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Role of magnetic resonance spectroscopy in the characterization of brain tumors

Dr. Hunar Shekhan Hamshin[1]*, Dr. Saeed Agha Nadhim[2], Dr. Falah Hasan Ali Karam[3]

[1]M.B.Ch. B, Trainee in Radiology and Medical Imaging-Rizgari Teaching Hospital- Erbil-Kurdistan Region, Iraq
[2]M.B.Ch. B, DMRD, PhD, Professor, Consultant Radiologist-Hawler Medical University, College of Medicine- Erbil- Kurdistan Region, Iraq
[3]M.B.Ch. B, CABHS (Rad.), Consultant Radiologist-Head of Radiology Department, Rizgari Teaching Hospital- Erbil- Kurdistan Region, Iraq

Abstract

Magnetic Resonance Imaging (MRI) plays a significant role in brain tumors diagnosis. However, the MRI had lower validity in grading of these tumors alone. To evaluate the role of Magnetic Resonance Spectroscopy (MRS) in the characterization of brain tumors, focusing on its utility in distinguishing tumor types and assessing tumor grade. A retrospective Cross-Sectional study implemented in MRI Unit-Radiology department of Rizgari Teaching hospital in Erbil City-Kurdistan region/Iraq for two years' duration from 1st of January, 2024 to 31st of December, 2025 on sample of 50 patients with brain lesions. The histopathology was done in private and governmental hospitals in Erbil city. High grade and low grade brain tumor categorization was done according to World Health Organization. Validity measures of MRS in diagnosis of brain neoplasm were (93.3% sensitivity, 85% specificity and 90% accuracy), which were higher than validity measures of MRI (80% sensitivity, 75% specificity and 78% accuracy). Validity measures of MRS in categorization of brain neoplasm were (92.3% sensitivity, 90% specificity and 91.3% accuracy), which were higher than validity measures of MRI (69.2% sensitivity, 70% specificity and 69.5% accuracy). The magnetic resonance spectrometry is valid technique for diagnosis and grading of brain tumors.

Keywords: Brain tumors, Histopathology, Magnetic resonance imaging, Proton spectroscopy

Introduction

Tumors of the brain are a serious health issue that is becoming more common every year. Gliomas are particularly prevalent type of fundamental brain tumor. The selection of suitable treatment approaches depends on the tumor's grade [1]. Brain tumors present a significant diagnosing and treatment challenge due to their variability and concordance in image characteristics. Properly differentiating brain lesions between neoplastic and non-neoplastic, as well as between low-grade and high-grade tumors, are crucial for making the right clinical judgments, evaluating prognosis, and planning therapy [2].

Traditional Magnetic Resonance Imaging (MRI) has become the gold-standard method for evaluating brain tumors because it offers such excellent anatomical information [3]. Regretfully, it is occasionally reliable to differentiate between various tumor stages and kinds only based on their physical characteristics. Certain lesions that are benign such as tumefactive demyelination or abscesses may show up on imaging as neoplastic lesions, and some low-grade tumors may look like high-grade malignancies [4].

Magnetic Resonance Spectroscopy (MRS) is a technology that integrates the molecular differentiation capabilities of Nuclear Magnetic Resonance (NMR) with the specific localised imaging qualities of MRI. This offers a "molecular window" into the chemical composition of certain tissues, facilitating distinct understanding of physiological or pathological mechanisms. MRS necessitates neither injected contrast agents nor ionising radiation, presenting clear safe advantages [5]. An attractive noninvasive supplement to magnetic resonance imaging is MRS [6]. It's a secure way to conduct in vivo biochemical investigations [7]. Additional details about the metabolic makeup of a region of tissue can be obtained by MRS. Physicians can assess aspects like neurone survival, neurotoxins and membranes cycle within the region of focus and, consequently, a probable cause of the disease by evaluating the different concentrations of metabolite like choline, *N*-acetyl-aspartate, creatine and choline [6]. The extensive application of accelerated MRS techniques with enhanced signal to noise ratio and spatial resolution

Correspondence: Hunar Shekhan Hamshin, M.B.Ch. B, Trainee in Radiology and Medical Imaging-Rizgari Teaching Hospital- Erbil-Kurdistan Region, Iraq, **e-mail:** hunarshblbas@yahoo.com, **Received:** April 21, 2026 **Accepted:** June 6, 2026

enables the identification of structural and metabolite alterations, thereby yielding greater insights into the precise characteristics of the tumor and the morphologic and physiologic modifications in the surrounding brain tissue [8].

