THE ROLE OF MULTIPARAMETRIC MR IMAGING IN DIFFERENTIATION OF BRAIN TUMORS

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ABSTRACT

Aim: The aim of our study is to assess the role of multiparametric MR imaging in differentiation of brain tumors.

Methods: This was a cross sectional, descriptive study which was conducted between August 2020 to September 2022 at Dr. D. Y. Patil Medical College and Hospital and Research Centre, Pimpri, Pune. Institutional scientific and Ethics committee clearance for conducting the study was obtained prior to starting the study.50 patients, who were meeting the inclusion criteria of the study, were included in the study. A written and informed consent was taken from all the patients.

Results: It was seen that in the present study, 56 % of the patients were males whereas 44 % were females. It was observed that headache was the presenting complaint in about 60 % of the patients and it was the common presenting symptom. Vomiting and seizures were the other common presenting symptoms accounting for 26% each. Giddiness was noted in 18% of the patients, whereas hemiparesis was seen in 14 % of the patients. It was observed that meningioma was the most common diagnosis accounting for about 20 % of the total cases, followed by astrocytoma which accounted for 18 % of the total cases. The other diagnosis observed were low grade glioma, glioblastoma multiforme observed in 12 % patients each.

Conclusion: Various newer advanced functional MR imaging sequences such as perfusion imaging and tensor imaging provide crucial additional information in the imaging of brain tumors. Conventional sequences help in diagnosing tumors and giving necessary information regarding appearance, however they have certain limitations for which newer advanced MR imaging techniques such as Diffusion weighted imaging (DWI) along with ADC ratios has opened up the possibilities to study tumoral and peritumoral tissue characteristics based on water diffusion findings, and providing clinicians a whole new approach towards better management of brain tumors and differentiation of low grade tumors from high grade tumors.

Keywords: Diffusion MRI, Perfusion MRI, MR Spectroscopy, Multiparametric MRI, Neuroimaging

INTRODUCTION

A brain tumor is an intracranial mass or growth which is caused due to unrestricted proliferation of cells which are normally seen in the brain such as glial cells, neurons, blood vessels, lymphatic tissue, pineal and pituitary gland or occur as a result of spread from primary cancers of other organs of the body which accounts for around 1.4% of all cancer cases annually. Most brain tumors diagnosed are metastatic. The lifetime risk in development of a brain tumor is 0.65% and 0.5% in men and women respectively. [1]. Brain tumors show peak incidence in ages between 65 and 79 years.

Focal neurological symptoms of various brain tumors depend on the involved lobe /region [2]. Personality and gait disturbances, expressive aphasia, hemiparesis, seizures are the common symptoms in patients with frontal lobe, symptoms such as receptive aphasia, hemianopia, and spatial disorientation are encountered in parietal lobe involvement. In patients in which temporal lobe is involved, incomprehension inabilities, symptoms of autism, memory loss, quadrantanopia are the most common symptoms, whereas in occipital involvement hemianopia is the most common symptom.

MRI is the most commonly used radiological modality for evaluation. Final diagnosis of brain tumor depends on various imaging modalities followed by histopathological confirmation. In recent times , evolution of physiology based sequences in MR imaging such as permeability imaging techniques and perfusion imaging techniques, diffusion tensor imaging and diffusion weighted imaging are proving to be extremely useful in the characterization of brain tumors and they have benefitted in the advent of many cutting-edge techniques, along with the including previously used MR imaging techniques .MR sequences such as T1, T2, MR spectroscopy, and DCE sequences are collectively part of a multiparametric imaging investigation of the brain which can be used to provide detailed characterization of the brain tumors [3]

Various physiology-based MR imaging techniques have helped in quantification of dynamic physiologic processes in the brain. Imaging biomarkers are measured as index variables and the various neuroimaging biomarkers can be used, such as water mobility, biochemical composition, cerebral blood flow (CBF) and cellularity. A primary objective of utilizing biomarkers is the capability to distinguish between abnormal and healthy biological processes [4]. Conventional MR sequences and the newer advanced imaging sequences have been a great boon to the field of diagnosis and characterization of brain tumors, and providing details about grades of the tumors wherever possible.

