MAK HILL Publications Research Journal of Medical Sciences

Research Article
doi: 10.59218/makrjms.2023.209.215

Role of MR Spectroscopy in Evaluation of Intra-Axial Brain Tumors by 3T MRI with Histopathological Correlation

[1]Pravin Arvind Lamdhade, [2]Amit Pendor and [3]Satyajeet S. Ghodake

[1]Department of Radiology, B.J. Medical College and Sassoon General Hospital, Pune

[2]Department of Radio-Diagnosis, Dr. Vaishyampayan Memorial Government Medical College Solapur, Maharashtra, India

[3]Department of Radio-Diagnosis, PCMC's Postgraduate Institute and YCM Hospital, Pimpri, Pune, Maharashtra, India

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Key Words
Intraaxial brain tumors, MR spectroscopy, glioma grading, neoplastic lesions

Corresponding Author
Satyajeet S. Ghodake,
Department of Radio-Diagnosis, PCMC's Postgraduate Institute and YCM Hospital, Pimpri, Pune, Maharashtra, India

Received: 5 June 2023
Accepted: 16 June 2023
Published: 29 June 203

Citation: Pravin Arvind Lamdhade, Amit Pendor and Satyajeet S. Ghodake, 2023. Role of MR Spectroscopy in Evaluation of Intra-Axial Brain Tumors by 3T MRI with Histopathological Correlation. Res. J. Med. Sci., 17: 209-215, doi: 10.59218/makrjms.2023.209.215

ABSTRACT

Intra-axial brain tumors refer to tumors that arise within the brain parenchyma, specifically within the cerebrum, cerebellum, or brainstem. The histopathological correlation remains the gold standard for definitive tumor diagnosis. However, MRS provides valuable functional and metabolic information that complements conventional MRI and assists in preoperative planning, tumor classification, grading and treatment response assessment. The current study is an open-ended, prospective and observational study conducted at the Department of Radiology in a tertiary care hospital. The study included a total of 30 patients were included in the study. The study subjects were selected from the patients referred to the Department of Radiology after meeting inclusion and exclusion criteria. The results indicate that for diagnosing intraaxial brain tumor, MRI with MR spectroscopy has 100% diagnostic accuracy in diagnosing Ependymoma, Medulloblastoma, Metastasis, Choroidp plexuspapilloma, Lymphoma and central neurocytoma, whereas diagnostic accuracy of 96.6% was observed in high-grade glioma. A diagnostic accuracy of 93.33% is observed in low-grade glioma and Oligodendroglioma. Accurate grading of gliomas on the basis of MRS alone may be difficult. Combining MRS with conventional and other advanced MR imaging techniques, grading becomes more precise.

INTRODUCTION

Intra-axial brain tumors are a significant health problem and present several diagnostic and treatment challenges[1]. We are witnessing a shift in imaging from merely providing anatomical information to providing information about tumor physiology[2]. Intra-axial brain tumors refer to tumors that arise within the brain parenchyma, specifically within the cerebrum, cerebellum, or brainstem. These tumors can be classified based on their histological origin and the most common types include Gliomas, Astrocytomas, Oligodendrogliomas, Ependymomas, Medulloblastomas, Brainstem gliomas, Metastatic brain tumors, Magnetic resonance spectroscopy (MRS)[3]. The histopathological correlation remains the gold standard for definitive tumor diagnosis. However, MRS provides valuable functional and metabolic information that complements conventional MRI and assists in preoperative planning, tumor classification, grading and treatment response assessment[4]. It helps in reducing the need for invasive procedures and provides additional insights into the tumor's biology. It's important to note that while MRS is a useful adjunct, it is not a standalone diagnostic tool and its interpretation should be done in conjunction with clinical and imaging findings[5].

MATERIALS AND METHODS

The current study is an open-ended, prospective and observational study conducted at the Department of Radiology in a tertiary care hospital. The study included a total of 30 patients were included in the study. The study subjects were selected from the patients referred to the Department of Radiology after meeting inclusion and exclusion criteria.

Inclusion criteria: In the current study, patients admitted to KEM hospital with a suspicion of Intra-Axialbrain tumors were included. Patients of allage groups and sex who were willing to participate in the study.

