Original Article

Evaluation Of Imaging Aspects Of Brain Lesions By Proton MR-Spectroscopy

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Abstracts: **Introduction**: Magnetic resonance spectroscopy (MRS) is a means of non- invasive physiological imaging of the brain that measures absolute and relative levels of various brain tissue metabolites. Conventional MR imaging provides highly detailed information for the diagnosis of suspected brain lesions. Despite this, MRI alone at times cannot answer few diagnostic questions in some patients. Proton MRS provides some extra information on the metabolic composition of the lesion under investigation. It provides biochemical picture of the underlying pathology and thus aids in the diagnosis. **Methods:** Retrospective study was done on 50 patients with brain lesions diagnosed on MRI in our radiology department of the Sardar Vallabhbhai Patel Institute Of Medical Science And Research(SVPIMSR) from March 2022 to Feb 2023. INCLUSION CRITERIA: Patients diagnosed with focal intracranial brain lesions and in whom MR spectroscopy was done. Cases of all age groups with no gender bias are included. EXCLUSION CRITERIA: Clinically unstable patients in whom the conventional MRI was done, However, MR spectroscopy could not be done. **Result:** Analysis of spectra of 50 patients with brain lesions was done; Out of 50 cases , 12 cases were of tuberculoma, 8 cases of meningioma , 5 cases of high grade glioma, 3 cases of low grade glioma , 4 cases of neurocysticercosis, 3 cases of lymphoma, 2 cases each of pilocytic astrocytoma, schwannoma, metastasis, oligodendroglioma, tumefective demyelination and brain abscess and 1 case each of ependymoma, medulloblastoma and choroid plexus papilloma noted. All the lesions had increased choline levels and decreased NAA and Cr levels with increased Cho/NAA and Cho/Cr ratio. MRS of gliomas shows high Cho content, decreased contents of NAA with a decreased level of Cr. High Lac-Lip concentration helps to distinguish high and low grade gliomas. mI is a useful metabolite and can be used for grading of gliomas. The MRS spectrum of oligodendrogliomas is very similar to that found in astrocytomas: high Cho signal, decreased NAA and Cr with present Lac-Lip and decreased mI. MR spectroscopy can be used to differentiate between ring enhancing granulomatous lesions like tuberculoma and neurocysticercosis. Tuberculomas on MR spectroscopy show lipid lactate peak and neurocysticercosis shows alanine peak. Lipid lactate was increased in high grade gliomas, metastasis and brain abscesses. **Conclusion:** MR Spectroscopy is complimentary to routine MR sequences. It helps in differentiating various neoplastic lesions from infective lesions of the brain. Granulomatous lesions like tuberculomas and Neurocysticercosis can be differentiated by MR Spectroscopy. MR spectroscopy can help in grading the gliomas. MR spectroscopy can help in differentiating high grade gliomas vs metastasis. [Rayani J Natl J Integr Res Med, 2023; 14(6):16-23, Published on Dated: 28/12/2023]

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Introduction: Magnetic resonance spectroscopy (MRS) is a means of non-invasive physiological imaging of the brain that measures absolute and relative levels of various brain tissue metabolites. Conventional MR imaging provides detailed information for the diagnosis of suspected brain lesions. Despite this, MRI alone at times cannot answer few diagnostic questions in some patients. Proton MRS provides some extra information on the metabolic composition of the lesion under investigation and thus aids in the diagnosis. Early in the development of human brain proton MRS, it was realized that brain lesions exhibited markedly different spectra from normal brain tissue. [1,2,3] Theoretically MRS can be performed with 1H, 13C, 19F, 23NA and 31P. However only 1H MRS is commonly used in clinical practice. Hydrogen 1 (1H) MR spectroscopy is complementary to MR imaging and adds clinically relevant information about metabolites in brain abnormalities.[1]

MR spectroscopy is clinic-ready for diagnostic, prognostic, and treatment assessment of brain lesions; it is expected to contribute to patient management in neurodegenerative disorders, epilepsy and stroke. Clinical MR spectroscopy can be performed successfully at either 1.5 or 3.0 T.

Magnetic resonance spectroscopy receives a sum

of individual metabolite signal amplitudes versus time in response to radiofrequency (RF) excitation similar to MR imaging. MRS presents the individual information as metabolite peak amplitude versus frequency. There are two classes of spatial localization techniques for MRS; single voxel techniques (commonly uses STEAM, ISIS & PRESS) and multi-voxel techniques (MRSI or CSI). The phenomenon of chemical shift forms the basis of the MR spectroscopy.

