

Quantitative Metabolite Mapping in Human Brain at 4T using Short TE ¹H LASER-CSI and Tissue Segmentation

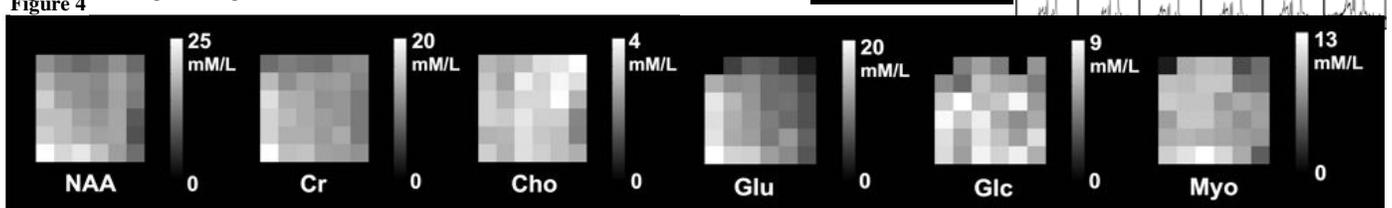
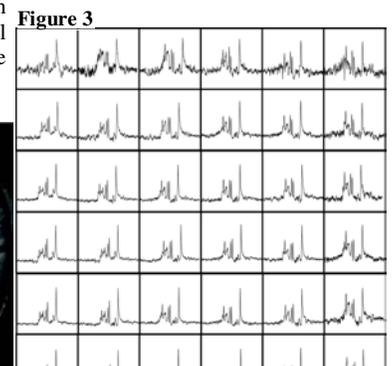
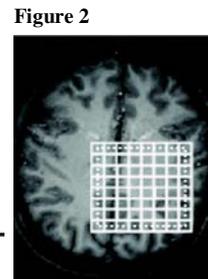
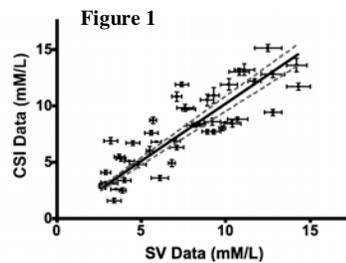
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Introduction Most current ¹H spectroscopy methods still limit clinical research studies to metabolite measurements from only a single-voxel and/or the detection of only four metabolites (N-acetyl-aspartate (NAA), creatine (Cr), choline (Cho) and lactate (Lac)) and/or do not provide the absolute quantitative measures that are required to make meaningful comparisons in longitudinal studies and between research centers. This study presents a new short echo-time (TE) ¹H chemical shift imaging (CSI) protocol that uses localization by adiabatic selective refocusing (LASER) for region of interest (ROI) pre-selection, macromolecule subtraction and tissue segmentation to produce absolute quantitative metabolite maps of glutamate (Glu), glucose (Glc) and myo-inositol (Myo) in addition to NAA, Cr and Cho from human brain at a nominal voxel size of 0.56 cm³. Metabolite measurements from LASER-CSI are compared to those made using LASER-single voxel spectroscopy (SVS).

