

# Magnetic Resonance Spectroscopic and Histopathological Findings in the Supratentorial Brain Space Occupying Lesions

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## ABSTRACT

**Objective:** Diagnosis of supratentorial space occupying lesion is a frequent dilemma in neurosurgical practice. MR spectroscopy that is an advanced MR imaging sequence can prove to be decisive in such cases. The objective of the study is to determine diagnostic accuracy of MRS in differentiating supra-tentorial brain space occupying lesions taking histopathology as gold standard

**Material and Methods:** The cross sectional study was conducted at Department of Neurosurgery, Jinnah Postgraduate Medical Centre, Karachi from August 2018 to July 2019. A calculated sample size of 156 patients aged between 18-50 years after informed consent. All patients underwent MR Spectroscopy pre-operatively. Surgery was performed and histopathological findings were compared with spectroscopic findings.

**Results:** The average age of the patients was  $32.41 \pm 10.02$  years. There were 84 (53.84%) males and 72 (46.15%) females. The sensitivity of MRS was 90.69% with a specificity of 97.34%.

**Conclusion:** MR Spectroscopy is an accurate diagnostic tool for establishing pre-operative differentiation between neoplastic and inflammatory lesion. It should be performed in all cases where contrast MRI is inconclusive in establishing the diagnosis.

**Keywords:** Magnetic Resonance Spectroscopy, Brain Abscess, Supratentorial lesion, Brain Tumor.

**Abbreviations:** MRS: Magnetic Resonance Spectroscopy. SOL: Space Occupying Lesion.

## INTRODUCTION

Diagnosis of supratentorial space occupying lesion (SOL) in brain is a frequent dilemma in neurosurgical practice.<sup>1</sup> These lesions may vary from simple arachnoid cysts requiring nothing but observation to brain abscess requiring emergency surgery. Inflammatory brain lesions are 50 times less common than neoplasm<sup>2,3</sup> and account for only 1-2 % of all brain SOL in the west. However, its incidence is as high as 8% in the developing countries.<sup>4</sup> An early diagnosis of SOL is of utmost importance in order to plan surgical intervention or conservative management.

Neuroradiology plays a pivotal role in the diagnosis of such SOL. These may include CT scan or

MRI. Recent advancements in MRI scanners have led to the availability of advanced sequences such as Diffusion weighted images. Magnetic Resonance Spectroscopy (MRS) is another state of the art technique which presents processed data as amplitude by frequency plots rather than images.<sup>5</sup> The important brain metabolites analyzed and plotted on spectrum are choline containing compounds (Cho) at 3.2 ppm, Creatine and Phosphocreatine (Cr) at 3.0 ppm, N-acetyl aspartate (NAA) at 2.02 ppm, Lactate (Lac) 1.32 ppm, Lipids at 0.9 – 1.5 ppm and Myo-inositol at 3.56 ppm.<sup>6-9</sup> Other metabolites include, Glutamine, Glutamate, Leucine and Alanine.<sup>10,11</sup> These levels of metabolites have their own significance. For example, the NAA is a marker of neuronal integrity, Cho is

linked to cell membrane turnover, Cr reflects energy storage and myo-inositol is a glial marker. Lipids and Lactate are absent in normal brain and are inflammatory markers of necrosis and anaerobic metabolism respectively.<sup>9</sup>

MRS has already been used for studying developmental behavior of human brain, hypoxic brain injury in neonates, congenital metabolic disorders, seizure disorders, brain tumors, neuro-degenerative and demyelinating diseases.<sup>12</sup>

MRS is primarily used to differentiate neoplastic lesions from inflammatory ones. The metabolites show a characteristic pattern different with pathologies. These are either interpreted as their peak levels or as a ratio. In brain abscess, NAA, Cho and Cr are typically absent because there is no normal neuron within the cavity. However, Lactate, lipids, amino acids including Leucine and alanine peaks are present.<sup>12</sup> Neoplastic lesions show increased Cho due to increased cellular turnover and decreased NAA levels. Cho/Cr and Cho/NAA ratios are also increased.<sup>13</sup>

MRS is a novel technique and therefore literature is scarce. The diagnostic accuracy of MRS varies from 90% to 94% in different studies.<sup>13</sup> The sensitivity and specificity varies from 80 to 98% and 70 to 78% respectively.<sup>14-17</sup> The studies conducted so far have included both supra and infra tentorial brain SOL. Presence of lesions near the bone and post fossa may augment the biochemical assay and affect the final diagnosis. Both national and international data is scarce on the comparison based findings related to MRS and Histopathology. This study will therefore focus on supra-tentorial brain SOL in order to determine diagnostic accuracy of MRS.

