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Evaluation of imaging aspects of brain lesions by proton mr spectroscopy

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Abstract
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. 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.
Result: Analysis of spectra of 50 patients with brain lesions was done. 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. 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 helping in differentiating various neoplastic lesions from infective lesions of the brain. MR spectroscopy can help in grading the gliomas. MR spectroscopy can help in differentiating high grade gliomas vs metastasis.

Keywords: Metabolite, spectroscopy, phenomenon

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. Proton MRS provides some extra information on the metabolic composition of the lesion under investigation and thus aids in the diagnosis [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.

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.

Normal Brain Metabolites

Table 1

Chemical compound	Chemical shift	Comments
N-Acetylaspartate (NAA)	2.0	Neuronal marker. Decreased: Degenerative disorders, multiple sclerosis, hypoxia, stroke, herpes encephalitis, epilepsy and some neoplasm. Increased: Canavan's disease
Creatine/phosphocreatine	3.0, 3.9	Energy metabolism. Decreased: acute destructive pathologies like malignant tumors, hyper metabolic state and hypoxia. Increased: hypo-metabolic states and trauma
Choline (Cho)	3.2	Cell membrane integrity marker. Decreased: hepatic encephalopathy and stroke Increased: active demyelinating lesions, chronic hypoxia, epilepsy, trauma, many brain tumours like glioma (more in higher- grade tumors due to increased membrane turnover)
Myo–inositol (ml)	3.6	Glial cell marker. Decreased: hepatic and hypoxic encephalopathy, stroke, central pontine myelinolysis Increased: dementia - Alzheimer's and frontal lobe dementia.
Lipid (lip)	0.9-1.4	Cell breakdown/ brain destruction indicator. Increased: tubercular granulomas and high grade

		brain tumors (necrosis).
Lactate (Lac)	1.3	An end product of anaerobic glycolysis Increased: stroke, mitochondrial myopathy, encephalopathy, lactic acidosis, recovery from cardiac arrest and neonatal hypoxia, cysts and abscesses.

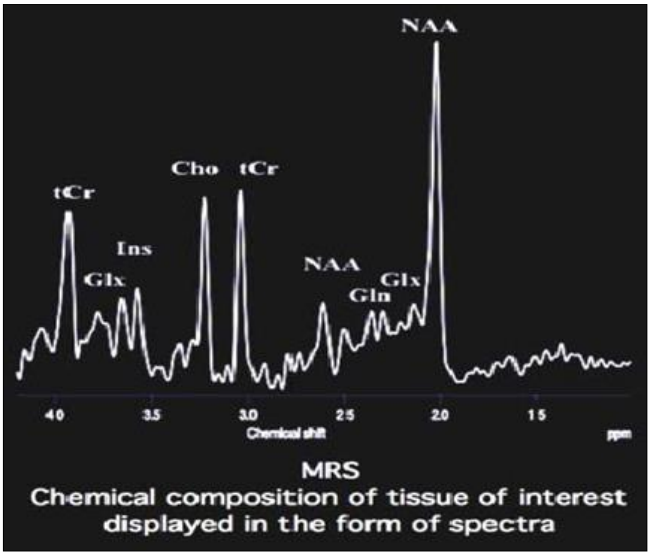

Fig 1: Normal Single Voxel MR Spectrum

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 45º angle to x axis when they are present in normal proportions, which is called as Hunters angle. It changes with echo time (TE), repetition time (TR) and change in location of voxel from cortex to midbrain [1].

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 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. Each stage (vesicular, colloid vesicular, granular nodular & nodular calcified) has 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 [6].

Meningioma

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

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. 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; 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].

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.

Methodology

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 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.
- Patients with hypoxic ischemic injuries, demyelinating diseases like neuromyelitis optica spectrum disorders, metabolic diseases and white matter diseases were excluded.

Sample Size

- Sample size of 50 cases.

Methods

- **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.