The incidence of brain tumors in Erbil city is more in males than females (2.9 vs. 2.3 per 100000 populations) with higher incidence among older age population [9]. Gliomas are the commonest types of brain tumors in Kurdistan region and Iraq [10, 11]. Rare literatures conducted nationally on diagnosis and categorization brain tumors although tumor significance urged us to implement this study that aimed to evaluate the role of MRS in the characterization of brain tumors, focusing on its utility in distinguishing tumor types and assessing tumor grade.

Patients and Methods: A retrospective cross-sectional study implemented in MRI Unit-Radiology department of Rizgari Teaching hospital in Erbil City-Kurdistan region/Iraq in duration of two years from 1st of January, 2024 to 31st of December, 2025 on patients with brain lesions referred for radiological investigations. Inclusion criteria were adult patients with brain lesions underwent both MRI and MRS with confirmed histopathology examination. Exclusion criteria included patients who had previously underwent brain surgery or chemotherapy, movement artifacts and missing or incomplete data.

As the design of study is retrospective cross sectional, the sample size calculation equation was: $n=Z^2 * P * (1-P)/d^2$. The expected MRS was 85% sensitivity (P=0.85) [4]. The sample size was 49.9 which approximated to 50 patients.

Information of patients was gathered by researcher retrospectively from saved data of selected patients regarding demographic characteristics (age and gender) diffusion-weighted MRI (DW-MRI) findings, MRS findings and histopathology findings.

DW images utilizing an echo based linear images sequences with TR/TE (3034 ms/100 ms), contrast-enhancing T1W order, FLAIR - sequences in coronary plane and T2W sequence in sagittal plane (1.5 Tesla), field of view (23 cm x 23 cm), number of excitations (3), slice thickness (5 mm), inter-slice gap (1.5 mm) and matrix size (256 x 256). Using diffusion sensitivity values of b = 0 and b = 1000 s/mm2, diffusion sensitizing gradients have been utilized along the three orthogonal axes.

There have been two localization techniques used, each with a unique echo time. The Point RE Solved Spectroscopy pulse sequence was used to collect the data, and post contrast T1WI was used for spectroscopic localization with automatic shimming. The measurement settings were section thickness of 10 mm, FOV of 120 x 120 mm, and TR/TE of 1500/135 ms. To prevent significant interference from the skull's lipids and subcutaneous fat, the region of interest was carefully positioned. SVS scans were performed using 1500/35 ms (TR/TE) measurement parameters and 1.5 cm3 voxel size. The cumulative scanning duration was 20 minutes. The primary metabolites discovered by 1H-MRS include N-Acetylaspartate (NAA) at 2.02 ppm, Creatine (Cr) at 3.0 ppm, and choline-containing compounds (Cho) at 3.2 ppm. The subsequent metabolic ratios were computed utilizing common commercial software: NAA/Cr, Cho/Cr, and Cho/NAA at both short and intermediate echo times. The Histopathology was done in private and governmental hospitals in Erbil city. High grade and low grade brain tumor categorization was done according to World Health Organization.

The Research Protocol Ethics Committee of the Kurdistan Higher Council of Medical Specialties approved this study. Confidentiality of patients' information was taken in consideration.

The study statistics was accomplished through using statistical package of social sciences, version 26 and apply of chi-square or fissures exact tests for categorical variables and independent sample t-test for continuous variable with level of significance was 0.05 or less. Two by two tables were used to measure validity findings.

