Localised 2D COSY of Human High-Grade Glioma Tumours

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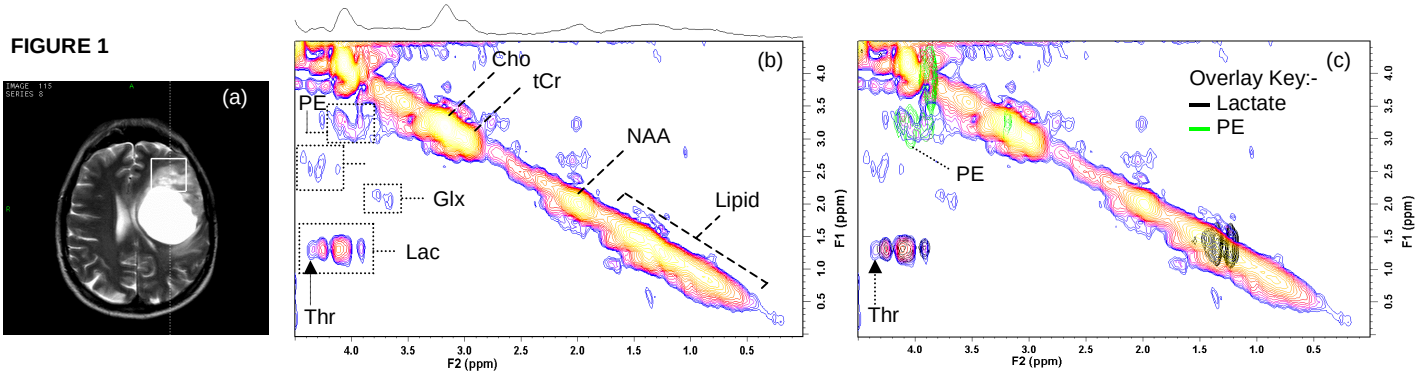
Introduction: Single-voxel 1D ^{1}H-MRS techniques such as PRESS and STEAM have been used extensively for characterising the metabolism associated with human intracranial tumours *in vivo* [1]. However, ^{1}H-MRS performed using clinical MRI systems is often hampered by poor spectral resolution and severe spectral overlap. As a result, spectral analyses of ^{1}H-MRS data have largely been restricted to the most prominent methyl (-CH_3) signals of N-acetyl aspartate (NAA), total creatine (tCr) and choline-containing compounds (Cho). Thomas *et al*. reported the implementation of a localised 2D COSY sequence, which facilitated the detection of an increased number of *J*-coupled metabolite resonances in normal human brain tissue at 1.5 T [2]. Recently, we employed a similar localised 2D COSY sequence for studying metabolism in human extracranial tumours *in vivo* [3]. However, the application of localised 2D COSY to human intracranial tumours *in vivo* has not been reported to date. The primary objective of this study was to evaluate the potential role of *in vivo* 2D COSY in a cohort of patients presenting with high-grade (HG) glioma tumours.

Materials and Methods: The localised 2D COSY sequence (90^o-180^o-90^o) was implemented on a 1.5 T Siemens (Erlangen, Germany) Vision whole-body MRI scanner. Six patients presenting with biopsy-proven HG glioma tumours have been examined to date. The head coil was used for radiofrequency (RF) transmission and signal reception in each study. T_2-weighted fast spin echo MR images (19 slices, TR/TE = 4700/120 ms, NEX = 1) were used to position the spectroscopy voxel (27 ml) within the region of interest (ROI). Localised 2D COSY spectra were recorded from the voxel using the following acquisition parameters: 48 t_1 increments, Δt_1 = 1.6 ms, t_1-sampling window centred at 102 ms, 16 averages per t_1 increment, 1024 complex points sampling t_2, TR = 2000 ms (26 minute acquisition time). Two identical SLR RF pulses were used for slice-selective excitation and coherence transfer and an optimised sinc RF pulse (Mao) used for slice-selective refocusing. All three slice-selective RF pulses were of 2.56 ms duration. Symmetric B_0 crusher gradients (maximum amplitude: 22 mT/m; duration: 6 ms) were positioned around the last slice-selective 90^o RF pulse to select the N-type signal. Water suppression was achieved using the WET sequence [4]. **Data processing:** performed using the FELIX 2002 NMR processing software (Accelrys Inc., San Diego, CA). The 2D raw data were initially zero-filled to provide a 2048 x 128 matrix. A skewed sine bell squared apodisation function was applied along t_2 (90^o phase-shifted) and an unshifted sine bell apodisation function was applied along the t_1 dimension. Following a complex 2D FT and magnitude calculation the 2D COSY spectra were referenced to the residual water peak at 4.7 ppm. The metabolite 2D peaks were assigned using chemical shift values taken from previously reported data [2] and using 2D COSY spectra acquired from separate phantoms containing individual metabolite species (each at a concentration of 50 mM with 5% bovine serum albumin).