Exclusion criteria: The patients having a history of claustrophobia and having absolute orrelative contraindications for contrast-enhanced MRI examination were excluded. The patients who are unable to cooperate with the procedure, pregnant females, mentally retarded patients and patients who are given an MRI diagnosis of intra-axial brain tumor but do not undergo further evaluation were also excluded.

Aims and objectives: The aim of the current study was: To determine biochemical markers of intra-axia lbrain tumors usingMR spectroscopy.

Toevaluate the role of Mr spectros copy in diagnosing and grading of intra-axial brain tumors with histo-pathologicalco-relation.

Statistical analysis: Data was entered into a Microsoft Excel worksheet and further analysis was done using IBM SPSS Statistics 26.0 software (IBM Corp. Released 2019. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp). The Descriptive statistics, frequencies and proportions were calculated and tabulated. The sensitivity, specificity, negative predictive value, positive predictive value and diagnostic accuracy were calculated to test the validity of MRS pectros copy with respect to histopathological examination. Fisher exact test was the test of significance for categorical data. $p<0.05$ was considered as statistically significant.

RESULTS

The current study included 30 study subjects with intra axial brain tumor and the majority (20%) of the study subjects were in the age group 31-40 years, followed by the age group 0-10 years and 41-50 years. The youngest study subject was 11 months old and the oldest study subject was 75 years old. The male preponderance in intra axial brain tumors is evident. Out f 30 study subjects, 22 (73.33%) were male and 8 (26.67%) were female (Table 1).

Table 2 indicates the distribution of study subjects according to the sample characteristics. According to the location of the brain tumor, out of 30 study subjects, the majority 22 (73.33%) had intraaxial brain tumors in the supratentorial location, followed by 6 (20%) in the infratentorial and 2 (6.672%) in both locations. The majority of the study subjects (43.33%) had a hypointense signal on T2 and 60% had a heterogenous signal on T2. Out of 30 study subjects, 14 (46.67%) had looming on the gradient, out of which the most common cause was bleed (92.8%) followed by calcification within the tumor (7.14%). It is observed that most of the brain tumors 24 (80%) present with Perilesional edema. Based on the degree of contrast enhancement, 6 (20%) had mild contrast enhancement, 5 (20%) showed moderate contrast enhancement, 17 (56.66%) showed intense contrast enhancement and in 1 (3.33%) subject, contrast enhancement was absent. According to the Solid/Cystic component, 19 (63.33%) subjects showed both solid and cystic components in the form of necrosis and in 11 (36.67%) brain tumors there was nonecrotic component. According to the characteristics, in 16 (53.33%) subjects the tumor margin was well-defined whereas among 14 (46.67%) subjects it was ill-defined with no definite tumor margins.

Table 1: Distribution of study subjects according to age and gender

	Frequency	Percentage
Age (years)		
0-10	5	16.67
11-20	4	13.33
21-30	1	3.33
31-40	6	20.00
41-50	5	16.67
51-60	2	6.67
61-70	4	13.33
71-80	3	10.00
Gender		
Male	22	73.33
Female	8	26.67

Table 2: Distribution according to sample characteristics

	Frequency	Percentage
Location		
Supratentorial	22	73.33
Infratentorial	6	20.00
Both	2	6.67
Signal characteristics on T1w		
Isointense	6	20.00
Hypointense	13	43.33
Hyperintense	0	0.00
Heterointense	11	36.67
Signal characteristics on T2w		
Isointense	2	6.67
Hypointense	0	0.00
Hyperintense	10	33.33
Heterointense	18	60.00
Blooming on T2 FFE/ GRE, within the brain tumor		
Present	14	46.67
Absent	16	53.33
GRE		
Bleed	13	43.33
Calcification	1	3.33
Perilesional edema		
Present	24	80.00
Absent	6	20.00
Degree of contrast enhancement of brain tumor		
Mild	6	20.00
Moderate	5	16.67
Intense	17	56.67
Absent	1	3.33
Component of the brain tumor		
Solid/cystic	19	63.33
Solid	11	36.67
Cystic	0	0.00
Characteristics of tumor margins		
Well defined	16	53.33
Ill defined	14	46.67

On the basis of MR Spectroscopy Findings, it is evident that allbrain tumors showed increased choline peak, choline/creatinine and choline/NAA ratios. Among all cases, absent or reduced NAA, creatinine peaks and reduced NAA/creatinine ratio was observed. In 60% of cases, there is a lipid and lactate peak and in 10% of cases, a myoinositol peak was seen (Table 3).

