Associations of Metabolite Concentration and Water Diffusivity in Normal Appearing Brain Tissue with Glioma Grade

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PURPOSE: Previous magnetic resonance spectroscopic studies of brain tumors have indicated that changes of tissue metabolism and water diffusion occur in tissue regions that are remote from the lesion and appear normal on conventional MRI [1-4]; however, the associations with tumor type or grade has not been reported. In this retrospective study the relationship of these imaging measures with tumor grade in gliomas was investigated.

METHODS: MR spectroscopic imaging of whole brain (TE=70 ms) and diffusion tensor imaging (DTI) was carried out at 3 Tesla in subjects with histology-proven untreated glioma for WHO grades 2, 3, and 4, resulting in 56 MRSI studies and 52 DTI studies. Normative data was also obtained for control subjects at two different sites (labeled Ctrl-1 and Ctrl-2). MRSI data was processed using the MIDAS package [5], which included normalization of individual metabolite values to tissue water as well as calculation of metabolite ratio maps. Mean metabolite and metabolite ratio values were obtained for grey- and white-matter with lobar regions on the contralateral side from the tumor location. Metabolite values were excluded from voxels having a fitted linewidth of >12 Hz. Mean ADC values were obtained from a region in parietal normal-appearing white matter. ANCOVA analyses were then used to test for differences in the mean values between subject groups while accounting for subject age.

RESULTS: Initial analysis indicated no differences in the associations of metabolite values with the different subject groups amongst the different brain lobes, and therefore mean value over the whole contralateral hemisphere were obtained. In Figure 1 are shown example distributions of data values for white-matter Cho/NAA and ADC from the different study groups. Analysis revealed a non-significant trend for decreased NAA and increased Cho in both grey- and white-matter with increasing tumor grade, and a trend for increasing ADC with tumor grade, with significant differences of the group-mean values for Cho/NAA between control and grade 4 glioma; however, with a relatively large overlap of data values between groups. Using data from all tumor grades, there was a weak and non-significant trend of increasing ADC value with Cho/NAA value (R^2=0.11).

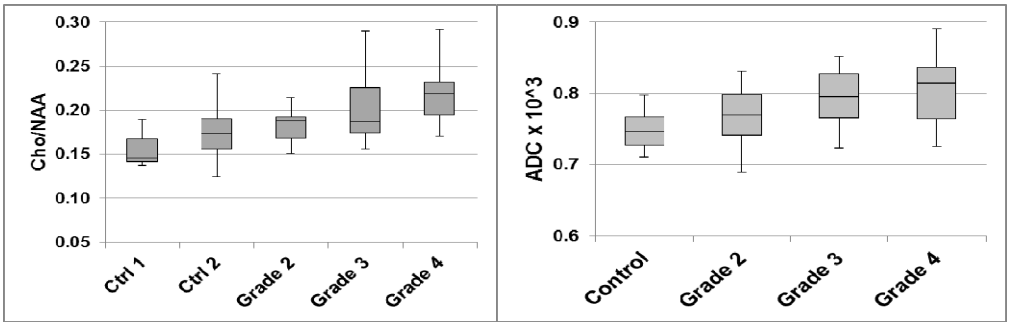

Figure 1. Box-and-whisker plots showing the minimum, first quartile, median, third quartile, and maximum data values for a) Cho/NAA and b) ADC for the different subject groups.

DISCUSSION: This study supports previous observations of altered tissue metabolism in normal-appearing white matter that is indicated by the Cho/NAA ratio, while additionally finding comparable changes in grey-matter and an association with tumor grade. While there was a trend to increased ADC with tumor grade this was non-significant after accounting for age, and there was no significant correlation between ADC and tissue metabolite concentrations. These findings indicate widespread metabolic alteration that increases with the degree of malignancy of the tumor. Diffuse infiltration of glioma cells into the healthy tissue has been proposed as a mechanism for such changes, although systemic metabolic depression caused by release of compounds from the tumor could also be considered.

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