Aims And Objectives : Main aim is to compliment routine MR sequences on differentiating various brain lesions into neoplastic vs non neoplastic lesions. It further aims to: To differentiate between high grade vs low grade gliomas. To differentiate between high grade glioma vs metastasis. To differentiate between ring enhancing lesions such as tuberculoma and neurocysticercosis.
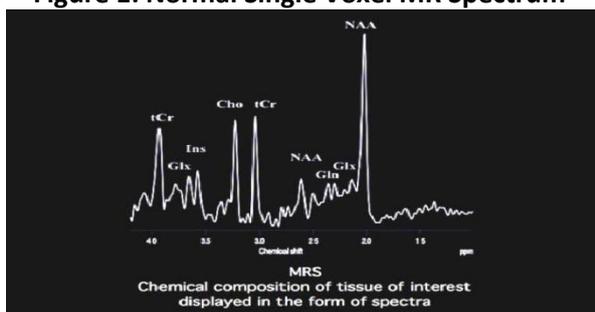
Table 1: Normal Brain Metabolites

CHEMICAL COMPOUND	CHEMICAL SHIFT	COMMENTS
N-Acetylaspartate (NAA)	2.0	Neuronal marker.
Creatine /phosphocreatine	3.0, 3.9	Energy metabolism.
Choline (Cho)	3.2	Cell membrane integrity marker.
Myo–inositol (ml)	3.6	Glial cell marker.
Lipid (lip)	0.9-1.4	Cell breakdown / brain destruction indicator.
Lactate (Lac)	1.3	An end product of anaerobic glycolysis

A normal MR spectrum is evaluated from right to left with metabolite peaks at various locations on x axis, starting from lipids at 0.9 and 1.4 ppm, lactate at 1.3 ppm (As a doublet), N-acetylaspartate (NAA) at 2.0 ppm, creatine (Cr) at 3.0 ppm and choline (Cho) at 3.2 ppm and Myo-inositol (mI) at 3.6 ppm. (Figure 1) A line joining mI, Cr, Cho and NAA forms 45° angle to x axis when they are present in normal proportions, which is called as Hunters angle. Hunters angle changes with short to long echo time (TE) changing repetition time (TR) and change in location of voxel from cortex to midbrain.[1]

Figure 1: Normal Single Voxel MR Spectrum

MRS
Chemical composition of tissue of interest displayed in the form of spectra

Brain Tumors: CNS neoplasms are a histologically diverse group that occur at many sites in the brain or its linings. World Health Organization (WHO) divides CNS neoplasms (fifth edition) into primary (9 basic groups) and secondary tumors (metastases).

Tuberculoma: Central nervous system involvement is the most devastating form of the tuberculosis. Parenchymal tuberculomas are the most common form of intracranial tuberculosis.

They occur due to conglomeration and coalescence of tubercular microgranulomas, which tend to occur at the grey-white matter junction. They can, however, occur in almost any possible location in the brain, including the sulcal spaces, brainstem, cerebellar hemispheres, basal cisterns, and the ventricular system. They also show a tendency to conglomerate and occur in clusters or coalesce into larger tuberculomas. It shows ring enhancement on post contrast T1WI. MR spectroscopy (MRS) at the site of lesions showed increased lipid peak, decreased N-acetylaspartate peak with increased Ch/Cr ratio.[5]

Neurocysticercosis: Neurocysticercosis is a neurologic parasitic disease caused by the encysted larva of the tapeworm Taenia solium. Each stage (vesicular, colloid vesicular, granular nodular & nodular calcified) has fairly distinctive imaging features although there is no sharp demarcation between later stages. A combination of elevated lactate, alanine, succinate, and choline levels and reduced levels of N-acetylaspartate and creatine are seen on MR Spectroscopy.[2-6]

Meningioma: Meningiomas are the most common non-glial tumours of the central nervous system (CNS), accounting for between 16 and 20 % of all intracranial tumours. Magnetic resonance imaging (MRI) is the modality of choice for the investigation of meningiomas, providing superior contrast differentiation and usually the ability to differentiate between intra and extra-axial lesions. After contrast administration, meningiomas typically

demonstrate avid, homogeneous enhancement. Meningiomas show an increase in alanine (Ala), choline (Cho) and decreased N-acetylaspartate (NAA) and creatine (Cr).[7]

