ORIGINAL RESEARCH PAPER

Volume-7 | Issue-3 | March-2018 | PRINT ISSN No 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

EVALUATION OF THE ROLE OF MAGNETIC RESONANCE SPECTROSCOPY AND DIFFUSION WEIGHTED IMAGING TECHNIQUES IN GRADING AND CHARACTERIZATION OF INTRACRANIAL TUMOURS

Radiodiagnosis

Dr Vikas Rastogi MD (Radiodiagnosis) Associate Professor Department of Radiodiagnosis, Army Hospital Delhi Cantt MD (Radiodiagnosis)

Dr Rajat Kumar Sharma* MD (Radiodiagnosis), Classified Specialist, Department of Radiodiagnosis, Base Hospital Delhi Cantt *Corresponding Author

ABSTRACT

The current standard of neuroimaging for brain tumor evaluation is anatomy-based magnetic resonance imaging (MRI) with intravenous contrast material (4, 5). Contrast enhanced MRI has its constraint in the form of inability to reflect the complicated biology of infiltrative tumours and has a limited capacity to differentiate a high-grade tumour from a single brain metastasis. In addition, anatomic MRI suffers from nonspecificity.
Grading of tumours is important for the determination of appropriate treatment strategies (6, 7) and in the assessment of prognosis (8).
For this purpose a total of 50 cases with different types of intracranial tumors were enrolled in the study in a standard Siemens Magneto Avanto 1.5 Tesla MRI scanner.
Results Grade I/II > Grade III > Grade IV > Meningioma ~ Metastasis (Table 17).Cho/Cr values ranged from 1.3 to 4.2 in different grades/types of tumors. Mean ADC was maximum in metastatic tumors (3.75±0.40) and minimum in Grade I/II (1.70±0.27). Statistically, the difference in ADC in different grades/types of intracranial tumors was significant. (Table 18). Mean difference in Cho/NAA was maximum between Grade I/II vs Meningioma (1.69±0.21) and minimum between Metastasis and Grade IV (0.19±0.25). Only Grade I/II had significantly lower mean Cho/NAA levels as compared to all the other types/grades. None of the other between grade/type differences were significant statistically. The order of ADC in different grades types was **Grade I/II < Grade III ~ Grade IV ~ Meningioma ~ Metastasis**

KEYWORDS

INTRODUCTION

Brain tumors comprise some of the most malignant tumors known to affect human beings and are generally refractory to all modalities of treatment (1). Malignant brain tumors are the leading cause of death from solid tumors in children and the third-leading cause of cancer-related death in patients aged 15 to 34 years old (2,3).

The current standard of neuroimaging for brain tumor evaluation is anatomy-based magnetic resonance imaging (MRI) with intravenous contrast material (4, 5). Contrast enhanced MRI has its constraint in the form of inability to reflect the complicated biology of infiltrative tumours and has a limited capacity to differentiate a high-grade tumour from a single brain metastasis. In addition, anatomic MRI suffers from nonspecificity.

Grading of tumours is important for the determination of appropriate treatment strategies (6, 7) and in the assessment of prognosis (8).

In high grade gliomas (HGGs) are usually treated with tumor resection and additional radiotherapy and chemotherapy, whereas in low-grade gliomas (LGGs), only surgical treatment for histological confirmation or tumor resection is performed in most patients (9, 10, 11). The variation in the treatment offered as per NCCN international guidelines is revised regularly. To reach a diagnosis though biopsy is the gold standard, it is always not possible to subject every patient with biopsy. The approach to treatment needs to be decided prior to the first line of treatment in many cases. Some of these cases are also offered treatment on urgent basis. Hence there is a pressing need to form a provisional diagnosis while approaching to manage patients found to have intracranial tumours.

