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

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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. Total 19 participants were 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%).

Key words: Magnetic Resonance Spectroscopy (MRS), Neoplastic brain lesion, sensitivity, Specificity.

Introduction:
The early detection of brain tumors is associated with significant clinical benefits, but presents a diagnostic challenge. Contrast-enhanced magnetic resonance imaging (MRI) is the current gold standard for guiding neurosurgeons when obtaining biopsy tissue for the diagnosis of brain tumors. However, the results of this technique can sometimes be ambiguous, and differentiating progressive or recurrent brain tumors from radiation-induced injury is difficult using MRI¹. Proton magnetic resonance spectroscopy (MRS) provides important metabolic information of tumors, such as N-acetyl-aspartate (NAA), choline (Cho), creatine (Cr) at different MRS echo times (TEs), and showed a major advantage without electromagnetic radiation exposure as an imaging technique for guiding brain tumor biopsy procedures². Several recent studies have reported the utility of MRS for brain tumor assessment, with the ability to differentiate between high-grade and low-grade gliomas, and between neoplastic and non-neoplastic brain lesions³.

Localized proton MR spectroscopy (MRS) of the human brain, first reported more than 20 years ago, is a mature methodology that is used clinically in many medical centers worldwide for the evaluation of brain tumors. While there have been studies of human brain tumors using heteronuclei such as phosphorus (³¹P) and sodium (¹¹Na), by far the most spectroscopy studies use the proton (¹H) nucleus, because of both its high sensitivity and ease of implementation on commercial MRI scanners⁴. There are two classes of spatial localization techniques for MR spectroscopy; single-voxel (SV) techniques (commonly used methods includes ‘PRESS’ and ‘STEAM’ which record spectra from one region of the brain at a time, or multi-voxel techniques ‘MR spectroscopic imaging’ (MRSI), also called ‘Chemical
Shift Imaging’ (CSI) which simultaneously record spectra from multiple regions and thereby map out the spatial distribution of metabolites within the brain5.

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. The decrease in NAA is widely interpreted as the loss, dysfunction or displacement of normal neuronal tissue since NAA is believed to be primarily of neuronal and axonal origin. The ‘Cho’ signal actually contains contributions from several different choline-containing compounds, which are involved in membrane synthesis and degradation; it has been suggested that it is increased in brain tumors due to increased membrane turnover6. A tCho/tNAA ratio greater than 2, a Lac/tNAA ratio greater than 0.25, and the presence of lipid at MR spectroscopic imaging with a long TE (144 msec) are characteristics of a high-grade tumor, allowing demarcation of brain parenchyma adjacent to MR imaging–delineated tumor7.

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:
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. Study period was from January 2017 to May 2018.

<table>
<thead>
<tr>
<th>Age group</th>
<th>Number of cases</th>
<th>Percentage of cases</th>
<th>Mean age (year)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Below 40 years</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>41 to 50 years</td>
<td>3</td>
<td>15.8</td>
<td></td>
</tr>
<tr>
<td>51 to 60 years</td>
<td>8</td>
<td>42.1</td>
<td>62.3</td>
</tr>
<tr>
<td>61 to 70 years</td>
<td>5</td>
<td>26.3</td>
<td></td>
</tr>
<tr>
<td>Above 70 years</td>
<td>3</td>
<td>15.8</td>
<td></td>
</tr>
</tbody>
</table>

Table 1 shows the distribution of all 19 patients according to their age group frequency. Highest number of patients was 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.

Table 2 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.

Table 3 shows the values of statistical analyses. Sensitivity and specificity were 85.71% and 91.67%

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

**Discussion:**
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

![Fig.-1: High Choline/Creatinin ration suggestive of Neoplastic lesion](image1)

![Fig.-2: Low Choline/Creatinin ration suggestive of non-neoplastic lesion.](image2)
the opportunity to compare the result of this study with the same of other international published studies.

Fayed N et al published their study on 24 patient brain neoplasia patients8. MRS reports were compared with the histopathology reports to determine the malignancy grades. A Choline/creatinine ratio 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 performed their study on 53 patients to evaluate the sensitivity, specificity, predictive values and diagnostic accuracy of MRS for intracranial neoplastic and non-neoplastic cases9. Percentage agreement between spectroscopy and histopathology was also calculated using kappa statistics. According to that study increased Choline/creatinine 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 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)10. The studies included to the analysis were originated from 10 countries or regions and were published between 1995 and 2013. 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 lesions11. The neoplastics 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 d’0.61 and rCBV e’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.

J Axford et al performed their study to quantify N-acetylaspartate (NAA), total creatines (tCr), total cholines (tCho), and myo-inositol (mI) levels in normal and abnormal appearing white matter of patients with neuropsychiatric systemic lupus erythematosus (NPSLE) in order to determine the specific changes in metabolite concentrations. Total 17 participants were included in that study12. Of them 9 were cases (seven female, mean age 40.3 years, range 16–65) with NPSLE and 8 were control (mean age 43 years, range 31–65). A significant rise of tCho (12.4%, p<0.05) and mI (31.4%, p<0.005) and a significant reduction in NAA (“12%, p<0.05) was found in normal appearing white matter compared with controls. Analysis according to severity of the clinical NPSLE features (sub-grouped as major or minor) showed that SLE major had reduced NAA compared with SLE minor (“18.4%, p<0.05) and controls (“20%, p<0.005). The SLE major group showed a significant rise of mI (32%, p<0.01) and the SLE minor group a significant increase in tCho (18.6%, p<0.05) compared with 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.

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**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.

**References:**


