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Radiology

DIFFUSION AND PERFUSION WEIGHTED MR IMAGING IN EVALUATION AND CHARACTERIZATION OF BRAIN TUMOURS

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ABSTRACT DWI and PWI give sufficient non-invasive functional and structural information at the cellular level, emphasising features of the underlying brain pathophysiology. Radiological evaluation of brain tumours done with DWI and PWI parameters using ADC and rCBV values in intra tumoral and peri tumoral region of different brain tumours. Histopathological data was collected and taken as a standard reference for correlation with the diffusion and perfusion parameters of brain tumours. 73 lesions are primary and 17 lesions are secondary out of 90 cases which were diagnosed histo-pathologically. Majority of the high-grade tumours show high relative cerebral blood volume value compared to lower grade tumours and lower ADC values in high grade tumours which is in strong correlation with the HPE analysis. So with DWI and PWI parameters we can conclude on the fact that these imaging techniques are strong and efficient imaging tools to evaluate and characterize brain tumours.

KEYWORDS : HPE= Histopathological Examination ,ROI= Regions of interest, HGG= High grade glioma, LGG= Low grade glioma, HGM = High grade meningioma, LGM= Low grade meningioma

INTRODUCTION:

Magnetic Resonance Imaging (MRI) has evolved into the most essential non-invasive diagnostic technique for brain tumour diagnosis, presurgical planning, and treatment outcome. Apart from its ability to provide high-resolution images, it is also possible to directly obtain information at molecular level. Despite its outstanding soft tissue imagery and wide range of imaging sequences, conventional MRI has limits when it comes to specific tumour features including infiltration and grading . The failure to detect infiltrating cells beyond the tumoral margin and precisely describe the tumour grading impedes surgical resection and post-surgical treatment.

DWI and PWI give sufficient non-invasive functional and structural information at the cellular level, emphasising features of the underlying brain pathophysiology.

Diffusion Weighted Imaging (DWI)captures images by utilising the Brownian motion of molecules. Water molecule diffusion ability varies by tissue and can be altered under certain pathological situations .

DWI allows for the evaluation of this tissue-related parameter, and the apparent diffusion coefficient (ADC) computation gives important diagnostic hints for evaluating intracranial lesions.

Perfusion Weighted Imaging (PWI) is linked to the biological aggressiveness of brain tumours, such as neo angiogenesis, which is essential for tumour growth. Perfusion Weighted MR imaging can detect these vascular abnormalities as well as variations in blood flow and volume . The most prevalent perfusion measures are cerebral blood volume (CBV), which reflects the quantity of blood present in a given amount of tissue at a particular time and is increased in tumours due to neoangiogenesis.

AIMS AND OBJECTIVES:

1. To provide significant non-invasive structural and functional information of brain tumours at cellular level.

2. To evaluate and characterize primary brain tumours by performing diffusion weighted and perfusion weighted MR Imaging

Subjects and Methods:

Subjects: Hospital based prospective study with due approval of the Institutional Ethical Committee conducted in Department of Radiodiagnosis, Gauhati Medical College & Hospital. The patients will be those who have already diagnosed brain tumours by all available modalities. 100 number of patients considered in the study population which were adult male, adult female and paediatric age group patients with presumptive diagnosis of intracranial space occupying lesion. Patient who had not undergone biopsy or whose HPE report was not available on follow up after MR evaluation were excluded from the study. So total of 90 patients were taken into data analysis as 10 patients did not have the HPE analysis of brain tumours or could not collect HPE report on follow up.

Imaging Protocol:

MR imaging was performed during a single session in all patients by using a superconducting 3 Tesla scanner (MAGNETOM SKYRA) with a maximum gradient strength of 45 mT/m @ 200 T/m/s. It has a bore size of 70 cm. 20 channels head matrix coil was used.

