Differentiation of Oligodendroglial Genotypes using Perfusion Weighted Imaging and Proton MR Spectroscopy

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Introduction: Treatment of patients with oligodendrogliomas depends on their histopathological grade and cytogenetic profile. Oligodendrogliomas with 1p and 19q loss of heterozygosity (LOH) are known to be more sensitive to the chemotherapy.[1] In the present study, we evaluated the utility of perfusion weighted imaging (PWI) and multivoxel proton magnetic resonance spectroscopy (^{1}H MRS) in differentiating the molecular subtypes of oligodendrogliomas which may potentially help in determining suitable patients for chemotherapy.

Materials and Methods: Magnetic resonance (MR) imaging and two dimensional multivoxel proton magnetic resonance spectroscopic imaging (^{1}H MRSI) were performed on a 3 Tesla MR system. Twenty-three patients diagnosed with oligodendrogliomas based on histopathology and availability of cytogenetic profile were recruited in this study. These patients were classified into two cytogenetic groups: 1p or 1p and 19q LOH (Group I; n=12), and 19q LOH only or intact alleles (Group II; n=11). Cerebral blood volume (CBV) maps were constructed using the Leonardo workstation and the Syngo software. ^{1}H MRSI grid was overlaid on the CBV maps to co-register the spectroscopic findings with CBV maps. In some cases, ^{1}H MRSI dataset was co-registered with FLAIR images and post contrast T1 weighted MPRAGE images using statistical parametric mapping software. Voxels that exhibited FLAIR hyperintensity and good spectral resolution were analyzed. CBV values were obtained by drawing regions of interest in the tumor region from all sections that corresponded to the approximate section thickness and location of the ^{1}H MRSI and were normalized with respect to contralateral white matter to obtain relative CBV (rCBV) values. Receiver operating characteristic (ROC) analysis was performed to obtain a threshold rCBV value in separating oligodendrogliomas into two regions, one with high rCBV and another with low rCBV. A cutoff value of 1.5 was used based upon the ROC analysis. 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 creatine (Cr). Voxels with maximum metabolite ratios were used to differentiate the two groups of the oligodendrogliomas using a two-tailed student t test. A probability (p) value of less than 0.05 was considered significant.

Results: Representative images from group I and group II oligodendrogliomas are shown in Fig. 1. Mean concentrations of Cho/Cr from high CBV regions in group I and II are shown in Fig 2. Cho/Cr was significantly higher in group I oligodendrogliomas only from regions of high rCBV compared to group II. No significant differences were observed from other metabolites between the two groups.

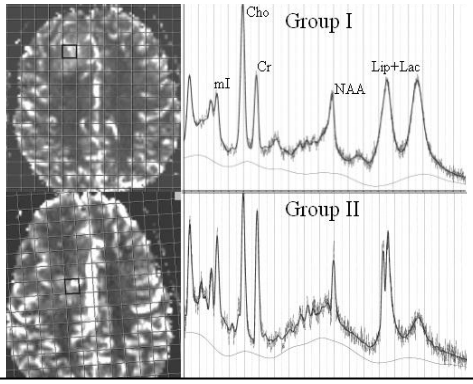

Fig 1.^{1}H MRSI grid overlaid on CBV maps from group I and group II oligodendrogliomas demonstrating representative voxels. Spectra from these regions are shown exhibiting various metabolites.

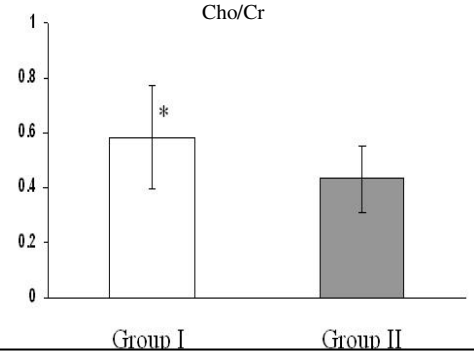

Fig 2. Bar diagram demonstrating variations in mean concentration of Cho/Cr between group I and group II oligodendrogliomas. Error bars indicate ±1SD. *Results from student t test are significant ($p<0.05$).

Discussion: Oligodendrogliomas harboring 1p/19q deletions have been reported to have high rCBV,[2] and increased ^{18}FDG and ^{201}TI uptake[3] compared to oligodendrogliomas with intact alleles. Thus it seems that high rCBV regions reflect a hypermetabolic state which have been correlated with increased mitotic activity, indicating high cell proliferation and thus increased Cho.[4] A previous study reported higher Cho/Cr in group I oligodendrogliomas compared to group II, however the difference was not significant.[5] This may be due to the inherent heterogeneity of the oligodendrogliomas which include varying degrees of cellular and nuclear pleomorphism, mitotic activity, vascular proliferation, and necrosis.[6] However, this limitation can be partially overcome by PWI guided voxel-by-voxel analysis of ^{1}H MRS as performed in this study and reported earlier.[7]

Conclusion:

Our results suggest that Cho/Cr from higher CBV regions may be helpful in distinguishing oligodendrogliomas with 1p/19q deletion from those with intact alleles and may help in identifying patient that might respond to chemotherapy

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