The two main techniques used in dynamic susceptibility contrast-enhanced (DSC) - MR imaging include

1. Steady-state dynamic contrast-enhanced (DCE) T1-weighted imaging and;
2. Perfusion DSC-MR imaging, that includes T2-weighted sequence of imaging [1]

This final method is selectively sensitive to changes in paramagnestism in the changes between magnetic susceptibility of the vessels and its surrounding tissue. Our study intents to assess helpfulness of conventional MR imaging protocols and newer advanced imaging sequences such as the perfusion imaging studies, ADC ratios and tensor imaging, which are beneficial and can offer added information in evaluation of brain tumors and can be linked with tumor cellularity and invasiveness. Thus, aim of our study was to assess the role of multiparametric MR imaging in differentiation of brain tumors.

MATERIALS & METHODS

This was a cross sectional, descriptive study which was conducted between August 2020 to September 2022 at Dr. D. Y. Patil Medical College and Hospital and Research Centre, Pimpri, Pune. Institutional scientific and Ethics committee clearance for conducting the study was obtained prior to starting the study.50 patients, who were meeting the inclusion criteria of the study, were included in the study. A written and informed consent was taken from all the patients.

INCLUSION CRITERIA

- All patients with brain tumor undergoing MRI study.

EXCLUSION CRITERIA

- Patients already operated for brain tumor
- Patients with deranged Renal Function test.
- Patients who are currently pregnant.
- Patients with a history of claustrophobia.
- Patient having cochlear implant, metallic foreign body.
- Patient with non compatibile MRI orthopaedic implant.

MRI SCAN TECHNIQUE

- Patient positioning: - Patient was positioned with head facing towards the magnet in a supine position. The patient is asked not to move during the study.
- Head positioned in head coil and immobilized with cushion. Laser beam localizer centered over glabella.
- Planes used: - Axial, Coronal and Sagittal.
- Sequences Used: -
  - T1 Weighted Imaging (T1WI).
  - T2 Weighted Imaging (T2WI).
  - Fluid attenuation Inversion Recovery (FLAIR).
  - Diffusion weighted Imaging.
  - Susceptibility weighted Imaging.
  - Mr spectroscopy
  - Post contrast T1 weighted Imaging.
  - MR Perfusion with DSC and DSE Imaging.
  - Diffusion tensor imaging.

Imaging was done on Siemens Magnetom Vida Magnetic Resonance Imaging 3 Tesla Machine using dedicated brain coils. **T1WI**: T1 weighted image (also referred to as T1WI or "spin-lattice" relaxation time) is one of the basic pulse sequences in MRI and it is based on the principle which demonstrates differences in the T1 relaxation times of tissues. (TR/TE ¼ 2,000/9 ms, flip angle 150, FOV ¼ 230 X 150 mm, slice/gap ¼ 4/1 mm, number of excitations ¼ 1, matrix ¼ 320 x 270)

- **T2 FLAIR** IN AXIAL, CORONAL and SAGITTAL: T2 weighted image (also referred to as T2WI "T2 weighted image") is another one of the basic pulse sequences which weighting highlights differences in the T2 relaxation time of tissues. (TR/TE ¼ 5,000/150 ms, flip angle 150, FOV ¼ 230 x 150 mm, slice/gap ¼ 4/1 mm, number of excitations ¼ 1, matrix ¼ 512 x 432 for T2WI) and (TR/TE ¼ 9,000/87 ms, flip angle 150, FOV ¼ 230 x 150 mm, slice/gap ¼ 4/1 mm, number of excitations ¼ 1, matrix ¼ 512 x 432 for FLAIR)