Results:

In current study, fifty patients were enrolled. Histopathology examination revealed that 60% of patients had neoplastic brain lesions and 40% of them had non-neoplastic brain lesions. Brain neoplasms present in 30 patients and divided into

high grade tumors in 13 patients (23.4% Glioblastoma grade III-IV, 10% Astrocytoma grade III-IV, 3.3% Oligodendroglioma grade III, 3.3% medulloblastoma and 3.3% anaplastic ependymoma), while low grade brain tumors were present in ten patients (30% Astrocytoma grade II, 6.7% Oligodendroglioma grade II and 6.7% Medullary glioma), metastases in 13.3% of patients and lymphoma in 10% of them. (*Table 1*)

Table 1: Histopathology findings of patients with brain lesions

Variable	No.	%
Lesion type		
Neoplastic	30	60
Non-neoplastic	20	40
Total	50	100
Neoplasm types		
High grade tumors		
Glioblastoma grade III-IV	7	23.4
Astrocytoma grade III-IV	3	10
Oligodendroglioma grade III	1	3.3
Medulloblastoma	1	3.3
Anaplastic ependymoma	1	3.3
Low grade tumors		
Astrocytoma grade II	6	20
Oligodendroglioma grade II	2	6.7
Medullary glioma	2	6.7
Metastasis	4	13.3
Lymphoma	3	10
Total	30	100

There was a highly significant association between increased age of patients and brain neoplasm (p<0.001). No statistically significant relationship was observed between brain histopathology finding and gender of patients. (*Table 2*)

Table 2: Demographic characteristics in relation to histopathology.

Variable	Neoplastic		Non-neoplastic		P value
	No.	%	No.	%	
Age					<0.001 S
<40 years	4	13.3	10	50	
40-49 years	6	20	8	40	
50-59 years	8	26.7	2	10	
≥60 years	12	40	0	-	
Gender					0.9 NS
Male	18	60	13	65	
Female	12	40	7	35	

S=Significant, NS=Not significant

Hypointense T1-weighted, hyperintense T2-weighted and hypointense FLAIR MRI parameters were significantly related to neoplastic finding of histopathology (p<0.05). Reduced DWI-ADC was significantly related to neoplastic brain lesions (p<0.001). Final diagnosis by MRI was significantly related to histopathology diagnosis (p<0.001). (*Table 3*)

Table 3: MRI results and histopathology findings for brain lesion

MRI measures	Neoplastic		Non-neoplastic		P value
	No.	%	No.	%	
T1-weighted					<0.001 S
Hypointense	22	73.3	3	15	
Isointense	6	20	9	45	
Hyperintense	2	6.7	8	40	
T2-weighted					0.003 S
Hypointense	4	13.3	6	30	
Isointense	3	10	8	40	
Hyperintense	23	76.7	6	30	
FLAIR					0.007 S
Hypointense	4	13.3	7	35	
Isointense	5	16.7	8	40	
Hyperintense	21	70	5	25	
DWI-ADC					<0.001 S
Increased	6	20	19	95	
Reduced	24	80	1	5	
Final					<0.001 S
Neoplastic	24	80	5	25	
Non-neoplastic	6	20	15	75	

S=Significant

Hypointense T1-weighted and hyperintense T2-weighted MRI parameters were significantly related to high grade brain finding of histopathology (p<0.05).

The DWI-ADC was significantly reduced in patients with high grade brain finding of histopathology (p=0.05). FLAIR MRI and final diagnosis by MRI were not significantly related to histopathology diagnosis (p>0.05). (*Table 4*)

Table 4: MRI results and histopathology findings for brain tumor differentiation

MRI measures	High grade		Low grade		P value
	No.	%	No.	%	
T1-weighted					0.003 S
Hypointense	8	61.5	0	-	
Isointense	5	38.5	7	70	
Hyperintense	0	-	3	30	
T2-weighted					0.004 S
Hypointense	1	7.7	6	40	
Isointense	2	15.4	3	30	
Hyperintense	10	76.9	1	10	
FLAIR					0.07 NS
Hypointense	2	15.4	6	60	
Isointense	4	30.8	2	20	
Hyperintense	7	53.8	2	20	
DWI-ADC					0.05 S
Increased	4	30.8	8	80	
Reduced	9	69.2	2	20	
Final					0.14 NS
High grade	9	69.2	3	30	
Low grade	4	20	7	70	

