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ROLE OF MR PERFUSION IN INTRA AXIAL BRAIN TUMORS- A PROSPECTIVE STUDY OF 50 CASES

Radiodiagnosis

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ABSTRACT

To study the role of MRI perfusion in grading and characterization of intra axial brain tumors. The aim of this paper is to determine the role of MR perfusion in differentiating low grade gliomas from high grade gliomas preoperatively. In this paper, the role of MR perfusion in differentiating between high grade gliomas and metastases is discussed.

KEYWORDS

INTRODUCTION: Conventional magnetic resonance imaging (MRI) is widely used to diagnose brain tumor patients, owing to its high sensitivity and exquisite delineation of anatomic relationships. It provides a "snapshot" in the time course of contrast enhancement, is largely inadequate to guide biopsy or treatment of brain tumors. The degree of contrast enhancement of glioblastomas has a relatively poor correlation with tumor grade. Precise delineation of tumor margins, and discrimination between tumors and non-neoplastic processes, and between low-grade and high-grade tumors, are all required for preoperative evaluation of space-occupying lesions in the brain.

Recently, advanced imaging techniques such as perfusion MR imaging and proton MR spectroscopy have been found useful in studying brain tumors.

MR perfusion also holds promise in providing a better delineation of tumor margins than conventional techniques. The principle of MR perfusion oncologic imaging is that as a tumor grows its metabolic demands increase due to rapid cell growth and increased cell turnover. Cellular hypoglycemia and hypoxia lead to the production of angiogenic cytokines leads to new blood vessel formation, or angiogenesis.

The net result of angiogenesis is a complex network of abnormal vessels in the peritumoral space. Tumor vessels are composed of immature vessels with large endothelial cell gaps, an incomplete basement membrane, and absent smooth muscle layers, rendering them more permeable.

TECHNIQUES AND METHODS: There are three main techniques used to perform MR perfusion imaging: T2*-weighted dynamic susceptibility, T1-weighted dynamic contrast-enhanced perfusion, and arterial spin labeling techniques.

The most established method of MR perfusion is T2*-weighted dynamic susceptibility imaging. This technique exploits the T2* susceptibility effects of gadolinium, rather than the T1 shortening effects routinely associated with contrast enhancement on conventional imaging. A double-dose of gadolinium (0.2 mmol/Kg) is typically injected via an 18- or 20-gauge i.e. catheter at a high rate (3–7 ml/sec) using a power injector, to allow for a tight bolus of contrast material. Successive images are then acquired during the first pass of contrast material through the brain. The drop in T2* signal caused by the susceptibility effects of gadolinium is computed on a voxel-by-voxel basis and used to construct a time-versus-intensity curve.

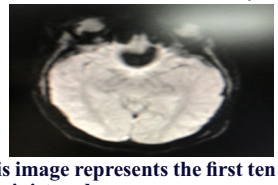


FIGURE 1 : This image represents the first ten slices before bolus of contrast is administered.

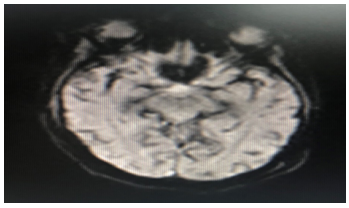


FIGURE 2 : This image is after administration of bolus of contrast. Look for the signal drop in the vessels due to T2 relaxation effect of gadolinium.

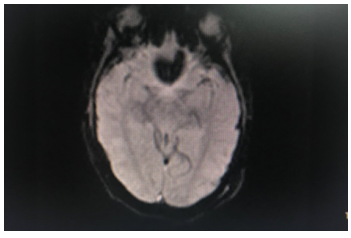


FIGURE 3 : This image indicates the redistribution of the administered contrast.

Both gradient-echo and spin-echo acquisitions can be used, but rapid spin-echo imaging is capable of dynamic perfusion measurements with echo-planar systems practically. Spin-echo techniques have been shown to be selectively sensitive to small vessels that are less than 20 μ in diameter, whereas gradient-echo images incorporate signals from larger tumor vessels as well as the micro vascularity.

REVIEW OF LITERATURE

Dean *et al.* demonstrated that the two most important predictors of tumor grade are mass effect and necrosis. The dilemma lies in the situation when a high grade glioma is mistaken for being low grade due to minimal edema, no contrast enhancement, no necrosis, and no mass effect. On the other hand, low-grade gliomas can be mistaken for being high grade due to peritumoral edema, contrast enhancement, central necrosis, and mass effect. Also, when using conventional T2-weighted MR images, the peritumoral hyper-intensity are nonspecific as it may represent vasogenic edema, tumor infiltration, or both.