Tumefactive Demyelination: Demyelinating diseases of the central nervous system are frequently encountered pathologic entities; multiple sclerosis is the most common. The typical appearance of these lesions on MRI is involvement of the major white tracts in a periventricular distribution. When the disease manifests as a single large or tumefactive demyelinating lesion within a cerebral hemisphere, the correct diagnosis is often not made until after surgical biopsy or resection. Diffusion imaging reveals mildly increased apparent diffusion coefficients within tumefactive demyelinating lesions. Proton MR spectroscopy provides insight into the chemical composition of lesions. Several non neoplastic brain lesions (including tumefactive demyelinating lesions) may produce a MR spectrum identical to glial tumors, mimicking a neoplastic process.[8]

Brain Abscess: A brain abscess is a focal area of necrosis starting in an area of cerebritis surrounded by a membrane. It is a potentially life-threatening condition requiring prompt radiological identification and rapid treatment. Fortunately, MRI is usually able to convincingly make the diagnosis, distinguishing abscesses from other ring enhancing lesions. The lesion shows diffusion restriction and peripheral ring enhancement. MR Spectroscopy shows elevation of the lipid/lactate peak and alanine peak; predominantly within the central necrotic portion of the lesion with marked depression and almost total nullification of the neural markers: N-acetyl aspartate (NAA) and creatine (Cr).[9]

Material and Methods: Source Of Data: Retrospective study was done on 50 patients with brain lesions diagnosed on MRI in radiology department of the Sardar Vallabhbhai Patel Institute Of Medical Science And Research (SVPIMSR) from March 2022 to Feb 2023.

Inclusion Criteria: Patients diagnosed with focal intracranial brain lesions and in whom MR spectroscopy was done. Cases of all age groups with no gender bias.

Exclusion Criteria: Clinically unstable patients in whom the conventional MRI was done, However, MR spectroscopy could not be done.
Sample Size: Sample size of 50 cases.

Equipment And Technique Used: Written consent for examination was taken in all cases. All the patients were explained the procedure. History of any allergy to contrast was obtained. Renal function tests were evaluated before giving contrast. All pre-procedure precautions for undergoing MRI were followed. The MRI scan was performed on MR SIEMENS MAGNETOM SKYRA 3T.

Sequences: Turbo spin echo sequences, axial T1 TSE, T2 TSE, CORONAL FLAIR, Sagittal T2 TSE; Post contrast T1 TSE axial and coronal; DWI; T2 SWI. Multi voxel csi slaser spectroscopy, multi voxel spectroscopy was performed. Spectroscopy was avoided in small lesions close to the bone and sinuses. Gadopentate Dimeglumine contrast was used with dosage being 0.1 mmol/kg bodyweight. Study voxel was chosen at the site of enhancement or at the region of solid lesion excluding cystic or necrotic areas.

Study Definition: MR spectroscopy is used as diagnostic test for diagnosing brain lesions. An increase choline peak at 3.2ppm, myoinositol peak at 3.6ppm, lipid peak at 0.9- 1.4 ppm, lactate peak at 1.3 ppm and reduced NAA peak at 2.0 ppm, creatinine peak at 3.0,3.9 ppm was considered significant for diagnosing brain lesions.

Result: Result are displayed in following tables and images

Table 2: No Of Cases According To Mri Diagnosis

Mri Diagnosis	No Of Cases	Percentage
Tuberculoma	12	24 %
Meningioma	8	16 %
Glioma(High Grade)	5	10 %
Ncc	4	8 %
Glioma(Low Grade)	3	6 %

Lymphoma	3	6 %
Pilocytic Astrocytoma	2	4 %
Metastasis	2	4 %
Schwannoma	2	4 %
Oligodendroglioma	2	4 %
Brain Abscess	2	4 %
Tumefactive Demyelination	2	4 %
Ependymoma	1	2 %
Medulloblastoma	1	2 %
Choroid Plexus Papilloma	1	2 %

