International Journal Dental and Medical Sciences Research
Volume 6, Issue 4, July. – Aug. 2024 pp 254-262 www.ijdmsrjournal.com ISSN: 2582-6018

Role of Magnetic Resonance Spectroscopy (Mrs) In Various Intracranial Lesions

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Date of Submission: 25-07-2024 Date of Acceptance: 05-08-2024

ABSTRACT: Introduction: Intracranial lesions are most common findings seen while neuroimaging. While considering intracranial lesions, consideration of shape of the lesion, wall thickness and size along with surrounding perilesional edema as well as clinical history of the patient should be done. It will help in accurately diagnosing the conditions and initiation of treatment with better management. In routine, MRI brain is very sensitive in the identification of ring enhancing lesions. Proton Magnetic Resonance Spectroscopy (MRS) is quite advanced imaging technique. It is found to be very useful in the diagnosing these lesions. MR spectroscopy also has a prognostic implication.

Materials & Methods: This prospective observational study conducted at GCS Medical College & Hospital assessed MRS's role in various intracranial lesion evaluation over one year. It included patients of all ages with suspected/knownintracranial pathology, utilizing advanced MRI scanners for high-quality imaging. Data collection involved comprehensive analysis of MRI+MRS findings and associated clinical features, adhering to ethical guidelines and IRB approval.

Result: In the present study of 50 patients presented with suspected intracranial pathology or having intracranial lesion, an attempt was made to evaluate correlation between MRI + MRS in evaluation of various intracranial lesions that included tumors and non-neoplastic lesions. The maximum number of patients were between 31 to 50 years of age. The approximate ratio of male:female was 2.1:1. The lesions were divided into neoplastic and non-neoplastic lesions. The later included tuberculoma (37%), demyelination (15%), encephalitis(15%), abscess (11%) and others (22%) like post ictal edema, cavernous angioma, tuberous sclerosis. Increase in choline was seen in 90% cases of tumors, 60% cases of non neoplastic lesions. Decrease in NAA was seen in 90% cases of tumors, in 74% of non neoplastic lesions and increase in single case of Canavan's disease. Increase in lipid was seen in 100% cases of tuberculoma and 60% of tumors.

Conclusion: MRI + MRS is more accurate in diagnosis of intracranial pathologies with a higher sensitivity and specificity compared to MRI alone.

Key words: Choline, Intracranial, Lipid, MRI, MR spectroscopy, Metabolic activity, N-acetyl alanine, Pathology

I. INTRODUCTION

MRS (Magnetic Resonance Spectroscopy) is a relatively advanced imaging technique that studies the chemical activity in the brain and detects the presence of certain chemical substances in a non-invasive manner. [1, 2]

Around every chemical substance that exists in the brain, an electron cloud is produced.Since in many pathologic processes, metabolic changes appear before the anatomic changes are apparent during disease progression, MRS offers a method of early detection of new disease and can influence therapeutic success or failure. The nuclei with an odd number of protons and neutrons such as hydrogen-1, phosphorous-31, carbon-13, fluorine-19 have a magnetic moment and interact with the external magnetic field and are commonly observed in MR SPECTRSCOPIC studies. MRS is frequently utilized to study disorders affecting the brain, as other techniques such as biopsy and microscopic studies cannot be performed. [3, 4]

The spectroscopic sequence's TE will determine how many observable metabolites are selected; the longer the TE (135 or 270 ms), the

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Volume 6, Issue 4, July. – Aug. 2024 pp 254-262 www.ijdmsrjournal.com ISSN: 2582-6018

more longT2 metabolites are chosen. Because there are more overlaid peaks in the spectrum at short TE (15 to 20 ms), there will be additional challenges with quantification and interpretation.

Classification of various intracranial lesions is as follows [5, 6, 7]:

