



## ROLE OF MR SPECTROSCOPY IN BETTER CHARACTERISATION OF RING ENHANCING LESIONS OF BRAIN- A NARRATIVE REVIEW

### Radiodiagnosis

<b>Rajasree Dhinadhayan</b>	Post Graduate, Department Of Radiodiagnosis, Mahatma Gandhi Medical College And Research Institute, Pondicherry
<b>Lokesh Kumar. T*</b>	Assistant Professor, Department Of Radiodiagnosis, Mahatma Gandhi Medical College And Research Institute, Pondicherry *Corresponding Author
<b>Vijayalakshmi. K</b>	Professor, Department Of Radiodiagnosis, Mahatma Gandhi Medical College And Research Institute, Pondicherry
<b>Prabhu. C. S</b>	Associate Professor, Department Of Radiodiagnosis Mahatma Gandhi Medical College And Research Institute, Pondicherry

### ABSTRACT

MR Spectroscopy identifies various metabolites in the ring enhancing lesions of brain thus enabling it to be widely used and to predict the functional changes of the brain lesion. Prognostic implication are also provided by MRS. The purpose of this review is to observe the intracranial ring enhancing lesions and thus giving a differential diagnosis with advanced MRI techniques, like MR Spectroscopy. Out of all ring enhancing lesions, Tuberculoma is found to be most common and shows a lipid lactate peak in MR Spectroscopy. Hence, MRS is used for better characterisation and accurate diagnosis of the ring enhancing lesions of brain which resemble each other in conventional MRI.

### KEYWORDS

MR Spectroscopy, Ring Enhancing Lesions, Tuberculoma, Neurocysticercosis, Metabolites.

#### INTRODUCTION:

Ring enhancing lesions are the challenging neuroimaging abnormalities witnessed by radiologists.<sup>1</sup> There are vast variety of causes that can lead to ring enhancing lesions of brain, including infections, neoplastic, vascular or inflammatory etiology.<sup>2</sup> Mostly these lesions are located in the gray white matter and sub-cortical region, deep or superficial in the brain parenchyma. Out of all the ring enhancing lesions, Tuberculoma is the most commonly occurring and creates a dilemma in diagnosis. These lesions almost appear same in conventional CT and MRI. The various stages of the disease such as progression, effects of treatment, management and prognosis can be established by HMRS. Due to its non-ionizing radiation free analytical technique, MR Spectroscopy helps in quantifying various metabolites in brain lesions. Parallel studies have shown that in vivo MRS is non invasive and enables us in disease monitoring, knowing about the progression and effects of treatment.<sup>3</sup>

The purpose of this review is to observe the intracranial ring enhancing lesions and thus giving a differential diagnosis with advanced MRI techniques, like MR Spectroscopy.<sup>4</sup>

#### METHODS:

##### DATASOURCE:

Articles were selected from indexed journals like Pubmed, Google scholar, Web of science. The key words used are MR Spectroscopy, Ring enhancing lesions, Tuberculoma, Neurocysticercosis and metabolites.

#### STUDY SELECTION:

A search strategy to find studies regarding MR Spectroscopy published during past 10 years. Those studies were reviewed which aimed at measuring the diagnostic accuracy of H-MRS. We obtained those information on study design and technique of H-MR spectroscopy.

#### NORMAL ANATOMY:

The contents of the cranial cavity are the brain parenchyma, cranial nerves, meninges and CSF spaces. The MRI anatomy of the head is studied using cross sectional images in three planes - Axial, sagittal and coronal planes.

#### MR SPECTROSCOPY:

Magnetic resonance spectroscopy is an advanced and non invasive imaging technique of the brain. MRS quantifies the relative and absolute levels of metabolites in different diseased brain tissues. The difference between MRS and MRI is only in the manner of which the data is processed and presented.

MRS collects the data on the metabolite signal and its amplitudes against time which is in response to radiofrequency (RF) excitation, that is nearly same as MR imaging. The process of chemical shift forms the basis of MR spectroscopy. For each peak on the plot created by relative resonance frequency position is dependent on chemical environment of that particular nucleus and determines its subtle chemical shifts in their absolute (Hz) or relative (ppm) resonance frequencies. The lactate peak splitting that occurs into doublets in the proton spectrum is mainly due to J coupling.