Table 3: Levels Of Metabolites In Mr Spectroscpy According To Brain Lesions

| BRAIN LESION	NO OF CASES	CHOLINE		NAA & CREAT		LIPID & LACTATE		CHO/ CR		CHO/ NAA		NAA/ CR		MI		ALANINE	
		I	D	I	D	I	D	I	D	I	D	I	D	I	D	I	D
Tuberculoma	12	12	0	0	12	11	0	12	0	12	0	0	12	0	0	1	11
Meningioma	8	8	0	0	8	0	0	8	0	8	0	0	8	0	0	8	0
Glioma (High Grade)	5	5	0	0	5	4	1	5	0	5	0	0	5	1	4	0	0
Ncc	4	4	0	0	4	0	0	4	0	4	0	0	4	0	0	4	0
Glioma(Low Grade)	3	3	0	0	3	0	3	3	0	3	0	0	3	3	0	0	0
Lymphoma	3	3	0	0	3	0	0	3	0	3	0	0	3	0	0	0	0
Pilocytic Astrocytoma	2	2	0	0	2	0	0	2	0	2	0	0	2	2	0	0	0
Metastasis	2	2	0	0	2	2	0	2	0	2	0	0	2	0	0	0	0
Schwannoma	2	2	0	0	2	0	0	2	0	2	0	0	2	0	0	0	0
Oligodendroglioma	2	2	0	0	2	2	0	2	0	2	0	0	2	0	2	0	0
Tumefactive Demyelination	2	2	0	0	2	2	0	2	0	2	0	0	2	0	0	0	0
Brain Abscess	2	2	0	0	2	2	0	2	0	2	0	0	2	0	0	0	0
Ependymoma	1	1	0	0	1	0	0	1	0	1	0	0	1	0	0	0	0
Medulloblastoma	1	1	0	0	1	0	0	1	0	1	0	0	1	0	0	0	0
Choroid Plexus Papilloma	1	1	0	0	1	1	0	1	0	1	0	0	1	0	0	0	0

Fig. 2 :Low Grade Glioma
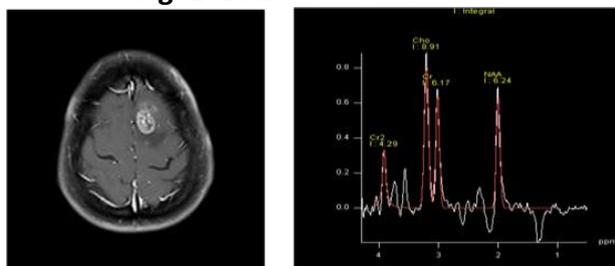
Fig. 3 : GBM
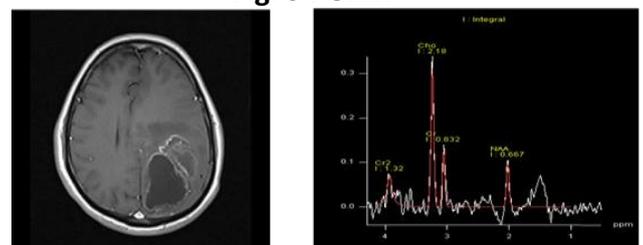
Fig. 2 shows raised choline, reduced NAA peaks, increased choline/NAA and choline/creat ratios (Figure 2) and choline/creat ratios suggestive of Low grade Glioma , while in Fig 3 we can see raised choline, reduced NAA peaks, increased choline/NAA and choline/creat ratios (Figure 3) and choline/creat ratios suggestive of GBM
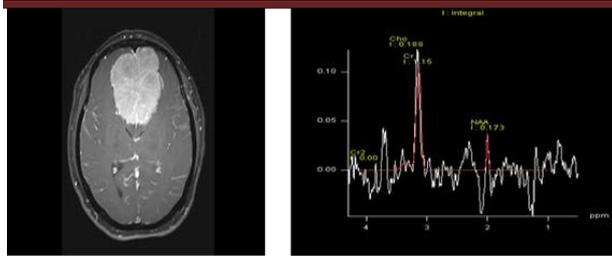
Fig 4: Meningioma

Fig 4 shows raised choline, reduced NAA peaks, increased choline/NAA and choline/creat ratios suggestive of Meningioma, while Fig 5 shows raised choline, reduced NAA peaks, increased choline/NAA and choline/creat ratios & lipid lactate levels and choline/ creat ratios suggestive of Tuberculoma.
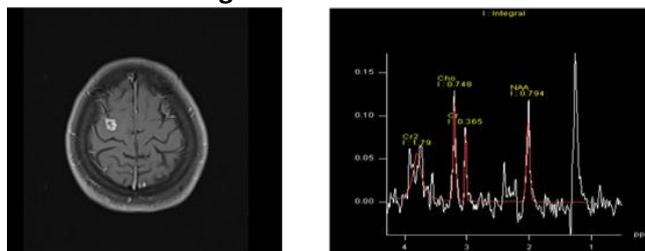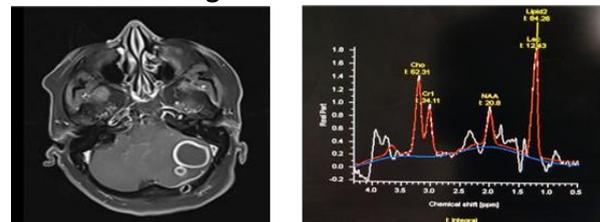
Fig 5.Tuberculoma

Fig 6 shows raised choline, reduced NAA level with characteristic lipid lactate peak and choline/creat ratios Suggestive of Brain Abscess

Fig 6: Brain Abscess

Discussion: Study of 50 patients of all age groups was carried out at our institute from March 2022 to Feb 2023 with no gender bias.