The present standard criterion for tumor grading is histopathological assessment. The presence of one or more criteria, such as, mitosis, nuclear atypia, vascular endothelial proliferation and necrosis (7). However, histological grading of primary gliomas has some limitations, in the form of few small samples of tissue are evaluated, particularly from stereotactic biopsy, the most malignant component of a tumor may not be included in the sample. It is difficult to sample the tumor involving the eloquent areas of brain by the surgeon. The dynamic spectrum of CNS tumors, with at least 50% dedifferentiating into more malignant grades (12, 13, 14) 3) in the numerous classifications/grading systems used by different institutions.

Hence the World Health Organization (WHO) classification scheme remains the standard reference for guiding therapy and predicting prognosis in patients with brain tumours (12).

In the last couple of years, there has been development and application of various advanced MRI techniques. These include diffusion-weighted MRI (DWI), perfusion and permeability MRI, diffusion-tensor MRI (DTI) and fiber tractography, and proton MR spectroscopy (MRS).

Diffusion is defined as the process of random thermal motion of molecules occurring at a microscopic scale (15). The apparent diffusion coefficient (ADC) is a value that describes microscopic water diffusibility in the presence of factors that restrict diffusion within tissues.

Measurements of the ADC would be expected to be useful in tumor assessment because variations in water content, which can be found within tumor for various reasons (eg. necrosis, variation in cellularity) and adjacent to tumors (eg, vasogenic edema) in contrast to conventional MRI (16).

Clinical MR Neurospectroscopy

It is a non-invasive qualitative and quantitative analysis of a number of metabolites within the brain (17). MRS provides a means to characterize the metabolite profiles of tumoral and non-tumoral lesions in the brain (18).

Neurochemistry in MRS

Figures 1 and 2 show examples of proton spectra recorded at short and intermediate echo time (TE). The assignment and significance of each of the resonances in the spectrum is discussed below.

N-acetyl aspartate

The largest signal in the normal adult brain spectrum, the N-acetyl group of N-acetyl aspartate (NAA) resonates at 2.01 ppm, with a smaller contribution from N-acetylaspartyl glutamate (NAAG) at 2.04 ppm, particularly in white matter (19, 20).

Myo-inositol

Myo-inositol (MI) observed at 3.5-3.6 ppm, is a pentose sugar, which is part of the inositol triphosphate intracellular second messenger system .

Glutamate and glutamine

Glutamate (Glu) and glutamine (Glm) are key components in brain metabolism and is the prominant neurotransmitter (34). Glu and Glm are difficult to separate in proton spectra at 1.5 T, and they are usually labeled as a composite peak "Glx", at 2.1 to 2.5 ppm (19, 21).

Lipid

Lipids (Lip) observed at 0.9 ppm and 1.3 ppm are found normally within cell walls and usually not evident on normal spectra.

Recent studies suggest the utility of this technique in making a specific diagnosis, determination of histologic grade, therapeutic planning, guiding biopsies and to monitor patients after treatment (17, 18).

Diffusion weighted MRI

Diffusion imaging examines the motion of water molecules, which is normally random or Brownian in the unimpeded isotropic state. Given that water moves within and across intracellular and extracellular domain, water also encounters impediments in the extracellular interstitium.

It is a measure of the magnitude of water diffusion. The greater the density of structures that impede water mobility the lower is the ADC. For this reason, ADC is considered a non-invasive indicator of cellularity or cell density.

MATERIAL AND METHODS

1. The **source of data** is from referred cases from Neurology and Neurosurgery department of a service hospital for evaluation of intracranial SOLs.

2. Method of data collection: The duration of study was over three years from April 2013 – May 2016. The sample size was that of a minimum of 50 cases.

a) Imaging protocols: Patients will be subjected to conventional MRI, Diffusion Weighted MR and MR Spectroscopy, according to the following protocols, in a standard Siemens Magneto Avanto 1.5 Tesla MRI scanner. The protocol followed was Fluid attenuated inversion recovery (FLAIR) sequences; T2 - weighted TSE, T1 weighted TSE, Post-Gadolinium T1 weighted TSE, Diffusion Weighted MRI**,** MR Spectroscopy.Findings of MR Spectroscopy and Diffusion Weighted MR would be compared and correlated with the histopathological data where ever possible.