All patients underwent standard MR imaging with the following sequences as non-enhanced axial T1-weighted spin-echo (TR/TE, 400/8.4), axial fluid-attenuated inversion recovery (FLAIR) (TR/TE/TI, 8000/95/2300) and T2-weighted (3500/90) images. Images were obtained in the three spatial planes with slice thickness of 4 to 5 mm with 1.2-1.5 mm gap. SWI sequence also done in all the cases with T2* weighted gradient-echo (GE) sequences (TR/TE,48/40). Axial contrast-enhanced T1WI were acquired in three orthogonal directions after intravenous administration of 0.1 mmol/kg of gadolinium contrast with gadobutrol. Contrast administration is accompanied by concurrent acquisition of perfusion sequences.

Before the administration of contrast material, all patients were studied with axial DWI by using SE EPI sequences (TR/TE 3550/61ms; FOV 32 cm; matrix 160×160; slice thickness 5 mm; gap 1.5 mm; b value 0 and 800-1000 mm2/s).

In perfusion study, we opted for dynamic susceptibility contrast MRI (DSC MRI). PWI was performed with T2-weighted single-shot EPI GRE sequences (TR/TE 1,790/30 ms, FA 60), matrix 128x128 (slice thickness 5mm and interslice distance 1.5mm) acquired during the first pass of a gadolinium (Gd) bolus. We used 1 M gadobutrol injected intravenously with the aid of a dual-syringe automatic injector via a 14–20-gauge needle cannula placed in the antecubital vein. During the first 10 s images were acquired before starting the contrast agent injection to establish a pre-contrast baseline.

All patients received the same dose of 0.15 mmol/kg at a flow rate of 5 ml/s followed by 20 ml of bolus saline solution (at 5 mL/s). In all cases, a few minutes before the dynamic phase, patients were administered 0.05 mmol/kg of Gd as a pre bolus to attenuate the T1 effects of blood–brain barrier (BBB) disruption. To analyse the complete lesion

region, we recorded a series of 20 slices that were repeated sequentially, yielding 1200-1400 pictures in 1 minute 42 seconds.

IMAGE POST PROCESSING & ANALYSIS:
After acquisition of images in mentioned protocol, all imaging data were analyzed and processed at console system via SYNGO software BY SIEMENS. Different steps need to be followed to get the rCBV maps and calculate rCBV.

ROIs (20-30 mm2) were placed on rCBV maps in solid portion of tumours where the maximum signal intensities were located. In SIEMENS software ROIs are selected as MCEval Ellipse ROI. In the tumor region, ROIs were placed in the areas of contrast enhancement and preferably on solid component if the tumour is of mixed type, while in the peritumoral area they were placed on the border between the tumor lesion and its surroundings, as shown on T2-weighted, FLAIR and T1-weighted post-contrast images. The ROI with the maximum mean signal intensity is chosen to represent the perfusion parameters in the tumour. Reference ROIs were placed in normal areas of the brain tissue on the contralateral side at same-level of the tumor automatically placed by software by mirror ROI. However manual interpolation of ROI in NAWM (Normal appearing white matter) in case of any vessel, cystic, haemorrhagic areas or areas of white matter T2 hyperintensity were noted on that region.

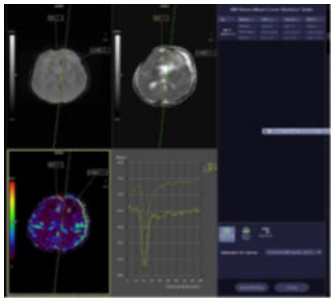


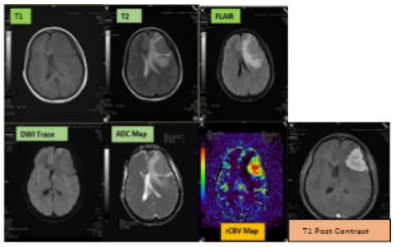
Figure 1: Reference Mirror ROI selection

rCBV Calculation: Finally, the rCBV (relative cerebral blood volume) value is calculated by dividing the signal intensity value either from the intra tumoral or peritumoral region, outlined above, with the signal intensity value from the contralateral ROI in NAWM.

For ADC all regions of interest (ROIs) are placed manually in the most hypointense regions on ADC maps corresponding to the tumor solid components with exclusion of cystic, necrotic, and hemorrhagic areas as mentioned earlier.

