Comparison of MRSI and Image Guided Histopathology in Treatment Naive and Treated Patients with Malignant Glioma

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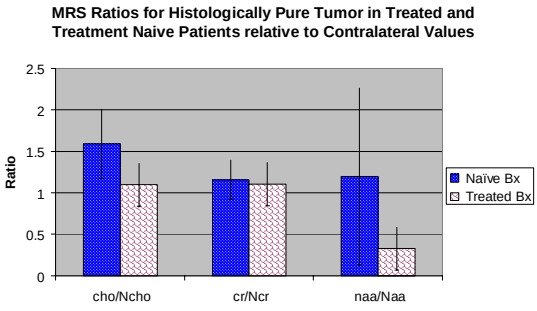
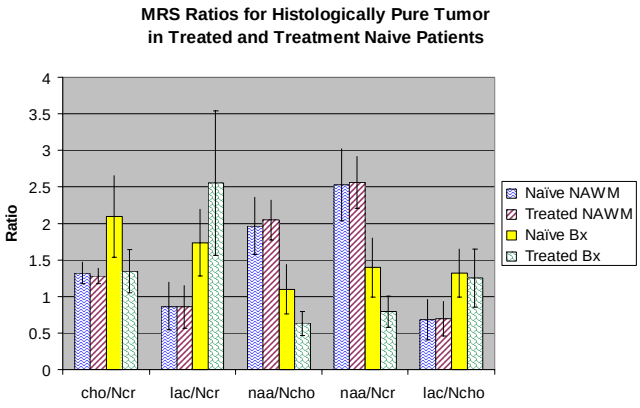
Introduction: Proton spectroscopic imaging (MRSI) has been used to characterize untreated brain tumors, assess response to therapy and evaluate previously treated patients for possible tumor recurrence. Effects of treatment, chemo or radiation, and tumor necrosis may result in partial volume contamination between normal tissue, recurrent tumor, and radiation necrosis (1). This complicates the comparison with pretreatment MRS. In this study we correlated MRSI with image guided stereotactic biopsies from both treatment naïve and treated patients to determine if the spectral patterns in pure tumor from treatment naïve patients correspond to confirmed pure tumor in treated patients. Knowledge of any differences in spectral patterns is important when following patients serially with MRS.

Methods MRSI from 13 patients previously treated (PT) with surgery, radiation, and chemotherapy were compared to MRSI from 37 treatment naïve (TN) patients. Image guided stereotactic biopsies were taken within 48hr of MRI and digitally referenced with 4 slice, 32x32 MRSI data (~.9cc voxels) collected during the 1.5T MRI examination. 8 different MRSI ratios formed from choline (Cho), lipid-lactate (Lac), n-acetylaspartate (NAA), and creatine (Cr) were analyzed where for example NCho refers to data taken from contralateral white matter (NAWM). Means/Standard deviations were used to describe MRSI ratios. Data from four tissues types were analyzed: 114 NAWM spectra without histologic confirmation from TN patients, 57 NAWM spectra from PT patients, MRSI corresponding to 55 biopsies characterized as pure tumor in TN patients, and MRSI corresponding to 23 biopsies characterized as pure tumor in PT patients. A double sided Students t-Test adjusted for unequal variance was used to determine if there were significant differences in spectral patterns between the treated and treatment naïve sample populations.





Results: Aggregate data for MRSI ratios are shown in the figures on the left . *p* values for 12 comparisons examined are shown in Table 1. No significant differences were found between NAWM spectral patterns in PT and TN patients. Significant differences were found between pure tumor spectra from TP and TN patients. These included lower cho/NCr and naa/NCr and higher lac/NCr in PT patients compared to TN patients.

Table 1 *p* values for selcted comparisons

	Naïve Normal vs. Treated NAWM	Treated Bx vs Naïve Bx
cho/Ncr	*p*=0.29901	*p*=0.00026
lac/Ncr	0.95575	0.00288
naa/cho	0.41609	0.0000001
naa/NCr	0.79032	0.00006
cho/Ncho		0.00223
cr/NCr		0.91120
naa/Nnaa		0.00398
lac/Nlac		0.63154

Discussion: When we restricted this study to pure tumor spectra characterized by stereotactic biopsy directly referenced with MRSI data, we found significant differences between TN and PT patients. These differences may be due to histologic differences between the two groups, or may be due to heterogeneity in the larger spectroscopic volume compared to the histology. The latter is consistent with partial volume of necrosis and the decreased Cho/NCr and increased Lac/NCr in the PT group (we did not distinguish between contributions from lipid or lactate in the latter). In either case, care must be taken in interpreting response to treatment in the context of pre treatment spectra. 0.9cc volume is the current practical limit for large coverage MRSI. We are currently extending this work to higher spectral resolution and SNR data acquired at 3T.

References:

Rock J, et al: Correlations between MRS and Image-guided Histopathology with Special Attention to Radiation Necrosis. **Neurosurgery** 51:912-920, 2002.