into consideration.

Exclusion Criteria: Patient with pacemakers, cochlear implants, metallic clips or metallic foreign bodies. Patient with histopathological diagnosis other than glioma.

Tools for Data Collection: MRS with tissue metabolites (Cho, Cr, NAA) with conventional MRI brain 1.5T Philips INGENIA. Gliomas are evaluated using the most recent WHO standard for histopathological diagnosis.

Statistical Analysis: Data was entered in Microsoft excel for data analysis will be performed using SPSS software.

MATERIALS

MRI Machine Specification with Head coil

Philips INGENIA (1.5T)

MRS CHARECTERISTICS OF GLIOMA

Low Grade Glioma

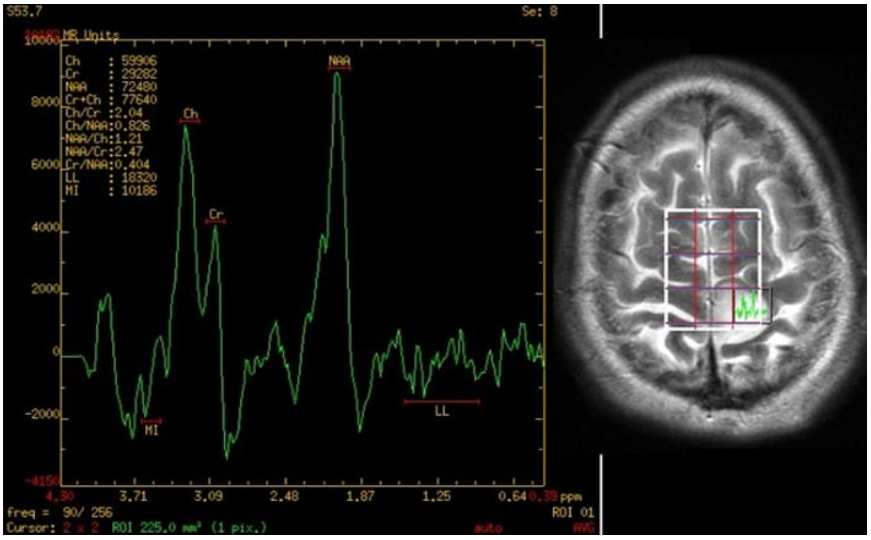

Fig 1: MRS Spectrum of Low-Grade Glioma

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Low-grade gliomas are characterized by low levels of choline, lactate, and lipids, along with a comparatively high quantity of N-acetyl aspartate (NAA). A rise in creatine levels may indicate earlier progression and malignant transformation in these tumours. The increase in NAA is attributed to cellular proliferation, inflammation, and edema, which can alter metabolic processes. Additionally, infiltration or mixing of tumor cells with normal brain tissue, including neurons and astrocytes, may contribute to elevated NAA levels.

The increase in creatine is associated with cellular density, turnover, metabolism, microenvironmental changes, inflammation, and tissue remodelling. On the other hand, a decrease in choline levels is linked to cellular differentiation, as differentiated cells typically exhibit lower levels of choline-containing compounds such as phosphocholine and glycerophosphocholine. This reduction is also indicative of decreased cell membrane turnover.

The absence of lipid and lactate peaks in low-grade gliomas is influenced by tumor cell characteristics. Glioma cells predominantly rely on aerobic glycolysis rather than anaerobic metabolism, leading to reduced lactate production. High cellularity minimizes extracellular lipids and lactate, which are more commonly found in necrotic regions. Additionally, adequate vascularization provides sufficient oxygen and nutrients, supporting aerobic glycolysis and reducing the need for anaerobic metabolism and lactate production.

