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Original Research Article

Dynamic Susceptibility Contrast Enhanced Imaging in Evaluation of Intracranial Tumours Using a 1.5 Tesla Magnetic Resonance Scanner

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ABSTRACT

Background: Brain tumors are a significant health problem and often are a diagnostic challenge. Role of imaging is no longer limited to merely providing anatomic details. Dynamic susceptibility contrast enhanced MRI advances allow knowing the hemodynamic characteristics of common intra axial tumors. Hence, present study aimed to evaluate perfusion parameters in evaluation of intracranial mass lesions and to find any correlation of these parameters with histopathological subtype and grade of malignancy of the tumor.

Materials And Methods: 33 patients with brain tumors, age 15 to 76 years, underwent dynamic contrast-enhanced susceptibility-weighted echo-planar perfusion magnetic resonance imaging (MRI) using a 3T MR scanner. The lesions were evaluated by measurements of relative cerebral blood volume (rCBV) and relative cerebral blood flow (rCBF). The ANOVA, Student 't' test was used to compare rCBV and rCBF measurements of tumor groups—5 low-grade and 11 high grade gliomas, five schwannoma, 11 meningiomas, and one haemangioblastoma. Peritumoral rCBV and rCBF measurements of tumours were also compared.

Results: Measurements of rCBV and rCBF were statistically significantly higher ($P < 0.05$) in meningioma than schwannoma. Measurements of rCBV and rCBF were statistically significantly higher ($P < 0.05$) in perilesional edema of high grade glioma as compared to perilesional edema of meningioma. The difference of rCBV and rCBF of tumour and perilesional edema was not statistically significant in comparing high-grade glioma and low grade glioma. However mean values of rCBV and rCBF of tumour and perilesional edema are higher in high grade glioma than low grade glioma.

Conclusion: CBV and CBF measurements provided by 3T dynamic susceptibility contrast enhanced (perfusion) MRI can help to predict intracranial tumor grading preoperatively, and differentiate between different brain tumors.

Keywords: Dynamic Susceptibility Contrast Enhanced; Perfusion 3T MRI; Brain Tumours.

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INTRODUCTION

The early and accurate diagnosis of a brain tumor is essential for disease management. Brain tumors are typically diagnosed after symptoms including headache, nausea, personality changes, seizure, or focal neurologic impairments appear. Brain tumors include gliomas, meningiomas, and pituitary tumors, among others. Magnetic resonance imaging (MRI) and computed tomography (CT), are the most common and preferred diagnostic modalities for detecting suspected primary brain tumors, can localize brain tumors and evaluate edema, hemorrhage, and hydrocephalus.[1]

Magnetic resonance imaging (MRI), is an indispensible imaging modality in the evaluation of the intracranial tumors. Conventional MRI techniques like T1, T2 and proton density weighted imaging, give overview of anatomical extension and different components of the tumor (like necrosis, hemorrhage, calcification, cysts, edema) depending on the signal characteristics, which aids in the most probable diagnosis of the tumor. However histopathology is the final verdict for the diagnosis. The role of imaging is no longer limited to merely providing anatomic details. In addition to conventional MR imaging techniques, a variety of advanced techniques such as diffusion-weighted imaging (including diffusion tensor imaging), perfusion imaging, MR spectroscopy, blood oxygen level–dependent (BOLD) imaging, and molecular imaging have found their place in clinical practice or are the subject of intense research.[2] These sophisticated magnetic resonance (MR) imaging techniques allow insight into such processes as the freedom of water molecule movement, the micro vascular integrity and hemodynamic characteristics, and the chemical makeup of certain compounds of masses. Currently, the first three techniques are more commonly used.

Dynamic susceptibility contrast-enhanced perfusion MR imaging of the brain provides hemodynamic information such as cerebral blood volume, cerebral blood flow, mean transit time that complements the anatomic information attainable with conventional MR imaging. In brain tumors, it quantitatively estimates cerebral blood volume that reflects the underlying microvasculature and angiogenesis.[3] Hence, present study aimed to evaluate perfusion parameters in evaluation of intracranial mass lesions and to find any correlation of these parameters with histopathological subtype and grade of malignancy of the tumor.

