

Quantitative 2D chemical shift imaging of glutamate in brain tumour patients

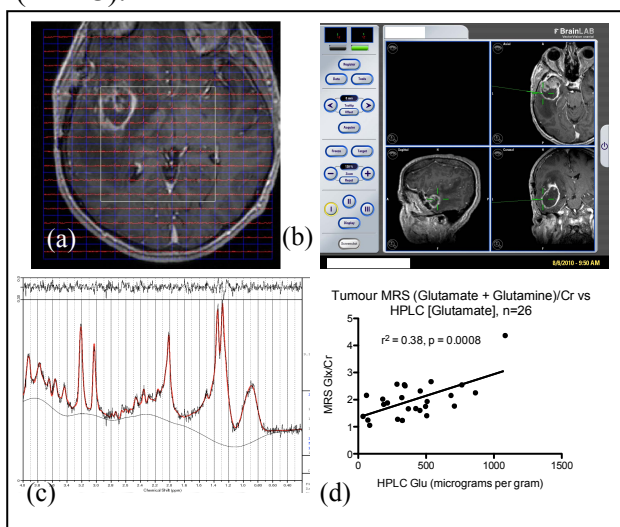
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Introduction:

The aim of this study was investigate the accuracy of 2D chemical shift spectroscopic imaging (2DCSI) quantification of glutamate (Glu) in patients with primary brain gliomas. Elevated Glu levels associated with gliomas have been implicated in tumour associated epilepsy and tumour invasion. 2DCSI is a non-invasive method of imaging the distribution of brain metabolites in-vivo. However, to date no study has investigated or validated its accuracy in quantifying Glu concentration in glioma patients. Such validation is necessary for translation 2DCSI for applied clinical research or clinical brain tumour management.

Methods: Water suppressed and non-suppressed 2DCSI data (2.5 min per image) were acquired on phantom solutions of known glutamate concentration, and 26 patients prior neurosurgery on a 3T Seimens scanner. In addition routine stereotactic gadolinium enhanced T1 weighted images were acquired. Glioma samples were obtained during surgery, and their location marked using stereotaxy hardware and software (BrainLab, Germany). These coordinates were used to locate the site of the MRS voxel anatomically corresponding to the site from which the tissue samples were taken. The MR spectra acquired from this voxel were analysed using LCModel™ to calculate estimates of Glu, and combine Glu and glutamine (Glx) levels [1]. The weight of Glu (micrograms per gram of tissue sample) was determined using high performance liquid chromatography (HPLC).

Results: The phantom MRS spectra were plotted against the phantom solution concentrations. The correlation between MRS measured glutamate (Glu) concentrations, and Glu to creatine ratio (Glu/Cr) were $r^2=0.89$ and 0.98 respectively. Representative *in vivo* 2DCSI data is shown in Fig. 1. The HPLC measured Glx was plotted against the MRS measured intensities of Glx and Glx/Cr (to date, n=26). Figure 1d shows the correlation between Glx/Cr and HPLC in tumoural tissue. Similar correlations were found for Glx vs HPLC in tumoural ($r^2=0.71$, $p=0.001$), and peritumoural tissue ($r^2=0.86$, $p=0.02$). Due to broadening of the spectra peaks Glu was not separable from glutamine in many of the brain tumour patients. This resulted in non-significant correlations between spectroscopic and HPLC Glu measurements.



Discussion and Conclusions: The heterogeneous nature of T2 and T1 relaxation in brain tumours has the potential to limit the ability to quantify tumour metabolites using MR spectroscopic techniques. However, this study has found that despite this, a good correlation exists between *in vivo* spectroscopic Glx concentration and “gold standard” HPLC concentrations of Glu. This suggests that quantification of Glx 2DCSI by lmodel is robust biomarker of *in vivo* Glu levels. This is one of a few if not the only study to directly correlate *in vivo* MR spectroscopic quantification of metabolic concentrations with HPLC data acquired on biopsy specimens.

References:

1. AZ Damyanovich *et al*, *MAGMA* (Suppl 1), 74 (1998)