Table 4 indicates the distribution of study subjects according to the Histopathological diagnosis and MRI Diagnosis. Out of 30 study subjects, histopathological diagnosis showed 15 (50%) cases of high-grade Glioma (Grade 3 and 4), 6 (20%) cases of low-grade Glioma (Grade 2 and 1), 1 (3.3%) case of Oligodendroglioma, 2 (6.7%) cases each of Ependymoma and Lymphoma. One (3.3%) case of each of the Medulloblastoma, Metastasis, Choroid Plexus Papilloma and Central Neurocytoma was seen. The MRI diagnosis showed

Table 3: Distribution of sample based on MR spectroscopy findings

	Frequency	Percentage
Choline		
Increased	30	100
Reduced	0	0
Naa and creat		
Increased	0	0
Reduced/absent	30	100
Lipid and lactate		
Increased	18	60
Absent	12	40
MI		
Increased	3	10
Reduced/absent	27	90
CHO/CR ratio		
Increased	30	100
Reduced	0	0
CHO/NAA ratio		
Increased	30	100
Reduced	0	0
NAA/CR ratio		
Increased	0	0
Reduced/absent	30	100

16 (53.3%) cases of high-grade Glioma (Grade 3 and 4), 4 (13.3%) cases of low-grade Glioma (Grade 2 and 1), 2 (6.7%) cases each of Oligodendroglioma, Ependymoma and Lymphoma was seen. One (3.3%) case of each of the Medulloblastoma, Metastasis, Choroid Plexus Papilloma and Central Neurocytoma was seen.

For high-grade glioma, low-grade glioma, Ependymoma, Medulloblastoma, Metastasis, CPP, Lymphoma and central neurocytoma, a significant association between MR Spectroscopy findings and Histopathological findings was seen ($p<.05$). For oligodendroglioma, no significant association between MR Spectroscopy findings and Histopathological findings was seen ($p = 0.1310$) (Table 5).

Table 6 shows the result of a diagnostic test. The results showed that for diagnosing intraaxial brain tumor, MRI with MR spectroscopy has 100% diagnostic accuracy in diagnosing Ependymoma, Medulloblastoma, Metastasis, Choroid plexus papilloma, Lymphoma and central neurocytoma. A diagnostic accuracy of 96.6% was observed in high-grade glioma. A diagnostic accuracy of 93.33% is observed in Low-grade glioma and Oligodendroglioma.

DISCUSSIONS

The current study included 30 study subjects from all age/sex groups. Brain neoplasms were most commonly found in 31-40 (n = 6) years followed by 41-50 (n = 5) and 0-10 (n = 5) years. McKinney[6] studied the incidence of brain neoplasms in all age groups and found that primary brain neoplasms occur most commonly in the 7th decade. The incidence of brain neoplasms was higher in males 73.33% (n = 22)[6]. In the current study out of 30 cases, 73.33% (n = 22) neoplasms were supratentorial, 20% (n = 6) were infratentorial and 6.67% (n = 2) were both supra and infratentorial in location. Supratentorial tumors were more common than infratentorial tumors.

Table 4: MRI diagnosis in correlation with histopathological diagnosis

	Histopathological diagnosis		MRI diagnosis	
Intra-axial brain tumor	No.	Percentage	No.	Percentage
High-Grade Glioma (Grade 3 and 4)	15	50.0	16	53.3
Low-Grade Glioma (Grade 2 and 1)	6	20.0	4	13.3
Oligodendroglioma	1	3.3	2	6.7
Ependymoma	2	6.7	2	6.7
Medulloblastoma	1	3.3	1	3.3
Metastasis	1	3.3	1	3.3
Choroid Plexus Papilloma	1	3.3	1	3.3
Lymphoma	2	6.7	2	6.7
Central Neurocytoma	1	3.3	1	3.3

Table 5: Association between MR spectroscopy findings and histopathological findings