STANDARD STATISTICAL TOOLS EMPLOYED

For the statistical analysis were employed such as SPSS (Statistical Package for Social Sciences) Version 15.0 statistical Analysis Software, Analysis of Variance: Analysis of Variance (ANOVA), Post-Hoc Tests (Tukey-HSD), Level of significance:

RESULTS

The present study was carried out with an aim to evaluate the role of MR spectroscopy and Diffusion Weighted MRI in diagnosis with focus on grading and characterization of brain tumors. For this purpose a total of 50 cases with different types of intracranial tumors were enrolled in the study.

Alanine peak was most common (n=12; 24%) followed by lipid and lactate peak (n=9; 18%) and lipid peak (n=6; 12%). There were 6 cases with no other metabolite. Myoinositol peak was observed in 4 (8%), raised lipid and lactate in 3 (6%), lactate peak, markedly raised lipid and raised lipid in 2 (4%) cases each. There was one case each with elevated lactate, markedly raised lipid and lactate, mildly raised lipid and raised lipid respectively.

All the cases had hyperintense images on diffusion weighted MRI – of these 2 had heterogeneously hyperintense and 1 had peripheral hyperintensity.

Age of patients ranged from 3 to 85 years. Maximum number of patients were aged 51-60 years (n=12; 24%) followed by those aged 31-40 years (n=11; 22.0%), 21-30 years (n=8; 16%), 61-70 years (n=7; 14%) and 41-50 years (n=6; 12%). There were 3 cases aged 71-80 years, 2 aged ≤10 years and 1 case in age group 11-20 years.

A total of 38 (76%) cases had hypointense images, 10 (20%) had hyperintense images. There was 1 (2%) case each with patchy hypointensity and peripheral hypointensity.

ADC values ranged from 660 to 1680. Mean ADC was 1048.22 with a standard deviation of 284.49.

On the basis of MRI, maximum number of cases (n=13; 26%) had meningioma, 9 (18%) cases each had anaplastic astrocytoma and glioblastoma multiforme respectively. There were 7 (14%) cases of low grade astrocytoma and 6 (12%) with metastasis. 2 (4%) cases had craniopharyngioma. 1 (2%) case had low grade glioma, medullobl astoma, pineal parenchymal tumor of indeterminate differentiation and supratentorial ependeymona respectively.

On histopathological correlation, meningioma was the most common finding followed by glioblastoma multiforme and anaplastic astrocytoma. In 3 (6%) cases the diagnosis was low grade astrocytoma. There were 4 (8%) cases in which correlation could not be done. There were 2 cases in which diagnosis was grade III astrocytoma. Adamantionomatous variant of craniopharyngioma, astrocytoma, astrocytoma low grade, craniopharyngioma, glioma, high grade PNET, infilterative astrocytoma, medulloblastoma and metastasis were the final diagnosis in 1 case each.

Grade IV was the most common (n=11; 22%) followed by grade III (n=10; 20%) and Grade I/II (n=10; 20%). There were 13 (26%) cases with meningioma and 6 (12%) with metastasis as the final diagnosis.

ADC ranged from 660 to 1680 in different grades/types of tumors. Mean ADC was maximum in Grade I/II (1490.30±135.57) and minimum in Meningioma (759.54±71.44). Statistically, the difference in ADC in different grades/types of intracranial tumors was significant.

Mean difference in ADC was maximum between Grade I/II vs Grade IV (730.76±41.77) and minimum between Meningioma and Metastasis (62.29±49.01). Except for difference between Meningioma and Metastasis, all the between grade/type differences were significant statistically. The order of ADC in different grades types was as follows: **Grade I/II > Grade III > Grade IV > Meningioma ~ Metastasis (Table 17).**Cho/Cr values ranged from 1.3 to 4.2 in different grades/types of tumors. Mean ADC was maximum in metastatic tumors (3.75±0.40) and minimum in Grade I/II (1.70±0.27). Statistically, the difference in ADC in different grades/types of intracranial tumors was significant. (Table 17).