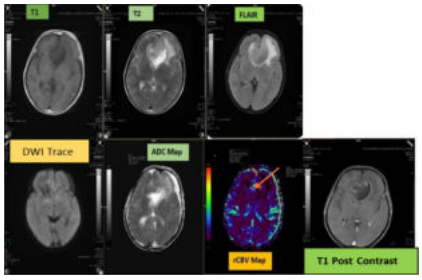
DATA ANALYSIS:
Radiological evaluation of brain tumours done with DWI and PWI parameters using ADC and rCBV values in intra tumoral and peri tumoral region of different brain tumours. For all tumors in SIEMENS software min/max, mean and SD value generated for each ROI for both rCBV map and ADC map.

Histopathological data was collected and taken as a standard reference for correlation with the diffusion and perfusion parameters of brain tumours (4–9). The histopathological data were collected both prior to the MR examination or follow up later on. Histopathological characterization and grading is done according to 'The 2021 WHO Classification of CNS Tumors'.



HPE Diagnosis	Intra tumoral ADC(x10^{-3}mm^2/s)	Intra tumoral rCBV	Peritumoral ADC(x10^{-3}m m^2/s)	Peri tumoral rCBV
GRADE 1 MENINGIOMA	0.95	2.6	1.5	1.8

Fig 2: 30-year-old woman presented with headache and seizure for 6 months, MR shows well-defined extra axial dural based mass lesion on left frontal lobar convexity, shows homogenous enhancement with increase perfusion on rCBV map. The lesion appears isointense on T1WI and heterogeneously hyperintense on T2 and FLAIR, it appears hyperintense on DWI & hypo intensity on ADC map.



HPE Diagnosis	Intra tumoral ADC(x10^{-3}m m^2/s)	Intra tumoral rCBV	Peritumoral ADC(x10^{-3}mm^2/s)	Peri tumoral rCBV
GLIOBLASTOMA	0.78	7.2	1.4	3.35

Fig 3: 55-year-old woman presented with headache and for 3 months, MR Imaging show an infiltrative lesion in bilateral frontal lobes in para falcine location. The lesion appears isointense on T1WI and heterogeneously hyperintense on T2 and FLAIR, On DWI there is hyperintensity which showing hypo intense on ADC map. On post contrast study it shows predominant peripheral enhancement with increase perfused component on PWI in centre of the lesion

RESULTS:
Brain tumours distributed primarily based on its origin as primary and secondary tumours of which 73 lesions are primary and 17 lesions are secondary out of 90 cases which were diagnosed histo-pathologically. Of the 90 patients under study, we found 35 patients are female and 55 patients are male with male: female ratio of 1.5:1 . In our study brain tumours in different age groups with a range of 13-69 yrs with mean age of 34 yrs. 14 of the 17 secondary cases have a known primary and 3 have an unknown primary.

Out of 73 cases of primary brain tumours 28 cases are of paediatric age group and 62 of adult age group. There are total 73 primary brain tumours in our study with highest frequency of glioma (36.98%) followed by meningioma (34.25%) among primary brain tumours. Glioblastoma is the most frequent high grade primary brain tumour among all age group (15.07%) and most frequent tumour among gliomas (40.74%). Among all meningioma in age wise distribution highest incidence noted in 51-60 years group (40.00%). Distribution of meningioma of different grade determined by HPE are 44 %, 20% and 36% in grade 1,2 and 3 respectively. Medulloblastoma has the highest number of cases (21.43%) in paediatric age group and most common tumour in embryonal and malignant pediatric brain tumour.