#### METABOLITES IN PROTON SPECTROSCOPY AND THEIR SIGNIFICANCE

##### LIPIDS:

Lipids are metabolites that show broad peaks at 0.9 and 1.3 parts per million (ppm). In normal spectrum, lipid peak is mostly obscured since very little lipid is noted in healthy tissue areas. Presence of lipid indicates necrosis and lactate which is seen in tuberculous granulomas and brain tumours.<sup>5</sup>

##### LACTATE:

Lactate generally presents as doublets (two peaks close together) which has frequency of 1.33 ppm. Lactate is not present in healthy tissue which makes it undetectable with MRS. In anaerobic glycolysis, lactate is a byproduct which is detected in diseased brain, that is oxygen deprived such as in stroke, encephalopathy, mitochondrial myopathy, lactic acidosis, neonatal hypoxia and recovery from cardiac arrest.<sup>5</sup>

##### CHOLINE:

The cell membranes of brain myelin has a common terminology called Choline or trimethylamine (TMA). Choline has a resonance value of 3.2ppm. Active demyelinating lesions has increased levels of choline because during active myelin breakdown, membrane phospholipids are released.<sup>5</sup>

##### CREATINE:

The primary resonance of creatine is 3.0 ppm. Creatine (Cr) is used for internal standards when resonance intensities of other metabolites are normal.<sup>5</sup>

The central energy marker of both neurons and astrocytes is phosphocreatine. In acute destructive pathologies such as malignant tumors, focal decrease in Creatine signal is seen.

##### N-ACETYLSPARTATE (NAA):

NAA is a derivative of amino acid which is synthesized in neurons and transported down the axons. The neuronal integrity can be assessed

from NAA as it acts as surrogate marker. In fetuses, NAA can be detected as early as 16 weeks of gestation. Rapid increase in levels of NAA/Cr can be observed during the first few years of life and after that its level increases less than 1% per year until 16 years of age to reach adult values.<sup>6</sup>

#### MYO-INOSITOL (MI) :

Increase in myo-inositol reflects the increased number of glial cells, which has high myo-inositol, thus more commonly seen in grade II Gliomas.<sup>6</sup>

A osmolyte and astrocyte marker , ml gives specificity in the diagnosis of dementia and also adds specificity in monitoring hepatic encephalopathy patients and brain syndromes involving hyponatremia.

#### GLUTAMATE-GLUTAMINE (GLX) :

They are a mixture of very closely related amino acid and amine. They both are involved in excitatory and inhibitory neuronal transmission which lies between 2.1 and 2.4 ppm. Glx is an important marker for MRS of lymphoma and metabolic brain disorders.

#### RING ENHANCING LESIONS OF BRAIN NEUROCYSTICERCOSIS :

Neurocysticercosis is the most common parasitic infection involving human CNS. Causative agent for Neurocysticercosis is pork tape worm called *Taenia solium*. Each of cyst measures around 3-18mm in diameter and it contains a scolex .

The locations usually involves meningo-basal, intraventricular, parenchymal or combination of these sites. Findings in image in each stages will reflect the underlying changes of the disease process and its host response.<sup>7</sup>

#### FOUR STAGES OF NEUROCYSTICERCOSIS:

1. Stage 1-Vesicular stage
2. Stage 2-Colloidal Vesicular stage
3. Stage 3-Granular Nodular stage
4. Stage 4-Nodular Calcified stage

In Cysticercosis, the MRS findings includes combinations of elevated levels of alanine, lactate, choline, succinate and reduction in levels of creatine and NAA.<sup>8</sup>

#### CEREBRAL ABSCESS :

High signal intensity on DWI is demonstrated in abscess, with corresponding decrease in values of apparent diffusion coefficients. Cellularity is directly related to viscosity of the pus present within the abscess cavity.<sup>9</sup>

Complex peaks at 0.9 ppm are seen indicating amino acids leucine, valine and isoleucine. succinate, pyruvate, Acetate and lactate are the metabolic byproducts which arises from microorganisms.<sup>10</sup>

#### TUBERCULOMA :

The Neuro TB is commonly seen in ages ranging between 25 and 45 years but can also present in any age. The most common brain parenchymal lesions are tubercular abscess and tuberculomas. Tuberculoma is seen in 15% to 30% cases of TB brain.<sup>11</sup>

In vivo, spectroscopy lipids are seen in T2 hypointense tuberculomas. Lesions with heterogeneous appearance shows Choline at 3.22 ppm with lipid. The lesions shows more amount of cellularity and less solid caseation. The cellular regions appears bright on MT imaging and shows Choline resonance in spectroscopy.<sup>12</sup>

#### METASTATIC DISEASE :

Metastases are located most commonly in supratentorial compartment (80 to 85%). The most common type of metastatic disease are intraparenchymal metastases that affects the intracranial space. Most common primary tumors causing brain secondaries are lung cancer, melanoma, breast cancer, renal cell carcinoma, gastrointestinal cancers and tumors of unknown primary.<sup>13</sup>