Table 1 :CLASSIFICATION OF INTRACRANIAL LESIONS

Brain tumors	**2. Vascular lesions:**	**3. Infections:**	**4. Metabolic, white matter and degenerative diseases:**
A) Primary brain tumors: **1) Glial tumors (glioma)** **•Astrocytoma** **•Oligodendroglioma** **•Ependymal tumors** **•Choroid plexus tumors** **2) Non-glial tumors** **•Neuronal and mixed neuronal-glial tumors** **•Meningeal and mesenchymal tumors** **•Pineal region tumors** **•Embryonal cell tumors** **•Cranial and spinal nerve tumors** **•Hemopoietic neoplasms** **•Pituitary tumors** **•Cysts and tumor like lesions** **B) Metastatic tumors**	A)Intracranial hemorrhage B) Intracranial aneurysms C) Vascular malformations D) Infarct	A) Congenital infections B) Bacterial infections C) Tuberculosis and fungal infections D) Parasitic infections E) Encephalitis	A) Inherited disorders: 1. Disorders that primarily affect white matter – leukodystrophies a) Metachromatic leukodystrophy b) Krabbe's disease c) Adrenoleukodystrophy d) Pelizaeus-Merzbacher disease e) Alexander disease f) Phenylketonuria and amino acid disorders 2. Disorders that primarily affect the grey matter a) Tay-Sach's disease and other lipidosis b) Hurler syndrome and other mucopolysaccharidosis c) Mucolipidosis and Fucosidosis d) Glycogen storage diseases 3. Disorders that affect both grey and white matter a) Leigh's disease and other mitochondrial encephalopathies b) Zellweger syndrome and other peroxisomal disorders 4. Basal ganglia disorders a) Huntington's disease b) Hallervorden-Spatz disease c) Fahr's disease d) Wilson's disease B) Acquired disorders: 1. White matter neurodegenerative disorders a) Multiple sclerosis b) Viral and post-viral disease c) Toxic demyelination d) Trauma e) Vascular disease 2. Grey matter neurodegenerative disorders a) Alzheimer disease and other cortical dementias b) Extrapyramidal disorders and other subcortical dementias c) Parkinson disease and other related striatonigral degenerations d) Miscellaneous cerebellar degenerations.

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AIMS AND OBJECTIVES

1. For diagnosis of intracranial pathologies.
2. To find out advantages of MR spectroscopy over routine MRI.
3. To differentiate neoplastic process from non-neoplastic process.
4. To assess the use of MR spectroscopy for characterization of intracranialmass lesions and to ascertain its reliability in grading of glioma and histopathology correlation.
5. To differentiate recurrent tumor from post-operative changes or radiation necrosis.

II. MATERIALS AND METHODS

During the period of May 2023 to May 2024, aprospective observational type of study of 50 patients was carried out at GCS Medical college, hospital and research centre, in Ahmedabad. All patients were analyzed by MRI brain and subsequent MR spectroscopy on 1.5 Tesla MR scanner (GE 1.5 T Signa MRI) of region of interest. Relevant present and past history was taken.

Inclusion criteria:

- All age and both sex
- Patients presented with suspected/ known intracranial pathology.
- Patients with positive/ indeterminate MR findings.
- Patients coming for follow up evaluation of intracranial pathology.

Exclusion criteria:

- Patient having claustrophobia.
- Patient with prior history of any metallic implant .
- Patient with history of contrast allergy and abnormal creatinine value.

MR spectroscopy was performed by using point resolved spectroscopy. After deciding the region of interest voxel was kept and 2D multivoxel proton spectroscopy (TR-1000 msec, TE- 144 msec, voxel size 20x20 mm) or single voxel proton spectroscopy (TR-1500 msec, TE-35 msec, voxel size 20x20 mm) was performed and spectra obtained.

On MR spectroscopy following metabolites were observed and spectrum was obtained:

N-acetyl-asparate (NAA) at 2.0 ppm
Creatine/phosphocreatine (Cr) at 3.0 ppm
Choline compounds (Cho) at 3.2 ppm
Myo-inositol (mI) at 3.56 ppm
Lactate (Lac) doublet at 1.35 and 4.1 ppm
Free lipids (Lip) wide resonance, doublet at 1.3 and 0.9 ppm

The metabolites were observed in the spectrum and any alteration in form of increase or decrease in above mentioned metabolites was noted.

In case of tumors final diagnosis was obtained by histopathology where possible while in case of non neoplastic lesions final diagnosis was obtained by clinical course and follow up.

III. OBSERVATIONS

In our study, maximum number of patients were in the age group of 31-50 years (27 %) and there was a male predilection (M:F – 2.15).

The lesions were divided into neoplastic and non-neoplastic lesions. The later included tuberculoma (37%), demyelination (15%), encephalitis(15%), abscess (11%) and others (22%) like post ictal edema, cavernous angioma, tuberous sclerosis.