MATERIALS AND METHODS

The present study includes patients who were referred to the department of Radiology, Krishna Institute of Medical Sciences, Secunderabad for imaging and subsequently either biopsied or operated in our Institute with histopathological diagnosis. Patients of all age groups with brain tumours who were imaged on 3 tesla MR scanner with dynamic susceptibility sequence and patients in whom histopathological confirmation of the diagnosis was available during the study period in our institute were included in the study. Patients with motion artifacts that interfered with optimal assessment, patients with susceptibility artifacts masking the abnormalities on PWI, patients with small lesions where exact placement of ROI was not possible for accurate assessment of perfusion parameters, patients with lesions adjacent to the base of the skull, if they were compromised by the bony susceptibility artifacts, where calculation of perfusion parameters was difficult, patients having no histopathological follow up, patients having known contrast adverse reaction/ high serum creatinine and patient already treated for brain tumour e.g. operated, radiotherapy, chemotherapy were excluded from the study

All patients were imaged on Philips ACHIEVA 3.0 Tesla MR unit using an 16-channel Head coil. MR imaging of the brain was performed using a tailor made protocol that consists of conventional sequences like fast spin echo T2 weighted images in axial, coronal and sagittal planes; T2 FLAIR,T1 weighted & diffusion images in axial plane.

Imaging was performed by using a T2* gradient-echo echo-planar imaging sequence acquired during contrast agent administration. After approximately 8 time points in sequence, 0.1 mmol/kg of gadolinium chelate (Gadoteric acid, DOTAREM) was injected at a rate of 5 mL/s, this was followed with an equivalent amount of saline flush with the help of MR-compatible pressure injector (Medrad Spectris Solaris, Indianola, PA,USA).

Raw PWI scans were transferred to the Philips advanced workstation **[**Extended Work Space (EWS)] for post-processing and to generate maps using 'Neuro T2* Perfusion' package Fig.1. The following functional maps were generated for dynamic susceptibility-weighted cerebral perfusion scans.

CBF, CBV, Mean Transit Time and Time to Peak were calculated. Calculation used was based on a deconvolution of a pre-defined Arterial Input Function (AIF) with the intensity curves on brain tissue. The CBV maps were taken for manual ROI placement. Unprocessed perfusion images were also assessed to make sure that regions-of-interest (ROIs) were not placed over blood vessels. Within the lesions, four to six ROIs with the highest rCBV values were selected and the highest rCBV value was recorded. In order to reduce confounding factors, the diameter of the ROIs was kept constant. Selection of very small ROIs allowed measurements to be obtained from lesion sites with the highest rCBV signal intensities, and the least partial volume with neighboring vascular structures and CSF-containing spaces. ROI's were placed in the lesion as follows. One in the centre of the lesion, in the margin, in the perilesional edema, in the opposite normal appearing white matter parenchyma in the same slice.

Figure 1 shows MR perfusion colour coded map (RED- hyper perfused, BLUE-hypo perfused) and curves.

