ORIGINAL ARTICLE

ANNALS OF PUNJAB MEDICAL COLLEGE

Diagnostic Accuracy of Magnetic Resonance Spectroscopy for Differentiation of Benign and Malignant Brain lesions using Histopathology as a Gold Standard

Amber Manzoor[1], Nayab Aliya[2], Marryum Mukhtar[3], Muhammad Qasim Khan[4], Aamna Gillani[5]

1 *Consultant Radiologist, Radiology Department, Mujahid Hospital, Faisalabad Pakistan*
Manuscript writing, Data collection

2 *Professor & HOD, Department of Radiology, Madina Teaching Hospital & University of Faisalabad, Faisalabad Pakistan*
Data analysis

3 *Senior Registrar, Department of Radiology, Madina Teaching Hospital, Faisalabad Pakistan*
Data collection, data analysis

4 *Post Graduate Resident, Department of Radiology, Madina Teaching Hospital, Faisalabad Pakistan*
Abstract writing, Critical analysis

5 *Senior Registrar, Department of Radiology, Madina Teaching Hospital, Faisalabad Pakistan*
Abstract writing, Critical analysis

CORRESPONDING AUTHOR
Dr. Marryum Mukhtar
Senior Registrar, Department of Radiology, Madina Teaching Hospital, Faisalabad Pakistan
Email: drmariam22@yahoo.com

Submitted for Publication: 15-07-2024
Accepted for Publication 05-09-2024

How to Cite: Manzoor A, Aliya N, Mukhtar M, Khan MQ, Gillani A. Diagnostic Accuracy of Magnetic Resonance Spectroscopy for Differentiation of Benign and Malignant Brain lesions using Histopathology as a Gold Standard. APMC 2024;18(3):242-245. **DOI: 10.29054/APMC/2024.1653**

ABSTRACT

Background: Academic sources showed that MRS has a high accuracy rate for recognizing malignant brain lesions and is more reliable than any other modality. However, there is much less data for the accuracy of MRS. So, more studies are needed to validate the evidence. MRS is a minimally disruptive technique that shows the neurochemical profile of the brain. **Objective:** To find the diagnostic precision of MRS for differentiation of aggressive & benign cerebral focal lesions taking1histopathology as the ultimate criterion. **Study Design:** Cross-sectional study. **Settings:** Imaging department, Madinah Teaching Health Institution, Faisalabad Pakistan. **Duration:** Six months from December 20, 2020 to June 21, 2021. **Methods:** A total of 155 Radiology Department patients fulfilling the selection criteria were enlisted. Then all patients underwent MRS using 3T. Findings were documented & patients were labeled as positive or negative. Then, the biopsy sample was sent to the hospital laboratory for histopathological evaluation after being under the supervision of the surgical team. **Results:** The mean age was 47.17±16.46 years. There were 69(44.5%) males & 86(55.5%) females in this study. The mean duration of symptoms was 11.44±2.79. The sensitivity and specificity of MRS were 90.79% and 86.08%, or PPV & NPV were 86.25% & 90.67%, respectively, and the 1overall diagnostic accuracy was 88.39%. **Conclusion:** Results demonstrate that the sensitivity (90.79%) and specificity (86.08%) of MRS are high enough to differentiate between malignant & benign brain lesions.

Keywords: *Diagnostic precision, Spectroscopic MRI, aggressive, Brain Lesions.*

INTRODUCTION

The precise assessment is necessary for ideal therapeutic management in patients having intracerebral tumors., Most tumors are surgically extracted when accessible; however, there's an equilibrium between eliminating maximum tumor tissue as possible while maintaining vital neural functions, and then radiation-based therapy is used to treat any residual neoplastic tissue.[1] It has been observed that most lesions are malignant, i.e., 62%, while 38% were benign brain lesions.[2]