Table 1: Tabular distribution of primary brain tumours according to HPE analysis and grading:

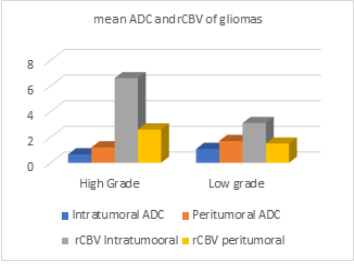
HPE diagnosis of primary brain tumours	Grade	Frequency
Meningioma	1	11
	2	5
	3	9
Pilocytic astrocytoma	Low grade	2
Oligodendroglioma	2	3
	3	2
Astrocytoma	2	1
	3	1
	4	3
Diffuse astrocytoma	Low grade	2
	High grade	1
Glioblastoma	High grade	11
diffuse high grade glioma	High grade	1
Medulloblastoma	High grade	5

Atypical teratoid rhabdoid tumour	High grade	1
Pineoblastoma	High grade	1
Germinoma	High grade	1
Schwannoma	Low grade	1
Choroid plexus papilloma	Low grade	2
Ependymoma	2	3
	3	2
Pituitary adenoma	Low grade	1
Papillary Craniopharyngioma	Low grade	2
Adamantinomous Craniopharyngioma	Low grade	2
Total		73

Table 2: Tabular distribution of secondary brain tumours as per HPE analysis:

Secondary	Frequency	Percentage
Adenocarcinoma Lung	2	11.8
Breast Cancer	3	17.6
Colorectal carcinoma	2	11.8
Ewing Sarcoma	2	11.8
Melanoma	1	5.9
No known primary	3	17.6
Renal cell carcinoma	3	17.6
SCC Lung	1	5.9
Total	17	100.0

Chart 1: Graphical representation of intra and peritumoral ADC and rCBV of glioma: -



This data indicates that higher rCBV values and lower ADC values in high grade glioma involving both intra tumoral and peri tumoral region.

Table 3: Tabular representation of intra and peritumoral ADC(x10³⁻mm²/s) and rCBV of glioblastoma

Tumour Group	Mean	
Glioblastoma	Intra tumoral mean ADC	0.65
	Intra tumoral mean rCBV	7.33
	Peritumoral mean ADC	1.03
	Peritumoral Mean rCBV	4.40

Table 4: Tabular representation of intra and peritumoral ADC (x10⁻³mm²/s) and rCBV of meningioma with HPE grading:

Tumour grade	ADC (mean±SD)		rCBV (mean±SD)	
	Intra tumoral	Peritumoral	Intra tumoral	Peritumoral
High	0.75±0.23	1.10±0.27	6.6±3.2	2.6±1.02
Low	1.00±0.33	1.32±0.31	3.1±1.1	1.5±0.53
P value	.04	.072	.008	.032

This data shows higher mean rCBV and lower mean ADC values are in high grade tumours in intra tumoral region. However, the peritumoral ADC values in high and low group is not statistically significant with p value of 0.072.

Table 5: Tabular representation of intra and peritumoral ADC (x10⁻³mm²/s) and rCBV of paediatric primary brain tumours with HPE grading:

Tumour grade	ADC (mean±SD)		rCBV (mean±SD)	
	Intra tumoral	Peritumoral	Intra tumoral	Peritumoral
High	0.72±0.23	1.24±0.34	6.6±3.2	2.6±1.02
Low	1.22±0.23	1.7±0.38	3.1±1.1	1.5±0.53
P value	<.001	<.001	<.001	<.001

This data indicates that higher rCBV values and lower ADC values in high grade pediatric age group tumours involving both intra tumoral and peri tumoral region.

Table 6: Tabular presentation of intra tumoral and peritumoral ADC and rCBV values of secondary brain tumours

Secondary	Intra tumoral ADC(x10⁻³m m²/s)	Intra tumoral rCBV	Peri tumoral ADC(x10⁻³m m²/s)	Peritumoral rCBV
Adenocarcinoma Lung	0.85±0.13	7.32±2.86	1.09±0.18	3.8±1.27
Breast Cancer	0.87±0.14	2.97±0.72	1.52±0.29	1.43±0.58
Colorectal carcinoma	0.76±0.28	4.2±3.82	1.12±0.16	1.6±0.53
Ewing Sarcoma	0.87±0.01	4.15±0.07	1.28±0.25	2.9±0
No known primary	1.23±0.23	5.67±2.78	1.49±0.3	1.75±0.95
Renal cell carcinoma	0.72±0.03	5.03±1.4	1.3±0.18	2.23±1.15
SCC Lung	1.13±0	1.2±0	1.9 ±0	1 ± 0
Melanoma	0.84±0	7.2±0	1.19±0	2.2±0

Melanoma & Renal cell carcinoma were having the high rCBV value among the all secondaries.