	Histopathology			
MR spectroscopy	High-grade glioma	Others	Total	Fisher exact test
High-grade glioma	15	1	16	p<0.001**
Others	0	14	14	
	Low-grade glioma	Others	Total	
Low-grade glioma	4	0	4	p<0.001**
Others	2	24	26	
	Oligodendroglioma	Others	Total	
Oligodendro glioma	1	1	2	p = 0.1310, NS
Others	1	27	28	
	Ependymoma	Others	Total	
Ependymoma	2	0	2	p = 0.0023**
Others	0	28	28	
	Medulloblastoma	Others	Total	
Medulloblastoma	1	0	1	p = 0.033*
Others	0	29	29	
	Metastasis	Others	Total	
Metastasis	1	0	1	p = 0.033*
Others	0	29	29	
	CPP	Others	Total	
CPP	1	0	1	p = 0.023*
Others	0	29	29	
	Lymphoma	Others	Total	
Lymphoma	2	0	2	p = 0.033*
Others	0	28	28	
	Central neurocytoma	Others	Total	
Central neurocytoma	1	0	1	p = 0.033*
Others	0	29	29	

Table 6: Sensitivity, Specificity, PPV, NPV and Diagnostic Accuracy of Brain Tumor Diagnosed in MRI in Correlation with Histopathological Diagnosis

Brain tumor	Sensitivity	Specificity	PPV	NPV	Diagnostic accuracy
High-grade glioma	93.80	92.90	93.75	100	96.66
Low-grade Glioma	66.67	100	100	92.31	93.33
Oligodendro glioma	50	96.43	50	96.43	93.33
Ependymoma	100	100	100	100	100
Medullo blastoma	100	100	100	100	100
Metastasis	100	100	100	100	100
Choroid plexus papilloma	100	100	100	100	100
Lymphoma	100	100	100	100	100
Central neurocytoma	100	100	100	100	100

Low-grade gliomas (grade I and II): In the current study, 3 out of 6 cases of Low-Grade glioma had perilesional edema. The cases which did not show perilesional edema were pilocytic astrocytoma and brainstem glioma (n = 3). All Low-Grade gliomas showed Mild to moderate enhancement except juvenile pilocytic astrocytomas which showed enhancement of mural nodule. These findings are in agreement with a study conducted by Felix *et al*.[7] and Broniscer *et al*.[8]. The current study showed that all low-grade Gliomas were mildly heterogenous lesions with predominant solid components except JPA which showed a predominant cystic component.

Diffuse infiltrative astrocytoma: Diffuse infiltrative astrocytoma are grade 2 astrocytomas. The current study observed four cases of diffuse astrocytoma. Among these two were diagnosed truly on MRI however two of them were wrongly interpreted on MRI as Oligodendroglioma and GBM. Two of them were seen in the age group of 11-20 years, one was of 47 years old and one more case was a9-year-old boy(brainstem glioma). There was an increased cho/creat ratio of 2.03 (±0.42), an increased cho/NAA ratio of 1.9 (±0.34) and a reduced NAA/creat peak at 0.9 (±0.33). mL creat^{-1} ratio was higher at 0.80 (±0.25). Both cases showed no choline peak in perilesional edema outside the tumor margin. Our findings were similar to the study conducted by Broniscer *et al*.[8].

JPAs are Grade I tumors. In the current study, 2cases of JPA were observed, both cases were less than 10 years of age (5 and 7 year-old).Both of them had infratentorial solid cystic lesions with predominant cystic components and enhancing mural nodule. No

perilesional edema was seen in either case. No blooming was observed on the T2 FFE sequence. On MRSI both cases showed increased choline peak, reduced NAA, increased mI peak and reduced creat peak. There was an increased cho/creat ratio of 1.97 (±0.36), an increased cho/NAA ratio of 1.85 (±0.31) and a reduced NAA/creat peak at 1.8 (±0.30). mL creat^{-1} ratio was higher at 0.80 (±0.25).

Oligodendroglial tumors: Oligodendroglial tumors can be low-grade/grade 2 oligodendroglioma or grade 3 anaplastic oligodendroglioma based on the WHO grading system. In the current study, two cases with oligodendroglioma were observed out of which one was misdiagnosed on MRI and turned out to be a diffuse infiltrative astrocytoma. On MRSI the tumor showed increased choline peak, reduced NAA, increased lipid lactate peak and reduced creat peak. There was an increased cho/creat ratio of 2.38 (±0.42), an increased cho/NAA ratio of 1.9 (±0.34) and a reduced NAA/creat peak at 0.9 (±0.33).The results of the current study indicated a specificity of 96.43% and a sensitivity of 50%. Diagnostic accuracy was 93.3%. These findings were in agreement with the study done by Spampinato *et al*.[9].

