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# A Cross Sectional Study to Evaluate the Sensitivity and Specificity of Magnetic Resonance Spectroscopy (MRS) in Diagnosing Intracranial Neoplastic Lesions

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## Abstract

Diagnosing intracranial neoplastic lesions accurately are always challenging. Often neurosurgeons face difficulties getting appropriate tissue from appropriate site for biopsy. Histopathology is the most confirm tool for tissue diagnosis though contrast Magnetic Resonance Imaging (MRI) gives some clue about the nature of the lesion. This is a cross sectional descriptive study to evaluate the sensitivity and specificity of Magnetic Resonance Spectroscopy (MRS) in diagnosing intracranial neoplastic lesions. There were total 19 participants in this study. Study place was neurosurgery department of the Al Haramain hospital of Sylhet, Bangladesh. Average age of the participants was 62.3 years. Magnetic Resonance Spectroscopy (MRS) results were compared with the histopathology reports to find out the Sensitivity (85.71%), specificity (91.67%), positive likelihood ratio (10.29), negative likelihood ratio (0.16), positive predictive value (85.71%), negative predictive value (91.67%) and diagnostic accuracy (89.47%).

## Keywords

Magnetic Resonance Spectroscopy (MRS); Neoplastic Brain Lesion; Sensitivity; Specificity

## Introduction

Early diagnosis of the nature of the brain tumour is always beneficial for management, but this is most of the time very challenging. So far Magnetic Resonance Imaging (MRI) with contrast is used to get an idea about the type of the brain tumour though biopsy is more confirmatory. The sensitivity of contrast MRI to differentiate between progressive or recurrent tumour with radiation induced tumour is not very high [1]. Proton magnetic resonance spectroscopy (MRS) can provide some important information regarding the metabolic status of tumours especially about creatine (Cr), N-acetyl-aspartate (NAA) and choline (Cho), at different MRS echo times (TEs), which gives a major advantage without electromagnetic radiation exposure for guiding intracranial tumour biopsy procedures [2]. There are several studies reported on the ability of MRS to differentiate between neoplastic and non-neoplastic brain lesions, and between high-grade and low-grade gliomas [3].

For the last two decades magnetic resonance spectroscopy has been used commercially in different medical centers to evaluate brain tumours. There are few reported studies of human brain tumours using heteronuclei such as sodium (11Na) and phosphorus (31P), by far the most spectroscopy studies use the proton (1H) nucleus. Proton has been proved most sensitive and also it is easy to implement on diagnostic MRI scanners [4].

There are two types of MR spectroscopy techniques. Single voxel (SV) technique includes PRESS and STEAM which records spectra from one area of brain at a time. Multi-voxel technique, also known as Chemical Shift Imaging (CSI) can record spectra from multiple areas of brain simultaneously at a time [5].

It has been proved earlier that brain tumours exhibit significantly different spectra from normal brain tissue.

Early in the development of human brain proton MRS, it was realized that brain tumors exhibited markedly different spectra from normal brain tissue. It was found that nearly all brain tumors have decreased N-acetyl aspartate (NAA) signals, and often also have increased levels of Choline (Cho), leading to increased Cho/NAA ratios. It is thought that NAA is primarily originated from neuronal and axonal tissue. Loss or displacement of normal brain tissue is widely interpreted with low NAA. Choline compounds are mainly related with membrane synthesis and degradation. Increased volume of brain tumour causes increased membrane turnover, which indicates high choline value in MRS [6]. A Lac/tNAA ratio greater than 0.25, a tCho/tNAA ratio greater than 2, and the presence of lipid

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at magnetic resonance spectroscopic imaging indicate a high-grade tumor, which allows a demarcation between brain parenchyma and adjacent tumor [7].

The aim of this study was to evaluate the sensitivity, specificity, likelihood ratios and predictive values of Magnetic Resonance Spectroscopy (MRS) of brain in diagnosing neoplastic brain lesions.

## Results and Discussion

This study was a cross sectional descriptive study with 19 patients (n=19) to evaluate the diagnostic accuracy of MR spectroscopy to differentiate between neoplastic and non-neoplastic brain lesions (Tables 1-3) (Figures 1 & 2).

This study was a cross sectional descriptive study with 19 patients to evaluate the diagnostic accuracy of MR spectroscopy to differentiate between neoplastic and non-neoplastic brain lesions. We had the opportunity to compare the result of this study with the same of other international published studies.