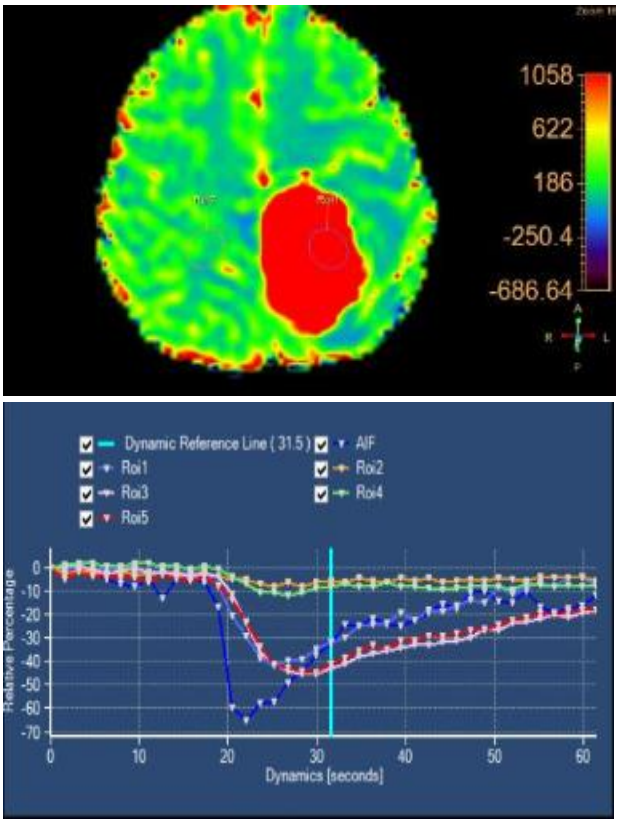


Fig 1: MR Perfusion colour coded map (RED- hyper perfused, BLUE-hypo perfused) and curves

rCBV ratio i.e. CBV of lesion /CBV contralateral hemisphere was calculated. When patients come for follow up similar procedure was repeated. Differences in CBV were tested for significance by using paired t tests (with P values < .05 regarded as significant). All the parameters obtained were tabulated, from which range, mean and standard deviations of various parameters of different groups were calculated.

All measured values are expressed in the following units

Cerebral blood volume- CBV: ml/100gm.

Relative cerebral blood volume- rCBV: CBV of lesion / CBV of normal brain

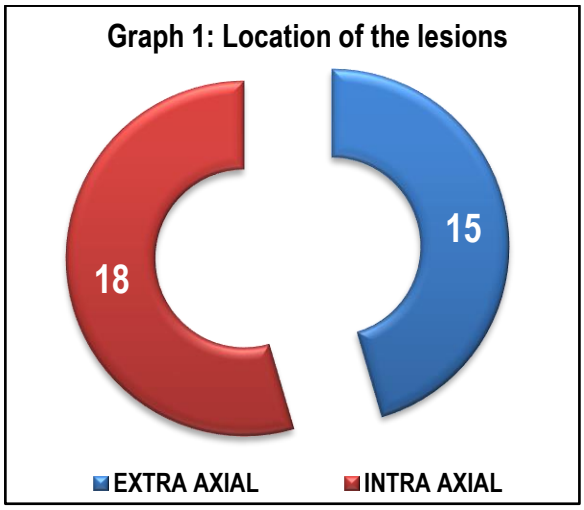
Cerebral blood flow – CBF: ml/min/100gm.

Relative cerebral blood flow- rCBF: CBF of lesion / CBF of normal brain.

Data was processed with help of Windostat Version 9.2 from Indostat services, Hyderabad. Analytical test such as ANOVA, student 't' test were used for statistical significance.

RESULTS

The present study included 33 patients, (18 males and 15 females), between an age range of 10-80 years. The lesions were intraaxial in 18 patients and extraaxial in 15 patients depicted in graph 1.



The study included 14 gliomas, 11 meningiomas, 5 schwanommas, and one each of medulloblastoma, PNET and haemangioblastoma. The distribution of the lesions is shown in graph 2.

Out of the 33 neoplastic lesions, 17 lesions were benign and 16 were malignant lesions.

