Role of MR spectroscopy and perfusion in treated brain tumours

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Purpose

INTRODUCTION:

Radiation necrosis can closely resemble recurrent tumour at MR imaging due to the following shared characteristics:

- **origin at or close to the original tumour site,**
- **contrast enhancement,**
- **growth over time,**
- **edema,** and
- **exertion of mass effect.[1]**

Anatomic imaging with contrast-enhanced MRI alone often cannot reliably discriminate between post treatment change and recurrent neoplasm. Physiological based imaging like MR Spectroscopy and Perfusion can help in differentiating these two entities.

PURPOSE:

- To differentiate tumour recurrence from post treatment changes using MR spectroscopy and Perfusion in treated cases of primary brain tumours.

- To define the cut off values of spectroscopy & perfusion parameters for labeling a case as recurrence.

- To evaluate changes in cerebral metabolites and in vascularity in patients with high or low grade cerebral gliomas after treatment.
Methods and Materials

- A prospective study of 55 treated cases of brain tumours (post operative + radiotherapy +/- chemotherapy) was done using conventional MRI along with MR Perfusion and MR Spectroscopy.

- MR images were acquired at 1.5T machine using a standard head coil.

- Axial T1,T2-weighted and FLAIR, sagittal T1 and coronal T2 weighted sequences were obtained with 5-mm section thickness and a 6-mm intersection gap.

- The perfusion MR images were obtained with a spin-echo echo-planar (SE-EPI) technique (2100/80) before, during, and after injection of 0.1 mmol/kg of gadolinium chelate at 3 mL/s, followed by a 20-mL saline flush. After data collection, the perfusion maps were derived on a voxel-by-voxel basis from the dynamic imaging sets.

- 2D Multivoxel MRS was run on areas appearing suspicious on conventional imaging. PRESS sequence was used with intermediate TE of 144ms.

- Post processing for multi voxel spectroscopy was done using functool software.

- On the basis of the clinical and imaging follow-up or histopathology from biopsy/ resection, final diagnosis was done.
Results

- On the basis of the clinical and imaging follow-up or histopathology from biopsy/resection, lesions of 31 patients were categorized as tumour recurrence and the lesions of 24 patients were categorized as post treatment change/radiation necrosis.

- For spectroscopy we used three metabolite ratios: Ch/Cr, Ch/Naa, Naa/Cr. rCBV (relative cerebral blood volume), CBF (cerebral blood flow) and MTT (mean time to transit) were the kinetic parameters used.

- Except for MTT, (Fig 1) on page 6 rest of the spectroscopic and perfusion parameters shows significant statistical difference between the means of two groups.

- Receiver operating characteristic (ROC) curve was used for spectroscopy and perfusion parameters to define the cut off values to differentiating recurrence and post treatment change.

- Values greater than 1.8 for both Ch/Cr and Ch/Naa were considered as tumour recurrence similar to study by Patrick Weybright [2]. When threshold of 1.8 is taken, sensitivity and specificity for Ch/Naa is more as compared to Ch/Cr. (Fig 2) on page 6

- In our study (fig 3) on page 7 24 cases out of 31 recurrent tumours showed Ch/Cr ratio of more than 1.8. However out of 7 cases that showed Ch/Cr ratio less than 1.8, 6 cases showed high Ch/Naa ratio (all more than 1.8 with max- 7.9) and one case showed elevated perfusion with rCBV of 1.75.

- 5 post treatment change cases showed elevated Ch/Cr however all of them showed decreased Ch/NAA levels and were hypo-perfused areas on perfusion studies. Similarly Ch/NAA was less than 1.8 only in 1 recurrent case that showed elevated perfusion with rCBV of 1.75.