Mean difference in Cho/NAA was maximum between Grade I/II vs Meningioma (1.69±0.21) and minimum between Metastasis and Grade IV (0.19±0.25). Only Grade I/II had significantly lower mean Cho/NAA levels as compared to all the other types/grades. None of the other between grade/type differences were significant statistically. The order of ADC in different grades types was **Grade I/II < Grade III ~ Grade IV ~ Meningioma ~ Metastasis (Table 18).**

FIGURES AND TABLES

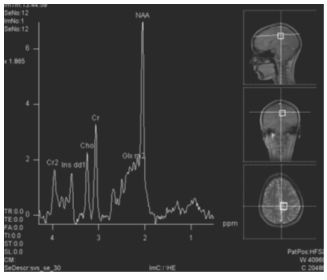


Figure 1. Single-voxel proton MRS of the normalappearing brain tissue shows normal metabolite levelsat echo time (TE) 30 ms.

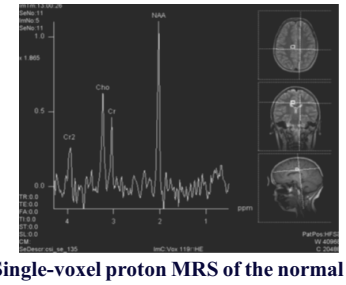


Figure 2. Single-voxel proton MRS of the normal appearing brain shows normal metabolite levels at echo time (TE) 135 ms.

All the cases had hyperintense images on diffusion weighted MRI – of these 2 had heterogeneously hyperintense and 1 had peripheral hyperintensity.

Table 1: ADC Findings

SN	Finding	No. of cases	Percentage
1.	Hyperintense	10	20.0
2.	Hypointense	38	76.0
3.	Patchy hypointensity	1	2.0
4.	Peripheral hypointnesity	1	2.0

A total of 38 (76%) cases had hypointense images, 10 (20%) had hyperintense images. There was 1 (2%) case each with patchy hypointensity and peripheral hypointensity.

Table 2: ADC Values

	N	Minimum	Maximum	Mean	Std. Deviation
ADC VALUE	50	660	1680	1048.22	284.49
ADC values ranged from 660 to 1680. Mean ADC was 1048.22 with a standard deviation of 284.49.					

SN	Finding	No. of cases	Percentage
1.	None	6	12.0
2.	Alanine peak	12	24.0
3.	Elevated lactate	1	2.0
4.	Lactate peak	2	4.0
5.	Lipid and lactate peak	9	18.0
6.	Lipid peak	6	12.0
7.	Markedly raised lipid	2	4.0
8.	Markedly raised lipid and lactate	1	2.0
9.	Mildly raised lipid	1	2.0
10.	Myoinositol peak	4	8.0
11.	Raised lactate	1	2.0
12.	Raised lipid	2	4.0
13.	Raised lipid and lactate	3	6.0

Cho/Cr and Cho/NAA values ranged from 1.3 to 4.5 and 1.4 to 4.3 units respectively. Mean Cho/Cr was 3.0±0.88 units while mean Cho/NAA was 2.8±0.77 .

Table 3. Level of metabolites

SN	Finding	No. of cases	Percentage
1.	Not done	4	8.0
2.	Adamantinomatous variant of craniopharyngioma	1	2.0
3.	Anaplastic astrocytoma	6	12.0
4.	Astrocytoma	1	2.0
5.	Astrocytoma low grade	1	2.0
6.	Craniopharyngioma	1	2.0
7.	Glioblastoma multiforme	10	20.0
8.	Glioma	1	2.0
9.	Grade III astrocytoma	2	4.0
10.	High grade PNET	1	2.0
11.	Infilterative astrocytoma	1	2.0
12.	Low grade astrocytoma	3	6.0
13.	Medulloblastoma	1	2.0
14.	Meningioma	13	26.0
15.	Metastasis	1	2.0

Table 6: Tumor Grade/Type vs ADC Count

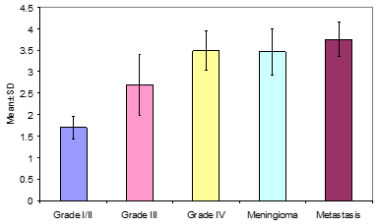
The order of ADC in different grades types was as follows:

Grade I/II > Grade III > Grade IV > Meningioma ~ Metastasis

SN	Grade/Type	No. of cases	Mean	SD	Range	
					Minimum	Maximum
1.	Grade I/II	10	1.70	0.27	1.3	2
2.	Grade III	10	2.69	0.70	2	4.5
3.	Grade IV	11	3.49	0.45	2.6	4.1
4.	Meningioma	13	3.46	0.54	2.7	4.2
5.	Metastasis	6	3.75	0.40	3.1	4.2

F=26.367; p<0.001 (ANOVA) (Significant)

Table 7: Tumor Grade/Type vs Cho/Cr



Statistically, the difference in ADC in different grades/types of intracranial tumors was significant.

Table 8: Between Grade/Type comparison of Cho/Cr levels (Tukey HSD test)

SN	Comparison	Mean Difference	SE	Significance "p"
1.	Grade I/II vs Grade III	-0.99	0.22	0.001
2.	Grade I/II vs Grade IV	-1.79	0.22	<0.001
3.	Grade I/II vs Meningioma	-1.76	0.21	<0.001
4.	Grade I/II vs Metastasis	-2.05	0.26	<0.001
5.	Grade III vs Grade IV	-0.80	0.22	0.006
6.	Grade III vs Meningioma	-0.77	0.21	0.006
7.	Grade III vs Metastasis	-1.06	0.26	0.002
8.	Grade IV vs Meningioma	0.03	0.21	1.000
9.	Grade IV vs Metastasis	-0.26	0.26	0.854
10.	Meningioma vs Metastasis	-0.29	0.25	0.773

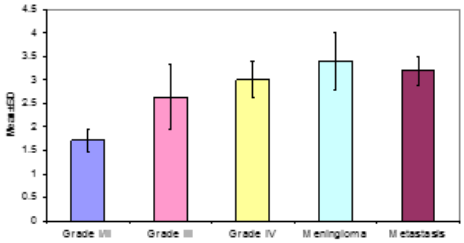
Mean difference in Cho/Cr was maximum between Grade I/II vs Metastasis (2.05±0.26) and minimum between Meningioma and Grade IV (0.03±0.21). Except for difference between Meningioma and Metastasis, Grade IV and Metastasis and Grade IV and Meningioma, all the between grade/type differences were significant statistically. The order of ADC in different grades types was as follows: **Grade I/II < Grade III < Grade IV ~ Meningioma ~ Metastasis**

Table 17: Tumor Grade/Type vs Cho/NAA

SN	Grade/Type	No. of cases	Mean	SD	Range	
					Minimum	Maximum
1.	Grade I/II	10	1.72	0.24	1.4	2.2
2.	Grade III	10	2.64	0.69	1.9	4.3
3.	Grade IV	11	3.01	0.39	2.09	3.5
4.	Meningioma	13	3.41	0.61	2.5	4.3
5.	Metastasis	6	3.20	0.31	2.9	3.8

F=18.178; p<0.001 (ANOVA) (Significant)

Table 4: Histopathological Correlation



Cho/NAA values ranged from 1.4 to 4.3 in different grades/types of tumors. Mean ADC was maximum in meningioma (3.41±0.61) and minimum in Grade I/II (1.72±0.24). Statistically, the difference in ADC in different grades/types of intracranial tumors was significant (p<0.001).