Soonmee Cha et al investigated dynamic susceptibility contrast-enhanced (DSC) MR imaging characteristics of the two most common subtypes of low-grade infiltrating glioma: astrocytoma and oligodendroglioma. Histopathologic evaluation remains the reference standard for diagnosis of glioma and classification of histologic subtypes, but is challenged by subjective criteria, tissue sampling error, and lack of specific tumor markers.

Edmond A.Knopp et al evaluated the role of T2* weighted echo planar

perfusion imaging by using a first pass gadopentetate technique to determine the association of CBV maps with histopathological grading & to improve the accuracy of stereotactic biopsy.

Meng Law et al evaluated the usefulness of Relative cerebral blood volume (rCBV) measurements derived from perfusion MR imaging and metabolite ratios from proton MR spectroscopy in predicting glioma grade as the sensitivity, positive predictive value (PPV), and negative predictive value (NPV) of conventional MR imaging in predicting glioma grade is not high compared with conventional MR imaging in grading primary gliomas.

Marco Essig et al evaluated whether preradiation and early follow-up regional cerebral blood volume (CBV) measurements can help predict treatment outcome in patients with cerebral metastases and to evaluate regional CBV changes in tumor and normal tissue after radiosurgery.

Kumar VA, Knopp EA et al evaluated the dynamic susceptibility-weighted contrast enhanced(DSC) MR Perfusion and MR imaging findings between hemangioblastomas and pilocytic astrocytomas retrospectively. The conclusion is that the rCBV"s of hemangi oblastomas were significantly higher when compared to pilocytic astrocytomas.

Raman F.Barajas et al investigated whether cerebral blood volume (CBV), peak height (PH), and percentage of signal intensity recovery (PSR) measurements derived from the results of T2*-weighted dynamic susceptibility-weighted contrast material enhanced (DSC) magnetic resonance (MR) imaging performed after external beam radiation therapy (EBRT) can be used to distinguish recurrent glioblastoma multiforme (GBM) from radiation necrosis.

Frederik wenz et al studied whether it is possible to measure radiation-induced changes in blood volume in low-grade astrocytomas and in normal brain tissue. The passage of a bolus of gadopentetate dimeglumine was monitored.

Takeshi Sugahara et al evaluated the differentiation of tumor recurrence from treatment-related changes which may be difficult with conventional MR imaging when newly enhancing lesions appear. Their aim was to determine the value of perfusion-sensitive contrast-enhanced MR imaging for differentiating recurrent neoplasm from non-neoplastic contrast-enhancing tissue.

MATERIALS AND METHODS

Fifty patients with intra axial brain tumors were included in this study. The group comprised 26 men and 24 women aged 5 to 68 (mean 36.5) years. All underwent conventional MR imaging along with MR perfusion prior to treatment, which included surgery, chemotherapy, and radiation therapy. MR spectroscopy was also performed on 40 out of the 50 patients using multivoxel CSI 135 sequence. The fifty patients included 16 cases of low grade gliomas, 18 cases of high-grade gliomas, 7 cases of metastases, 3 cases of oligodendrogliomas, 2 cases of hemangioblastomas, 1 case of lymphoma and 2 cases of tumor like appearance on MRI but proved to be infective lesions. Confirmed histopathological diagnoses of 30 cases were obtained (5 metastases, 3 low grade / pilocytic astrocytomas, 3 grade I oligodendrogliomas , 1 grade I astrocytoma, 1 diffuse astrocytoma, 7 glioblastoma multiformes, 1 anaplastic astrocytomas, 2 anaplastic oligodendrogliomas,1 anaplastic oligoastrocytomas and 1 gliosarcoma), one lymphoma, two hemangioblastomas and two of non-neoplastic etiology like abscess) . The seven metastatic tumors arose from squamous cell carcinoma of the lung in two patients, and large cell carcinoma of the lung in two patients, from undifferentiated carcinoma, lobular carcinoma, sarcomatous tumor and adenocarcinoma of the thyroid and kidney in one patient each. The histopathological confirmation in rest of the patients could not be obtained.

EXCLUSION CRITERIA:

1. Brain aneurysm clip
2. Implanted neural stimulator
3. Implanted cardiac pacemaker
4. Cochlear implant
5. Ocular foreign body
6. Metal shrapnel
7. Other implanted medical devices
8. Patients with surgery of uncertain type where the presence of metal clips or wires cannot be excluded.

All patients underwent preoperative conventional and perfusion MR imaging using SIEMENS B17 AVANTO 1.5 Tesla MRI Machine. For the latter, we used a gradient-echo single-shot echo-planar imaging (EPI) sequence. A series of images (20 slices, 50images/slice) was obtained at 2-second intervals before, during, and after administration of the contrast agent. After 10 seconds, during which time the first five images were acquired and an imaging baseline thus established, a bolus of 10 ml (0.2 mmol /kg) gadopentetate dimeglumine (Magnilek) was power injected at a rate of 5 ml/second through an 18- or 20-gauge intravenous catheter. In each case, multi-section data acquisition was used to record a tumor in its entirety.

