4 Tesla 1H MR Spectroscopy and 23Na Imaging in Low Grade Glioma

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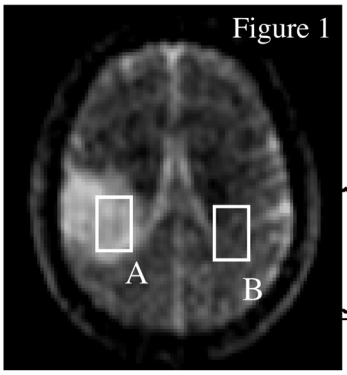
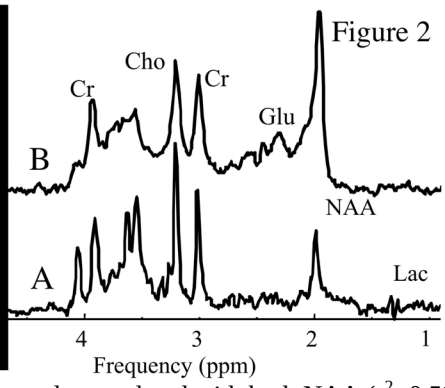
Introduction: The potential for high field short echo-time ^{1}H MR spectroscopy (MRS) to discriminate cell types and determine tumor malignancy from metabolic characteristics continues to grow as the sophistication and reliability of MRS techniques matures. Recent advances in the measurement and removal of the macromolecule baseline from the spectrum further increases the reliability of these measures and allows accurate quantification of glutamate (Glu) and myo-inositol (Myo) in addition to *N*-acetylaspartate (NAA), choline containing compounds (Cho), and total creatine (Cr) (1). Metabolic changes in cerebral tumors are also accompanied by altered tissue sodium concentration reflecting modified cell packing and ion concentrations. The purpose of this study was to characterize the metabolic profile associated with human low-grade glioma and to correlate metabolite levels with changes in tissue sodium signal measured non-invasively by ^{23}Na MRI.

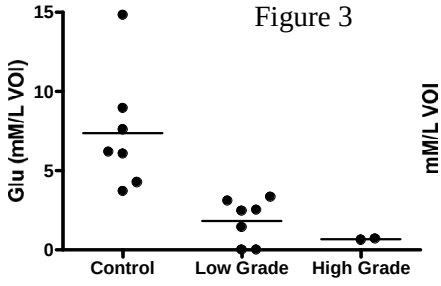
Methods: Prior to surgery, eight patients (6 male/2 female, mean age 45 ± 11 years) with suspected low-grade glioma were studied using a Varian (Palo Alto, CA) 4T whole body MRI including a Siemens (Erlangen, Germany) Sonata gradient coil. 3D inversion-prepared axial T_1-weighted anatomical images (FOV = 24x24x16 cm^3, TI/TR/TE = 500/10/5 ms, 256x256x64 acquisition matrix) were acquired to position a LASER (2) localized single voxel for short echo-time ^{1}H MRS (128 averages, TR/TE = 2200/46 ms (full spectrum), TI_1/TI_2/TR/TE = 2200/700/4200/46 ms (macromolecule spectrum), 128 averages) within the tumor (biopsy confirmed low grade glioma: N=6, high grade: N=2) and in normal tissue on the contralateral side (N=7). Spectra were lineshape corrected by QUECC (3), residual water subtracted, and the macromolecules baseline removed (1) prior to time domain fitting in fitMAN (1) incorporating prior knowledge of 19 metabolite lineshapes. Metabolite levels were normalized to the unsuppressed water signal from the same voxel after correcting for relaxation effects and water concentration (4) to yield metabolite levels in absolute units (1). 3D axial T_2*-weighted ^{23}Na images were also acquired (FOV = 24 x 24 x 16 cm^3, TR/TE = 23/3.8 ms, 64x64x16 acquisition matrix) and used to calculate sodium signal intensity within each voxel studied by ^{1}H MRS normalized to the signal intensity in normal parietal-occipital white matter after correcting for T_2 relaxation (5). Metabolite levels were compared (two-tailed ANOVA with $p<0.05$ considered statistically significant) between low and high-grade tumor and normal tissue and correlated with ^{23}Na signal intensity.



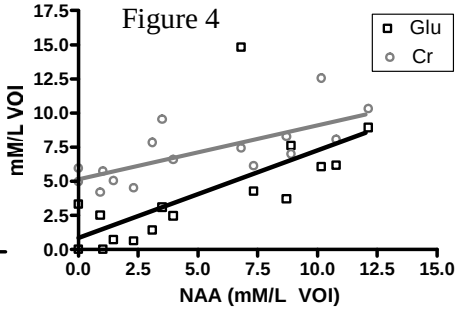


Results: Figure 1 depicts a typical transverse T_2*-weighted ^{23}Na image from one subject with low-grade glioma showing voxel positions (A-tumor, B-control) that correspond to the processed spectra in Figure 2. The tumor is clearly visible in the ^{23}Na image as a hyperintense region in the right hemisphere. Significantly lower NAA ($p<0.01$) and Glu ($p<0.05$, Fig 3) were observed in low and high grade glioma compared to control, while increased levels of Myo ($p<0.05$ in low grade only), and ^{23}Na ($p<0.01$) were also observed. Pooling all data from control and tumor, both Glu and Cr were positively correlated with NAA levels but had significantly different intercepts ($p<0.01$, Fig 4). ^{23}Na signal intensity was inversely correlated with both NAA ($r^2=0.59$, $p<0.01$) and Cr ($r^2=0.37$, $p<0.05$).

Discussion: Consistent with reduced neuronal density accompanying glial-cell proliferation and previous reports (4), decreased NAA was observed in low-grade glioma. Additional metabolite changes included decreased glutamate and increased myo-inositol. Correlations suggest that all NMR visible glutamate is localized with NAA and is therefore contained within neurons, while the concentration of Cr in glioma cells is ~ 5 mM/L VOI. Increased ^{23}Na signal in tumors is also consistent with previous studies (6).



*In one low grade patient, spectra were acquired from two different tumor regions



Acknowledgements and References: Funding provided by the Robarts Research Institute. (1) Kassem and Bartha, Magn Reson Med 2003; 49: 918-927, (2) Garwood and DelaBarre. J Magn Reson 2001; 153: 155-177, (3) Bartha *et al*, Magn Reson Med 2000; 44: 641-645, (4) Tong *et al*, Magn Reson Imaging 2004; 22: 735-742 (5) Bartha and Menon, Magn Reson Med 2004; 52: 407-410, (5) (6) Ouwerkerk *et al*, Radiology 2003; 227: 529-537.