In this study, out of 50 cases , 12 cases were of tuberculoma, 8 cases of meningioma , 5 cases of high grade glioma, 3 cases of low grade glioma , 4 cases of neurocysticercosis, 3 cases of lymphoma, 2 cases each of pilocytic astrocytoma, schwannoma, metastasis, oligodendroglioma, tumefective demyelination and brain abscess and 1 case each of ependymoma, medulloblastoma and choroid plexus papilloma noted.

Patients from all age groups were included in this study. Brain lesions were most commonly found in 31-40 (n=11) years age group. The second most common age group was 41-50 (n=10) and 21-30 (n=10) years of age. The youngest patient

was 2 years old and the oldest patient was 72 years old. P A McKinney studied the incidence of brain neoplasms in all age groups and found that primary brain neoplasms occur most commonly in 7th decade.[10] In this study, the incidence of brain lesions was found to be more in males, 56% (n=28).

In this study of 50 cases, 74% (n=37) lesions were supratentorial, 20%(n=10) were infratentorial and 6%(n=3) were both supra and infratentorial in location

While MRI is the most sensitive modality available for the detection of brain lesions, its specificity is low and several different lesions may share a similar MRI appearance. Two particularly important imaging diagnoses are the differentiation between high- grade and low-grade tumors or between neoplastic and non-neoplastic lesions respectively.

The occurrence of a brain mass represents a change in the cell population at that location and the MR spectrum of a voxel containing a brain tumor may reflect this new cell type that is partially or completely displacing the normal cells of the brain. The biochemical information provided by MRS is always to be interpreted within the context of the other available imaging information, including structural (T1, T2, post contrast imaging, etc.) and functional (diffusion, perfusion) data when available. The typical H1 MR spectrum of a neoplasm depicts a substantial elevation of Cho, a reduction of NAA and little or minor changes in Cr.[1]

In astrocytomas, several studies, but not all, have suggested an association between tumor grade and Cho levels, with the higher grade tumors having greater Cho concentrations.[11,12,13] However, some studies have found high-grade tumors (e.g. grade IV glioblastoma multiforme (GBM)) to have lower levels of Cho than grade II or grade III astrocytoma.[14] This may be due to the presence of necrosis in high grade tumors.[15] Hence, the region of interest chosen for analysis will have a large influence on the results and as stated above, MRSI is generally considered preferable since it allows metabolic heterogeneity to be evaluated and the voxel with the maximum Cho signal to be chosen for analysis.[10-16]

In this study, we had 3 patients with lymphoma

which on MR Spectroscopy showed raised choline levels along with increased Cho/NAA and Cho/Cr ratios. Sanjeev Chawla et al. demonstrated that elevated Cho/Cr levels were noted in PCLs compared with those in metastases. In addition, PCLs also demonstrated significantly higher lipids + lactate/Cr levels.[17]

If a lesion can be confidently diagnosed as non-neoplastic, an invasive brain biopsy procedure may be avoided and a different treatment course may be considered. Differentiation between few of the non-neoplastic and neoplastic lesions using conventional MRI may be challenging. While MRI is a sensitive technique for detection of brain lesions, the specificity and capability of conventional MRI for distinguishing between benign and malignant lesions is limited. The use of a contrast agent may also not increase diagnostic specificity since various non-neoplastic processes are often associated with disruption of the blood-brain barrier and not all tumors enhance. Since tumors typically exhibit elevated Cho and decreased NAA, the greatest benefit of adding MRS to a clinical examination may be in including (or excluding) diagnoses with markedly different spectroscopic patterns. Conversely, differentiation between tumors and acute demyelinating lesions based on MRS alone may be difficult as both entities typically present with elevated Cho and decreased NAA as well as often increased lactate.[8]

All the brain lesions in this study showed increased choline levels and decreased NAA & Creat levels, increased Cho/NAA, Cho/Cr ratio and decreased NAA/Cr ratio.