MRS in metastatic disease shows increased choline levels and high choline/ creatine ratio. There is a high incidence of solitary metastasis which is estimated to range between 30% to 50% and are commonly seen in melanoma, breast and lung carcinoma.<sup>14</sup>

#### DEMYELINATING DISORDERS :

Several acute demyelinating disorders presents as multiple ring enhancing lesions. Presence of incomplete ring or open ring lesions helps us to differentiate between demyelinating lesion, large brain tumors and brain abscess. Atypical ring-enhancing lesions in patients with mass effect often undergo biopsy from lesion to confirm the diagnosis.<sup>15</sup> MRS in demyelination shows lactate peak, choline peak, NAA and creatine peak.

#### RADIATION NECROSIS :

Radiation therapy in treatment of malignancy of head, neck or any brain tumour commonly causes radiation necrosis of brain. Conventional magnetic resonance (MR) imaging of radiation necrosis and recurrent tumour often overlap each other. In histopathologic analysis also tumor mixed with radiation necrosis is found commonly. MR spectroscopy, Diffusion tensor imaging ,perfusion MR imaging and positron emission tomography are useful in differentiating between recurrent tumor and radiation necrosis.<sup>16</sup> MRS shows lipid lactate peak and low choline levels.

A study by **Bava DJS, Sankhe DA, Patil DS** involving 50 patients concluded that MRI done along with MRS to be the most sensitive modality in identifying and differentiating intracranial ring enhancing lesions . MRI was helpful in identification of exact anatomical location and the extent of lesions. In their study they found, MRS was useful in differentiating and characterizing various ring enhancing lesions on the basis of metabolites which enables for accurate diagnosis.<sup>17</sup>

Similarly, another study by **Morales H Alfaro D et al**, in 13 cases of tuberculomas, a singlet peak at ~3.8 ppm is noted in most of the cases of tuberculomas when compared to malignant tumours, where singlet peak is absent. MRS which shows a dominant lipid peak and near absence of other metabolites has been reported to have high sensitivity and specificity in differentiating tuberculomas from other non-neoplastic and neoplastic lesions.<sup>18</sup>

A study with 10 patients done by **Weybright P et al**, showing MRI evidence of ring- like enhanced lesions after administration of GDPA. The study says that a combination of MRS and other methods including DW echo planar MRI has greater potential for establishing the differential diagnosis between pyogenic brain abscess and other cystic tumours with similar neurologic appearance.<sup>19</sup>

In 2016, 40 patients of intracranial brain tumours were observed by **Darwiesh AMN and Maboud NMA-E et al**, which included glioblastoma multiforme, pilocytic astrocytoma and metastasis. They found that MRS can differentiate between lesions, showing similar aspects on conventional MRI. In their study Choline was considered as the most specific marker of intracranial neoplasm. The increase in Choline levels and Choline/NAA ratios shows malignancy of the neoplasm.<sup>20</sup>

In 2004, a study by **Garg M et al** obtained 75 patients with brain abscess and observed the in vivo-MR Spectroscopy in the visualizing metabolite pattern of Brain abscess. They have proved that the information is useful in prompt and appropriate treatment of disease in these patients with brain abscess.<sup>21</sup>

#### DISCUSSION :

Based on the results obtained by review articles, most common lesion seen is Tuberculoma with seizure being the most common presenting complaint. All Tuberculoma cases shows elevated lipid peak in MRS. Metastasis appears as well defined hyperintense lesions on T2 with significant perilesional edema and shows high choline peak on MRS. Abscess shows a hypointense rim on T2 with complete diffusion restriction. MRS shows Lactate and Amino Acids. All the neoplastic lesions like primary brain tumours show a high choline creatine ratio. MRS helps to differentiate between benign and malignant lesions. MR Spectroscopy is used for differentiating infectious, inflammatory and neoplastic causes of ring enhancing lesions. In tuberculomas, choline/ creatine ratio > 1.

#### CONCLUSION :

Based on the results of study on review articles, MRI is used for the diagnosis of ring enhancing lesions, but MR Spectroscopy plays a vital role in accurate diagnosis of the lesion and helps in avoiding the dilemma in diagnosing similar lesions. However, no lesion can be diagnosed based on the findings of MRS as sole criteria. Hence, it is

recommended to use MR Spectroscopy sequence along with routine sequences in all cases of Ring enhancing lesions which will narrow down the differential diagnosis and contribute towards accurate diagnosis.

