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Diagnostic accuracy of magnetic resonance spectroscopy (mrs) in differentiating neoplastic and non-neoplastic brain lesions

Maryam Rauf[1] , Aliya Ahmed[2]

ABSTRACT

Background: Magnetic Resonance Spectroscopy (MR Spectroscopy) is one of the tools used to determine the molecular structures of compounds or to detect the compound presence. MR Spectroscopy can help in differentiating neoplastic from non-neoplastic lesions. Lesions can be categorized into neoplastic and non-neoplastic on the basis of certain criteria including Cho/Cr and Cho/ NAA ratio and choline and NAA peak on MR Spectrum.

MATERIALS AND METHODS: To determine the diagnostic accuracy of magnetic resonance spectroscopy (MRS) in differentiating neoplastic from non-neoplastic brain lesions, taking biopsy as gold standard. A total of 191 patients with patients with focal brain lesions on conventional MRI of age 30-60 years of either gender were included. Patients with history of previous brain surgery, pregnant or breast feeding females, claustrophobia and contraindication to MRS were excluded. All the patients then underwent MRS and were looked for Choline peak, NAA/ Cr Ratio, NAA/ Cho Ratio and Cho/ Cr Ratio for neoplastic or non-neoplastic lesion and findings were correlated with histopathology.
To determine the diagnostic accuracy of magnetic resonance spectroscopy (MRS) in differentiating neoplastic from non-neoplastic brain lesions, taking biopsy as gold standard.

RESULTS: Mean age was 47.93 ± 8.13 years. Out of these 191 patients, 112 (58.64%) were male and 79 (41.36%) were females with ratio of 1.4:1. In 108 MRS positive patients, 95 were True Positive and 13 were False Positive. Among 83 MRS negative patients, 09 were False Negative where as 74 were True Negative (p=0.680). Overall sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of MRS in differentiating neoplastic from non-neoplastic brain lesions was 91.35%, 85.06%, 87.96%, 89.16% and 88.48% respectively.

CONCUSION: This study concluded that magnetic resonance spectroscopy (MRS) is the non-invasive modality of choice with high diagnostic accuracy in differentiating neoplastic from non-neoplastic brain lesions.

Keywords: Brain lesions, neoplastic, spectroscopy, diagnostic accuracy

INTRODUCTION:

Brain tumors may originate from neural elements within the brain, or they may represent spread of distant cancers. Primary brain tumors arise from CNS tissue and account for roughly half of all cases of intracranial neoplasms.1 Gliomas, metastases, meningiomas , pituitary adenomas, and acoustic neuromas account for 95% of all brain tumors.2 Aydin H et al3 in his study has shown the prevalence of neoplastic brain lesions as 53%. When a patient comes for the evaluation of a focal brain lesion, it is often difficult to differentiate between tumoral and non-tumoral brain lesions and frequently creates a dilemma for physicians and surgeons for further management.4 Diagnosis is usually by medical examination along with computed tomography or magnetic resonance imaging. This is then often confirmed by biopsy.5

During the last century, central nervous system (CNS) imaging has witnessed a revolution with advances that have impacted all aspects of neuroscience practice in general and the management of intra-axial brain tumors in particular.6 Intra-axial brain lesions present several imaging challenges. The role of imaging is no longer limited to merely providing anatomic

[1] , FCPS Consultant Radiologist- Diagnostic Radiologist- Advanced Diagnostic Center- Islamabad

[2] , FCPS Associate Professor- Diagnostic Radiology- Pakistan Institute of Medical Sciences (PMS) Islamabad

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For Correspondence:
Dr. Maryum Rauf
mmrauf@hotmail.com

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The morphological characterization of intracranial mass lesions using conventional Magnetic Resonance Imaging (MRI) alone, even after contrast administration may be difficult without the histopathological examination of the suspected tissue.8 Therefore, advanced MR imaging techniques as Diffusion Weighted Imaging (DWI), Perfusion Weighted Imaging (PWI), and proton Magnetic Resonance Spectroscopy (1HMRS) have been employed in the differential diagnosis of these lesions.9

The Introduction of magnetic resonance imaging (MRI) has created many important advances in the detection and characterization of brain lesions and is considered to be the state of the art technology in the evaluation of the brain. The detection rate of most types of brain lesions by MRI exceeds 90%, compared to 77% for CT - without the invasiveness or risk of iodinated intravenous contrast agents or the inherent problem of the radiation effect of X-rays. These safety features make MRI especially advantageous for the pediatric and elderly populations.8,10

In vivo proton MR spectroscopy (1H-MRS) produces a non invasive analysis of the metabolism of the tissue, determining the relative concentrations of their metabolites and the interactions produced between them, which may be used in tumor diagnosis and and has been proved to be a sensitive method in identifying malignant tumours.3,4,6 The sensitivity and specificity of MR Spectroscopy for differentiating neoplastic from non-neoplastic brain lesions as observed by Surur A et al6 is 97% and 90% respectively while Alam MS et al10 evaluated the role of 1HMRS in focal brain lesions and found the sensitivity of 93% and specificity of 70% in differentiating neoplastic from non-neoplastic brain lesions.