PERFUSION IN EXTRAAXIAL MASSES

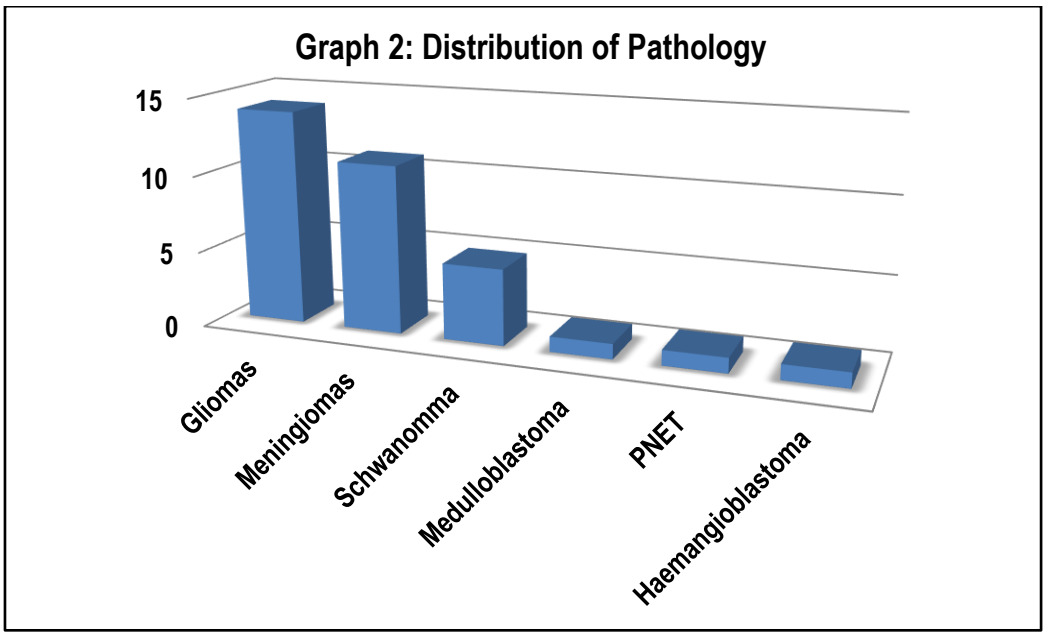
We have included in our study extraaxial masses mainly meningioma and schwanomma. We found significant difference ($p < 0.05$) of rCBV between meningioma and schwanomma (figure 2).

Meningioma

The mean rCBV was 5.38 ± 3.83 (ranging between 1.8 – 12.3). The lowest rCBV (1.8) was noted in angimatous meningioma. The mean rCBF was 7.6 ± 5.5 (ranging between 2 – 19). The lowest rCBF (2) was noted in fibroblastic meningioma. Perilesional edema in meningiomas had a mean rCBV of 0.49± 0.05 (range 0.4-0.6) and mean rCBF 0.62±0.25 (range 0.3-1.1) with lowest perilesional rCBV in the fibroblastic meningioma. There is no significant correlation between rCBV values and meningioma grading.

Schwannoma

Perfusion parameters in schwannoma were calculated. The mean rCBV was 1.26± 1.32 (ranging between 0.3 – 3.6). The mean rCBF was 2.01± 1.7 (ranging between 0.9 – 5.1).



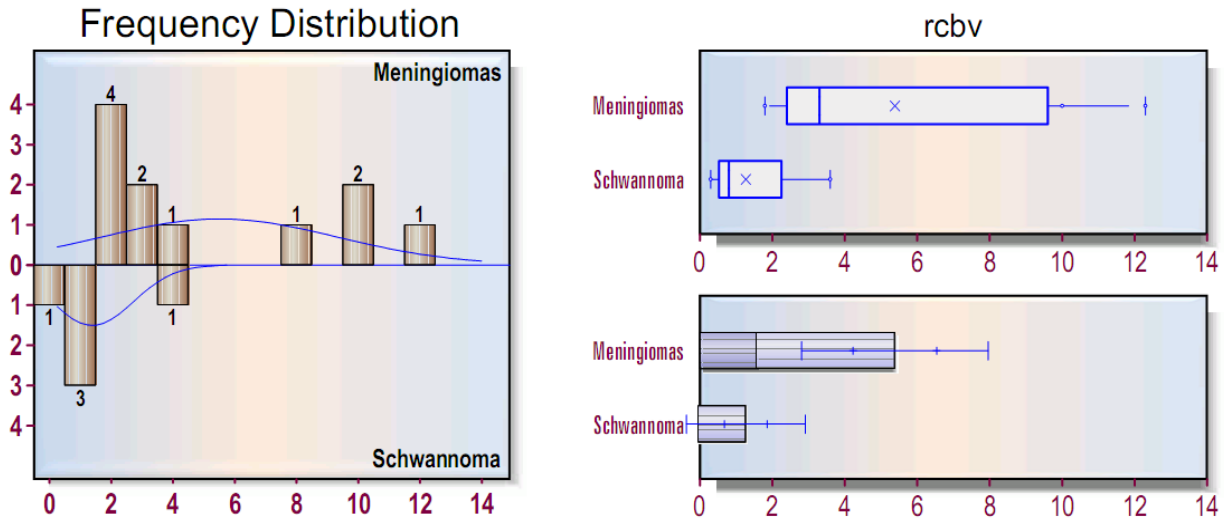


Figure 2: Distribution of extraaxial masses (Meningioma & Schwannoma)