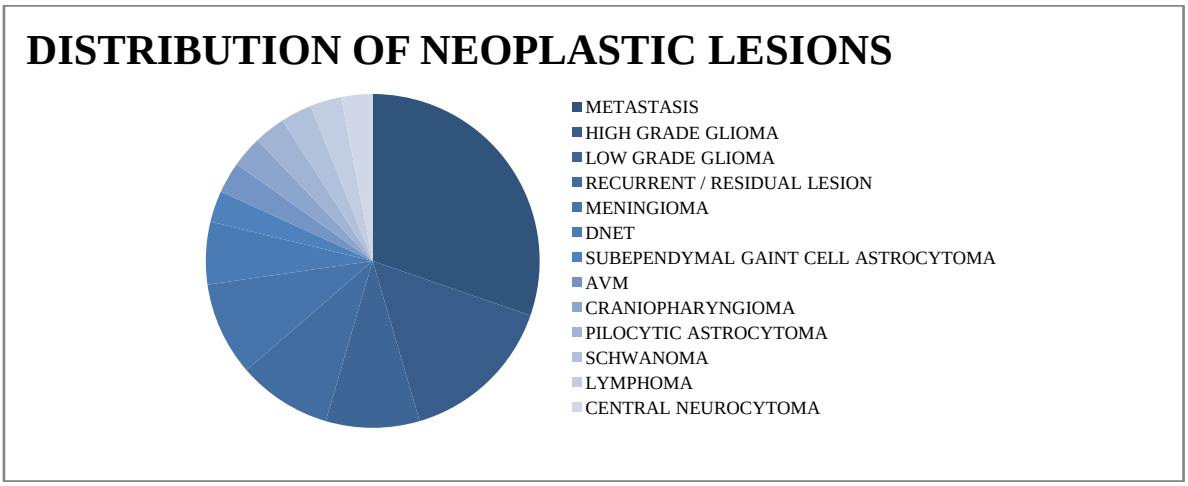

Fig-1: Distribution of Neoplastic Lesions

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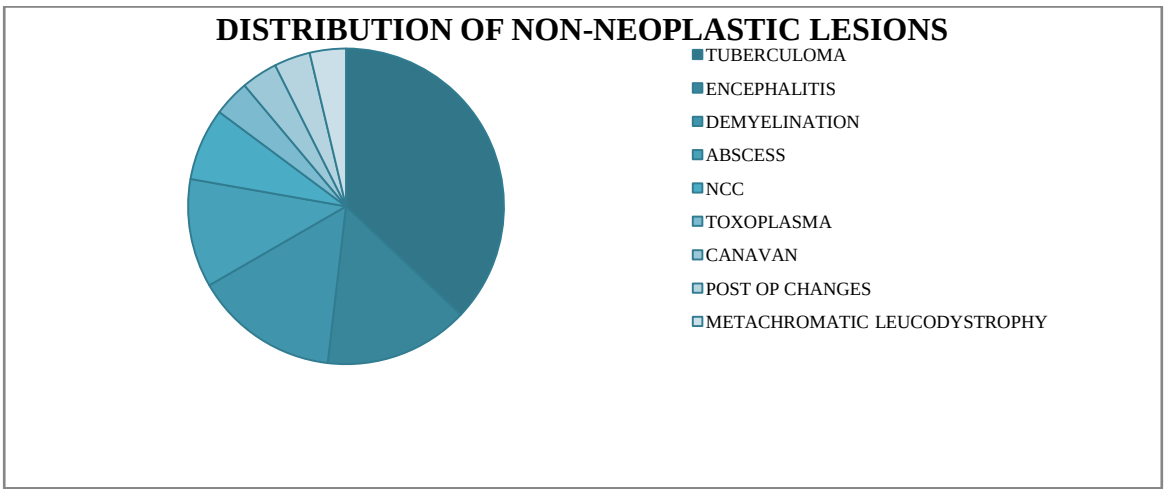

Fig. 2 - Distribution of Non-Neoplastic Lesions

85% of total tumors showed contrast enhancement while 70% of non-neoplastic lesions showed contrast enhancement. Increase in choline was seen in 90% cases of tumors, 60% cases of non neoplastic lesions. Decrease in NAA was seen in 90% cases of tumors, in 74% of non neoplastic lesions and increase in single case of Canavan's disease. Increase in lipid was seen in 100% cases of tuberculoma and 60% of tumors.