Other less common intra axial and extra axial primary tumours including ependymoma, pilocytic astrocytoma, chorooid plexus papilloma, craniopharyngioma, pineoblastoma and pituitary adenoma show varying rCBV values depending upon the histological type. Majority of them are low grade tumours.

Discussion:

90 out of total 100 patients underwent HPE evaluation were taken into the study. In patient demographics maximum incidence of brain tumour cases in the age group of 51-60 years is in concordance with previous studies done by Othman et al. (2020)(10) and Barciszewska et al. (2014)(11). We found a male: female ratio of 1.5:1. Which is in partial concordance with other studies Mondal et al (12)(Ratio 1.8:1) & Othman et al. (2020) (Ratio 0.80:1). (10)

In Comparison of intra tumoral rCBV of glioma in previous study Soliman et al (7)found to be 1.90 ± 0.70 and 4.20 ± 1.83 respectively. In peritumoral region LGG was 0.68 ± 0.19 and HGG was 1.37 ± 0.66 with significant difference (P=0.002) . These values are slightly higher than our values (chart 1) but with the same inference of higher rCBV values in HGG.

In evaluation of meningioma ,previous studies Tsai et al. (2022)(9) and Surov et al , 2015(13) shows significantly higher intra tumoral ADC in LGMs than HGMs. All the study shows significantly higher intra tumoral ADC in LGMs than HGMs.

Table 7: Comparison of Intra tumoral mean ADC (x10 ⁻³m²/s) of meningioma

Study	High grade	Low grade	P value
Tsai et al. (2022)	0.79	0.92	<00001
Surov et al. (2015)	0.80	0.96	0.006
Our study	0.75	1.00	.04

In evaluation of pediatric age group primary brain tumors , previous study of Mert Doğan et al. (14) showed intra tumoral mean ADC value.49±0.36 (x10³⁻mm²/s) in low-grade tumors and 0.68±0.12 (x10³⁻mm²/s) in high-grade tumors.(p<0.05). In peritumoral region low grade and high-grade tumor showed meanADC 1.04±0.41(x10³⁻mm²/s) and 0.84±0.20 respectively (p=0.029). In comparison of our study (Table 3) it shows that peritumoral and intra tumoral ADC are much lower in high grade tumors.

In our study relative cerebral blood volume (rCBV) in peritumoral edema was significantly higher in glioblastomas than in metastases 4.409±1.84 and 2.12±1.048 respectively (P < 0.0001).

In previous studies Askaner K et al.(15) , Tsougos et al. 2012(6) and Hakyemez et al. 2010 (16) did comparison between high grade glioma and metastasis by assessing peritumoral rCBV shows peritumoral infiltration.

Table 8: Comparison of peritumoral rCBV of HGG and secondary brain tumours with previous study

Study	GBM	Metastasis
Askaner K, et al	3.2 ±1.4	0.9 ± 0.7
Tsougos et al	1.68 ± 0.59	1.06 ± 0.38
Hakyemez et al	0.89 ±0.51	0.31 ±0.12
Our study	4.409±1.84	2.12±1.048

All studies show that peritumoral rCBV is significantly high in GBM than metastases.

Conclusion:

Tumour characterization which is not feasible on conventional MR imaging can be achieved by DWI and PWI techniques using parameter ADC and relative CBV. Majority of the high-grade tumours show high relative cerebral blood volume value compared to lower grade tumours and lower ADC values in high grade tumours which is in strong correlation with the HPE analysis. Our study also shows strong correlation of peri tumoral infiltration of more malignant and high-grade brain tumour as evident by low ADC and higher rCBV value in most of the occasions. So, the study support the hypothesis of increase mitotic activity in higher grade tumours and neo angiogenesis by evaluating through ADC and rCBV respectively. So, evaluating and assessing brain tumours with DWI and PWI parameters along with the reference HPE correlation we can conclude on the fact that these imaging techniques are strong and efficient imaging tools to evaluate and characterize brain tumours.

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