- Useful threshold relative cerebral blood volume (rCBV) values that accurately distinguish the 2 entities- recurrence and post treatment change do not exist.
• We used cut off 1 showed high specificity of 95.8 % with lower sensitivity of 67.7%. Lowering the threshold to 0.75 shows specificity(71%) and sensitivity(71%) as against study by Hu\textsuperscript{a,g}, L.C. Baxter et al showed sensitivity of 91.7% and specificity of 100% with threshold of 0.71.[3] (Fig 4 on page 6 Fig5 on page 8)

• Most of the recurrent as well as post therapy change show heterogenous enhancement. Hence enhancement cannot reliably differentiate these entities. (Fig 6) on page 9

• We also classified glial neoplasms as high and low grade based on the previous histopathological report (pre Radiotherapy) and studied the spectroscopic and perfusion parameters. (fig 11) on page 13

• Low grade gliomas included grade I and II tumours where as high grade included grade III and IV.

• In low grade gliomas, except for Ch/Cr rest of the parameters show statistical significance between the means in two groups (Fig 12) on page 14. For high grade gliomas, all the parameters show significant statistical difference between the means (Fig 13) on page 15.

• The mean Ch/NAA ratio was 4.1 for both recurrent low as well as high grade gliomas. Mean rCBV in recurrent low grade gliomas was 1.28 which was slightly more as compared to that of recurrent high grade tumor suggesting that low grade tumors showed conversion and progression to higher grade tumour.
Fig. 0: Table showing means of various spectroscopy and perfusion parameters in recurrent as well as post treatment change group.

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**Fig. 0:** Receiver operating characteristic (ROC) curve for spectroscopy parameters: Ch/Cr and Ch/Naa.

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Values greater than 1.8 for either Ch/Cr or Ch/Naa ratios were considered evidence of tumour, similar to study by Patrick Weybright et al.
**Fig. 0:** Table showing distribution of cases when threshold for Ch/Cr and Ch/Naa was taken as 1.8

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<table>
<thead>
<tr>
<th>Cut off</th>
<th>Sensitivity%</th>
<th>Specificity%</th>
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<tbody>
<tr>
<td>rCBV</td>
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<tr>
<td>0.50</td>
<td>93.5</td>
<td>29.2</td>
</tr>
<tr>
<td>0.75</td>
<td>71</td>
<td>71.8</td>
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<td>1.00</td>
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<td>95.8</td>
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<tr>
<td>1.50</td>
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<td>100</td>
</tr>
<tr>
<td>CBF</td>
<td></td>
<td></td>
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<tr>
<td>0.50</td>
<td>93.5</td>
<td>20.8</td>
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<tr>
<td>1.50</td>
<td>19.4</td>
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</table>

**Fig. 0:** Receiver operating characteristic (ROC) curve for perfusion parameters: rCBV and CBF.

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Values greater than 1.00 were considered as recurrent cases and less than 1.00 were considered as post treatment change.

**Fig. 0:** Table showing distribution of cases when threshold for rCBV and CBF was taken as 1

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Fig. 0: Table showing enhancement patterns in recurrent as well as post therapy change group.

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This is a k/c/o GBM left parietooccipital region, 8 months post treatment. Post contrast axial and coronal MR images show stellate pattern of heterogeneous enhancement in the region of prior tumour.

**Fig. 0:** K/c/o GBM in left parieto-occipital region, 8 months post treatment showing heterogeneous enhancement.

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Fig. 0: MR spectroscopy and MR perfusion are consistent with post treatment change.

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AFTER 3 MONTHS
**Fig. 0:** Follow up scan after 3 months showing hyperintensity involving entire left temporal lobe with areas of gliosis in left occipital region. Patchy enhancement is seen in the anterior left temporal lobe.

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**MRS and MRP show features consistent with radiation induced necrosis. No e/o tumor recurrence is seen.**

**Fig. 0:** MR spectroscopy shows reduced Naa,Ch and Cr levels with/without lactate doublet. The area is hypo perfused as compared to contra lateral normal brain parenchyma. These features are s/o radiation induced change.

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**Fig. 0:** Grading of Glial tumours based on previous histopathological report.

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<table>
<thead>
<tr>
<th></th>
<th>RECURRENCE (n=11)</th>
<th>POST TREATMENT CHANGE (n=4)</th>
<th>P value</th>
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<tr>
<td>Ch/Cr</td>
<td>2.6</td>
<td>1.45</td>
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<tr>
<td>Ch/Naa</td>
<td>4.1</td>
<td>1.35</td>
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<tr>
<td>rCBV</td>
<td>1.28</td>
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<tr>
<td>CBF</td>
<td>1.04</td>
<td>66.75</td>
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**Fig. 0:** Spectroscopy and Perfusion parameters in low grade gliomas.