Since there was a controversy in previous literature, so there was need of more research on this topic. The rationale of this study was to determine the diagnostic accuracy of magnetic resonance spectroscopy (MRS) in differentiating neoplastic from non-neoplastic brain lesions. If its diagnostic accuracy would be found high, then our general population would be provided with a non invasive pre-operative diagnostic technique for accurate diagnosis and take management measures accordingly in order to reduce the morbidity and mortality of these particular patients. Moreover, it would also help to reduce pure diagnostic biopsies in focal brain lesions which would also reduce complications of this invasive procedure.

Tumors have characteristics that allow determination of its malignacy, how it will evolve and it will allow the medical team to determine the management plan.

MATERIAL AND METHODS:

A total of 191 patients with patients with focal brain lesions on conventional MRI of age 30-60 years of either gender were included. Patients with history of previous brain surgery, pregnant or breast feeding females, claustrophobia and contraindication to MRS were excluded. All the patients then underwent MRS for were looked for Choline peak, NAA/ Cr Ratio, NAA/ Cho Ratio and Cho/ Cr Ratio for neoplastic or non-neoplastic lesion and findings were correlated with histopathology.

STUDY DESIGN:

Descriptive, Cross-sectional study.

SETTING:

Department of Radiology, PIMS, Islamabad.

DURATION OF STUDY:

05th January 2022 to 10th December 2022.

SAMPLE SIZE:

Sample size of 191 cases has been calculated with 95% confidence level, expected prevalence of neoplastic brain lesions as 53%3, 5% desired precision for sensitivity of 93%10 and d = 10% for specificity of 70%10 of magnetic resonance spectroscopy in differentiating neoplastic and non-neoplastic brain lesions.

SAMPLE TECHNIQUE:

Non-probability, consecutive sampling.

SAMPLE SELECTION:

a. Inclusion Criteria:
a. All patients with focal brain lesions on conventional MRI (hypointense lesion on T1-weighted imaging, no contrast enhancement, perifocal edema and rim enhancement).
b. Duration of lesion 0-6 months.
c. Patients with 30-60 years of age of both genders.
b. Exclusion Criteria:
a. Patients with already diagnosed type of tumour.
b. Patients with history of previous brain surgery.
c. Pregnant or breastfeeding females.
d. Patients with lesion that will not suitable for spectroscopy on the basis of location
e. Patients who have contraindication to MRS i.e. MRS incompatible prosthesis or cardiac pacemaker holders.
f. Patients not willing for biopsy.
g. Patients not willing to be included in the study.

DATA COLLECTION PROCEDURE:

After approval from ethical review committee, total number of 191 patients who were referred by clinician to the Radiology department of PIMS, Islamabad. Fulfilling the inclusion/exclusion criteria were selected. Informed written consent from each patient was taken. After this, proton magnetic resonance spectroscopy (1H MRS) was performed in every patient using 1.5 Tesla MR system with gradient strength of 33 mT/m. A fast scout scan in sagittal, axial, and coronal planes were obtained. The scan technique used

was the point-resolved spectroscopy single-voxel technique. It was followed by water suppression pulses to be followed by data acquisition. Each MRS was interpreted by one consultant radiologist (with post-fellowship experience of at least 5 years) and were looked for Choline peak, NAA/ Cr Ratio, NAA/ Cho Ratio and Cho/ Cr Ratio for neoplastic or non-neoplastic lesion as per-operational definition. Magnetic resonance spectroscopy findings were correlated with biopsy report. All this data was recorded on a specially designed proforma .

DATA ANALYSIS PROCEDURE:
Collected data was analyzed through computer software SPSS 20.0. Mean and standard deviation were calculated for quantitative variables i.e. age and duration of disease. Frequency and percentage were calculated for qualitative variables i.e. gender and neoplastic or non-neoplastic brain lesion. 2×2 contingency table was used to calculate sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy in differentiating neoplastic from non-neoplastic brain lesions, taking biopsy as gold standard. Effect modifiers like age, gender and duration of disease were controlled through stratification and post-stratification chi square was applied. P value ≤ 0.05 was considered as significant.