- **Diffusion MRI**: DWI was done in axial plane using b values of 0 and 1000 s/mm^2 (TR/TE ¼ 5,000/150 ms, flip angle 150, FOV ¼ 230 X 150 mm, slice/gap ¼ 4/1 mm, number of excitations ¼ 1, matrix ¼ 512 x 432, slice number ¼ 30).
- **Perfusion MRI**: Gadolinium (Multi- Hence) was administered and during the first pass of a bolus of contrast, DSC perfusion imaging was done using a 3D Principles of Echo Shifting and it was taken in 60 phases with effective TR/TE ¼ 1840/30 ms, matrix ¼ 128 x128.
- **MR Spectroscopy**: After administration of gadolinium contrast, multi-voxel chemical shift imaging was done. For mutlivoxel TE value of 135 ms was used. For all acquisitions during MR spectroscopy, the volume of interest was manually placed on co-registered axial FLAIR images or contrast-enhanced axial T1-weighted images. For single- voxel MRS, the VOI was adapted to the size and extent of the lesion, with TE value of 35 ms.
- **Diffusion tensor imaging**- Diffusion tensor imaging was done in 20 directions with color coded FA maps which depicted about information about the anatomy and orientation of fibers.
- **Planes Used**: Axial, Sagittal and Coronal Planes.
- **Slice Thickness**: 4 mm

RESULTS

Table 1: Sex & age wise distribution of cases in study group

Sex	**Male**		**Female**	
	28 (56%)		22 (44%)	
Age (in years)	0-15	16-30	31-50	>50
	3 6%	8 16%	22 34%	17 44%

It was seen that in the present study, 56 % of the patients were males whereas 44 % were females, showing male predominance male to female ratio of 1.28: 1.

Table 2: Symptoms wise distribution of cases in study group

Symptoms	**No. of patients**	**Percentage**
Headache	30	60%
Vomiting	13	26%
Seizures	13	26%
Giddiness	9	18%
Hemiparesis	7	14%
Loss of consciousness	3	6%
Slurring of speech	3	6%
Blurring of vison	3	6%
Imbalance	2	4%

It was observed that headache was the presenting complaint in about 60 % of the patients and it was the common presenting symptom. Vomiting and seizures were the other common presenting symptoms accounting for 26% each. Giddiness was noted in 18% of the patients, whereas hemiparesis was seen in 14 % of the patients.

Table 3: Tumor composition & Location wise distribution of cases in study group

Composition	Solid	Solid-cystic
	27 54%	23 46%
Location	Intra-axial	Extra-axial
	36 72%	14 28%

It was observed that in 54% of the patients, tumors were solid in composition, whereas in 44% of the patients, tumors showed mixed solid cystic composition. In the present study, it was seen that 72 % of the tumors were intra-axial in location, whereas only 28 % of the tumors were extra-axial in location**.**

Table 4: Diagnosis wise distribution of cases in study group

Tumors	**Number (n=50)**	**Percentage**
Meningioma	10	20%
Astrocytoma	9	18%
Low grade glioma	6	12%
Glioblastoma multiforme	6	12%
High grade glioma	5	10%
Oligodendroglioma	4	8%
Pituitary macroadenoma	2	4%
Schwannoma	2	4%
Medulloblastoma	2	4%
CNS lymphoma	2	4%
Metastases	2	4%

It was observed that meningioma was the most common diagnosis accounting for about 20 % of the total cases, followed by astrocytoma which accounted for 18 % of the total cases. The other diagnosis observed were low grade glioma, glioblastoma multiforme observed in 12 % patients each. Other observed diagnosis was high grade gliomas (10%), followed by oligodendroglioma in 8 % of the patients.

Table 5: Signal wise distribution of cases in study group

Signal on T1	Hypointense	Isointense	Hyperintense
	43 86%	5 10%	2 4%
Signal on T2	Isointense	Heterogeneously hyperintense	Hyperintense
	3 6%	25 50%	22 44%
Signal on FLAIR	Hypointense	Isointense	Hyperintense
	4 8%	2 4%	44 88%
Signal on SWI	Blooming present		Blooming absent
	29		21

	58%	42%

In the present study, it was seen that on T1 weighted imaging, there were 86% of the total cases showing hypointense signal, whereas about 10 % showed isointense signal and only 4 % cases showed hyperintense signal. It was observed that 50% of the total cases showed heterogeneously hyperintense signal on T2 weighted imaging, whereas 46 % cases showed hyperintense signal on T2. T2 Isointense signal was noted in 6% of the total cases. It was observed that hyperintense signal on FLAIR was seen in 88% of the cases , while only 8 % cases showed hypointense signal and 4 % showed isointense signal on FLAIR respectively. It was noted that 58% of the cases showed on blooming on SWI whereas 42 % of the cases showed no blooming on SWI in the present study.