Fayed N et al. [8] published their study on 24 patient brain neoplasia patients. MRS reports were compared with the histopathology reports to determine the malignancy grades. A Choline/creatineratio equal or larger than 1.55 predicted malignancy grade with 92% sensitivity and 80% specificity respectively. The area under the Receiver-operating characteristic (ROC) curve was 0.92 (CI: 95%; 0.81-1). In the Blood Brain Barrier (BBB) damaged patients the specificity was increased to 90%.

Alam MS et al. [9] performed their study on 53 patients to evaluate the sensitivity, specificity, predictive values and diagnostic accuracy of MRS for intracranial neoplastic and non-neoplastic cases. Percentage agreement between spectroscopy and histopathology was also calculated using kappa statistics. According to that study

| Age group | Number of cases | Percentage of cases | Mean age (year) |
|---|---|---|---|
| Below 40 years | 0 | 0 | 62.3 |
| 41 to 50 years | 3 | 15.8 | |
| 51 to 60 years | 8 | 42.1 | |
| 61 to 70 years | 5 | 26.3 | |
| Above 70 years | 3 | 15.8 | |

**Table 1:** Distribution according age frequency-shows the distribution of all 19 patients according to their age group frequency. Highest number of patients were in 51 to 60 years age group. They were 8 in number and 42% of the total cases. Both 41 to 50 year and above 70 year groups had 3 patients (15.8%) each. Nearly one-quarter (26.3%) patients were in 61 to 70 years age group. None of the patient aged below 40 year. Average age of the patients was 62.3 year.

| | MRS reported neoplastic | MRS reported non-neoplastic | |
|---|---|---|---|
| **Biopsy reported neolastic** | 6 (TP- a) | 11 (TN-d) | 17 |
| **Biopsy reported non-neoplastic** | 1 (FP- c) | 1 (FN- b) | 2 |
| | 7 | 12 | |

**Table 2:** Distribution according to MRS and biopsy result-Demonstrates the 2 X 2 epidemiological table according to the MRS and biopsy result. Out of 19 patients 7 patients were reported as neoplastic/glioma (a+c). Other 12 patients (b+d) were reported as non-neoplastic. Among the 7 neoplastic patients 4 were primary glioma and other 3 were secondary glioma. Biopsy confirmed 6 (true positive-a) out of these 7 patients as glioma. One neoplastic reported patient's biopsy report was non-neoplastic (false positive-c).On the other hand out of the 12 non-neoplastic MRS reported patients 1 patient's (false negative-b) biopsy was reported as primary glioma (grade 2 astrocytoma). So, 11 non-neoplastic patient's (true negative-d) biopsy report supported the MRS report.

| Statistics | Formula | Value | 95% Confidence Interval (CI) |
|---|---|---|---|
| Sensitivity | a/a+b | 85.71% | 42.13% to 99.64% |
| Specificity | d/c+d | 91.67% | 61.52% to 9.79% |
| Positive Likelihood Ratio (PLR) | Sensitivity/1-specificity | 10.29 | 1.54 to 68.82 |
| Negative Likelihood Ratio (NLR) | 1-Sensitivity/ Specificity | 0.16 | 0.03 to 0.96 |
| Positive Predictive Value (PPV) | a/a+c | 85.71% | 47.28% to 97.57% |
| Negative Predictive Value (NPV) | d/b+d | 91.67% | 64.00 to 98.55% |
| Accuracy | a+d/a+b+c+d | 89.47% | 66.86% to 98.70% |

**Table 3:** Statistical analysis to evaluate sensitivity, specificity, likelihood ratios and predictive values-shows the values of statistical analyses. Sensitivity and specificity were 85.71% and 91.67% respectively. Positive Likelihood Ratio (PLR) was 10.29 and Negative likelihood ratio was 0.16. Positive Predictive Value (PPV) and Negative Predictive Value (NPV) were same as sensitivity and specificity respectively. Accuracy was determined as 89.47%.

increased Choline/creatine and Choline/NAA ratio were noted in neoplastic lesions compared to non-neoplastic lesion with significant p-value. MR Spectroscopy had a sensitivity of 93.02%, specificity of 70%, positive predictive value of 93.02%, negative predictive value of 70% and diagnostic accuracy of 88.67% in differentiating neoplastic and non-neoplastic brain lesions. Kappa statistics showed a good agreement between MR Spectroscopy and histopathology (k=0.630).

