Case Study: 2D L-COSY of Low-Grade Gliomas at 7T

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Introduction: Magnetic Resonance Spectroscopy (MRS) has proven an effective modality for the assessment of brain tumors *in vivo*, particularly in establishing the elevated presence of choline and lactate as biomarkers for high grade tumors. The recently-demonstrated two-dimensional (2D) localized correlated spectroscopy (L-COSY) technique at 7T (1) could potentially improve the capability of MRS techniques by uniquely resolving lactate from background lipids resonances and identifying individual species of choline-containing metabolites (glycerophosphocholine (GPC) + phosphocholine (PC), glycerophosphoethanolamine (GPE) + phosphoethanolamine (PE) and ethanolamine (Eth)). Reliable quantification of PC could be of particular interest as previous studies have correlated glioma grade with increased PC (2). The primary goal of this study was to evaluate 2D L-COSY at 7T in characterizing the biochemical properties of brain tumors in greater detail than is possible at lower fields or with conventional spectroscopy techniques.

Materials & Methods: Two patients, both with pathologically-confirmed low grade gliomas – in the temporal lobe and in the occipital lobe – were scanned using a 32-channel head coil on a Siemens 7T whole-body scanner. T_1-weighted and T_2 fluid attenuated inversion recovery (FLAIR) MRI scans were used to place the 2D L-COSY voxel in the tumor. The 2D L-COSY scan parameters were as follows: TE/TR = 20/2000ms, 64 Δt_1 increments of 0.4ms, F_2/F_1 bandwidth = 4000/2500 Hz, 8 averages, 2.5x2.5x2.5 cm^3 (15.6 ml) voxel size, 17-minute scan time. The data was processed offline in MATLAB, quantified with the volume integral method and compared with data from a previous reproducibility study using the same sequence and parameters and taken from the occipital lobe of six healthy volunteers (age 30-72) (1). Creatine was used as an internal reference and all metabolite peaks were normalized to the volume integral of the 3.0 ppm diagonal resonance of creatine.

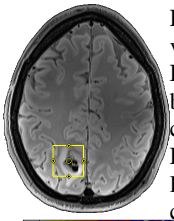
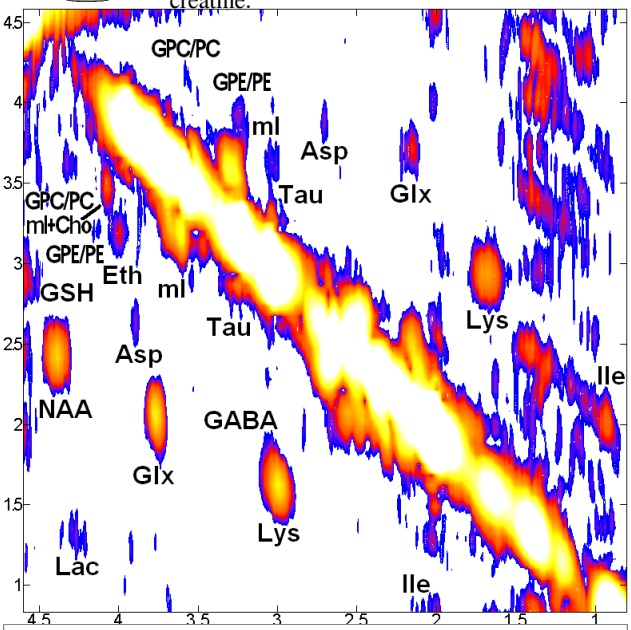
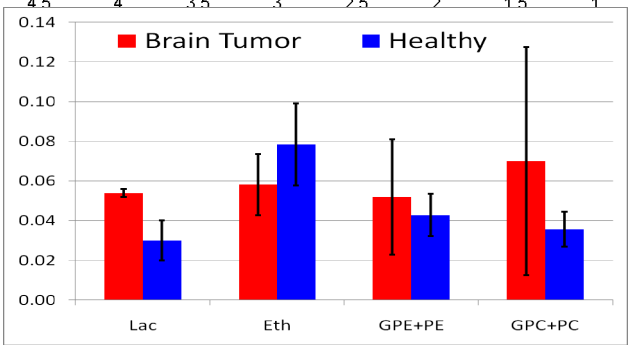


Figure 1 (left): Localization of 2D L-COSY voxel in occipital lobe using T_2 FLAIR MRI.

Figure 2 (below): 2D L-COSY spectrum from brain tumor. Several identifiable metabolite cross peaks have been labeled

Figure 3 (bottom): Quantified values of Lac, Eth, GPE+PE and GPC+PC normalized to creatine.





Results & Discussion: Figure 1 shows the image with the 2D L_COSY voxel placed on the tumor in the occipital lobe. Figure 2 shows the 2D L-COSY spectrum acquired from the tumor . Several metabolite cross-peaks, including aspartate (Asp), γ-aminobutyric acid, glutamate/glutamine (Glx), glutathione, isoleucine (Ile), Lac, lysine (Lys), N-acetylaspartate (NAA), taurine (Tau) and the choline-containing compounds (Eth, GPC/PC, GPE/PE and mI+free Cho) (3). L-COSY facilitated the quantification of Lac despite the presence of overlapping lipid peaks from the scalp. The cross-peak resonance of lactate at [F_2, F_1] = 4.1, 1.2 ppm, were clearly visible and were not subject to spectral overlap with lipids.

Figure 3 shows normalized values for Lac, Eth, GPE+PE and GPC+PC from the two brain tumor patients and the six healthy volunteers. Among these metabolites, Lac and GPC+PC appeared elevated in patients while Eth was lower although firm conclusion from this study must be reserved until a large sample size is acquired. The detection of NAA in the spectrum suggests the presence of healthy neurons in addition to tumor in the localized voxel. Future applications of L-COSY using multi-voxel acquisition could lead to smaller individual voxels and thereby reduce partial volume effects such as this.

Conclusion: 2D L-COSY was successfully implemented to study brain tumors at 7T. The cross peak of lactate was identified separate from the background lipid peaks and choline-containing metabolites were detected separate from each other. Although only low-grade tumor patients were scanned in this preliminary study, the sequence could potentially be used to resolve high grade from low grade tumors and potentially be used to detect the 2-hydroxy glutamate cross peak, which has been suggested to be a specific biomarker of secondary gliomas with IDH1 mutation.

References: 1. Verma G et al., JMRI 2013 *in press*, 2. Poptani H et al. Amer Journal Neuroradiology 1995;16(8):1593-1603 3. Velan S., Magn Reson Med 2007;26:405-409