Table 6: Signal on Phase wise distribution of cases in study group

Signal on Phase	**Number (n=29)**	**Percentage**
Low signal on Mag with low signal on Phase	5	17%
Low signal on Mag with high signal on Phase	22	76%
Low signal on Mag with mixed signal on Phase	2	7%

In the present study, 76 % of the cases showed low signal on Mag with high signal on Phase images which indicated presence of hemorrhage, whereas 17% showed low signal on Mag with low signal on Phase which suggested calcifications.7% cases showed both mixed signal on phase which indicated presence of both calcifications as well as hemorrhagic foci.

Table 7: Tumors showing Diffusion restriction on DWI with corresponding low ADC values wise distribution, MR Spectroscopy metabolites in cases and DTI findings wise distribution of cases in study group

Diffusion restriction	**Number (n=50)**	**Percentage**
Diffusion Restriction present	20	40%
No diffusion restriction	30	60%
Metabolites	**Increase**	**Decrease**
NAA	0	42
Choline	42	0
NAA/Cr	6	36
Chol/Cr	42	0
DTI findings	**Number (n=40)**	**Percentage**
Displacement only	24	60%
Displacement and destruction	14	35%
Infiltration	2	5%

It was observed that there was evidence of diffusion restriction on DWI with corresponding low ADC values in 40 % of the cases, whereas 60 % of the cases showed no diffusion restriction. In our study, multivoxel spectroscopy showed interpretable results in 42 cases. It was observed that there was decrease in NAA values and increase in Choline values. In our study, 40 patients had analyzable diffusion tensor imaging results. It was observed that 60% of cases showed displacement of tracts, whereas 35% showed displacement and destruction of tracts.5% of cases showed infiltration of tracts.

DISCUSSION

Magnetic resonance imaging is the gold standard modality of choice in diagnosing and classifying brain neoplasms. However, the virtue of complex delineation and specification is a limitation that is met with conventional MRI, as in scenarios of discrimination of glioblastoma from solitary metastases, CNS lymphoma or other grades of glioma. Initial and proper differentiation of such tumors is crucial in terms of accuracy as the prognosis and management of them depends on these variables to a considerable extent. With the above limitation in mind, functional MRI techniques are considered beneficial in order overcome this issue.

We performed our study on 50 patients, out of which 28 were male (56%) and 22 were female (44%). It was seen that in our study, there was male predominance with 56% of patients being male. Male to female ratio was observed to be 1.28:1. A near similar study population was seen in studies by Malik et al[5], Fink et al[6] and Meng et al.[7]

In our study that involved 50 patients, it was observed that age group of 31-50 years had maximum number of patients (22), that constituted to 44 % followed by the age group of 50 years and above, constituting to 34%. Age groups 16 to 30 years and less than 15 years comprised of 8(16%) and 3(6%) patients respectively. These findings were comparable to study done by Fink et al[6] and Weber et al.[8]

The common presenting complaint observed in our study were headache, vomiting and seizures seen in 30 (60%), 13(26%) and 13 (26 %) patients respectively followed by giddiness, hemiparesis seen in 9(18%), and 7 (14%) patients respectively. This has been reported in number of studies like Chandana et al[9], Goffaux et al[10], Purdy RA et al[11], Pfund Z et al.[12] The most common histological tumor type observed in our study were the tumors of neuroepithileal origin which constituted about 60 % of the total tumors, which included 11(22%) patients of gliomas out of which 6(12%) were low grade gliomas and 5(10%) were high grade gliomas, then followed by 9 (18%) patients of astrocytoma and 6(12%) patients of glioblastoma multiforme. The other histologic tumor type was tumors of meningeal tumors such as meningioma which accounted for 10 (20 %) patients. The other tumors which were noted included embryonal tumors such as medulloblastoma (4%), tumors originating from cranial nerves such as schwannoma (4%). Similar findings were noted in studies done by Ng S et al[13] and Zouaoui S et al.[14] In our study, there were 36 (72%) cases of intra-axially located tumors whereas 14(28%) were extra-axial in location.