Wenzhi et al. [10] published their meta-Analysis on the diagnostic performance of MRS in brain tumours. Total 24 studies were reviewed. Number of participants was 1013 (605 cases and 408 controls). The studies were performed in 10 countries or regions. The sample sizes of the included studies ranged from 12-160 (mean 40). The meta-analysis revealed that the overall sensitivity and specificity of MRS were 80.05% (95% CI: 75.97–83.59%) and 78.46% (95% CI: 73.40%–82.78% respectively. The overall PLR after logarithmic transformation was 1.28 (95% CI: 1.05–1.52) corresponding to 3.53 (95% CI: 2.71–4.60. The NLR after logarithmic transformation was −1.31 (95% CI: −1.53 to −1.09) corresponding to 0.29 (95% CI: 0.24–0.36). The DOR after logarithmic transformation was 2.86 (95% CI: 2.42–3.30) corresponding to 14.66 (95% CI: 9.81–21.92). They concluded that MRS demonstrated high diagnostic accuracy.

Alena and Peter published their article on utility of MRS to differentiate between neoplastic and non-neoplastic brain lesions and to compare spectroscopic characteristics of those lesions [11]. The neolastics were anaplastic astrocytoma WHO grade II, infiltrating astrocytoma WHO grade III, gliomatosis cerebri WHO grade II, oligodendroglioma WHO grade II, ganglioglioma WHO grade II. On the other hand the non-neoplastic lesions were demyelination, radiation necrosis, postsurgical gliosis, and stable lesions not confirmed on pathologic examination. They found 84% of the 69 brain lesions (36 tumors) were correctly classified using the ratios NAA/Cho, NAA/Cr, and Cho and NAA signal areas normalized to signal areas in a control region. By combining both MRSI and perfusion MRI, a sensitivity of 72.2% and specificity of 91.7% in differentiating tumors from nonneoplastic lesions was achieved with cutoff points of NAA/Cho ≤ 0.61 and rCBV ≥ 1.50 corresponding to tumor diagnosis. When comparing the result of MRS to histopathology it was revealed that the accuracy, sensitivity, and specificity of the classification strategy was 90%, 97%, and 67% respectively.

