

# Perfusion Weighted Imaging Directed Proton MR Spectroscopy: A New Approach to Identify Oligodendroglial Genotypes

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**Introduction:** Oligodendrogliomas patients harboring loss of heterozygosity (LOH) on chromosomes 1p and 19q demonstrate better prognosis and improved response to radiation and chemotherapy than those with intact 1p/19q alleles.<sup>1</sup> It is thus important to accurately diagnose and distinguish between the two types for better patient management. Unfortunately, due to the inherent heterogeneity of oligodendrogliomas, any imaging parameter or even <sup>1</sup>H-MRS from contrast enhancing regions alone might have limited value in separating these two different genotypes.<sup>2</sup> We hypothesized that an integrated approach using <sup>1</sup>H-MRS voxels guided by dynamic susceptibility contrast-perfusion weighted imaging (DSC)-PWI can provide higher accuracy in discriminating molecular genotypes of oligodendrogliomas. **Materials and Methods:** MRI and <sup>1</sup>H MRSI studies were performed on a 3 Tesla MR system. <sup>1</sup>H MRSI was acquired using a single slice 2D CSI (PRESS) sequence. The parameters included: TR/TE = 1700/30ms, NEX = 3, FOV = 16x16 cm<sup>2</sup>, BW=1200 Hz, matrix size = 16x16. The slice thickness was varied from 15-20mm. For PWI, T2\*-weighted gradient-echo, EPI was performed during the first pass of standard dose (0.1 mmol/kg) of intravenous contrast agent. Sequence parameters included: TR/TE = 2000/45ms, FOV = 22x22cm<sup>2</sup>, number of slices=20, in-plane resolution 1.72x1.72x3mm<sup>3</sup>, flip angle 90°, EPI factor=128 and echo spacing=0.83. Forty-five images were acquired for each slice with a temporal resolution of 2.1 seconds. Thirty-four patients with histologically confirmed oligodendrogliomas and availability of cytogenetic profile were recruited in this study. These patients were classified into two groups: 1p or 1p and 19q LOH (Group I; n=19), and 19q LOH only or intact alleles (Group II; n=15). Cerebral blood volume (CBV) maps were constructed using Leonardo workstation and Syngo software. CBV values were obtained by drawing regions of interest in the neoplasm region from all sections that corresponded to the approximate section thickness and location of the CSI slice and were normalized with respect to contralateral white matter to obtain relative CBV (rCBV) values. <sup>1</sup>H-MRSI grid was overlaid on the CBV maps. Concentrations of metabolites [N-acetyl aspartate (NAA), choline (Cho), myo-inositol (mI), glutamate/glutamine (Glx) and lipid+lactate (Lip+Lac)] were computed using LC model software and normalized with respect to ipsilateral creatine (Cr) for the voxel corresponding to the maximum rCBV areas. Differences in rCBV and <sup>1</sup>H-MRSI parameters between the two groups were analyzed using two-sample t-test with unequal variances. Logistic regression analyses were performed to ascertain the best model to distinguish two groups. Areas under the curves (AUC) of receiver operating characteristic (ROC) curves were determined to ascertain the accuracy.

**Results:** Representative images from a patient with group 1p and 19q LOH are shown in Fig 1. We observed higher Cho/Cr in this group (0.51±0.19) compared to group II oligodendrogliomas (0.41±0.11) with a trend towards significance (p=0.07). The sensitivity, specificity and AUC for Cho/Cr in distinguishing two groups were 47%, 68% and 0.66 respectively. However, addition of maximum rCBV value and Cho/Cr from corresponding maximum rCBV voxel resulted in a p value of 0.005 with a sensitivity of 73%, specificity of 84% and AUC of 0.82 in distinguishing two groups (Fig. 2).

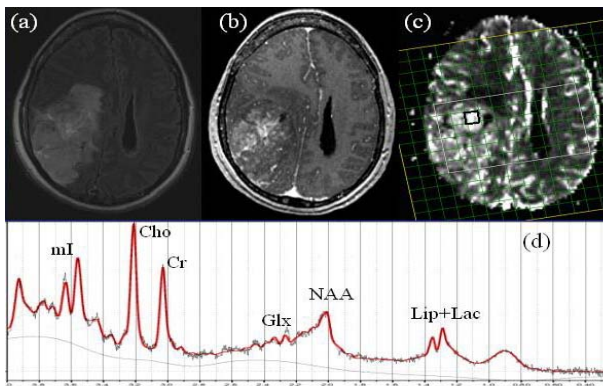


Figure 1: Flair image (a), post contrast T1 weighted image (b) and <sup>1</sup>H MRSI grid overlaid on CBV map (c) from group I oligodendrogloma demonstrating a voxel from maximum rCBV region (black). Corresponding spectra (d) from this voxel is shown exhibiting various metabolites.

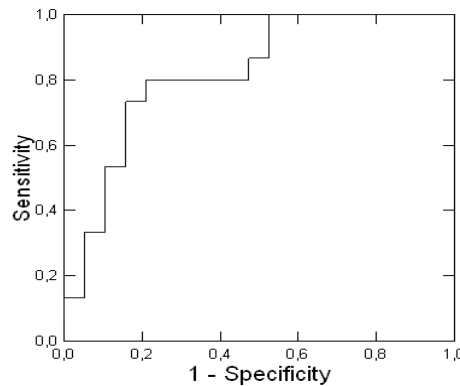


Figure 2: ROC curve obtained after incorporating maximum rCBV and Cho/Cr as interacting variables. The ROC curve demonstrates an AUC of 0.82 with a sensitivity of 73% and specificity of 84% in distinguishing the two groups of oligodendrogliomas

**Discussion:** It has been reported that oligodendrogliomas harboring 1p/19q LOH demonstrate elevated rCBV<sup>3</sup>, increased glucose metabolism and higher proportion of viable cells<sup>4</sup> compared to oligodendrogliomas with intact alleles. It appears that high rCBV regions in our study reflect a hypermetabolic state which correlates with increased mitotic activity and high cell proliferation as indicated by increased

Cho/Cr.<sup>5</sup> A previous study reported higher Cho/Cr in group I oligodendrogliomas compared to group II, however the differences were not significant.<sup>2</sup> This may have been due to the inherent heterogeneity of oligodendrogliomas that include varying degrees of cellular and nuclear pleomorphism, mitotic activity, vascular proliferation, and necrosis.<sup>6</sup> Our logistic regression analysis indicates that this limitation can be partially overcome by PWI guided analysis of <sup>1</sup>H MRSI as performed in this study and also reported earlier.<sup>7</sup>

**Conclusion:** These results suggest that Cho/Cr from maximum rCBV region may be helpful in distinguishing oligodendrogliomas with 1p/19q deletion from those with intact alleles and may help in identifying patients who might show better therapeutic response.

## References:

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