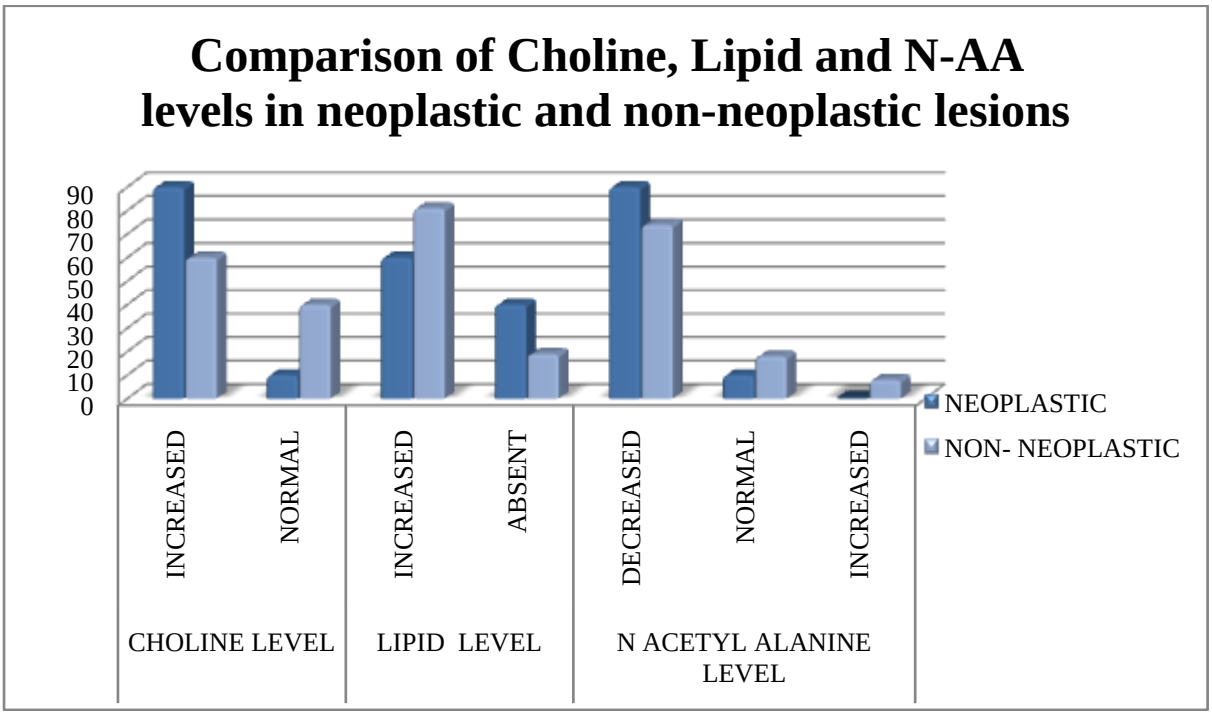

Fig. 3- Comparison of Choline, Lipid and N-AA levels in neoplastic and non-neoplastic lesions

Table 1 shows comparison between MRI and MRI + MRS; MRI + MRS is more sensitive and specific than MRI for diagnosis of tumors. MRI + MRS is more sensitive but equally specific as compared to MRI for diagnosis of demyelination, abscess, low grade glioma , high grade glioma, demyelination and tuberculosis.

International Journal Dental and Medical Sciences Research
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Table 1- Comparison of Sensitivity, Specificity, PPV and NPV between MRI and MRI+MRS in diagnosis of various pathologies

PATHOLOGIES	SENSITIVITY		SPECIFICITY		PPV		NPV	
	MRI	MRI + MRS	MRI	MRI + MRS	MRI	MRI + MRS	MRI	MRI + MRS
LOW GRADE GLIOMA	66	100	100	100	100	100	98	100
HIGH GRADE GLIOMA	80	100	100	100	100	100	98	100
TUBERCULOSIS	80	90	100	100	100	100	96	98
ENCEPHALITIS	100	100	100	100	100	100	100	100
DEMYELINATION	75	100	100	100	100	100	98	100
ABSCESS	66	100	100	100	100	100	98	100
METASTASIS	70	80	100	100	100	100	94	96
MENINGIOMA	100	100	100	100	100	100	100	100

In our study, we also observed that MRI alone is useful in detection of intracranial pathologies, however, when used along with MR Spectroscopy, it becomes more sensitive in giving the correct diagnosis in terms of histopathological correlation.

GRADING OF GLIOMA USING CHO/Cr AND CHO/NAA RATIO

Table 2- Grading of gliomas using Cho/Cr and Cho/NAA ratios

	CHOLINE/CREATININE RATIO		CHOLINE/NAA RATIO	
	<2.2	>2.2	<2.2	>2.2
LOW GRADE GLIOMA	3	0	2	1
HIGH GRADE GLIOMA	0	5	1	4

Table 2 shows that the sensitivity and specificity of choline / creatinine ratios on MRS in grading of low and high grade gliomas are 100 % and 100 % respectively. The positive predictive value and negative predictive value are 100 % and 100 % respectively if a cut off value of >2.2 is used.