RESULTS:

Age range in this study was from 30-60 years with mean age of 47.93 ± 8.13 years. Majority of the patients 80 (41.88%) were between 51 to 60 years of age .
Out of these 191 patients, 112 (58.64%) were male and 79 (41.36%) were females with ratio of 1.4:1 . Mean duration of disease was 3.23 ± 1.32 months .
All the patients were subjected to magnetic resonance spectroscopy (MRS) of brain. MRS supported the diagnosis of neoplastic brain lesion in 108 (56.54%) patients. Histopathology findings confirmed neoplastic brain lesion in 104 (54.45%) cases. In MRS positive patients, 95 were True Positive and 13 were False Positive. Among 83, MRS negative patients, 09 were False Negative where as 74 were True Negative (p=0.680) .
Overall sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of MRS in differentiating neoplastic from non-neoplastic brain lesions was 91.35%, 85.06%, 87.96%, 89.16% and 88.48% respectively .

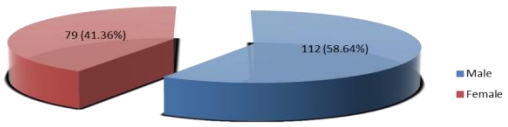


Table: Male to Female ratio in Diagnostic accuracy of MRS for differentiating brain lesions

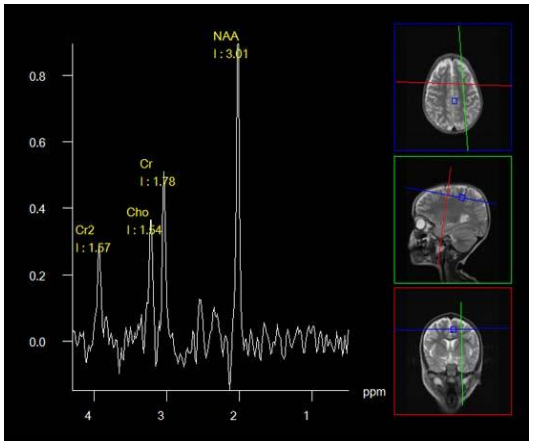


FIG 1 a: Normal MR spectra showing the various metabolites

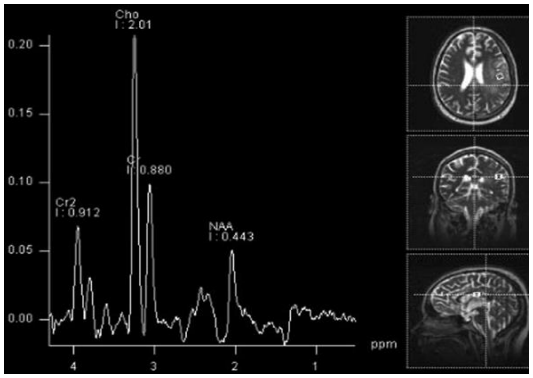
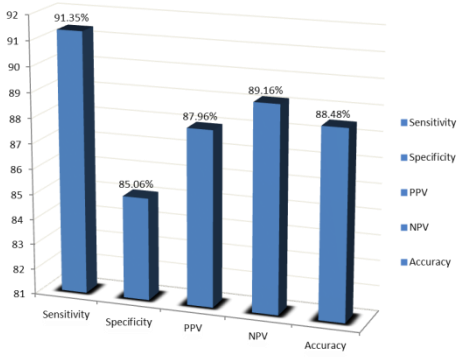


FIG 1 b: MR spectra showing the raised choline peak in a glioma

Summary of Results.

Positive result on MRS P-value	Negative result on MRS	
Positive on Histopathology	95 (TP)*	09 (FN)***
0.680		
Negative on Histopathology	13 (FP)**	74 (TN)****

Positive result on MRS	Negative result on MRS P-Value
Positive on Histopathology 02 (FN)	15 (TP)
0.820	
Negative on Histopathology 19 (TN)	03 (FP)



DISCUSSION:

Magnetic resonance spectroscopy (MRS) is a non-invasive diagnostic test that uses strong magnetic fields to measure and analyze the chemical composition of human tissues. MRS relies on the fact that chemicals in the body emit radiofrequency signals when stimulated by a strong magnetic field. By analyzing the different chemical compounds or metabolites in a diseased tissue area (e.g., in the brain) and comparing these with the normal metabolite composition of corresponding tissue, MRS has the potential to provide information that can assist in diagnosing pathologic states.11 MRS, which evaluates the metabolite profile of the lesion when combined with conventional MR imaging, has been reported to increase diagnostic accuracy.11 A number of studies have identified metabolic patterns utilizing MRS in various pathologies such as brain tumours,12-19 infections15,16and inflammatory conditions.17 Although a few studies have evaluated the role of MRS in differentiating brain tumours from abscesses,18,19and high-grade gliomas from low-grade gliomas,21 there appears to be little information elucidating a neurosurgical perspective of the value, or otherwise, of MRS.

The sensitivity and specificity of MR Spectroscopy for differentiating neoplastic from non-neoplastic brain lesions as observed by Surur A et al6 is 97% and 90% respectively while Alam MS et al10 evaluated the role of 1HMRS in focal brain lesions and found the sensitivity of 93% and specificity of 70% in differentiating neoplastic from non-neoplastic brain lesions.