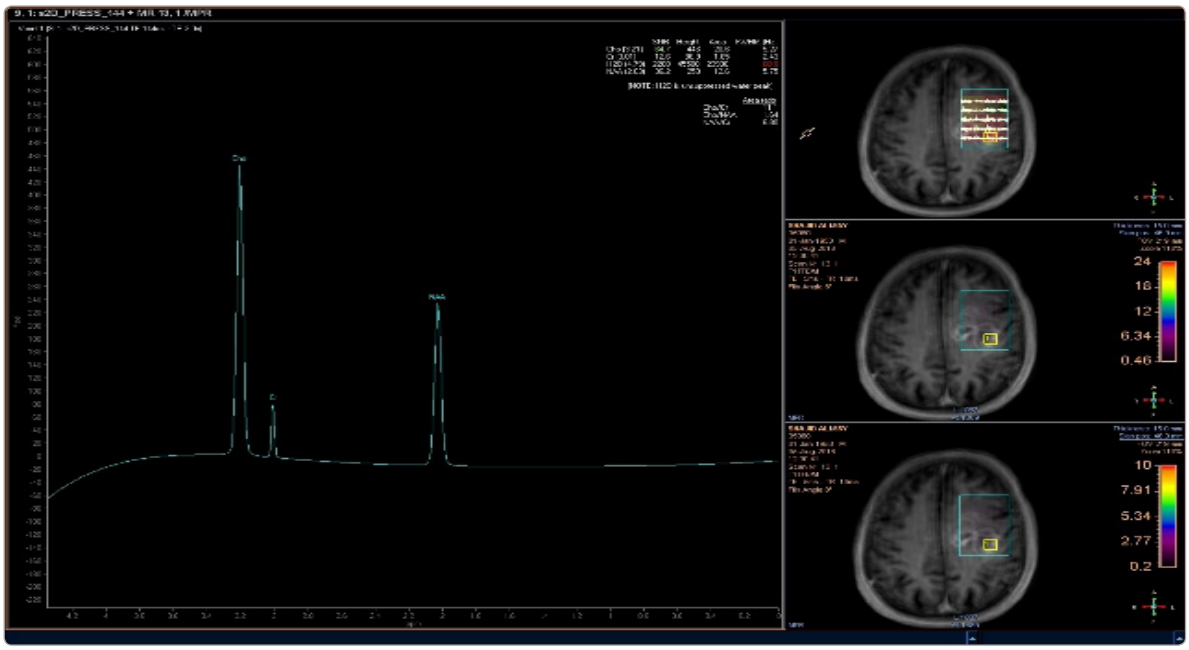


**Figure 1:** High Choline/Creatinin ration suggestive of Neoplastic lesion

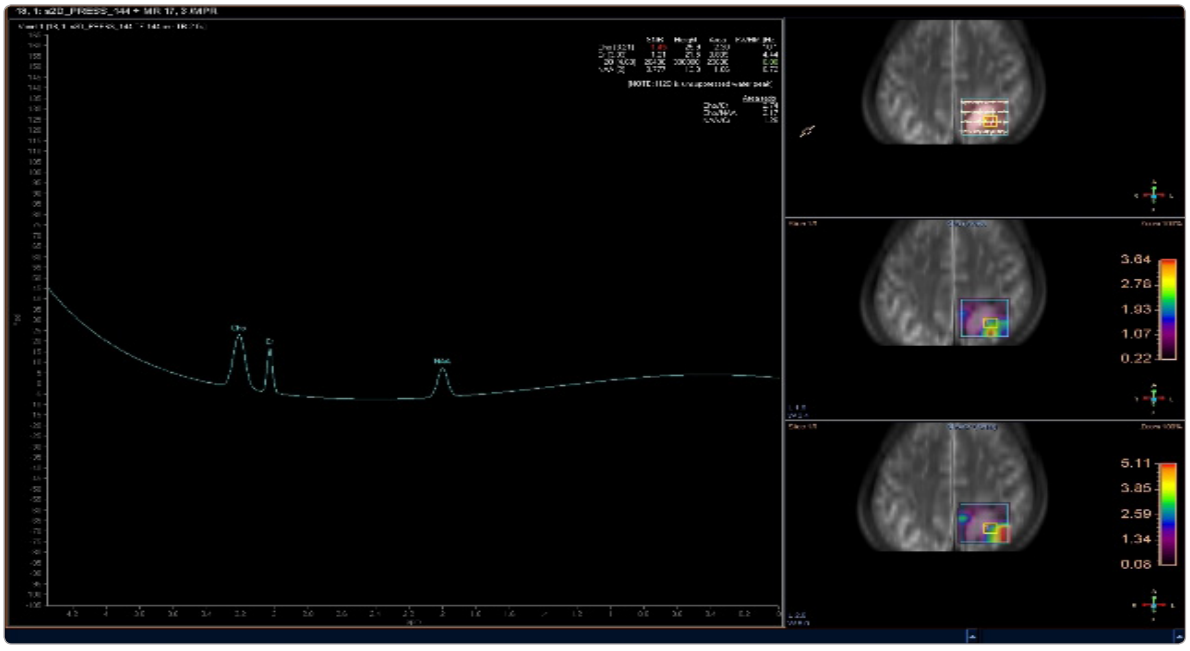


**Figure 2:** Low Choline/Creatinin ration suggestive of non-neoplastic lesion

J Axford et al. [12], performed their study to quantify total creatines (tCr), total cholines (tCho), N-acetylaspartate (NAA) and myo-inositol (mI) levels in the normal and abnormal white matter of brain of the patients with Neuropsychiatric Systemic Lupus Erythematosus (NPSLE) to determine the deficinte changes in metabolite concentrations. Total 17 participants were included in that study [12]. In the study nine were cases (7 female with the mean age of 40.3 years.) with neuropsychiatric systemic lupus erythematosus and eight were control (with the mean age of 43 years). A significant rise of Choline (12.4%, $p<0.05$) and a significant reduction in N-acetylaspartate (−12%, $p<0.05$) was found in normal appearing white matter in comparison to the controls. Analysis according to severity of the neuropsychiatric systemic lupus erythematosus features (with major or minor sub groups) revealed that SLE major had reduced N-acetylaspartate (NAA) in comparison to SLE minor (−18.4%, $p<0.05$) and controls (−20%, $p<0.005$). The SLE major group had a significant rise of ml (32%, $p<0.01$) and the SLE minor group showed significant increase of Choline (18.6%, $p<0.05$) compared with the controls.

In this study the mean age of all the patients was 62.3 years. Sensitivity and specificity were 85.71% and 91.67% respectively. PLR was 10.29 and NLR was 0.16. PPV and NPV were 85.71% and 91.67% respectively. The overall diagnostic accuracy was 89.47%. These results had similarity with those of other previously published international studies.

## Conclusion

Magnetic Resonance spectroscopy (MRS) is a non-invasive sensitive diagnostic tool to diagnose neoplastic brain lesions. The sensitivity, specificity and diagnostic accuracies are not significantly high when calculate at high confidence interval. This tool may be used as an adjunct to differentiate between neoplastic and non-neoplastic brain lesions but yet to replace histopathological evaluation.

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## Conflict of interest

There was no conflict of financial, academic or other interest declared among any of the co-authors.

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