High Grade Glioma

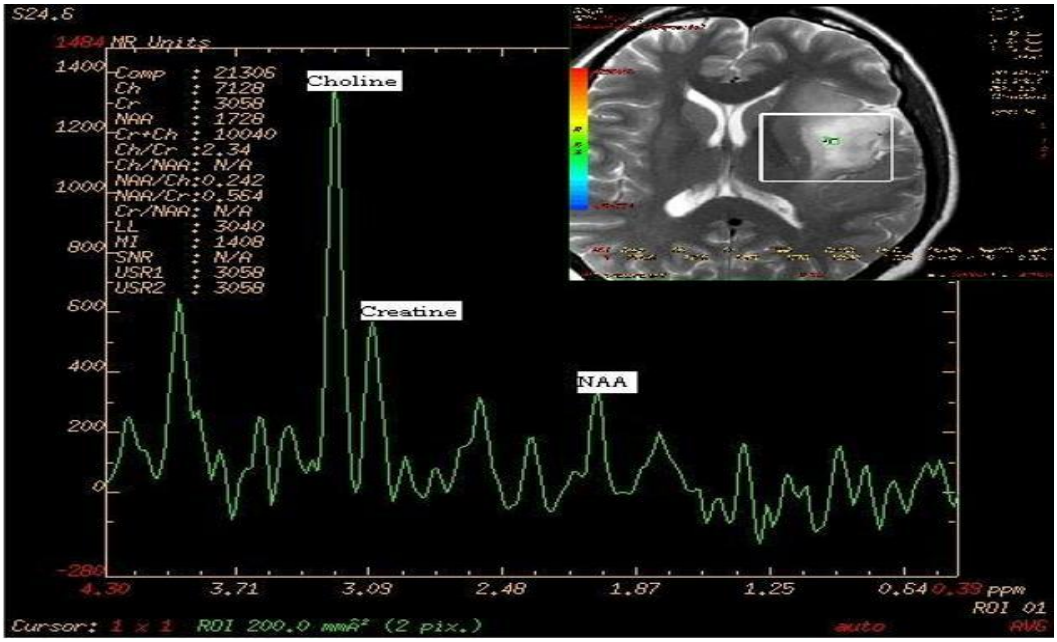

Fig 2: MRS Spectrum of High-Grade Glioma

A decrease in N-acetyl aspartate (NAA) levels in gliomas is primarily due to neuronal loss and dysfunction. As tumor cells proliferate and replace normal brain tissue, the proportion of neuronal tissue is reduced, leading to lower NAA levels. Neurons are particularly sensitive to ischemia and hypoxia, and their dysfunction, along with inflammatory responses, tumor necrosis, and edema, further contribute to the decline in NAA levels detected by MRS.

An increase in choline levels is associated with cellular proliferation, increased turnover of cellular membranes, loss of cellular regulation, inflammation, and tissue damage. Similarly, elevated creatinine levels result from increased cellular density and proliferation, as well as the presence of necrotic tissue and damage, which release cellular components, including creatinine, into the extracellular space.

The presence of lipid and lactate peaks is a distinguishing feature of high-grade gliomas. In necrotic regions, the lack of oxygen and nutrients forces tumor cells into anaerobic metabolism, leading to lactate accumulation and an elevated lactate peak in the MRS spectrum. Additionally, necrotic areas contain cellular debris, including lipids, which contribute to the lipid peak observed in high-grade gliomas.

RESULT

Case Study:
A total of five cases were analysed, each presenting with high-grade glial neoplasms based on MRS and imaging findings.

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The first case, a 69-year-old female (Patient ID: 2002317), exhibited an increased choline peak with a Cho: NAA ratio of ~2 and a lipid lactate peak. Imaging revealed a circumscribed, intensely heterogeneously enhancing solid lesion in the tectal/pineal region with restricted diffusion, increased perfusion parameters, and surrounding mild FLAIR signal changes, suggestive of a high-grade glioma. Histopathology confirmed a High-Grade Glial Neoplasm, WHO Grade 3.

The second case, a 62-year-old female (Patient ID: 2040993), showed an increased choline peak with a Cho: NAA ratio of ~2.5 and a lipid/lactate peak. Imaging differentials included a high-grade ependymal tumor versus glioblastoma, with metastasis being a less likely possibility. Histopathology confirmed Glioblastoma, WHO Grade 4. The third case, a 74-year-old male (Patient ID: 1990664), presented with an elevated choline peak and a choline-creatinine ratio greater than 1.5. An ill-defined intra-axial lesion was observed in the left posterior parietal lobe and peri-trigonal white matter, showing features of haemorrhage and mass effect, suggestive of high-grade glioma. Histopathology confirmed Anaplastic Oligodendroglioma, WHO Grade 3.