## REFERENCES

- Shetty G. Ring-Enhancing Lesions in the Brain: A Diagnostic Dilemma. 2014;8(3):4.
- Elsadway ME, Ibrahim Ali H. Verification of brain ring enhancing lesions by advanced MR techniques. Alexandria Journal of Medicine. 2018 Jun 1;54(2):167–71.
- Kadota o, kohnno k, ohue s, kumon y, sakaki s, kikuchi k, miki h. Discrimination of brain abscess and cystic tumor by in vivo proton magnetic resonance spectroscopy. Neurologia medico-chirurgica. 2001;41(3):121-6.
- Morita N, Harada M, Otsuka H, Melhem ER, Nishitani H. Clinical Application of MR Spectroscopy and Imaging of Brain Tumor. MRMS. 2010;9(4):167–75.
- Verma A, Kumar I, Verma N, Aggarwal P, Ojha R. Magnetic resonance spectroscopy—Revisiting the biochemical and molecular milieu of brain tumors. BBA clinical. 2016 Jun 1;5:170-8.
- Horská A, Barker PB. Imaging of Brain Tumors: MR Spectroscopy and Metabolic Imaging. Neuroimaging Clinics of North America. 2010 Aug;20(3):293–310.
- Lerner A, Shiroishi MS, Zee CS, Law M, Go JL. Imaging of neurocysticercosis. Neuroimaging Clinics. 2012 Nov 1;22(4):659-76.
- Pandit S, Lin A, Gahbauer H, Libertin CR, Erdogan B. MR spectroscopy in neurocysticercosis. Journal of computer assisted tomography. 2001 Nov 1;25(6):950-2.
- Desprechins B, Stadnik T, Koerts G, Shabana W, Breucq C, Osteaux M. Use of Diffusion-Weighted MR Imaging in Differential Diagnosis Between Intracerebral Necrotic Tumors and Cerebral Abscesses. 1999;6.
- Kim YJ, Chang KH, Song IC, Kim HD, Seong SO, Kim YH, Han MH. Brain abscess and necrotic or cystic brain tumor: discrimination with signal intensity on diffusion-weighted MR imaging. AJR. American journal of roentgenology. 1998 Dec;171(6):1487-90.
- Chowdhury FH, Mohammad N, Haque MR, Hossain Z, Salam A, Sarker MH. Tubercular Lesions in Brain Parenchyma. 5(2):16.
- Poptani H, Gupta RK, Roy R, Pandey R, Jain VK, Chhabra DK. Characterization of Intracranial Mass Lesions with In Vivo Proton MR Spectroscopy. 1995;8.
- Potts DG. National Cancer Institute Study: Evaluation of Computed Tomography in the Diagnosis of Intracranial Neoplasms. 1980;8.
- Meyer PC, Reah TG. Secondary Neoplasms of the Central Nervous System and Meninges. Br J Cancer. 1953 Dec;7(4):438–48.
- Maarouf M, Kuchta J, Miletic H, Ebel H, Hesselmann V, Hilker R, et al. Acute demyelination: diagnostic difficulties and the need for brain biopsy. Acta Neurochirurgica. 2003 Nov 1;145(11):961–9.
- Shah R, Vattoth S, Jacob R, Manzil FFP, O'Malley JP, Borghei P, et al. Radiation Necrosis in the Brain: Imaging Features and Differentiation from Tumor Recurrence. RadioGraphics. 2012 Sep;32(5):1343–59.
- Bava DJS, Sankhe DA, Patil DS. Role of MR Spectroscopy in Evaluation of Various Ring Enhancing Lesions in Brain. 2013;5(7):3.
- Morales H, Alfaro D, Martinot C, Fayed N, Gaskill-Shiple M. MR spectroscopy of intracranial tuberculomas: A singlet peak at 3.8 ppm as potential marker to differentiate them from malignant tumors. The neuroradiology journal. 2015 Jun;28(3):294-302.
- Weybright P, Sundgren PC, Maly P, Hassan DG, Nan B, Rohrer S, et al. Differentiation Between Brain Tumor Recurrence and Radiation Injury Using MR Spectroscopy. American Journal of Roentgenology. 2005 Dec;185(6):1471–6.
- Darwiesh AMN, Maboud NMA-E, Khalil AMR, ElSharkawy AM. Role of magnetic resonance spectroscopy & diffusion weighted imaging in differentiation of supratentorial brain tumors. The Egyptian Journal of Radiology and Nuclear Medicine. 2016 Sep;47(3):1037–42.
- Garg M, Gupta RK, Husain M, Chawla S, Chawla J, Kumar R, et al. Brain Abscesses: Etiologic Categorization with in Vivo Proton MR Spectroscopy. Radiology. 2004 Feb;230(2):519–27.