## MATERIAL AND METHODS

### *Study Design and Setting*

The Cross-sectional study was conducted at Department of Neurosurgery, Jinnah Postgraduate Medical Centre, Karachi from August 2018 to July 2019.

### *Sampling*

Sample Size was calculated using a sample size calculator for sensitivity and specificity. Taking sensitivity as 90.16%<sup>14</sup> with precision of 9.5% and specificity as 70%<sup>15</sup> with precision of 10%, at 95% confidence interval with a prevalence of 17%,<sup>15</sup> the sample size was calculated as 156 patients. Non-

probability consecutive sampling technique was used to collect data.

### *Inclusion Criteria*

Patients included of either gender, aged 18 to 50 years who consent to participate in the study with newly diagnosed Supratentorial Brain SOL appearing hypo or hyper-intense on MRI with post contrast enhancement.

### *Exclusion Criteria*

Pregnant females, patients with any previous intracranial surgery, multiple SOLs on initial MRI, diagnosed neoplasm of any other region of body and bleed within the SOL on initial MRI were excluded from the study.

### *Data Collection and Data Analysis*

Data was collected on a pre-designed questionnaire data statistical analysis was done using SPSS version - 23. MRS and histological findings were tabulated using 2x2 tables. Sensitivity, specificity, positive and negative predictive values were calculated.

## RESULTS

### *Age Range*

A total of 156 patients with were included in this study. The average age of the patients was  $32.41 \pm 10.02$  years (range 18 – 50 years).

### *Gender Distribution*

There were 84 (53.84%) male and 72 (46.15%) female.

### *Clinical Presentation*

The mean height of patients was  $1.51 \pm 0.21$  m, the mean weight was  $57.96 \pm 10.33$  kg and the mean BMI of patients was  $25.59 \pm 4.93$  kg/m<sup>2</sup>. The average duration of symptoms was  $8.41 \pm 3.79$  weeks. Altered level of consciousness was the most common symptom in our patients (81.4%) followed by fever (19.9%) and history of ENT infection (10.9%).

### *Sensitivity & Specificity*

The sensitivity of MRS was 90.69% with a specificity of 97.34%. The Positive predicted value of MRS

calculated as 92.85% and Negative predictive value as 96.49% (Table 1 – 3). The agreement between MR

**Table 1:** Accuracy of MR spectroscopy (n = 156).

MR Spectroscopy Report		Histopathology Diagnosis	
Inflammatory	42	39	3
Neoplastic	114	4	110
Total	156	43	113

spectroscopic and histological findings was measured as 0.887 with approximate significance of < 0.005. The diagnostic accuracy of MRS was calculated as 95.51% with 39 true positive and 110 true negative results.

**Table 2:** Calculation of Measures of Accuracy.

Sensitivity	= a/a + c	= 39/39 + 4	= 90.69%
Specificity	= d/d + b	= 110/110 + 3	= 97.34%
Positive predictive value (PPV)	= a/a + b	= 39/39 + 3	= 92.85%
Negative predictive values (NPV)	= d/d + c	= 110/110 + 4	= 96.49%

**Table 3:** Types of lesions on histopathology.

Inflammatory Lesions (n = 43)		Neoplastic Lesions (n = 113)	
Tuberculoma	14	Oligodendroglioma	32
Abscess	26	Astrocytoma	41
Fungal lesion	3	Glioblastoma	21
Total	43	Metastatic tumor	7
		Lymphoma	12
		Total	113

### Stratification Analysis

Stratification analysis was performed with respect to effect modifiers. This showed that the sensitivity of MRS in males (86.95%) was less than females (95.0%). It was also lower in patients aged between 31 – 40 years (87.50%) compared to age groups 18 – 30 (91.30%) and 41 – 50 (91.67%). The sensitivity was also halved if the duration of symptoms was more than 8 weeks. Low BMI (< 20.0 kg/m<sup>2</sup>) also reduced sensitivity to 66.67%.

### DISCUSSION

MR Spectroscopy provides chemical analysis of cerebral lesion that aids in establishing non-invasive diagnosis. It is being used for differentiating cerebral inflammatory lesions from neoplastic lesions. The diagnosis was based on amount of certain chemical marker on spectroscopy and their ratios.

Choline (Cho) levels of 2.15 mmol/l and Choline to NAA ratio above 1 is considered as diagnostic of neoplastic lesion.<sup>14,18</sup> However, these values are not absolute and vary a great deal in the literature. Moreover, different cut off values of these makers may affect the diagnostic accuracy of MRS.