Results: Figure 1(a) shows the axial T_2-weighted MR image recorded from a 48 year-old male patient presenting with a HG astrocytoma in the left parietal lobe. The localised 2D COSY spectrum recorded from the spectroscopy voxel (white box) is presented in figure 1(b) with the F2-summed projection displayed above the 2D spectrum. Resonances observed along the diagonal spectrum ($F_1 = F_2$) have been assigned to lipids (saturated protons: 0.5 - 2.0 ppm), NAA (2.0 ppm), tCr (3.0 ppm) and Cho (3.2 ppm). The cross peaks of a number of metabolites can be seen below the $F_1 = F_2$ spectrum. The cross peaks have been assigned to NAA (F_2/F_1 = 4.35/2.7 ppm), to the glutamate and glutamine pool (Glx: 3.75/2.1 ppm), lactate (lac: 4.1/1.3 ppm) and phosphoethanolamine (PE: 4.0/3.2 ppm). The identical 2D COSY spectrum is displayed in figure 1(c) overlaid with the 2D COSY spectra recorded from Lac and PE phantoms. The cross peaks seen at 4.1/1.3 ppm and 4.0/3.2 ppm show good overlap with the cross peaks of Lac and PE, respectively. An intense Lac cross peaks was observed in all five 2D COSY spectra and a cross peak was assigned to PE in two of the five patient spectra. In addition, note the presence of an additional signal downfield from the Lac cross peak (indicated by an arrow), which corresponds to threonine (Thr) in phantom studies. Thr has previously been identified in HG human brain tumour samples using high-resolution ^{1}H-MRS methods *in vitro* [5]. A cross peak was assigned to Thr in two of the five patient spectra. **Discussion;** In contrast to the common Lac-editing methods (e.g. 1D ^{1}H-MRS with long TE), the localised 2D COSY sequence may permit the simultaneous detection of Lac and tumoural lipid proton resonances. Furthermore, the localised 2D COSY data acquired thus far suggests that, in some tumours, the Lac -CH_3 doublet resonance (1.3 ppm) may contain an additional contribution from the corresponding -CH_3 doublet resonance of Thr. Finally, the severe spectral overlap associated with 1D ^{1}H-MR spectra recorded at 1.5 T hampers the identification of the PE methylene protons at 3.2 and 4.0 ppm. PE levels have been monitored in human tumours using ^{31}P-MRS, which requires specialised hardware and effective ^{1}H/^{31}P decoupling. The localised 2D COSY technique may provide a unique ^{1}H-MRS method for PE-detection in human tumours.

FIGURE 1



Conclusion: This exploratory study has demonstrated, for the first time, the application of a localised 2D COSY sequence for investigating human brain tumour metabolism *in vivo*, confirming the presence of Lac in tumours with high lipid content, and detecting PE and Thr in some patients. An increased number of patient studies are required to evaluate the potential role of 2D COSY in HG glioma patients. The 2D COSY sequence will be used to investigate the metabolism associated with other brain tumour histologies including meningiomas and metasteses.

References: [1] Howe *et al*., Magn Reson Med 2003;49(2):223-232. [2] Thomas *et al*., Magn Reson Med 2001;46(1):58-67. [3] Prescot *et al.* Proc ISMRM 2002;10:2048. [4] Ogg *et al*. Magn Reson B 1994;104(1):1-10. [5] Florian *et al*., NMR Biomed 1995;8(6):253-26.