Quantitative 1H MRS and Diffusion MRI of Untreated Pediatric Primitive Neuroectodermal Tumors

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Introduction: Primitive neuroectodermal tumors (PNETs) include a heterogeneous group of tumors thought to originate from primitive neuroepithelial cells that typically occur in pediatric patients. These tumors are surgically removed and patients are treated with radiation and chemotherapy. Staging and resultant patient stratification have been major components of patient management. However, clinical variables permitting broad distinctions between patient risk groups have proved to be unreliable factors for assessing tumor malignancy and assigning appropriate individual therapy (1). It has been hypothesized that characterization of tumors *in vivo* before resection may provide additional information which may guide therapeutic decisions and prognosis in individual patients. Elevated taurine (Tau) was detected *in vitro* in PNET (2, 3) and it was suggested that high Tau may be an indicator for high tumor malignancy (2). Also, MR diffusion weighted imaging (DWI) can assess the degree of cellularity (4). The goals of this study were to (i) quantify Tau with quantitative 1H MRS, (ii) assess tumor cellularity with DWI, and (iii) determine their correlation in untreated PNET *in vivo*.

Materials and Methods: 13 patients with newly diagnosed, untreated brain tumors, retrospectively classified as PNET, were studied on a 1.5T GE clinical scanner. Single voxel 1H MRS spectra of the tumors were acquired using a single voxel PRESS sequence with an echo time of TE = 35 ms, a repetition time of TR = 1.5 s, and NEX=128. The regions of interest (ROIs) were placed in the center of solid lesions and did not include any partial volume with surrounding normal appearing tissue in all cases. Single voxel 1H MRS quantification included determination of the fractions of tissue and of necrotic/cystic fluid. This measurement was based on the differences in the T2 relaxation time of tissue water and necrotic/cystic fluid (5) as apparent on T2 images and was used to correct metabolite intensities for the varying degree of necrosis of individual tumors. Spectra were processed using the LCModel V6.0 software (6) and absolute concentrations in institutional units (i.u.) of taurine ([Tau]) were determined. Processing of MRS data was completely automated and did not require user interaction. DW-EPI (TE=70ms, matrix=128×128, slice thickness=5mm, b=1000 s/mm^2) was performed in a subgroup of 8 PNET patients and apparent diffusion coefficient (ADC) maps were computed using software provided by GE. Mean ADC values were obtained from ROIs placed in tumors excluding any obvious necrotic areas within the lesion, normal appearing white matter, and CSF. Control data for 1H MRS were obtained in the occipital cortex from 14 age-matched subjects with unrelated and comparably minor clinical indications for MR such as developmental delay on the basis of a normal MRI report. 21 patients with other brain tumors were also included for comparison. For ADC measurements, patients served as their own controls because ADC values were computed from normal white matter distant from the brain mass and CSF.

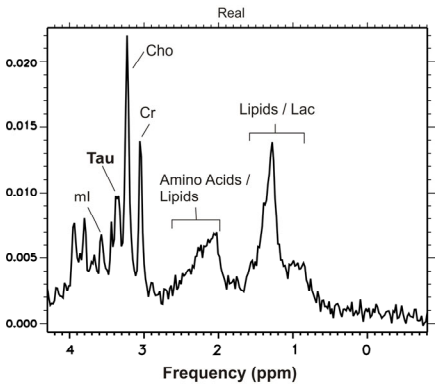

Figure 1: 1H MRS spectrum of PNET with high taurine signal.

Results: Peaks attributed to Tau were readily observed in all PNET patients and Tau was quantified with a high degree of reliability (Cramer-Rao bounds < 20%) (Fig. 1). [Tau] was significantly higher in "PNET" than in "Control" (3.94 ± 1.45 vs. 0.96 ± 0.50, p<1e-7) or "Other Tumor" (0.47 ± 0.57, p<1e-10) and separated all (but one) "other tumor" patients from PNET (Fig.2). A considerable variation in [Tau] was observed in individual patients. ADC values in white matter (869±118 μm^2/s) and CSF (3146±415 μm^2/s) were in good agreement with literature. Mean ADC in PNET was 1007±314 μm^2/s (min: 683 μm^2/s, max: 1500 μm^2/s), not significantly different from that in white matter and larger than what has been measured earlier in a single patient by Wilke et al. (7). When the ADC values were plotted against [Tau], generally lower ADCs were measured in tumors with higher [Tau] and a weak linear correlation was found (r=0.75, p<0.03, Fig. 3).

Discussion: In PNET, although clinical variables permit broad distinctions between patient risk groups, when used alone they have proved an unreliable basis for assigning therapy. A recent joint Children's Cancer Group and Pediatric Oncology Group study which randomized 'standard risk' PNET patients to receive reduced versus standard neuroaxis radiotherapy, was closed early after an increased risk of relapse was detected among patients in the reduced treatment arm (1). These data suggest that additional markers other than clinical variables are needed to accurately assess disease risk/tumor aggressiveness *in vivo* and individualize treatment. 1H MRS and diffusion imaging are standard MR techniques available on most clinical MR systems and can be readily incorporated into the pre-surgical MR examination of candidates for brain surgery. Results are immediately available after an MR examination and can thus be used for treatment decisions. Individual PNET tumors were well separated by their different levels of Tau and ADC. The significance of these parameters to predict malignancy needs to be evaluated by following-up individual patients and careful correlation with clinical outcome.

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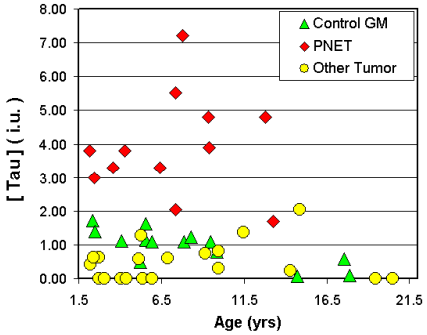

Figure 2: Taurine distinguished all (but one) PNET from other tumors.

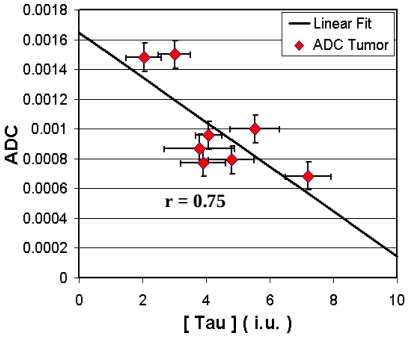

Figure 3: Low ADC values corresponded with high Taurine levels.