Gluch (2005) stated that ex vivo and in vivo applications of MRS have been developed, which aid in distinguishing malignant from normal tissues. Studies of breast, colon, cervix, esophageal, and prostate cancer reveal both the successes and failings of present technology. The author noted that verification that these non-invasive tests might supplant conventional histology in obtaining spatial diagnostic and chemical prognostic information remains for the time being illusive.22 Previous studies evaluating a heterogeneous group of patients, some with known prior tumour, some with unknown new masses, showed variable diagnostic test characteristics for MRS with sensitivities ranging from 79% to 100% and specificity ranges from 74% to 100%. The positive predictive values ranged from 92% to 100%, while the negative predictive values ranged from 60% to 100%.23 Lai PH et al24 has suggested that MRS might noninvasively contribute to the establishment of the differential diagnosis between brain abscesses and cystic or necrotic brain tumours with sensitivity, specificity, PPV, NPV and diagnostic accuracy as 93.2%, 85.7%, 100%, 100%, and 88.5% respectively. In a large clinical study which included 98 patients with intracranial mass lesions, Poptani et al25reported 89% diagnostic accuracy with proton MR spectroscopy. In a prospective clinical study including 120 patients with intracranial lesions reported a diagnostic accuracy of 85.6% with proton MR spectroscopy.26Moller-Hartmann et al27 reported that the addition of proton MR spectroscopy increased the diagnostic accuracy of conventional MR imaging by 15.4% in their series.

According to Jung and Westphalen (2012) studies have demonstrated that the addition of proton magnetic resonance spectroscopic imaging (1H-MRSI) to T2-weighted MR imaging improves tumor localization, volume estimation, staging, tissue characterization, and identification of recurrent disease after therapy. A recent multicenter study supported by the American College of Radiology Imaging Network, however, showed that the combination of 1H-MRSI and T2-weighted MR images does not improve tumor detection in patients with low-grade, low-volume

disease selected to undergo radical prostatectomy. These results suggest that positive 1H-MRSI findings are more likely to reflect higher tumor grade and/or volume.28 Horska A et al29 noted that the utility of MRS in diagnosis and evaluation of treatment response to human brain tumors has been widely documented. These researchers discussed the role of MRS in tumor classification, tumors versus non-neoplastic lesions, prediction of survival, treatment planning, monitoring of therapy, and post-therapy evaluation. Horska and Barker (2010)30 noted that the utility of MRS in diagnosis and evaluation of treatment response to human brain tumors has been widely documented. These researchers discussed the role of MRS in tumor classification, tumors versus non-neoplastic lesions, prediction of survival, treatment planning, monitoring of therapy, and post-therapy evaluation.

Dyke et al (2007)31 explored (1)H MRSI as a means to assess peri-tumoral tissue response post-resection and Gliadel (R) implantation in patients with high-grade gliomas. Pilot (1) H MRSI data are presented that demonstrate non-invasive, serial monitoring of metabolic changes at the tumor site following Gliadel implantation. Three patients with newly diagnosed glioblastoma multiforme (GBM) underwent MRI and (1) H MRSI at 3.0 Tesla prior to resection and at 3 to 5 and greater than or equal to 12 weeks post-operatively. Baseline MRS spectra of tumor tissue from all patients were characterized by marked increases of choline (CHO) and lactate (LAC), and a decrease of N-acetylaspartate (NAA), typical of GBM compared with normal contra-lateral brain tissue.

In a prospective clinical study including 120 patients with intracranial lesions reported a diagnostic accuracy of 85.6% with proton MR spectroscopy.32 Moller-Hartmann et al33 reported that the addition of proton MR spectroscopy increased the diagnostic accuracy of conventional MR imaging by 15.4% in their series.

On the whole, it is concluded that magnetic resonance spectroscopy (MRS) is the non-invasive modality of choice with high diagnostic accuracy in differentiating neoplastic from non-neoplastic brain lesions, and has not only dramatically improved our ability of differentiating benign and malignant brain tumour pre-operatively but also helps the surgeons for proper decision making.

Conclusion:

This study concluded that magnetic resonance spectroscopy (MRS) is the non-invasive modality of choice with high diagnostic accuracy in differentiating neoplastic from non-neoplastic brain lesions, and has not only dramatically improved our ability of differentiating neoplastic from non-neoplastic brain lesions pre-operatively but also helps the surgeons for proper decision making. So, we recommend that magnetic resonance spectroscopy (MRS) should be done routinely in all suspected cases of intracranial mass lesion for accurate differentiation of differentiating neoplastic from non-neoplastic brain lesions pre-operatively and opting proper surgical approach.

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