Also, it shows that the sensitivity and specificity of choline / NAA ratios on MRS in grading of low and high grade gliomas are 67 % and 80 % respectively. The positive predictive value and negative predictive value are 67 % and 80 % respectively if a cut off value of >2.2 is used. Thus, it can be concluded that if the Cho/Cr and Cho/NAA ratio is <2.2, possibility is low grade glioma is more likely in contrast to the ratios being >2.2, which would suggest the possibility of high grade glioma.

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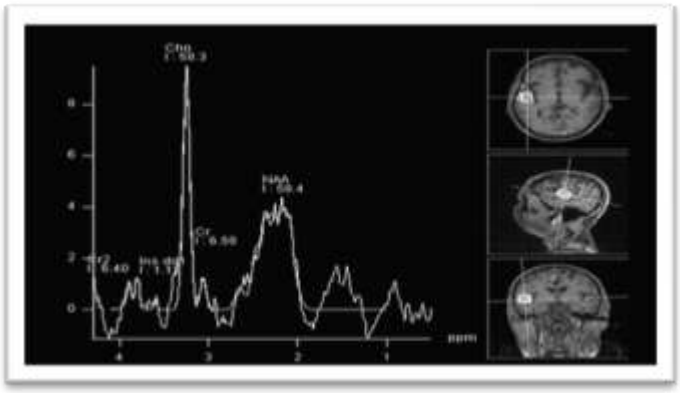

Figure showing increased NAA and Choline peak on spectroscopic study in case of meningioma

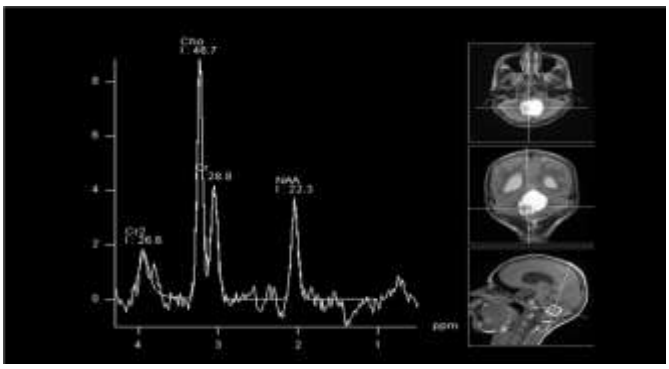

Figure showing increased Choline, Creatine and NAA peak on spectroscopic study in case of Pilocytic astrocytoma

IV. DISCUSSION

The results of the present study are discussed as follows:

1. AGE DISTRIBUTION:

In our study the age distribution in intracranial lesions is from 1 to 80 years. It is observed that the intracranial tumors and other intracranial lesions are more prevalent in 31-50 year age group (44%) which is in accordance with a study by Zeng Q et. Al (8). In our study, the mean age for intracranial lesions is 36 years. The mean age for tumors is 43.5 years while the same for non-neoplastic lesions is 31.1 years.

2. SEX DISTRIBUTION:

The observation in our study regarding sex distribution in intracranial lesions is 68% males and 32% females with the ratio of M:F being 2.1:1. In intracranial tumors, the ratio of M:F is 3:1 and in case of non-neoplastic lesions, the ratio is 1.5:1.

3. CONTRAST ENHANCEMENT:

In our study contrast enhancement was seen in 85% of the tumours. According to Zohu ZR et al [(9)]94% of the cases showed contrast enhancement. This may be secondary to significant difference in the size of sample in both studies.

4. INCREASES IN CHOLINE:

In our study, 90% of tumors show an increase in choline levels. In the study by Poptani H et al [(10)], the choline is increased in all 100% of tumors. This difference may be due to reduced choline in high grade gliomas (glioblastoma multiform) secondary to necrosis [(11)]. Increase in choline is also not seen in pineal germinoma in our study which is consistent with the findings of Panigraphy et al [(12)]. In our study, the choline is increased in 60% of non neoplastic lesions.