A general diversity of noncancerous lesions may mimic cerebral focal lesions from a radiologic perspective. Magnetic resonance imaging (MRI) and magnetic resonance spectroscopy (MRS) are the most popular methods for assisting in lesion specification of various neurological conditions & diffusion-weighted imaging.[3]

A rapidly growing area of neuroimaging called magnetic resonance spectroscopy (MRS) enables noninvasive in vivo metabolite analysis.[3] The MRS can identify the resonance spectrum of various chemical compounds in tissues, which in turn exposes structural details about the chemical1component and details about the metabolic state of the tissues.[4]

However, in the case of malignancy, citrate levels diminish or are undetectable because of a conversion from citrate-producing to citrate-oxidating metabolism.[5] MRS was a more reliable diagnostic tool for the

distinction & treatment planning of cerebral focal lesions than other radiological modalities assessments.[3]

The justification of this research project is to evaluate the detective accuracy of spectroscopic MR for the differentiation of aggressive and nonaggressive brain lesions taking histopathology as the ultimate criterion. Literature showed that MRS has a high accuracy rate for recognizing malignant brain lesions and is more reliable than any other modality. However, there is variability in the accuracy of MRS in local studies available in the literature. So additional studies are needed to validate the evidence. Thus, to confirm the evidence, we want to conduct this study to establish reliable results regarding the predictive accuracy of MRS aiming to avoid unnecessary invasive procedures. This will help to enhance our practice, and we tend to imply the results in a local setting to commence the application of MRS for the correct detection of malignant & benign brain lesions.

The objective of the study was to find the diagnostic precision of magnetic resonance spectroscopy for differentiation of aggressive & benign cerebral focal lesions using taking1histopathology as the ultimate criterion

METHODS

This cross-sectional evaluation study was conducted at the Imaging Department, Madinah Teaching Health Institution, Faisalabad Pakistan. The duration of the study was six months from 20-12-2020 to 21-6-2021.

Sample count of 155 cases was analyzed with a 95.0% confidence level & taking expected1percentage of malignant lesions, i.e., 62%, and sensitivity of MRS, i.e., 87.5% with a 10% margin of error & specificity of MRS, i.e., 93.3% with 6.5% margin of error taking histopathology as the reference standard.

Non-probabilistic consecutive sampling technique was used.

Patients aged 16-75 years diagnosed with suspicious brain lesions detected on CT scan and planned to undergo biopsy were enrolled.

Patients with recurrent disease or metastasized disease were excluded from the study.

A total of 155 patients were referred to the Radiology Department. Informed consent was taken. All patients underwent MRS using 3T (Magnetom Skyra, Siemens) without an endorectal coil machine by a single chief radiologist with at least 4 years of relevant work experience in Radiology with the help of a researcher. Results were noted, and patients were given a positive or negative label. It was labeled as positive if Cho > 3.2 ppm, Cr > 3 ppm, NAA >2.02 ppm and negative if Cho ≤ 3.2 ppm, Cr ≤ 3 ppm, NAA ≤2.02 ppm. Then biopsy was performed on these patients by a surgical team under spinal anesthesia. The biopsy sample was sent to the hospital laboratory for histopathological assessment of the biopsy sample. Reports were assessed & patients were labeled as positive or negative for malignant lesions. On histopathology, it was classified as positive if >30% of cells got an H&E stain and negative if <30% of cells got an H&E stain on histopathology slides. All this information was documented.

Data was entered and analyzed in SPSS 21. To determine the sensitivity,1specificity, 1PPV, 1NPV & accuracy of MRS using histopathology as the gold standard, a 2 x 2 table was made.

RESULTS

The mean age was 47.17 ± 16.46 years. There were 69 (44.5%) males & 86 (55.5%) females. The male-to-female ratio was 1: 1.2. The mean duration of symptoms was 11.44±2.79 months. As per BMI criteria, 63 (40.6%) patients' BMI was normal, 44 (28.4%) were excessive weight, and 48 (31%) were highly overweight. The mean size of the lesion on the CT scan was 5.64 ± 0.73 mm.