Additionally, these values may also be used to differentiate low and high grade neoplasm with Mean Cho value of 1.65 ± 1.03 mmol/l in low-grade Gliomas and 2.36 ± 1.15 mmol/l in high-grade astrocytoma.<sup>14</sup> Similarly, Choline to Creatinine ratio in low-grade Gliomas was 2.98 ± 2.73 whereas in high-grade Gliomas it was 3.93 ± 3.33. It was reported in a study that the former was 1.26 ± 0.38 and the latter was 2.11 ± 0.93.<sup>19</sup> another study suggested the cut off value to differentiate between the two grades as 1.56.<sup>20</sup> On the other hand, a study concluded this value as 1.84 ± 1.22 for metastatic lesions against 3.92 ± 3.31 for high grade Gliomas.

Interpretation of the results is also be falsified by the contents. For instance, inflammatory metabolites can be accumulated in necrotic high-grade Gliomas resulting in reduced levels of choline in addition to NAA and creatine. It also resulted in tall lipid/lactate peak. On the contrary, invasive infections (e.g. fungus) can produce high level of choline and lower the levels of creatinine and NAA.<sup>21</sup>

The mean age of presentation in our study was similar to previously conducted local studies. Our patients were predominantly males; this was also similar to other studies.<sup>14-16</sup>

Our study showed sensitivity of 90.69% which is similar to previously conducted studies which ranged from 79% to 100%.<sup>14-16,22-26</sup> The specificity reported in the literature is 74% to 100%.<sup>14-16,22-26</sup> However, specificity calculated in our study (97.34%) was slightly higher than some studies including one conducted at our center in the past.<sup>16</sup> This may be attributed to the fact that our study only included patients with supra-tentorial lesions whereas, other studies have included both supra and infra-tentorial lesion. Since the compact bony anatomy in the posterior fossa hinders the spectroscopic signal

estimation, that may affect the specificity of the test. Another possible explanation is the difference of placement of voxels and interpretation of results which may have improved over time. Correct Voxel placement of utmost importance in accuracy of the diagnosis. The prospect of including viable proliferating tumor in the spectroscopic volume is improved by placing it on the leading edge of enhancing lesion thus minimizing the possibility of necrotic focus.<sup>15</sup>

Moreover, this study was conducted on adult patients between ages 18 and 50 years only however, previous studies included both adults and children. Nonetheless, the diagnostic accuracy of our study was similar to previously conducted local studies.<sup>14-16</sup>

### Limitations of the Study

This study was conducted on patients from a single institution. Although the sample size was adequate, but inflammatory lesions were considerably lesser than the neoplastic lesions. This may be attributed to the fact that many of the inflammatory lesions are treated medically.

The results were based on single voxel technique and may have significant inter-observer interpretation bias compared to multi-voxel technique. The diagnostic accuracy of MRS was based on the overall interpretation of the biochemical markers. However, individual biomarkers and their ratios may have different diagnostic accuracy.

### Implications for Future Research

Future studies may be conducted on the basis of individual biochemical analysis for the diagnosis of inflammatory vs. neoplastic lesions. Moreover, these values may also be investigated for differentiating different types of tumors and their grades. Differentiation between causes of inflammatory lesions such as tuberculomas or fungus may be useful fronts for future research. Different cut off absolute values of biochemical markers may be studied and their effect on overall diagnostic accuracy.

### CONCLUSION

This study concluded the high diagnostic accuracy of MRS for inflammatory and neoplastic lesions. MRS therefore may be used as non-invasive investigation for differentiating neoplastic from inflammatory lesions. However, in cases where differentiation is

difficult, the implication of MRS becomes more profound in establishing pre-operative diagnosis and early treatment.

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### Additional Information

**Disclosures:** Authors report no conflict of interest.

**Ethical Review Board Approval:** The study was conformed to the ethical review board requirements.

**Human Subjects:** Consent was obtained by all patients/participants in this study.

### Conflicts of Interest:

In compliance with the ICMJE uniform disclosure form, all authors declare the following:

**Financial Relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work.

**Other Relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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**AUTHORS CONTRIBUTIONS**

<b>Sr.#</b>	<b>Author's Full Name</b>	<b>Intellectual Contribution to Paper in Terms of:</b>
1.	Asad Abbas	Study design and methodology.
2.	Farrukh Javeed	Paper writing, referencing, data calculations and
3.	Lal Rehman	Data collection and calculations
4.	Ali Afzal	Analysis of data and interpretation of results etc.
5.	Raza Khairat Rizvi	Literature review and manuscript writing

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