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### HIGH GRADE TUMOURS

<table>
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<tr>
<td>rCBV</td>
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<tr>
<td>CBF</td>
<td>1.27</td>
<td>62.33</td>
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**Fig. 0:** Spectroscopy and Perfusion parameters in high grade gliomas.

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A 60 year female with grade II astrocytoma operated and taken radiation 9 yrs back came with focal seizures. Present MR study: Post contrast axial, MRS and MRP. Heterogeneous enhancing mass with necrosis, markedly elevated choline and reduced Naa and elevated rCBV all indicate high grade recurrence.

Fig. 0: A case of grade II astrocytoma operated and taken radiation taken 9 yrs back. Present MR study: shows a heterogenously enhancing mass with necrosis in left temporal region with markedly elevated choline and reduced Naa and elevated rCBV, indicating a high grade recurrence.

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**Fig. 0:** follow up scan after 6 cycles of temazolamide, shows reduction in the size of enhancing mass. MR spectroscopy shows elevated Ch and lactate peak with reduction in Naa. There is makedly reduction in rCBV s/o response to temazolamide.

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**Fig. 0:** K/c/o GBM 6 months post treatment shows a peripherally enhancing heterogeneous lesion. MR Spectroscopy shows markedly elevated Cho and lipid peak
with reduced NAA and Cr. MR Perfusion shows hyper as well as hypo perfused areas. the features are consistent with recurrent lesion.

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**Fig. 0:** Images show surgical cavity in right occipital region with enhancing duramater. MR spectroscopy and Perfusion are suggestive of post treatment change. No e/o residual/ recurrent lesion is seen.

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Fig. 0: A 35 yr old female, k/c/o Glioblastoma multiforme, post op. and RT 4 months back: MR study: Axial flair and post contrast images show heterogeneously enhancing mass in left frontal region involving genu of corpus callosum and crossing the midline. It also involves septum pellucidum and shows mass effect on frontal horn of left lateral ventricle. MRS shows elevated Choline and lipid peak with reduction of Naa. The lesion is hyperperfused as compared to contra lateral brain parenchyma. The features are s/o recurrent lesion.

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<tr>
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<th>SPECTROSCOPY</th>
<th>PERFUSION</th>
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<tbody>
<tr>
<td>SENSITIVITY</td>
<td>96.7%</td>
<td>67.7%</td>
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<tr>
<td>SPECIFICITY</td>
<td>91.6%</td>
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<tr>
<td>PPV</td>
<td>93.7%</td>
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<tr>
<td>NPV</td>
<td>91.6%</td>
<td>69.6%</td>
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<tr>
<td>ACCURACY</td>
<td>94.5%</td>
<td>80%</td>
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</table>

**Fig. 0:** Table comparing sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy between spectroscopy and perfusion in our study.

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Conclusion

• Our results confirm significant elevations of the Ch/NAA and Ch/Cr ratios with a concomitant reduction in the NAA/Cr ratio in contrast-enhancing lesions representing tumour recurrence compared with lesions representing post treatment change. Further, although all three metabolic ratios significantly predicted tumour, the most significant correlation was noted with Ch/Cr and Ch/NAA (p<0.001) similar to results by Smith et al.[4]

• An elevated Ch/Naa and Ch/Cr ratio of more than 1.8 correlated with evidence of tumour recurrence and allowed creation of a prediction rule to aid in lesion classification. rCBV and CBF cut off of 1 showed specificity of 95.8%.

• Low grade tumours may convert to high grade tumours over a period of time.

• High sensitivity is noted with spectroscopy and perfusion increases the specificity thus combination of both can reliably predict tumour recurrence from post treatment change.

• In these lesions, the Ch/Naa and Ch/Cr ratios and perfusion parameters rCBV and CBF may be the best numeric discriminators.
References


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