Table 1: Demographic features of patients (n=155)

Age (years)		47.17 ± 16.46
Gender	Male	69 (44.5%)
	Female	86 (55.5%)
Duration of Symptoms		11.44 ± 2.79
BMI of patients	Normal	63 (40.6%)
	Overweight	44 (28.4%)
	Obese	48 (31.0%)
Size of lesion on CT scan (mm)		5.64 ± 0.73

The sensitivity & specificity of MRS was 90.79% & 86.08%, respectively, PPV & NPV was 86.25% & 90.67%, respectively, and 1 overall diagnostic accuracy was 88.39%.

Table 2: Diagnostic precision of spectroscopic MR for differentiation of benign and nonaggressive cerebral lesions

MRS	**Histological Pathology**		**Total**
	Malignant	**Benign**	
Malignant	69 (90.8%)	11 (13.9%)	**80**
Benign	7 (9.2%)	68 (86.1%)	**75**
Total	**76**	**79**	**155**

	Value	**95% CI**
Sensitivity	90.79%	82.19, 95.47
Specificity	86.08%	76.76, 92.04
PPV	86.25%	77.03, 92.15
NPV	90.67%	81.97, 95.41
Diagnostic Accuracy	88.39%	82.39, 92.53

DISCUSSION

MRI is a sensitive detection method being used for characterizing cerebral lesions, although due to overlapping symptoms, it's frequently impossible to tell the difference between benign & malignant nature. Non-invasive spectroscopic MR can identify the chemical makeup of the focal lesion. Neoplastic masses can be distinguished from other lesions with the help of MRS. After placing an appropriate voxel on the focal lesion, the MR spectrum is performed.[6] Choline and NAA peak, Cho/Cr & Cho/NAA ratio & other criteria can be used to evaluate lesions based on MR spectrum analysis.[7]

Primary brain tumors are defined as primary intracranial tumors that develop from their surrounding membranes (meninges), neuro-epithelial tissues, pituitary & associated structures, cranial nerves, blood-forming organs, germ cells, or a distant nonapparent primary tumor. The predicted 23,380 new cases diagnosed in 2014, followed by 14,320 fatalities, malignant tumors in adults are rare, accounting for 1.4% of all the fresh cases of cancer & 2.4% of all cancer deaths. The peak frequency occurs between the ages of 55 and 64, and men have a slightly higher probability than women to experience it. A lifetime diagnosis of brain or other nervous system cancer carries a risk of 0.6%.[8,9]

In this study, sensitivity, specificity, PPV (positive predictive value), NPV (Negative predictive value), and overall detective accuracy of Magnetic resonance spectroscopy were 90.79%, 86.08%, 86.25%, 90.67%, and 88.39%, respectively.

One study found that MRS had 87.5% sensitivity, 93.3% specificity, 95.5% PPV, 89.7% NPV & 92.1% accuracy.[10] Another study reported that the overall sensitivity, specificity, PPV, NPV, and diagnostic precision of MRS were 90.7%, 94.4%, 98.3%, 73.9%, and 91.5%, respectively.[11] One more study reported that The sensitivity, specificity, and accuracy of MRS for all examined malignant and neoplastic lesions are around 95.3%, 97.1%, and 96%, respectively.[3] Results of this study align with the above-mentioned studies showing higher sensitivity and slightly lower specificity for MRS for differentiating benign and malignant brain lesions. The diagnostic accuracy of MRS reported in this study is slightly lower as compared to the above-mentioned studies, but it is still strong enough to be used for diagnosis and differentiating brain lesions.