PERFUSION IN INTRAAXIAL MASSES

We have included in our study intraaxial masses mainly, the gliomas. These gliomas are divided by WHO grading from Grade I to Grade IV. Grade I and Grade II are known as low grade gliomas, whereas Grade III and Grade IV are considered as High grade gliomas.

In our study we have total 16 gliomas. 5 gliomas were Grade II, 4 gliomas were Grade III, and 7 gliomas were Grade IV. We didn't have a single case of Grade I glioma. Hence, total number of low grade glioma is equal to Grade II tumours i.e. 5. Total number of high grade gliomas is equal to Grade III and Grade IV i.e. 11.

1) Low Grade Gliomas

In our study we noted only Grade II tumours as low grade glioma. Therefore total 5 numbers of patients were considered. Perfusion parameters in low grade gliomas were calculated**.** The mean rCBV was 1.43 ± 0.58 (ranging between 0.8 – 2.2). The lowest rCBV (0.8) was noted in a gemistocytic astrocytoma and highest in oligodendrglioma. The mean rCBF was 1.98 ± 0.93 (ranging between 1 – 3). The lowest rCBF (1) was noted in fibrillary astrocytoma. Perilesional edema in low grade gliomas had a mean rCBV of 1.25 ± 0.07 (range 1.2-1.3) and mean rCBF 1.64 ± 0.49 (range 1.3-2) with highest perilesional rCBV in the fibrillary astrocytoma.

2) High Grade Gliomas

Total high grade gliomas of Grade III and Grade IV were 11 in number. The mean rCBV was 2.25± 0.91 (ranging between 0.4 – 3.7). The lowest rCBV (0.4) was noted in a primitive neuroectodermal tumour and highest (3.7) in glioblastoma multiforme. The mean rCBF was 2.23± 1.75 (ranging between 0.4 – 6.3). The lowest rCBF (0.4) was noted in primitive neuroectodermal tumour and highest rCBF (6.3) was noted in glioblastoma multiforme. Perilesional edema in high grade gliomas had a mean rCBV of 1.72 ± 0.60 (range 0.9-2.5) and mean rCBF 3.17 ± 4.46 (range 0.7-13.1) with highest perilesional rCBV and rCBF in the anaplastic oligoastrocytoma. Increased rCBV and rCBF is noted in lesion and perilesional edema without statistical significance.

Significant difference ($p < 0.05$) was noted between perilesional rCBV of meningioma and high grade glioma. However no statistical significance of rCBV and rCBF between low grade and high grade glioma was observed.

Table 1: Mean perfusion parameters of Extraaxial tumors

	rCBV	rCBF
Meningioma	5.38±3.83	7.6 ± 5.5
Schwannoma	1.26± 1.32	2.01± 1.7

*Significant difference ($p < 0.05$) of rCBV between meningioma and schwanomma is noted.

Table 2: Mean perfusion parameters of Intraaxial tumors (GLIOMA)

	Tumour		Perilesional Edema	
	rCBV	**rCBF**	**rCBV**	**rCBF**
Low grade glioma (Grade II)	1.43 ± 0.58	1.98 ± 0.93	1.25 ± 0.07	1.64 ± 0.49
High grade glioma (Grade III + Grade IV)	2.25± 0.91	2.23± 1.75	1.72 ± 0.60	3.17 ± 4.46