High-grade gliomas (grade III and IV) It include Glioblastoma multiforme, Gliomatosis cerebri, anaplastic astrocytoma and gliosarcoma. Out of 15 cases of High-grade gliomas diagnosed on MRI, 9 were GBM,4were anaplastic astrocytoma and 2 were gliomatosis cerebri, 1 case was misdiagnosed as GBM on MRI which turned out to be low-grade glioma on histopathology.

Anaplastic astrocytomas are grade 3 astrocytomas. Four patients with anaplastic astrocytoma were evaluated in our study. On MRSI all the tumors showed increased choline peak, reduced NAA, reduced mI peak and reduced creat peak. There was an increased cho/creat ratio of 4.5 (±0.55), an increased cho/NAA ratio of 2.5 (±0.22) and a reduced NAA/creat peak at 0.9 (±0.33). ml creat^{-1} ratio was lower at 0.33 (±0.15). Two of the cases showed increased choline peak with raised cho/creat ratio in perilesional edema probably due to tumoral infiltration. These results were similar to the study done by Magalhaes *et al*.[10] and Castillo *et al*.[11]

GBM are grade 4 astrocytomas. 9 patients with Glioblastoma multiformae were evaluated in our study. All GBM cases were found in adults between the 3rd to 8th decades. One case of GBM did not correlate with histopathology. It was diagnosed as GBM on MRI which turned out to be a Diffuse astrocytoma on histopathology. On conventional MR sequences, all cases were heterogeneously hypointense on T1W and heterogeneously hyperintense on T2W imaging. Blooming was a prominent feature observed in almost all cases.

On MRSI all tumors showed increased choline peak, reduced NAA, reduced mL peak at 3.6 ppm and reduced creat. There was an increased cho/creat ratio of 6.5 (±0.55), an increased cho/NAA ratio of 3.5 (±0.22) and a reduced NAA/creat peak at 0.8 (±0.33). mL creat^{-1} ratio was lower at 0.15 (±0.15). All the cases showed increased choline peak with raised cho/creat ratio in perilesional edema probably due to tumoral infiltration.

Gliomatosis cerebri is a grade 3 tumor. We had two patients with gliomatosis cerebri, they were in 4th and 6th decade. On conventional MR sequences, the lesions were T1 hypointense and T2 hyperintense. On MRSI both the tumors showed increased choline peak, reduced NAA, increased mL peak and reduced creat peak. There was an increased cho/creat ratio of 4.5 (±0.55), an increased cho/NAA ratio of 2.5 (±0.22) and a reduced NAA/creat ratio of 0.9 (±0.33). mL creat^{-1} ratio was higher at 0.80 (±0.25). The results indicate a diagnostic accuracy of 100% with a significant association between MR Spectroscopy findings and Histopathological findings for Gliomatosis Cerebri. Our study is in agreement with previous studies done by Mohana-Borges *et al*.[12], Galanaud *et al*.[13] and Peretti-Viton *et al*.[14].

Ependymoma has been graded as grade 2. We had two patients with ependymoma and both patients belonged tothe pediatric age group (<10 years). On conventional MR, the lesions showed heterogeneously hypointense on T1 and heterogeneously hyperintense on T2. The lesion was well-defined with intense post-contrast enhancement on T1 FFE. One of the cases was showing blooming on T2 FFE s/o calcification which was a plastic tumor that extends along the foramen of luschka and the foramen of megendie.

On MRSI both the tumors showed increased choline peak, absent NAA, reduced mI peak and reduced creat peak. There was mI peak noted in one of the tumors. There was an increased cho/creat ratio of 2.03 (±0.42), an increased cho/NAA ratio of 1.9 (±0.34) and a reduced NAA/creat peak at 0.9 (±0.33). And one of the lesions showed increased mL creat^{-1} of 0.82+/-0.25. A diagnostic accuracy of 100%, specificity of 100% and sensitivity of 100% were observed. Our study shows similar results obtained in a study done by Fouladi *et al*.[15].