Another recently published local study reported the Sensitivity, specificity, PPV, NPV & accuracy of MRS as 87.4%, 93.2%, 95.4%, 89.6% & 92.1%.[12] These results confirm the high sensitivity & specificity of MRS as well as in line with the results of this study. Another locally published study reported lower sensitivity (72.20%) and low negative predictive value (57.70%) for MRS, which contradicts the findings of this regarding higher sensitivity value for MRS.[13]

Zeynep B Aydın, in his study, showed that high-resolution MR imaging methods like diffusion-weighted imaging, MRS, and a fusion of these systems predicted 100.0% sensitivity for the distinction of noncancerous & aggressive lesions, making MRP superior to conventional MRI. Diffusion-weighted imaging +MRS was considered to have 100.0% sensitivity for the identification of benign & malignant mass lesions in the absence of intravenous contrast agent injection.[14]

Magnetic resonance spectroscopy (MRS) is shown may significantly improve diagnosis accuracy by lighting the dark regions of conventional MRI when utilized as an addition. A non-invasive diagnostic method called MRS can measure the concentration of a certain metabolite in a pre-selected tissue volume.[15,16]

Spectroscopic MR could be introduced into standard MRI protocols during the first-line diagnostic imaging to ensure accurate diagnosis further. The absence of data acquisition protocols, assessment methods & quality assurance procedures for particular clinical situations has until now hampered MRS deployment. It is difficult to accurately interpret data, evaluate the quality of spectra, and process to convey information. There's a scarcity of research to implement the diagnostic indication from MRS, but more research is needed to assess the effectiveness of MRS as a common diagnostic1tool.[17]

The benefit of MRS has increased diagnostic possibilities and allowed for molecularly-based tissue characterization. It gives more knowledge about cell growth, cellular aging, neural vitality & energy metabolism. These characteristics are used by MRS to distinguish between malignant or benign brain lesions.

Based on the above discussion, it can be said that MRS can help differentiate malignant lesions from benign brain lesions. Thus, an invasive biopsy of brain procedures can be avoided in many situations where the diagnosis is clear-cut, minimizing the risk of morbidity and death associated with such procedures as well as the manpower, the time needed to begin therapy & economic cost.

CONCLUSION

Results of this study demonstrate that the sensitivity (90.79%) and specificity (86.08%) of magnetic resonance spectroscopy are high enough to differentiate between malignant & benign brain lesions in patients presenting with suspicious brain lesions.

FUNDING

The project received its funding from the hospital.

SHORTCOMINGS / LIMITATIONS

Technical issues such as low resolution or inadequate signal-to-noise ratio in MRS could affect diagnostic accuracy and lead to suboptimal differentiation.

SUGGESTIONS / RECOMMENDATIONS

Longitudinal Studies: Implement longitudinal studies to track changes in metabolic profiles over time in patients with known benign or malignant lesions. This could provide insights into the progression of disease and the potential for early detection of malignancy.

Advanced Analytical Techniques: Utilize machine learning and artificial intelligence to analyze MRS data. These technologies can improve pattern recognition and enhance the accuracy of differentiating between lesion types.

CONFLICT OF INTEREST / DISCLOSURE

The authors declare that there are no conflicts of interest related to this study.

ACKNOWLEDGEMENTS

We extend our heartfelt thanks to the hospital for their generous funding and support, which made this research project possible. We also appreciate the invaluable contributions of our research team and collaborators. Your dedication has been crucial to our success.