Observations and Results

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

Images

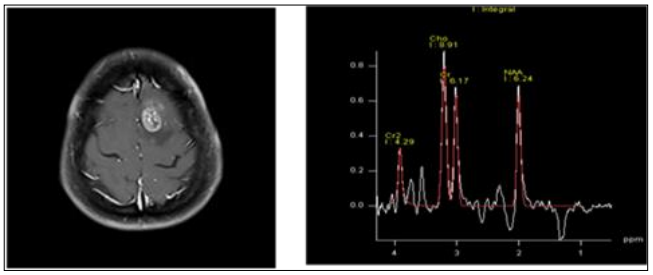

Fig 2

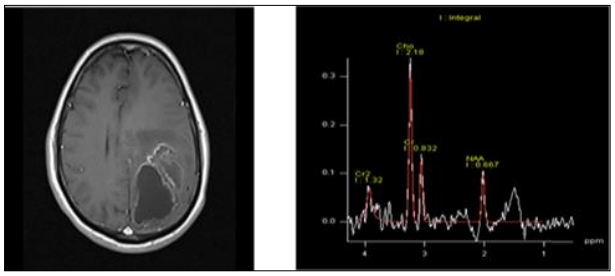

Fig 3

LOW GRADE GLIOMA
MR spectroscopy shows raised choline, reduced NAA peaks, increased choline/NAA and choline/creat ratios (Figure 2)

GBM
MR spectroscopy shows raised choline, reduced NAA peaks, increased choline/NAA and choline/creat ratios (Figure 3)

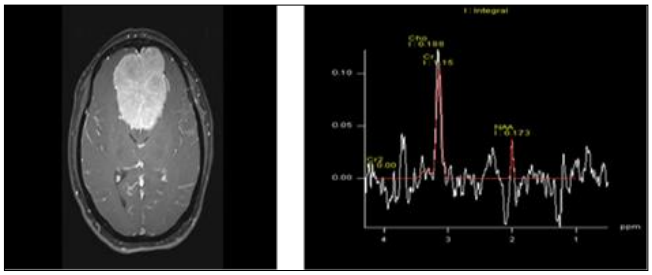

Fig 4

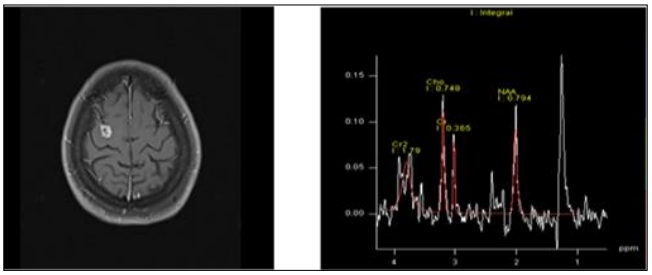

Fig 5

MENINGIOMA
MR spectroscopy shows raised choline, reduced NAA peaks, increased choline/NAA and choline/creat ratios

TUBERCULOMA
MR spectroscopy shows raised choline, reduced NAA peaks, increased choline/NAA and choline/creat ratios & lipid lactate levels (Figure 5)

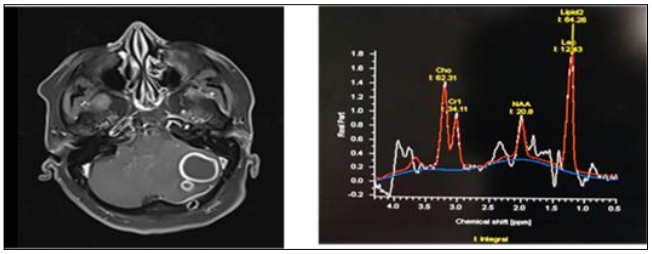

Fig 6

BRAIN ABSCESS
MR spectroscopy shows raised choline, reduced NAA level with characteristic lipid lactate peak and choline/creat ratios (Figure 6)

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 72 years

old. P A McKinney studied 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. 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 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 [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 and lipids + lactate/Cr levels were noted in PCLs compared with those in metastases [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. 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 [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.

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 as studied by H Poptani *et al*. differentiating it from schwannomas [22].

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 [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]. The role of proton MRS in biopsy guidance is to recognize regions of high metabolic activity, represent a good target for biopsy [26, 27]

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.