Methods Data from eight healthy volunteers were acquired using a 16-element quadrature hybrid birdcage RF coil on a 4.0 Tesla Varian whole-body MRI equipped with a Siemens Sonata gradient coil. LASER-CSI data were acquired (6cmx6cmx1cm volume, 8x8 phase-encodes, nominal voxel size=0.56cm³) in left posterior brain superior to the ventricles. K-space-dependent averaging ($N_{av}=25*(0.5+0.5*\cos(\pi k/k_{max}))+1$) was employed during the water-suppressed acquisition. Total spectroscopic imaging time was 47 min. LASER-SVS (128 averages, TR/TE=2200/46ms (full spectrum), T₁/T₂/TR/TE=2200/700/4200/46ms (macromolecule spectrum) spectra² were acquired in a homogeneous region of parietal white matter from a volume equal to the effective voxel size of the spectroscopic imaging protocol (1.5 cm x 1.5 cm x 1cm based on the full width at half maximum of the point spread function). A CSI voxel was aligned with the SVS location during post-processing. After spatial reconstruction of the full, macromolecule and water spectra, the CSI spectra were processed identically to the SV spectra on a voxel-by-voxel basis. Spectra were lineshape corrected by QUECC³, residual water subtracted, and the macromolecule baseline removed² prior to time domain fitting using prior knowledge of 19 metabolite lineshapes. CSI spectra were compared to SVS spectra on the basis of: linewidth of the unsuppressed-water signal, SNR (NAA/standard deviation of the noise) and absolute metabolite concentrations. The T₁-weighted MR images were segmented using SPM2^{4,5} to generate white matter (WM), grey matter (GM) and cerebrospinal fluid (CSF) maps. Tissue class maps were point spread function (PSF)-weighted at the location of each CSI voxel prior to calculating the proportional contribution of each component. Tissue composition estimates were used to determine water concentration (using 71%, 81% and 100% for WM, GM and CSF respectively, where [H₂O at 38°C]=55.12M). Tissue composition was also used to estimate T₁ and T₂ signal attenuation based on literature values^{6,7,8,9,10}. Metabolite levels were normalized to the unsuppressed water signal from the same voxel after correcting for relaxation effects, water concentration and CSF fraction (assuming negligible metabolite levels present in CSF) to yield tissue metabolite levels in absolute units².

Results and Discussion Figure 1 presents a linear-regression analysis of the concentration measurements from LASER-SVS and matching LASER-CSI voxels from all eight subjects (slope=1.01±0.03, r²=0.73). Figure 3 displays spectra from the inner 6x6 voxels of the LASER-CSI acquisition depicted in Figure 2 (dotted line = LASER excitation, solid lines=acquisition matrix). High spectral quality was observed throughout although a slight decrease in SNR



was noted in the top row. Average unsuppressed-water linewidths in SVS and the corresponding CSI voxels were 7.1 ± 0.6 Hz, and 8.7 ± 2.7 Hz respectively. Average SNR for SVS and CSI spectra were 10 ± 3 and 14 ± 5 respectively. Figure 4 displays quantitative metabolite maps corresponding to the acquisition shown in Figures 2 and 3.

Conclusion Quantitative metabolite maps for six metabolites (NAA, Cr, Cho, Myo, Glu and Glc) in healthy human brain have been generated from short TE ¹H LASER-CSI data for the first time. Tissue segmentation using SPM2 and PSF characterization accounted for the tissue composition of each voxel facilitating absolute quantification in voxels with mixed tissue content. Though the metabolite maps for NAA, Cr and Glu do show a few abnormally high values in the lower left corner, the remaining concentration measurements are physiologically reasonable and in good agreement with previously published values. By combining three very desirable attributes: a multi-voxel acquisition, detection of more than four metabolites and quantitative concentration measurements, in a time frame that is feasible for clinical research studies, LASER-CSI represents a viable and attractive option for future ¹H NMR spectroscopic investigations.

Acknowledgements and References Funding provided by Robarts Research Institute and CIHR/UWO Strategic Training Initiative in Cancer Research and Technology Transfer. (1) Garwood M, DelaBarre L. *JMR*. 153:155-177 (2001). (2) Kassem M, Bartha R. *MRM*. 49:918(2003). (3) Bartha R, Drost D, Menon R, Williamson P. *MRM*. 44:641-645 (2000). (4) Wright IC et. al. *Neuroimage*. 2:244-252 (1995). (5) Ashburner J, Friston K. *Neuroimage* 6:209-217 (1997). (6) Micaeli S et. al. *MRM* 47:629-633 (2002). (7) Bartha R et. al. *MRM* 47:742-750 (2002). (8) Mason GF et. al. *MRM* 126:18-29 (1997). (9) Posse S. *MRM* 33:246-252 (1995). (10) Choi CG et. al. *MRM* 41:204-207 (1999).