REFERENCES

1. Aboelnor MI, Elhawary ME, Mahmoud MAE, Saad MAM. Evaluating the role of proton magnetic resonance spectroscopy in characterization of intracranial lesions. Acta Sci Intellect 2017;3(5):61-83.
2. Tanvir I, Malik R, Khan R, Khan H, Wahid Z, Riaz S. Frequency of brain tumors in childhood and adults, a hospital based study. Pakistan Journal of Medical and Health Sciences. 2014;8(1):109-11.
3. Ahmed HA, Mokhtar H. The diagnostic value of MR spectroscopy versus DWI-MRI in therapeutic planning of suspicious multi-centric cerebral lesions. Egyptian Journal of Radiology and Nuclear Medicine. 2020 Dec;51:1-1.
4. Tognarelli JM, Dawood M, Shariff MI, Grover VP, Crossey MM, Cox IJ, Taylor-Robinson SD, McPhail MJ. Magnetic resonance spectroscopy: principles and techniques: lessons for clinicians. Journal of clinical and experimental hepatology. 2015 Dec 1;5(4):320-8.
5. Suh CH, Park SH. Successful publication of systematic review and meta-analysis of studies evaluating diagnostic test accuracy. Korean journal of radiology. 2016 Feb 1;17(1):5-6.
6. Majós C, Aguilera C, Alonso J, Julià-Sapé M, Castañer S, Sanchez JJ, et al. Proton MR spectroscopy improves discrimination between tumor and pseudotumoral lesion in solid brain masses. American Journal of Neuroradiology. 2009 Mar 1;30(3):544-51.
7. Elmoneim BA, Hafez H, Omar SF, Fawzy T. The role of proton magnetic resonance spectroscopy in grading of brain gliomas. Menoufia Medical Journal. 2016;29(1):136-40.
8. Perkins A, Liu G. Primary brain tumors in adults: diagnosis and treatment. American family physician. 2016 Feb 1;93(3):211-7B.
9. Howlader NN, Noone AM, Krapcho M, Garshell J, Miller D, Altekruse SF, et al. SEER cancer statistics review, 1975–2012. National Cancer Institute. 2014 Nov.
10. Jesrani A, Ajmal R, Asad M, Zehra SN. Diagnostic accuracy of magnetic resonance spectroscopy in differentiating neoplastic from non-neoplastic enhancing brain lesions taking histopathology as gold standard, experience at Liaquat National Hospital, Karachi, Pakistan. Acta Scientific Cancer Biology. 2019;3(10):3-8.
11. Amin U, Ahmad A, Ather S, Ahmed A. Diagnostic Accuracy of Magnetic Resonance Spectroscopy in Diagnosing Glioblastoma by taking Histopathology As A Gold Standard. PJR. 2019 Mar 30;29(1):8-13.
12. Jesrani A, Ajmal R, Asad M, Zehra SN. Diagnostic accuracy of magnetic resonance spectroscopy in differentiating neoplastic from non-neoplastic enhancing brain lesions taking histopathology as gold standard, experience at Liaquat National Hospital, Karachi, Pakistan. Acta Scientific Cancer Biology. 2019;3(10):3-8.
13. Nisar S, Rauf M, Sarfraz L. Diagnostic Accuracy (sensitivity and specificity) of Magnetic Resonance Spectroscopy as an imaging tool in the differentiation of benign vs malignant intracranial space occupying lesions. PJMHS. 2020;14(3):528.
14. Aydın ZB, Aydın H, Birgi E, Hekimoğlu B. Diagnostic Value of Diffusion-weighted Magnetic Resonance (MR) Imaging, MR Perfusion, and MR Spectroscopy in Addition to Conventional MR Imaging in Intracranial Space-occupying Lesions. Cureus. 2019 Dec 18;11(12):e6409.
15. Zhang X, Chen YL, Lim R, Huang C, Chebib IA, El Fakhri G. Synergistic role of simultaneous PET/MRI-MRS in soft tissue sarcoma metabolism imaging. Magnetic resonance imaging. 2016 Apr 1;34(3):276-9.
16. Ostrom QT, Gittleman H, Fulop J, Liu M, Blanda R, Kromer C, et al. CBTRUS statistical report: primary brain and central nervous system tumors diagnosed in the United States in 2008-2012. Neuro-oncology. 2015 Oct 1;17(suppl_4):iv1-62.
17. Manias K, Gill SK, Zarinabad N, Davies P, English M, Ford D, et al. Evaluation of the added value of 1H-magnetic resonance spectroscopy for the diagnosis of pediatric brain lesions in clinical practice. Neuro-oncology practice. 2018 Mar 2;5(1):18-27.