COMPARISON OF IN VIVO MRS GLUTAMATE/GLUTAMINE LEVELS IN TUMOR-ASSOCIATED EPILEPSY

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Aim: The pathogenesis of tumour associated seizures (TAS), a common co-morbidity with brain tumors remains poorly understood [1-2]. Glutomate has been implicated in many types of epilepsy [3-5]. In a pilot study of 9 patients we analyzed the concentration of glutamate/glutamine associated with gliomas using *in vivo* MRS, and correlated that with observed pre-operative seizures.

Methods: 9 Patients scanned between January 2008 and June 2009 for clinical purposes. All scans were performed on a 3T Siemens MRI System with the usual preoperative anatomical neurosurgical planning contrast MRI scan. A dedicated head phased array coil was used and all proton spectra was acquired using a point resolved spectroscopy (PRESS) pulse sequence. MR spectra was obtained from three 8cm3 voxels; one of which was placed in the tumor (central non necrotic area within the tumor), one in the peritumoral region (within 2cm from the outer border of the tumor and not including any macroscopic tumor) and one in the contralateral brain (mirroring the position of the brain tumor) with and without water saturation. Placement of the voxels was determined by one clinician (TIY). Water saturated and non-water saturated spectra were required to calculate absolute concentration of glutamate [3]. The acquisition parameters were: Flip angle = 90, TR/TE = 3000/30 ms, 5kHz bandwidth, 2048 points per spectra and voxel dimensions of 2x2x2 cm3. For the water saturated spectra the data was averaged 64 times, while the non-water saturated spectra were average twice. Proton MRS spectra was processed using the software program LCModel® (USA) [6] according to previously described methods for quantifying water normalised concentration of brain metabolites

Results: When comparing ipsilateral to contralateral sides, there was a significant difference in levels of glutamate/glutamine for both the **gross tumour (p**=0.024**)**, but not for the **peritumoral oedema (p**= 0.12). In addition, there was a significant difference in the levels of glutamate/glutamine between the **gross tumour** and **peritumoral** regions of all glioma patients (**p** < 0.047). Finally, a significant difference (**p** = 0.02) (see Fig1 (b)) was observed in the **peritumoral** glutamate levels between TAS positive patients (those with pre-operative seizures) and TAS negative (no pre-operative seizures), whereas there was no direct correlation when comparing the **gross tumour** regions (**p** = 0.4)

Conclusion In this pilot study, we found elevated glutamate/glutamine levels in the peritumoral area of tumours who experienced pre-operative seizures compared to those which did not. Due to the small sample size, we are in the process of acquiring a larger MRS and *ex vivo* prospective data set (N>100) to confirm these findings.

References: **1:** Glantz MJ et al. Neurology 2000;54:1886-93, **2:** van Breemen et al Lancet 2007;6:421 – 30. **3:** Rego AC et al. Neurochem Res 2003;28:1563-74. **4:** Schousboe A et al. Neurotoxicity research 2005;8:221-5. **5:** During MJ et al. Lancet 1993;341:1607-10**. 6:** LCModel, S. W. Provencher

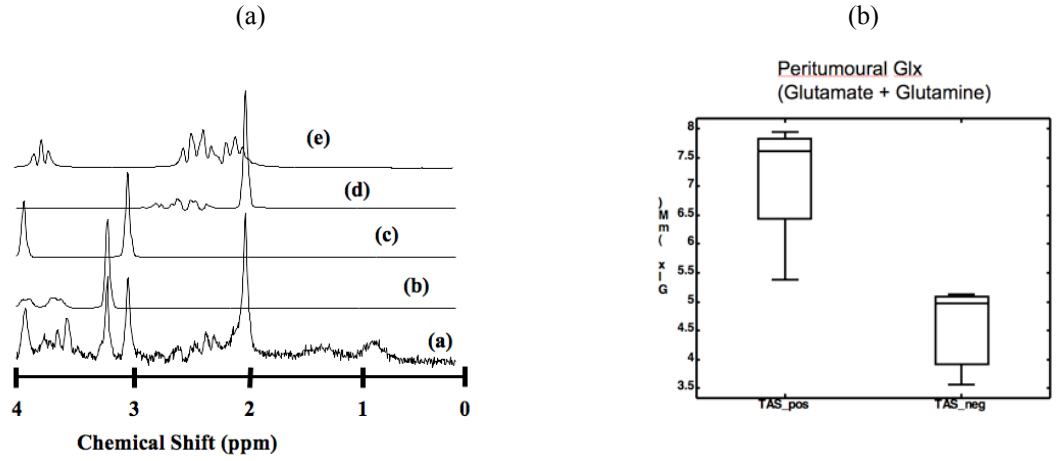

Figure 1: *In vivo* MRS (a) of the peritumoural region from a TAS positive glioma patient. The spectrum is from an 8 cm^3 voxel using a PRESS pulse sequence. Using linear combinations of model spectra, including Cho (b), Cr (c), NAA (d) and Glx (e), a best fit model can be estimated (LC Model) and used to calculate metabolite concentrations. In a pilot study of 9 glioma patients (b) we found a statistically significant (p=0.02) greater concentration of Glx (7.1+/-1.2) in the peritumoural region of TAS positive patients (n=4) compared to TAS negative patients (4.6 +/- 0.9, n=3).