The fourth case, a 55-year-old female (Patient ID: 1995200), had an elevated choline peak in the peripheral rim with a Cho: NAA ratio greater than 2, along with elevated lipid and lactate peaks in the cortical necrotic area. Imaging suggested a high-grade glial neoplasm with areas of dedifferentiation, which was histopathologically confirmed as High-Grade Glial Anaplastic Astrocytoma, WHO Grade 3. The fifth case, a 63-year-old male (Patient ID: 1966179), displayed an increased choline peak with a Cho: NAA ratio of ~2.5 and elevated lipid and lactate peaks. Imaging findings included an interval increase in confluent T2/FLAIR hyperintensity with altered diffusivity and peripheral enhancement, suggestive of a high-grade glial neoplasm. Histopathology confirmed High-Grade Glioma, WHO Grade 4.

STATISTICAL ANALYSIS

		No. of respondents
Gender	Female	24
	Male	26
Glioma Grade	Grade 1	2
	Grade 2	12
	Grade 3	14
	Grade 4	22
Age	0-19	0
	20-39	10
	40-59	17
	60-79	21
	80-99	2
Glioma grade	Low	27
	High	33

Correlation Analysis

Hypothesis

H0 – There is no corelation between MR spectroscopy grading and histopathology grading of glioma

H1 -There is correlation between MR spectroscopy grading and histopathology grading of glioma

Table 6: Correlation Analysis

Parameter	**Value**
Pearson correlation coefficient (r)	**0.7365**
r^2	0.5424
P-value	1.09E-09
Covariance	0.3204
Sample size (n)	50
Statistic	7.5435

Our P value (0) is <0.05, Therefore H1 is accepted. Hence, we conclude that there is correlation between MR spectroscopy Grading and Histopathology Grading of Glioma.

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DISCUSSION

This study was designed to find whether there is a correlation between MRS and histopathological grading regarding glioma. MRS is a powerful non-invasive imaging technique that provides metabolic information about brain tumours, particularly gliomas. This information is crucial for grading these tumours, as it correlates closely with their histopathological features and clinical behaviour.

By analysing the levels of various metabolites within the tumour tissue like Cho, Cr, NAA, Lac, and lipid peaks and the ratios of these metabolites, such as Cho/Cr, Cho/NAA, and Lac/Cr, can indicate the degree of cellularity, proliferation, and metabolic activity within the tumour.

One of the most striking findings is Clinically the ability of MRS to provide metabolic profiles of gliomas helps in several ways:

- Diagnostic Accuracy
- Treatment Planning
- Monitoring Response to Therapy

Furthermore, the findings emphasize the correlation between MRS findings and final histopathological grading is robust, although MRS has some limitations such as spatial resolution and susceptibility to artifacts. Nevertheless, its non-invasive nature and ability to provide functional information make it an invaluable tool in the clinical management of gliomas

CONCLUSION

This study confirms a strong correlation between Magnetic Resonance Spectroscopy (MRS) and histopathological grading of gliomas, highlighting the value of MRS as a non-invasive diagnostic tool. By analysing key metabolites such as NAA, choline, creatine, lactate, and lipids, MRS provides crucial insights into tumor metabolism, aiding in accurate glioma classification. High-grade gliomas exhibited reduced NAA, elevated choline, and increased lactate and lipid peaks, consistent with aggressive tumor behaviour. The statistical analysis demonstrated a significant correlation ($r = 0.7365$, $p < 0.05$) between MRS metabolic profiles and histopathological findings.

MRS enhances diagnostic accuracy, guides targeted biopsies, and informs treatment planning by distinguishing tumor grades more effectively. Despite limitations such as spatial resolution and susceptibility to artifacts, its integration with conventional MRI and histopathology significantly improves glioma assessment. This study underscores the clinical utility of MRS in neuro-oncology, facilitating better patient management and prognosis prediction.

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