Correlation of quantitative in vivo 1H MRS of untreated pediatric medulloblastoma with quantitative histological features

X. Liu[1], I. Gonzalez-Gomez[2], A. Panigrahy[1], M. D. Krieger[3], G. J. McComb[3], M. D. Nelson[1], F. H. Gilles[2], S. Bluml[1,4]

[1]Radiology, Childrens Hospital Los Angeles, Los Angeles, CA, United States, [2]Neuropathology, Childrens Hospital Los Angeles, Los Angeles, CA, United States, [3]Neurosurgery, Childrens Hospital Los Angeles, Los Angeles, CA, United States, [4]Rudi Schulte Research Institute, Santa Barbara, CA, United States

Introduction: Childhood neuroglial tumors are complex disease processes. Various patterns of histologic features differentiate these tumors one from another (1). However, childhood neuroglial tumors of the same diagnostic name or grade contain histologic subsets that differ markedly in survival expectation (2,3) reflecting the histologic heterogeneity within each diagnosis or grade. Similarly, in vivo biochemical profiles of tumors with same diagnoses and grade vary substantially (4-6) as well. The goal of this study was to correlate tumor metabolite concentrations with *quantitative* brain tumor factors.

Material and Methods: 13 patients with cerebellar primitive neuroectodermal tumors (medulloblastoma) were studied. Single voxel 1H spectra were acquired using a PRESS sequence with TE = 35 ms, a repetition time of TR = 1.5 s, and 128 signal averages on a 1.5T GE clinical scanner. Spectra were processed using the LCModel V6.0 software (7) with water as the internal reference for absolute quantitation. This version of the LCModel has additional simulated model spectra for macromolecules and lipid resonances which improves the quantitation of the metabolites. Concentrations were corrected for the fraction of necrotic/cystic volume within the ROI (8). All tumors were resected within 3 days of the MR examination and 3-5 tissue samples were submitted for histological analyses. Five quantitative histological scores named "Spongy", "Proliferative", "Ring", "Fibrillary", and "Nuclear" factors were determined from 26 histologic features that are reliably recognized such as the presence or absence of microcysts, mitosis, adaptosis, the cell size and shape etc. (9). A set of five brain tumor factors is calculated from all samples from one patient and represents quantitative histological features of the *tumor as a whole*.

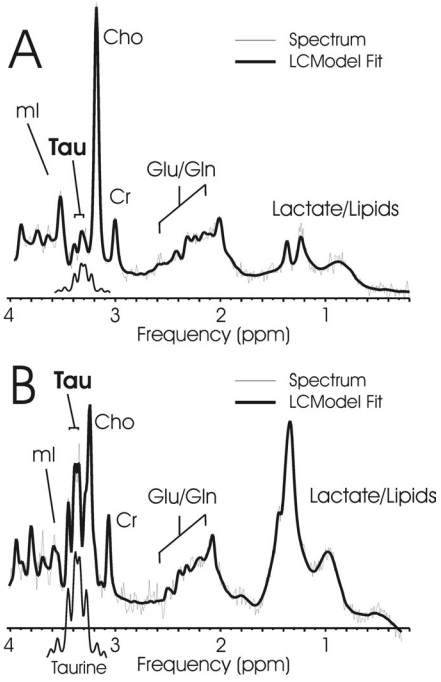

Fig. 1: ^{1}H MRS of medulloblastoma

Results: Medulloblastomas exhibited a considerable heterogeneity in their metabolic profile (Fig.1). Significant (linear) correlations with histologic factors were found for glutamate (Glu) with "Fibrillary" (Fig. 2), glutamate+glutamine (Glx) with "Fibrillary", and for glucose with "Nuclear". Concentrations or concentration ratios of other metabolites or the absolute lipid level did not correlate significantly with histologic factors.

Discussion: Although only a small number of medulloblastomas were studied, it appears that there is little correlation between the metabolic profile and histologic features. Histology and in vivo MRS complement each other. The significance of the metabolic information in respect to tumor malignancy and survival expectation is uncertain. Only a small number of patients were studied and long-term follow-up is required. On the other hand, the significance of factor scores to predict 5 year survival likelihood has been established (10). The "Fibrillary" factor contained three defining features: fine fibrillary stroma, low cell density, and astrocytes. In medulloblastoma a low score for "Fibrillary" is associated with a better chance for 5 year survival. In that context, the significant correlation of glutamate with "Fibrillary" is important. In vivo MRS could provide valuable information about tumor malignancy prior to the initial resection of the brain mass, the most important, therapeutical intervention. The accuracy of the quantitation of glutamate is compromised in low quality spectra due to its complex pattern and the overlap in spectral appearance with glutamine by a significant covariance with glutamine. The more robust sum of glutamate+glutamine (Glx) also correlated with "Fibrillary", however, less significantly than glutamate alone.

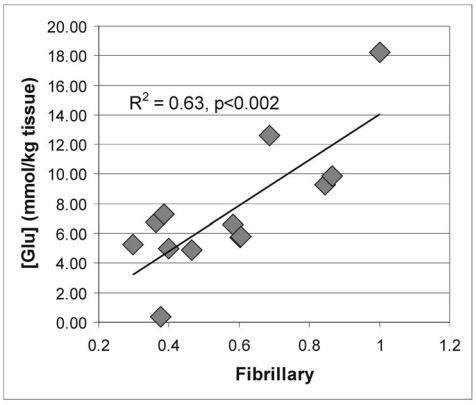

Fig. 2: Correlation of factor scores with ^{1}H MRS

References: 1.Yates AJ, Becker LE, Sachs LA. Childs Brain 1975;5(1):31-39. 2. Brown WD, Gilles FH, Tavare CJ, et al. J Neuropathol Exp Neurol 1998;57(11):1035-1040. 3. Gilles FH, Brown WD, Leviton A, et al. Children Brain Tumor Consortium. Cancer 2000;88(6):1477-1483. 4. Negendank WG, Sauter R, Brown TR, et al. J Neurosurgery 1996;84:449-458. 5. Howe FA, Barton SJ, Cudlip SA, et al. Magn Reson Med 2003;49(2):223-232. 6. Kovanlikaya A, Panigrahy A, Krieger MD, et al. Radiology 2004;in print. 7. Provencher SW. Magn Reson Med 1993;30(6):672-679. 8. Ernst T, Kreis R, Ross BD. J Magn Reson 1993;102:1-8. 9. Gilles FH, Sobel EL, Leviton A, et al. Pediatr Pathol Lab Med 1997;17(5):809-834. 10. Sobel EL, Gilles FH, Leviton A, et al. Neurosurgery 1996;39(1):45-54.

Acknowledgment: This work was supported by grant 5R33-CA096032-03 (National Cancer Institute).