Medulloblastoma has been graded as a grade 4 brain tumor by WHO. We had one patient (8-year-olds) with medulloblastoma. On conventional MR, the lesions appeared isointense to grey matter on both T1 and T2. They were well-defined and showed intense contrast enhancement on T1 FFE. No blooming on T2 FFE. On MRSI, the tumor showed an increased choline peak, an increased lipid lactate peak, reduced NAA and a reduced creat peak. There was an increased

cho/creat ratioof 4.5 (±0.55), an increased cho/NAA ratio of 2.5 (±0.22) and a reduced NAA/creat ratio of 0.9 (±0.33).

We got diagnostic accuracy of 100% and a significant association between MR Spectroscopy findings and Histopathological findings for Medulloblastoma with p = 0.033 (p<0.05 being significant). Our study is in agreement with the study done by Koeller *et al*.[16].

Metastasis was seen in one case (65 years old). On conventional MR, Multiple heterogeneous to hypointense on T1 and heterogenously hyperintense on T2, with perilesional edema. On MRSI, Strong Cho peak at long TE without elevation in surrounding peritumoral edema. Reduced NAA and creatinine. Increased lipid/lac peak in one of the tumors. There was an increased cho/creat ratio of 6.5 (±0.55), an increased cho/NAA ratio of 3.5 (±0.22) and a reduced NAA/creat peak at 0.8 (±0.33). cho/creat ratio was not elevated in peritumoral edema. The diagnostic accuracy of 100% was observed along with a significant association between MR Spectroscopy findings and Histopathological findings for Metastasis with p = 0.033 (p<0.05). These findings were is in agreement with the study done by Law *et al*.[17].

Choroid plexus papilloma is a grade 1 intra-axial brain tumor. In the current study, one case of choroid plexus papilloma was observed (a 2-year-old child). On MRSI, there was increased choline, an increased lactate peak, reduced NAA and a reduced creat peak was seen.An increased cho/creat ratio of 2.03, increased cho/NAA ratio of 1.93 and reduced NAA/creat ratio of 0.8 were also observed. The diagnostic accuracy was 100% and a significant association between MR Spectroscopy findings and Histopathological findings with p = 0.033 (p<0.05) was seen. Our findings are in agreement with the study done by Sarkar *et al*.[18].

In the current study, two patients (40 and 55 years old) with lymphoma were seen. On conventional MR, T2/FLAIR mildly hpyointense lesions were seen involving the left parietal and adjacent occipital and posterior temporal lobes including the hippocampus, posterior body and splenium of the corpus callosum with corresponding diffusion restriction. On MRSI elevated choline and lipid lactate peaks, reduced NAA and creat peaks were observed. An increased cho/creat ratio of 2.04 and cho/NAA ratio of 2.2 and a reduced NAA/creat ratio of 1.4. The results of the current study are similar to the results obtained in the study by Koeller *et al*.[19]. A diagnostic accuracy of 100% with a significant association between MR Spectroscopy findings and Histopathological findings for Lymphoma p = 0.0023 (p<0.05) was observed.

CONCLUSION

Accurate grading of gliomas on the basis of MRS alone may be difficult. Combining MRS with conventional and other advanced MR imaging techniques, grading becomes more accurate. Some features of tumors on conventional MRI (contrast enhancement, surrounding edema, signal heterogeneity, necrosis, hemorrhage and midline crossing) suggest a high grade. MRS is complementary and helpful for glioma grading. High-grade gliomas demonstrate marked elevation of Cho, decreased NAA and presence of Lac and Lip. Myo-inositol is high in low-grade gliomas and decreases with increasing grades of tumors. The results of the current study conclude that in vivo MR spectroscopy can be used as a reliable method for glioma grading. It is useful in discrimination between WHO grade I, II vs grade III, IV astrocytomas as well as other intraaxial brain tumors such as gliomatosis cerebri, ependymoma, medulloblastoma, oligodendroglioma, lymphoma, metastasis and choroid plexus papilloma. Our study also demonstrates that spectroscopic MR measurements in the peritumoral region can be used to demonstrate differences in solitary metastases and high-grade gliomas and also the peritumoral infiltrative nature of certain intraaxial brain tumors.