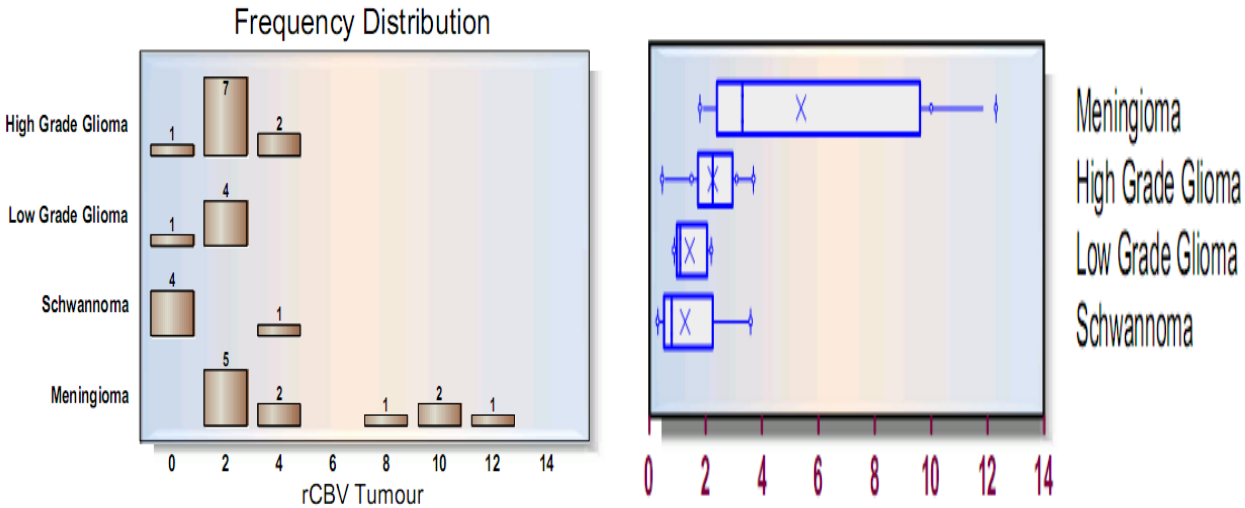


Figure 3: Distribution of Intraaxial and extraaxial masses.

DISCUSSION

Role of imaging is no longer limited to merely providing anatomic details. MRI advances allow knowing the hemodynamic characteristics and chemical makeup of common intra axial tumors. Mass effect and necrosis may correlate with tumor grade and indicate aggressive behaviour. Strong contrast enhancement is generally used as criteria for high grade gliomas; however lack of contrast enhancement does not indicate low grade glioma. The risk of high grade tumor is increased with the age of the patient.[4]

In such cases differentiation on conventional MRI is difficult. Perfusion weighted imaging is now used to asses tumor vascularity in vivo. Relative CBV maps and measurements have been shown to correlate reliably with tumor grade and histological finding of tumor microvascular density, which is the current standard for assessing the degree of angiogenesis.

In the evaluation of brain masses this technique is used to determine the additional information such as microvascular integrity, hemodynamic characteristics of the lesion, which are useful in preoperative and pre radiotherapy evaluation. In our study, we evaluated perfusion MR imaging parameters in intracranial masses and looked for their significance in differentiating tumor types and grades.

We included histopathologically proven 11 meningioma and 5 schwannoma cases. CBV in all meningiomas in our series was more than normal brain, which can be attributed to extra axial lesions no BBB barrier and higher permeability result in increased blood flow through these vessels and intravascular component increases, increasing CBV. Yang et al[5] reported mean rCBV's in 15 typical and 7 atypical meningiomas as 8.02 ± 4.74 and 10.5 ± 2.1 respectively, with no significant correlation with tumor grading. Zhang et al[6] also studied rCBV in 25 benign and 8 malignant meningiomas and found no significant correlation between rCBV and meningioma grading. Our study is consistent with these studies in that there is no significant ($p>0.05$) correlation between rCBV meningioma grading.

Maeda et al[7] studied perfusion in meningiomas and neuromas and revealed showed a higher mean rCBV in meningiomas than neuromas ($p <0.001$), which correlated with our study. Thus, preoperative evaluation of rCBV could help differentiating meningiomas and schwanommas especially at cerebellpontine angle and middle cranial fossa.