Meningioma-related MRI signal intensities are typically defined as T1 isointensity to mild hypointensity compared to grey matter, T2 isointensity to slight hyper intensity relative to grey matter on the T2 sequence, and avid homogenous enhancement on post contrast scans. The majority of the meningioma cases in our study had a similar pattern on standard MRI sequences. Homogenous post contrast enhancement was noted in 9(90%) of cases on meningioma in our study. In our study, blooming was noted in susceptibility weighted imaging in 29 (58%) cases. Further signal characterization of these cases who showed blooming on SWI was done using Magnitude and phase images, which showed there was evidence of intratumoral hemorrhage in 22 (76%) of our cases, whereas 5 (17%) cases showed calcifications. There were both hemorrhagic foci along with calcifications in 2(7%) cases in our study. Phase images played a very significant role in differentiation of hemorrhagic foci and calcifications. There are previous studies conducted by Berberat J et al[15] which has proved efficacy of phase images for differentiation of hemorrhagic foci and calcifications. There was evidence of hemorrhagic foci in 5 out of 6 cases of Glioblastoma multiforme in our study. There were comparable findings in previously conducted studies by Deistung A et al.[16]

In our study, there was significant hyperperfusion on perfusion imaging in 44% of cases, whereas 26% showed mild hyperperfusion. There was hypoperfusion in 18% of cases in our study group. On further DSC perfusion imaging relative cerebral blood volume of various tumors were quantitatively analyzed. In our study it was observed that low grade glial tumors showed a mean rCBV value of 1.23± 0.35, whereas high grade glial tumors showed a mean rCBV value of 3.27±0.67. There were comparable findings in previously conducted studies by Cho SK, et al.[17]

In our study, it was observed that there was evidence of diffusion restriction on DWI with corresponding low ADC values in 40 % of the cases, whereas 60 % of the cases showed no diffusion restriction. In our study, multivoxel spectroscopy showed interpretable results in 42 cases. It was observed that there was decrease in NAA values and increase in Choline values which helps in confirming diagnosis of neoplasms rather than neoplastic lesions. Similar findings were noted in previously conducted study by Hourani R et al.[18]

In our study, Chol/Cr ratio showed a mean value of 3.94 ± 2.25 in low grade gliomas whereas, Chol/Cr ratio showed a mean value of 2.45±0.96 in high grade gliomas. Comparable findings were noted in previously conducted studies by Zeng Q et al.[19] Diffusion tensor imaging was interpretable in 40 cases of our study due to certain technical limitations. The findings of DTI observed in our study showed that out of total 40 analyzable cases, that 24 (60%) of cases showed displacement of tracts, whereas 14(35%) showed displacement and destruction of tracts. There were 2(5%) of cases which showed infiltration of the adjacent tracts. These findings were comparable with study done by Witwer BP et al.[20]

CONCLUSION

Multiparameteric imaging plays a key role in imaging of brain tumors with regards to diagnosis and grading of tumors. Various newer advanced functional MR imaging sequences such as perfusion imaging and tensor imaging provide crucial additional information in the imaging of brain tumors. Conventional sequences help in diagnosing tumors and giving necessary information regarding appearance, however they have certain limitations for which newer advanced MR imaging techniques such as Diffusion weighted imaging (DWI) along with ADC ratios has opened up the possibilities to study tumoral and peritumoral tissue characteristics based on water diffusion findings, and providing clinicians a whole new approach towards better management of brain tumors and differentiation of low grade tumors from high grade tumors. SWI has proved to be a great boon in providing information regarding intratumoral hemorrhage and calcifications in various brain tumors.MR spectroscopy helps in differentiation between etiologies of infection and neoplasm and in certain cases, the grading of tumors. DTI aids in providing knowledge about tumor in relation to the white matter tracts in terms of displacement, disruption and infiltration. Hence, radiodiagnostic approach towards diagnosis and assessment of prognosis of brain tumors become more holistic with the use of newer MR imaging techniques in addendum to the conventional MR imaging.

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