K H Chang Et Al showed that in most gliomas and metastases, only a lactate resonance was observed. There was a trend toward a higher lactate peak in high-grade gliomas. A few tumors, including malignant gliomas and metastases showed lipid signal combined with lactate signal. If the lesion does not exhibit mobile lipid signals, anaplastic glioma is more likely. In this study, all the oligodendroglioma, choroid plexus papilloma , metastasis and 4 of the high grade gliomas showed increased lipid lactate levels.[18]

For discriminating solitary metastasis from primary brain tumors, it has been suggested that investigation of perienhancing tumor regions may be useful; whereas gliomas are often invasive lesions which show elevated Cho in surrounding tissue, metastatic lesions tend to be more encapsulated and do not typically show high Cho signal or other abnormalities outside the region of enhancement. [19,20] In this study, 2 lesions were metastatic lesions and did not show choline peak in perilesional edema outside the tumor margin.

In this study, tumors were reported as low grade or high grade astrocytoma , pilocytic astrocytoma, oligodendroglioma, ependymoma , choroid plexus papilloma , medulloblastoma, schwannoma and meningioma according to the MR characterization of tumors. Both conventional sequences and different parameters of MR spectroscopy were used to optimize the results.

M Castillo Et Al showed a trend toward lower mI levels in the presence of anaplastic astrocytomas and GBMs compared with those of low-grade astrocytomas. mI levels may have implications in the grading of cerebral astrocytomas.[21] All the 3 low grade gliomas and 2 pilocytic astrocytomas in this study showed increased mI levels whereas all the oligodendroglioma and 4 of the high grade gliomas showed decreased mI levels.

MR Spectroscopy helps in differentiating 2 most common granulomatous lesions of brain like tuberculoma and neurocysticercosis. Sameer Pandit showed that a combination of elevated lactate, alanine, succinate and choline levels and reduced levels of N - acetylaspartate and creatine in a cystic brain lesion helped in characterizing the neurocysticercosis.[6] In this study, out of 16 patients of ring enhancing granulomatous lesions (12 tuberculomas and 4 neurocysticercosis) , 11 of the tuberculomas showed increased lipid lactate levels and all the neurocysticercosis showed increased alanine levels. 2 patients of brain abscess were noted and both of them showed lipid lactate peak.

Most of the brain abscesses need to be differentiated from metastasis. Brain abscess typically shows increased lipid lactate, choline levels and Cho/NAA and Cho/Cr ratio. K H Chang et al. showed that both gliomas and metastasis can show lactate peak However, in abscesses, there were various combinations of lactate, acetate, succinate, amino acids (including valine, alanine, and/or leucine) and/or unassigned resonances.[9]

All the 8 meningiomas showed increased alanine peaks on MR Spectroscopy. H Poptani et al. also showed in their study that meningiomas could be differentiated from schwannomas by the presence of alanine in the meningiomas. [17-22]

Proton MRSI and other physiological imaging techniques may assist the surgeon in obtaining representative samples of the tumour tissue for histology and surgical resection by identifying regions of active tumor. As described above, MRSI provides information on tumour heterogeneity, including distinguishing normal tissue, infiltrating tumor and vasogenic edema. [23] This information is also of great potential value in planning targeted radiotherapy as well as to help to differentiate residual or recurrent tumor from radiation necrosis on follow-up. [23-24]

The primary therapeutic goal in neuro-oncology is complete removal of the tumor; therefore, it is essential to know the exact tumor borders.[25] However, in high- grade gliomas, the tumor boundaries and the degree of infiltration are difficult to define due to their diffuse growth pattern. By evaluating metabolic abnormalities, proton MRS can also enhance the diagnostic yield of stereotactic brain biopsy. In high-grade heterogeneous tumors, there is a possibility that an unspecific or lower- grade tumor tissue is sampled or that important functional tracts are damaged. Ideally, regions of increased angiogenesis, vascular permeability and high metabolic activity should be sampled.[26] The role of proton MRS in biopsy guidance is to recognize regions of high metabolic activity, represent a good target for biopsy.[27,28,29]

Conclusion: MR Spectroscopy is complimentary to routine MR sequences. It helps in differentiating various neoplastic lesions from infective lesions of the brain. Granulomatous lesions like Tuberculomas and Neurocysticercosis can be differentiated by MR Spectroscopy. It can help in grading the gliomas. It can help in differentiating high grade gliomas vs metastasis.

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