REFERENCES

1. Abdolmohammadi, J., M. Shafiee, F. Faeghi, D. Arefan and A. Zali *et al*., 2016. Determination of intra-axial brain tumors cellularity through the analysis of T2 relaxation time of brain tumors before surgery using MATLAB software. Electron. Physician, 8: 2726-2732.
2. Huisman, T.A.G.M., 2009. Tumor-like lesions of the brain. Cancer Imaging, 9: S10-S13.
3. Lapointe, S., A. Perry and N.A. Butowski, 2018. Primary brain tumours in adults. Lancet, 392: 432-446.
4. Press, R.H., J. Zhong, S.S. Gurbani, B.D. Weinberg, B.R. Eaton, H. Shim and H.K.G. Shu, 2018. The role of standard and advanced imaging for the management of brain malignancies from a radiation oncology standpoint. Neurosurgery, 85: 165-179.
5. Carrete, L.R., J.S. Young and S. Cha, 2022. Advanced imaging techniques for newly diagnosed and recurrent gliomas. Front. Neurosci., Vol. 16. 10.3389/fnins.2022.787755.
6. McKinney, P.A., 2004. Brain tumours: Incidence, survival and aetiology. J. Neurol., Neurosurg. Psychiatry, 75: ii12-ii17.

7. Felix, R., W. Schörner, M. Laniado, H.P. Niendorf, C. Claussen, W. Fiegler and U. Speck, 1985. Brain tumors: MR imaging with gadolinium-DTPA.. Radiology, 156: 681-688.
8. Broniscer, A., A. Gajjar, R. Bhargava, J.W. Langston and R. Heideman *et al*., 1997. Brain stem involvement in children with neurofibromatosis type 1: Role of magnetic resonance imaging and spectroscopy in the distinction from diffuse pontine glioma. Neurosurgery, 40: 331-338.
9. Spampinato, M.V., J.K. Smith, L. Kwock, M. Ewend, J.D. Grimme, D.L.A. Camacho and M. Castillo, 2007. Cerebral blood volume measurements and proton MR spectroscopy in grading of oligodendroglial tumors. Am. J. Roentgenol., 188: 204-212.
10. Magalhaes, A., W. Godfrey, Y. Shen, J. Hu and W. Smith, 2005. Proton magnetic resonance spectroscopy of brain tumors correlated with pathology[1]. Acad. Radiol., 12: 51-57.
11. Castillo, M., J.K. Smith and L. Kwock, 2000. Correlation of myo-inositol levels and grading of cerebral astrocytomas. AJNR Am. J. Neuroradiol., 21: 1645-1649.
12. Mohana-Borges, A.V.R., S.G. Imbesi, R. Dietrich, J. Alksne and D.K. Amjadi, 2004. Role of proton magnetic resonance spectroscopy in the diagnosis of gliomatosis cerebri: A unique pattern of normal choline but elevated Myo-inositol metabolite levels J. Comput. Assisted Tomogr., 28: 103-105.
13. Galanaud, D., O. Chinot, F. Nicoli, S. Confort-Gouny and Y.L. Fur *et al*., 2003. Use of proton magnetic resonance spectroscopy of the brain to differentiate gliomatosis cerebri from low-grade glioma. J. Neurosurg., 98: 269-276.
14. Peretti-Viton, P., H. Brunel, O. Chinot, C. Daniel and M. Barrié *et al*., 2002. Histological and MR correlations in Gliomatosis cerebri. J. Neuro-Oncol., 59: 249-259.
15. Fouladi, M., K. Helton, J. Dalton, E. Gilger and A. Gajjar *et al*., 2003. Clear cell ependymoma: A clinicopathologic and radiographic analysis of 10 patients. Cancer, 98: 2232-2244.
16. Koeller, K.K. and E.J. Rushing, 2003. From the archives of the AFIP: medulloblastoma: A comprehensive review with radiologic-pathologic correlation. Radiographics, 23: 1613-1637.
17. Law, M., S. Cha, E.A. Knopp, G. Johnson, J. Arnett and A.W. Litt, 2002. High-grade gliomas and solitary metastases: Differentiation by using perfusion and proton spectroscopic MR imaging. Radiology, 222: 715-721.
18. Sarkar, C., M.C. Sharma, S. Gaikwad, C. Sharma and V.P. Singh, 1999. Choroid plexus papilloma: A clinicopathological study of 23 cases. Surg. Neurol., 52: 37-39.
19. Koeller, K.K., J.G. Smirniotopoulos and R.V. Jones, 1997. Primary central nervous system lymphoma: Radiologic-pathologic correlation.. Radiographics, 17: 1497-1526.