References

1. MRI Made Easy (for Beginners): Chavhan, Govind B, Bruhn H, Frahm J, Gyngell ML, *et al*. Noninvasive differentiation of tumors with use of localized H-1 MR spectroscopy *in vivo*. Radiology,1989:172(2):541–548.
2. Langkowski JH, Wieland J, Bomsdorf H, *et al*. Pre-operative localized *in vivo* proton spectroscopy in cerebral tumors at 4.0 Tesla. Magn Reson Imaging,1989:7(5):547–555.
3. WHO Classification of Tumours, 5th Edition, Central Nervous System Tumours – IARC, 2022, 6.
4. Naphade PS, Raut AA, Pai BU. Magnetic resonance perfusion and spectroscopy in a giant tuberculoma, 2011.
5. Pandit S, Lin A, Gahbauer H, Libertin CR, Erdogan B. MR spectroscopy in neurocysticercosis. J Comput Assist Tomogr,2001:25(6):950-2. doi.
6. Watts J, Box G, Galvin A, Brotchie P, Trost N, Sutherland T, 2014.
7. Saindane AM, Cha S, Law M, *et al*. Proton MR spectroscopy of tumefactive demyelinating lesions. AJNR Am J Neuroradiol,2002:23(8):1378–1386.
8. Chang KH, Song IC, Kim SH, *et al*. *In vivo* single-voxel proton MR spectroscopy in intracranial cystic masses. AJNR Am J Neuroradiol,1998:19(3):401–405.
9. PA McKinney. Brain tumours: incidence, survival, and aetiology. J Neurol Neurosurg Psychiatry, 2004, 75. ii12-ii17 doi: 10.1136/ jnnp. 2004.040741.
10. Arnold DL, Shoubridge EA, Villemure JG, *et al*. Proton and phosphorus magnetic resonance spectroscopy of human astrocytomas *in vivo*. NMR Biomed,1990:3(4):184–189.
11. Hourani R, Horska A, Albayram S, *et al*. Proton magnetic resonance spectroscopic imaging to differentiate between nonneoplastic lesions and brain tumors in children. J Magn Reson Imaging,2006:23(2):99–107.
12. Gill SS, Thomas DG, Van Bruggen N, *et al*. Proton MR spectroscopy of intracranial tumours: *in vivo* and *in vitro* studies. J Comput Assist Tomogr,1990:14(4):497–504.
13. Howe FA, Barton SJ, Cudlip SA, *et al*. Metabolic profiles of human brain tumors using quantitative *in vivo* 1H magnetic resonance spectroscopy. Magn Reson Med,2003:49(2):223–232.
14. Preul MC, Leblanc R, Caramanos Z, *et al*. Magnetic resonance spectroscopy guided brain tumor resection: differentiation between recurrent glioma and radiation change in two diagnostically difficult cases. Can J Neurol Sci,1998:25(1):13–22.
15. Senft C, Hattingen E, Pilatus U, *et al*. Diagnostic value of proton magnetic resonance spectroscopy in the noninvasive grading of solid gliomas: comparison of maximum and mean choline values. Neurosurgery,2009:65(5):908–913. discussion 13.
16. Poptani H, Gupta RK, Roy R, Pandey R, Jain VK, Chhabra DK. Characterization of intracranial mass lesions with *in vivo* proton MR spectroscopy. AJNR Am J Neuroradiol,1995:16(8):1593–1603.
17. Chang KH, Song IC, Kim SH, *et al*. *In vivo* single-voxel proton MR spectroscopy in intracranial cystic masses. AJNR Am J Neuroradiol,1998:19(3):401–405.
18. Fan G, Sun B, Wu Z, *et al*. *In vivo* single-voxel proton MR spectroscopy in the differentiation of high-grade gliomas and solitary metastases. Clin Radiol,2004:59(1):77–85.
19. Chiang IC, Kuo YT, Lu CY, *et al*. Distinction between high-grade gliomas and solitary metastases using peritumoral 3-T magnetic resonance spectroscopy, diffusion, and perfusion imagings. Neuroradiology,2004:46(8):619–627.
20. Castillo M, Smith JK, Kwock L. Correlation of myo-inositol levels and grading of cerebral astrocytomas. AJNR Am J Neuroradiol,2000:21(9):1645-9. PMID: 11039343; PMCID: PMC8174883.
21. Poptani H, Gupta RK, Roy R, Pandey R, Jain VK, Chhabra DK. Characterization of intracranial mass lesions with *in vivo* proton MR spectroscopy. AJNR Am J Neuroradiol,1995:16(8):1593–1603.
22. Majos C, Aguilera C, Alonso J, *et al*. Proton MR spectroscopy improves discrimination between tumor and pseudotumoral lesion in solid brain masses. AJNR Am J Neuroradiol,2009:30(3):544–551.
23. Crawford FW, Khayal IS, McGue C, *et al*. Relationship of pre-surgery metabolic and physiological MR imaging parameters to survival for patients with untreated GBM. J Neurooncol,2009:91(3):337–351.
24. Weber MA, Giesel FL, Stieltjes B. MRI for identification of progression in brain tumors: from morphology to function. Expert Rev Neurother,2008:8(10):1507–1525.
25. Barker PB. N-acetyl aspartate--a neuronal marker? Ann Neurol,2001:49(4):423–424.
26. Dowling C, Bollen AW, Noworolski SM, *et al*. Preoperative proton MR spectroscopic imaging of brain tumors: correlation with histopathologic analysis of resection specimens. AJNR Am J Neuroradiol,2001:22(4):604– 612.