A signal intensity curve is obtained which shows the fall in the signal intensity in relation to time which corresponds to the perfusion. The curve is inverted because there is fall in signal intensity with time due to the T2 relaxation effect of gadolinium and hence represented as an inverted curve. Two signal intensity curves represent that of the reference vessel and that of the region of interest. In lesions with high perfusion there is significant fall in the signal intensity. The difference in the level of drop in the two signal intensities is directly proportional to the degree of perfusion in the lesion.

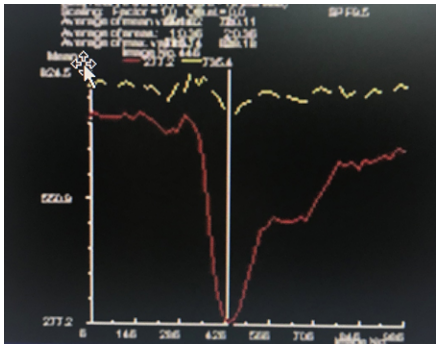
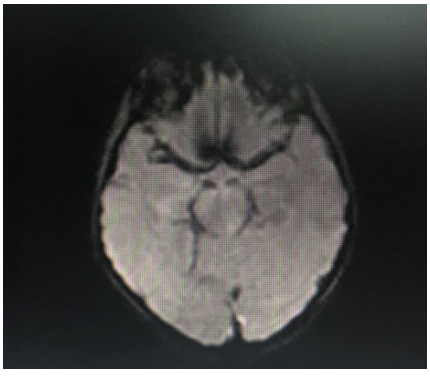


FIGURE 4 : This image shows the time intensity curves of the reference vessel and the region of interest where the signal intensity is represented on Y axis and time is represented on X axis.

For the post processing of perfusion MR data, the "PERF P2" sequence was loaded in the software provided along with the Magnetom Avanto MRI machine. The changes in the relaxation rate (ΔR2) can be calculated from signal intensity using the following equation: ΔR2= ln (S/S0)/TE, where ln is the natural logarithm, S is signal intensity, and S0 is baseline signal intensity.



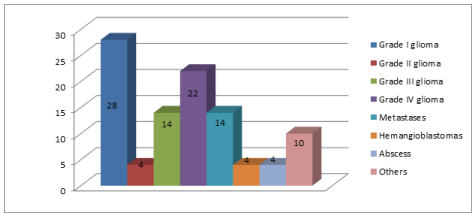
Qualitative and Quantitative Analysis:

For quantitative analysis, normal white matter within the contra lateral hemisphere was used as the internal reference standard.

Observations and Tables :

Sex distribution: Male 52% and female 48%

Distribution of cases:



Low grade gliomas :
These include both grade I and grade II gliomas.

GRADE I :
We studied 14 patients with grade I gliomas.

rCBV values	Number of patients
0.8-1.1	1
1.2-1.5	6
1.6-1.9	5
2.0-2.3	1
2.4-2.7	0
2.8-3.1	0
3.2-3.5	1

GRADE II Gliomas :
We studied 2 patients with grade II gliomas.

rCBV values	Number of patients
0.8-1.1	0
1.2-1.5	0
1.6-1.9	1
2.0-2.3	0
2.4-2.7	0
2.8-3.1	0
3.2-3.5	1

High grade gliomas :
These include grade III gliomas, grade IV gliomas and metastases.

GRADE III :
We studied 7 patients with grade III gliomas.

rCBV values	Number of patients
2-2.5	2
2.6-3.0	2
3.1-3.5	1
3.6-4.0	0
4.1-4.5	0
4.6-5.0	0
> 5	2

GRADE IV gliomas :
We studied 11 patients with grade IV gliomas.

rCBV values	Number of patients
2-2.5	1
2.6-3.0	1
3.1-3.5	1
3.6-4.0	1
4.1-4.5	1
4.6-5.0	1
> 5	5

Metastases:
We studied 7 patients with metastases from different primaries.

rCBV values	Number of patients
2.5 – 5.0	5
5.1 – 7.5	0
7.6 – 10	1
10.1 – 12.5	0
> 12.5	1

Peritumoral rCBV values in metastases:

Peritumoral rCBV values	Number of patients
0.7 – 1.0	2
1.1 – 1.4	3
1.5 – 1.8	1
1.9 – 2.2	0
> 2.2	1

Hemangioblastomas :
We studied 2 patients with hemangioblastomas. Both the patients with hemangioblastomas had exceptionally high rCBV values (more than 10) inspite of these being low grade malignancies.