S=Significant, NS=Not significant

Table 5: MRS results and histopathology findings for brain lesion

Metabolites	Neoplastic		Non-neoplastic		P value
	No.	%	No.	%	
Choline/creatine ratio					<0.001 S
Increased	30	100	1	5	
Reduced	0	-	19	95	
Choline/ N-acetylaspartate ratio					<0.001 S
Increased	30	100	2	10	
Reduced	0	-	18	90	
N-acetylaspartate/creatine ratio					<0.001 S
Increased	0	-	19	95	
Reduced	30	100	1	5	
Lipid-Lactate					0.003 S
Increased	20	66.7	4	20	
Reduced	10	33.3	16	80	
Final diagnosis					<0.001 S
Neoplastic	28	93.3	3	15	
Non-neoplastic	2	6.7	17	85	

S=Significant, NS=Not significant

Increased choline/creatine, choline/N-acetylaspartate ratio and lipid-lactate ratios were significantly prevalent in patients with brain neoplasm ($p<0.05$), while reduced N-acetylaspartate/creatine ratio was significantly related to brain neoplasm ($p<0.001$). MRS final diagnosis was significantly related to histopathology diagnosis of brain neoplasm ($p<0.001$). (*Table 5*)

Increased choline/creatine, choline/N-acetylaspartate ratio and lipid-lactate ratios were significantly prevalent in patients with high grade brain neoplasm ($p<0.05$), while reduced N-acetylaspartate/creatine ratio was significantly related to high grade brain neoplasm ($p<0.001$). MRS final diagnosis was significantly related to histopathology diagnosis of high grade brain neoplasm ($p<0.001$). (*Table 6*)

Table 6: MRS results and histopathology findings for brain tumor differentiation

Metabolites	High grade		Low grade		P value
	No.	%	No.	%	
Choline/creatine ratio					<0.001 S
Increased	13	100	1	10	
Reduced	0	-	9	90	
Choline/ N-acetylaspartate ratio					<0.001 S
Increased	13	100	2	20	
Reduced	0	-	8	80	
N-acetylaspartate/creatine ratio					<0.001 S
Increased	0	-	9	90	
Reduced	13	100	1	10	
Lipid-Lactate					0.02 S
Increased	10	76.9	2	20	
Reduced	3	23.1	8	80	
Final diagnosis					<0.001 S
High grade	12	92.3	1	10	
Low grade	1	7.7	9	90	

S=Significant, NS=Not significant

Validity measures of MRS in diagnosis of brain neoplasm as compared to histopathology were (93.3% sensitivity, 85% specificity and 90% accuracy), which were higher than validity measures of MRI in diagnosis of brain neoplasm as compared to histopathology (80% sensitivity, 75% specificity and 78% accuracy). Validity measures of MRS in categorization of brain neoplasm as compared to histopathology were (92.3% sensitivity, 90% specificity and 91.3% accuracy), which were higher

than validity measures of MRI in categorization of brain neoplasm as compared to histopathology (69.2% sensitivity, 70% specificity and 69.5% accuracy). (*Table 7*)

Table 7: Validity measures of MRS and MRI in comparison to histopathology.

Parameters	MRS	MRI
Neoplastic vs. non-neoplastic brain lesions		
Sensitivity	93.30%	80%
Specificity	85%	75%
PPV	90.30%	82.70%
NPV	89.40%	71.40%
Accuracy	90%	78%
High grade vs. low grade brain tumors		
Sensitivity	92.30%	69.20%
Specificity	90%	70%
PPV	92.30%	75%
NPV	90%	63.60%
Accuracy	91.30%	69.50%

Discussion

Earlier and accurate detection of brain tumors with optimal categorization of these tumors is essential in planning for management strategies. Although high cost and longtime disadvantages, the magnetic resonance spectroscopy is considered nowadays as an encouraging method in diagnosis of brain tumors [12].