Zimny A et al[8] studied contribution of perfusion-weighted magnetic resonance imaging in the differentiation of meningiomas and other extra-axial tumors. They found cases of CPA tumors, a lesion with low relative cerebral blood volume values and should be suspected to be schwannoma, allowing exclusion of meningioma to be made. We also found similar result in our study significantly high rCBV in meningiomma as compared to schwannoma.

Major intraaxial group in our study were gliomas (n=16). Out of which five were histologically proven low grade glioma. High grade gliomas, are heterogenous lesions with different components within, like enhancing, non-enhancing and cystic/necrotic components.

Contrast enhancement on conventional MRI represents pathological alteration of BBB, whereas MRP depicts tumor neoangiogenesis. Areas with high rCBV in a heterogeneous tumor may be targeted for stereotactic biopsy. Elevated rCBV is also present in the peritumoral regions due to tumor infiltration. In low grade tumors peritumoral area contains less infiltrating tumor cells. This interpretation is consistent with increasing blood volume prior to tumor enhancement. Hence tumor enhancement differs from tumor perfusion.[4]

Sughara et al[9] and Meng law et al[10,11] in their studies postulated that rCBV is more in high grade glioma compared to low grade glioma with a statistical significance ($p< 0.0001$).Our study is consistent with the above studies that rCBV of high grade glioma (2.4) is greater than low grade glioma (1.4) (II vs III/IV), but there was no statistical significance($p > 0.05$). This could be because of the smaller number of patients in our study.

Cho SK[12] studied fifty seven patients & found that highest rCBV were seen in hemangioblastomas, followed by high-grade gliomas, metastases, lowgrade gliomas, and lymphomas. Hemangioblastomas showed the highest rCBV and lymphomas the lowest. Our study is consistent with findings of this study. Haemangioblastoma in our study also showed highest mean rCBV similar to this study. We have not included lymphoma as there is false low rCBV due to disruption of BBB.

There were no side effects related to either the rapid injection of contrast material or to the contrast agents used in the study. One potential pitfall of rCBV maps derived from DSC MR imaging occurs in the setting of high capillary permeability when substantial contrast material leakage is present. An rCBV map is generated by analyzing a time–signal intensity curve after infusion of MR contrast material. The passage of the contrast material through blood vessels produces a decrease in signal intensity on T2*-weighted images. Thereafter, the signal intensity of tissue returns to (or near) baseline. However, in lesions that are associated with disruption of the blood-brain barrier (eg, contrast-enhancing tumors), the signal intensity as seen on the time–signal intensity curve can actually increase above baseline owing to the T1-shortening effects of leakage of contrast material. If the limits of integration (which are operator derived) are drawn to include the region of the curve that is above baseline, the rCBV of the region is underestimated.

Thus, with our study of dyanamic suscepyibility contrast enhanced MR imaging in intracranial masses we conclude that this advanced technique is of significant importance in differentiation and characteriasation of the brain tumors. Our findings were consistent with the literature available, however few were contradicting with the literature. These techniques can also help the surgeons for planning their surgeries, biopsies and radiotherapists for radiotherapy planning. Small patient number was a limitation of our study and we recommend studies in larger groups. Also our study group included heterogenous histopathologic types of tumors which is the most important limitation of study.

CONCLUSION

There was no significant correlation between rCBV values and meningioma grading. Meningiomas have a higher rCBV values than schwannomas with a statistical significance and particularly very useful in cerebellopontine angle. Statistically significant difference is noted in the perilesional edema rCBV values of meningiomas and high grade glioma. rCBV and rCBF values in grade III+IV gliomas are more than that of grade II gliomas, but without statistical significance. Contrast enhanced dynamic susceptibility weighted MR imaging is helpful in grading of gliomas as low (grade I & II) versus high (III & IV). MR perfusion is also

helpful in evaluation of peritumoral areas as high grade tumors were more infiltrative. Conventional contrast enhanced MRI lacks this ability. The results suggest that MR perfusion is a useful tool in assigning patients with intracranial lesions to either invasive biopsy or conservative management.

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