Patient	rCBV values
1	10.6
2	17.7

Oligodendrogliomas :
We studied 3 patients with oligodendrogliomas. All the 3 patients had high rCBV values of more than 3.

Patient	rCBV
1	10.6
2	3
3	5.5

DISCUSSION :

Low grade gliomas :
Low grade gliomas include both grade I and grade II gliomas. MR perfusion is a very helpful tool in evaluation of low grade neoplasms.

We studied 16 patients of low grade gliomas – 14 with grade I gliomas and 2 patients with grade II gliomas.

High grade gliomas :
High grade gliomas include both grade III and grade IV gliomas as well as metastases. MR perfusion is a very helpful tool in evaluation of high grade neoplasms.

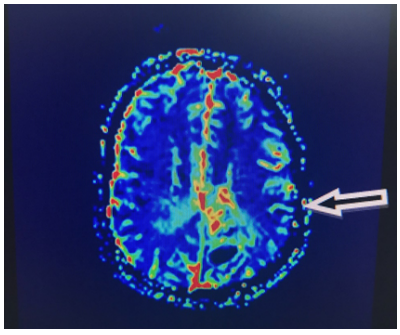


FIGURE 6: The above image shows the markedly elevated CBV (areas in red) within a grade IV glioma (GBM). Note that the peritumoral region laterally also shows areas of significantly elevated CBV (arrows)

Metastases :
MR perfusion is a very helpful tool in evaluation of metastases. We studied 7 patients with metastases. The rCBV values within the tumor were elevated in all the patients and the rise in CBV was significant (more than 2.5) in all of them.

The peritumoral rCBV values were of great use in differentiating high grade gliomas from metastases. High grade gliomas being aggressive in nature show increased rCBV in the peritumoral region as well.

However, metastases on the contrary show normal values of rCBV in the peritumoral region. Six out of the seven patients showed peritumoral CBV values of less than 1.8

We first applied these tests taking into consideration the histopathologically confirmed cases with histopathological grading as the gold standard.

Histopathological diagnosis		
MR perfusion	**High grade**	**Low grade**
High grade	17 (True positives)	1 (False positives)
Low grade	0 (False negatives)	9 (True negatives)
Total	17	10

Sensitivity = Number of true positives / True positives + False negatives x 100

Sensitivity = 17/17 x 100 = 100.00 %
Specificity = Number of true negatives / False positives + True negatives
Specificity = 9/10 x 100 = 90 %

Hemangioblastomas:
MR perfusion plays an important role in evaluation of hemangioblastomas as it helps in distinguishing small hemangioblastomas from Pilocytic astrocytomas. Both these appear as a solid cystic lesion with intensely enhancing mural nodule. We studied 2 patients with Hemangioblastoma and both showed rCBV values of more than 10.

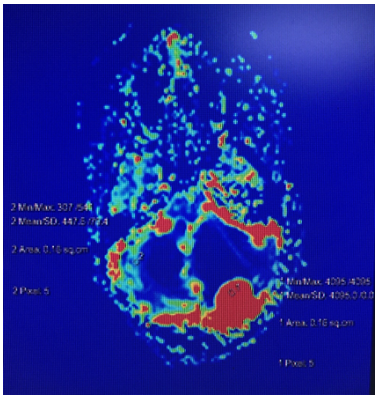


FIGURE 7: CBV color map showing very high CBV values within the enhancing nodule with rCBV more than 10 suggesting it to be a hemangioblastoma. This was proven histopathologically to be a hemangioblastoma.

Tumor recurrence:

MR perfusion has an important role in determining whether there is tumor recurrence or not. Most of the times, post-operative patients show heterogeneous enhancement on conventional MRI because conventional post-contrast imaging is based on the extra vascular leakage of contrast. Hence it is difficult to comment on the recurrence based on conventional MRI alone.

CONCLUSION:

MR perfusion has a definite role in the grading and characterization of intra axial brain tumors. MR perfusion can effectively differentiate low grade gliomas from high grade gliomas preoperatively. MR perfusion can help in distinguishing between the high grade gliomas and metastases based on the cerebral blood volume in peritumoral region. High grade gliomas show increased intratumoral as well as peritumoral CBV, whereas metastases do not show significantly increased peritumoral CBV values. MR perfusion can differentiate between pilocytic astrocytomas and hemangioblastomas based on the values of the rCBV in the enhancing component, which is extremely high in cases of hemangioblastomas and low in cases of pilocytic astrocytomas. An exception to the overall principle of MR perfusion that rCBV corresponds to the grade of tumor is seen in cases of hemangioblastomas and grade I and II oligodendrogliomas as these show exceptionally high values of rCBV, despite being low grade tumors. MR perfusion offers good prediction in the recurrence of tumor versus post-operative changes in operated cases, which is very difficult on conventional post contrast MRI.

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