In present study, histopathology examination revealed that 60% of patients had neoplastic brain lesions and 40% of them had non-neoplastic brain lesions. These proportions are better than results of recent retrospective observational study conducted in India which found by histopathology that 93.27% of patients had neoplastic brain lesions, while 6.73% of them had non-neoplastic lesions [13]. This difference might be attributed to discrepancies in diagnostic techniques used before histopathology and differences in risk factors between different communities. Our study showed that brain neoplasms were divided into high grade tumors (commonly glioblastoma) and low grade brain tumors (commonly astrocytoma). These findings are in agreement with results of recent cross-sectional study implemented in Iraq which reported that glioblastoma tumors were the most common high grade brain tumors and astrocytoma tumors were the main low grade brain tumors [14]. In our study advanced age of patients was significantly related to neoplastic brain lesions ($p<0.001$). This finding coincides with results of different literatures [9, 15].

MRI findings in current study showed that hypointense T1-weighted, hyperintense T2-weighted, hypointense FLAIR MRI and Reduced DWI-ADC were significantly related to neoplastic finding of histopathology ($p<0.05$). Similarly, recent Italian review study revealed that findings of magnetic resonance imaging technique are predictive for neoplastic brain lesions especially hyperintense T2-weighted, hypointense FLAIR MRI and Reduced DWI-ADC [16]. In our study, final diagnosis of brain neoplasm by MRI was significantly related to histopathology diagnosis ($p<0.001$). This finding is similar to results of recent study carried out in Brazil [17]. In current study, high grade brain tumors were significantly related to hypointense T1-weighted and hyperintense T2-weighted and reduced DWI-ADC of MRI ($p<0.05$). Consistently, recent review Italian study documented that DWI-MRI findings are valid in grading and differential diagnosis of brain neoplasms [18].

Current study found that increased choline/creatine, choline/N-acetylaspartate ratio and lipid-lactate ratios were significantly prevalent in patients with brain neoplasm ($p<0.05$), while reduced N-acetylaspartate/creatine ratio was significantly related to brain neoplasm ($p<0.001$). These findings are consistent with results of different literatures [19, 20]. MRS final diagnosis in our study was significantly related to histopathology diagnosis of brain neoplasm ($p<0.001$). This finding is parallel to results of recent cross-sectional study carried out in Pakistan which stated the high validity of MRS in differentiating between neoplastic and non-neoplastic brain lesions [21]. Our study showed that increased choline/creatine, choline/N-acetylaspartate ratio and lipid-lactate ratios were significantly prevalent in patients with high grade brain neoplasm ($p<0.05$), while reduced N-acetylaspartate/creatine ratio was significantly related to high grade brain neoplasm ($p<0.001$). These findings are consistent with results of many authors which revealed that MRS parameters are valuable in grading of brain tumors [22, 23]. MRS final diagnosis in present study was significantly related to

histopathology diagnosis of high grade brain neoplasm (p<0.001). This finding is similar to results of recent retrospective study implemented in Turkey which found that MRS is useful in grading of brain tumors [24].

This study showed that validity measures of MRS in diagnosis of brain neoplasm as compared to histopathology were (93.3% sensitivity, 85% specificity and 90% accuracy), which were higher than validity measures of conventional MRI in diagnosis of brain neoplasm as compared to histopathology (80% sensitivity, 75% specificity and 78% accuracy). These findings are close to results of recent prospective hospital-based observational study in India which reported higher validity findings of MRS in diagnosis of brain neoplasms than MRI (as compared to histopathology) [2]. Our study found that validity measures of MRS in categorization of brain neoplasm as compared to histopathology were (92.3% sensitivity, 90% specificity and 91.3% accuracy), which were higher than validity measures of conventional MRI in categorization of brain neoplasm as compared to histopathology (69.2% sensitivity, 70% specificity and 69.5% accuracy). These findings are close to results of different literatures which reported higher validity of MRS in grading of brain tumors [8, 25].

In conclusion, the magnetic resonance spectrometry is valid technique for diagnosis and grading of brain tumors. Validity findings of magnetic resonance spectrometry in diagnosis and grading of brain tumors are higher than validity findings of magnetic resonance imaging. This study encouraged use of magnetic resonance spectrometry in diagnosis and grading of brain lesions in addition to encouraging further national studies on role of magnetic resonance spectrometry in brain lesions.

Conflict of interest

None

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