5. DECREASE IN N-ACETYL ALANINE:

According to our findings, 90% of neoplastic diseases had reduced NAA levels. Except for DNET, all neoplastic diseases exhibit decreased NAA. Reduction in NAA is commonly seen in tumors, indicating a decrease in the number and viability of neurons, according to Brandao LA (11). NAA levels are reportedly lower in cases of meningioma, glioma, and metastases (Otto D. et al., 2013). Saindane AM et al. (14) state that NAA is reduced in all neoplasms that result in the

displacement of neurons or their replacement by malignant cells. A reduction in or lack of NAA was observed in all instances (100%) of glioma, lymphoma, and metastases in the study conducted by Poptani H et al. (10). According to their statement, NAA is a neuronal marker that declines in all malignancies due to the tumor cells' invasiveness into the normal tissue.
In our study, NAA is elevated in one case of Canavan's disease and decreased in 74% of non-neoplastic lesion cases.

6. INCREASE IN LIPID:

In our study, 60% of tumor cases had higher lipid levels. In 83% of the cases in the research by Krouwer HG et al. (15), the lipid peak was increased. According to Poptani H et al.'s study (10), there is an increase in lipid in all cases of high-grade glioma and most cases of metastasis, while it is absent in all cases of low-grade glioma. The discrepancy between the results of our investigation and the previously stated research may be caused by differences in the percentage of high- and low-grade glioma cases that were included in the analysis. In our research, lipid levels are elevated in all (100%) cases of tuberculoma. According to Poptani H et al.'s study (10), lipid levels are elevated in 100% of tuberculoma patients. This is consistent with what we found.

7. GRADING OF GLIOMA:

In our research, we utilized a choline/creatinine ratio of 2.2 to classify gliomas as either low or high grade, achieving 100% sensitivity and specificity. Similarly, a choline/NAA ratio of 2.2 had a sensitivity of 67% and specificity of 80%. A study conducted by Zeng Q(8) on 39 patients who were suspected of having gliomas found that the Cho/Cr and Cho/NAA ratios were notably higher in high-grade gliomas compared to low-grade gliomas (P<.001). Conversely, the NAA/Cr ratios were significantly lower in high-grade gliomas than in low-grade gliomas (P<.001). A Cho/Cr ratio of 2.04 has been determined as the threshold value, achieving sensitivity, specificity, PPV, and NPV rates of 84.00%, 83.33%, 91.30%, and 71.43%, respectively. A threshold value of 2.20 for the Cho/NAA ratio yielded sensitivity, specificity, PPV, and NPV of 88.00%, 66.67%, 84.62%, and 72.73%, respectively.

8. **INTRACRANIAL TUMORS: MRI AND HISTOPATHOLOGY/FOLLOW-UP CORRELATION**

In our study, in detection of intracranial tumors with the help of MRI, the true positive results were obtained in 81% and false positive results were obtained in 9% cases. In our study, the sensitivity & specificity of MRI in tumor are 81% and 88% respectively. The positive predictive value &negative predictive value are 90% and 80% respectively. The comparison of our study data with other similar study is tabulated in Table 3. The results are almost similar except NPV which is higher in our study.

Table-3: Intracranial Tumors: MriAnd Histopathology/Follow-Up Correlation

MRI in diagnosis of tumors	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
Our study	81	88	90	80
Meng Law[16]	72	65	82	41

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8. INTRACRANIAL TUMORS: MRI +MRS AND HISTOPATHOLOGY/FOLLOW-UP CORRELATION:

In our study, in detection of intracranial tumors with the help of MRI and MRS, the true positive results were obtained in 31 (93%) and false positive results in 1(4%)of cases.False negative cases were 2 suggesting that MRI with MRS can be used to exclude the possibility of a tumor in all doubtful cases with very high confidence.

In our study the sensitivity & specificity or MRI + MRS in tumor are 94% and 96 % respectively. The positive predictive value &negative predictive value are 97 % and 93 % respectively.

MRI+MRS in diagnosis of tumors	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
Our study	94	96	97	93
Rand SD et al [17]	85	74	92	61

The above table shows comparison of our study data with others. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy are more in our study as compared to others. This could be due to use of multivoxel spectroscopy technique. This can also be due to small sample size in our study. In addition, we have taken both MRI and MRS for the diagnostic consideration that enhances the accuracy of diagnosis as compared to MRS alone.

V. CONCLUSIONS

Thus, after careful evaluation of a variety of intracranial lesions, we conclude that MRI + MRS is more accurate in diagnosis of intracranial pathologies with a higher sensitivity and specificity compared to MRI alone.

It is also possible to give a better pathological basis as well as classification of the lesions based on MR spectroscopy findings, thus serving the purpose of guiding the further course of action in lesions that are not approachable for biopsy or resection.

Acknowledgement: We are sincerely thankful to all the participants who took part in our study
Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Review Board

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