Table 18: Between Grade/Type comparison of Cho/NAA levels (Tukey HSD test)

SN	Comparison	Mean Difference	SE	Significance "p"
1.	Grade I/II vs Grade III	-0.92	0.22	0.001
2.	Grade I/II vs Grade IV	-1.29	0.22	<0.001
3.	Grade I/II vs Meningioma	-1.69	0.21	<0.001
4.	Grade I/II vs Metastasis	-1.48	0.26	<0.001
5.	Grade III vs Grade IV	-0.37	0.22	0.452
6.	Grade III vs Meningioma	-0.77	0.21	0.006
7.	Grade III vs Metastasis	-0.56	0.26	0.210
8.	Grade IV vs Meningioma	-0.40	0.20	0.306
9.	Grade IV vs Metastasis	-0.19	0.25	0.942
10.	Meningioma vs Metastasis	0.21	0.25	0.916

Mean difference in Cho/NAA was maximum between Grade I/II vs Meningioma (1.69±0.21) and minimum between Metastasis and Grade IV (0.19±0.25). Only Grade I/II had significantly lower mean Cho/NAA levels as compared to all the other types/grades. None of the other between grade/type differences were significant statistically. The order of ADC in different grades types was as follows: **Grade I/II < Grade III ~ Grade IV ~ Meningioma ~ Metastasis**

REFERENCES

1. Newton HB et al Overview of brain tumor epidemiology. In: Newton HB, Jolesz FA (eds) Handbok of Neuro-oncology Neuroimaging. Elsevier, New York, 2008 pp 3-8.
2. Mechtler L. et al Neuroimaging in Neuro-oncology. Neurol Clin; 27(1):171-201. 2009 Feb
3. Jemal A, e al Cancer statistics, 2007. CA Cancer J Clin. 2007 Jan-Feb;57(1):43-66.
4. Gerstner ER et al. Advances in neuroimaging techniques for the evaluation of tumor growth, vascular permeability, and angiogenesis in gliomas. Curr Opin Neurol. 2008 Dec; 21(6):728-35.
5. Sorensen AG et al Response criteria for glioma. Nat Clin Pract Oncol. 2008 Nov;5(11):634-44.
6. Inoue T et al Diffusion tensor imaging for preoperative evaluation of tumor grade in gliomas. Clin Neurol Neurosurg. 2005;107:174–180.
7. Sugahara T, Korogi Y, Kochi M, Ikushima I, Shigematu Y, Hirai T, Okuda T, Liang L, Ge Y, Konohara Y, Ushio Y, Takahashi M. Usefulness of diffusion-weighted MRI with echo-planar technique in theevaluation of cellularity in gliomas. J Magn Reson Imaging. 1999;9:53–60.
8. Zonari P et al Multimodal MRI in the characterization of glial neoplasms: the combined role of single-voxel MR spectroscopy, diffusion imaging and echo-planar perfusion imaging. Neuroradiology. 2007;49:795–803.
9. Goebell E et al, Low-grade and anaplastic gliomas differences in architecture evaluated with diffusiontensor MR imaging. Radiology. 2006;239:217–222.
10. Chang SM et al Chemotherapy for gliomas. Curr Opin Oncol. 1995;7:207–213.
11. Krauseneck P et al. Chemotherapy of malignant gliomas. Recent Results Cancer Res. 1994; 135:135–147.
12. Lacerda S et al, Magnetic resonance perfusion and permeability imaging in brain tumors. Neuroimaging Clin N Am. 2009 Nov;19(4):527-57.
13. Gilles FH et al, Limitations of the World Health Organization classification of childhood supratentorial astrocytic tumors. Children Brain Tumor Consortium. Cancer. 2000 Mar 15;88(6):1477-83.
14. Jackson RJ et al Limitations of stereotactic biopsy in the initial management of gliomas. Neuro Oncol. 2001 Jul;3(3):193-200.
15. Cha S et al,. Neuroimaging in neuro-oncology. Neurotherapeutics. 2009 Jul;6(3):465-77.
16. Provenzale JM et al Diffusion-weighted and perfusion MR imaging for brain tumor characterization and assessment of treatment response. Radiology. 2006 Jun;239(3): 632-49.
17. Leclerc X et al, The potential of proton magnetic resonance spectroscopy ((1)HMRS) in the diagnosis and management of patients with brain tumors. Curr Opin Oncol. 2002 May;14(3):292-8.
18. Law M et al, MR spectroscopy of brain tumors. Top Magn Reson Imaging. 2004 Oct;15(5):291-313.