In-vivo Short-Echo-Time Single-Voxel Proton LASER Spectroscopy at 7 Tesla Incorporating Macromolecule Subtraction

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Background: Metabolite levels measured by short-echo-time proton (^{1}H) MR spectroscopy (MRS) may provide indicators of disease progression in conditions such as Alzheimer's disease (AD). The use of high fields increases signal to noise ratio and spectral dispersion leading to improved metabolite quantification. Metabolite level changes have been demonstrated in multiple brain regions in AD at lower fields. Furthermore, it has been postulated that these levels can be used to detect the early onset of AD. Short echo-time spectroscopy measurements must account for the broad macromolecule baseline [1], either by fitting [2], or by direct measurement and subtraction [3]. The purpose of this study was to develop a method of acquiring quantitative short-echo-time ^{1}H MRS at 7T, that incorporated metabolite nulling for accurate measurement of the macromolecule baseline, and to quantify metabolites using prior knowledge from ex-vivo aqueous metabolite solutions and correction for tissue relaxation and partial volume.

Method: A 7T Varian/Siemens MRI system with a 15 channel transmit and receive head coil (built in-house) was used to acquire single-voxel short-echo-time ^{1}H MR spectra as previously described [4], from the parietal-occipital region of young healthy volunteers and from 19 separate ex-vivo aqueous metabolite phantoms. A conventional localization by adiabatic selective refocusing (LASER) sequence [3] was modified as described by Marjanska et al [5], which consisted of a 2 ms slice selective 90° excitation pulse followed by two pairs (one pair for each remaining orthogonal dimension) of slice-selective adiabatic full-passage pulses (hyperbolic secant, R10, 3.5 ms) (TR/TE = 3700/38 ms). Eight global 5 ms gaussian pulses were used for variable pulse power and optimized relaxation delays (VAPOR) water suppression [6]. T_1-weighted gradient echo images were used for voxel placement. Single inversion recovery was used to determine the in-vivo T_1 values of N-acetylaspartate (NAA), glutamate (Glu), creatine (Cr), and choline (Cho) by acquiring spectra from a 3x3x3 cm^3 voxel in the parietal-occipital region of 7 volunteers (24 - 31 years old) with inversion times (TI) ranging from 0.14 s to 4.44 s, and then fitting their peak heights ($M_z(t)$) at each inversion time (t = TI) to the longitudinal relaxation equation ($M_z(t) = M_o[1 - \exp(-t/T_1)]$). Two non-selective 5 ms adiabatic full-passage pulses were used for double inversion recovery [7], and the optimal inversion times TI1/TI2 for metabolite nulling to measure the macromolecule baseline were calculated from the measured T_1 values. Ex-vivo data was obtained from 19 plastic balls (5.1 cm diameter) each filled with an aqueous solution of one of 19 metabolites at a concentration of 100 mM. Each metabolite spectrum was fitted to produce the prior knowledge lineshape for that metabolite. T_1-weighted anatomical images were acquired using a 3D FLASH sequence and segmented into gray matter, white matter, and cerebral spinal fluid using FMRIB's Automated Segmentation Tool (FAST) [8] to compute tissue partial volumes within the measurement voxel.

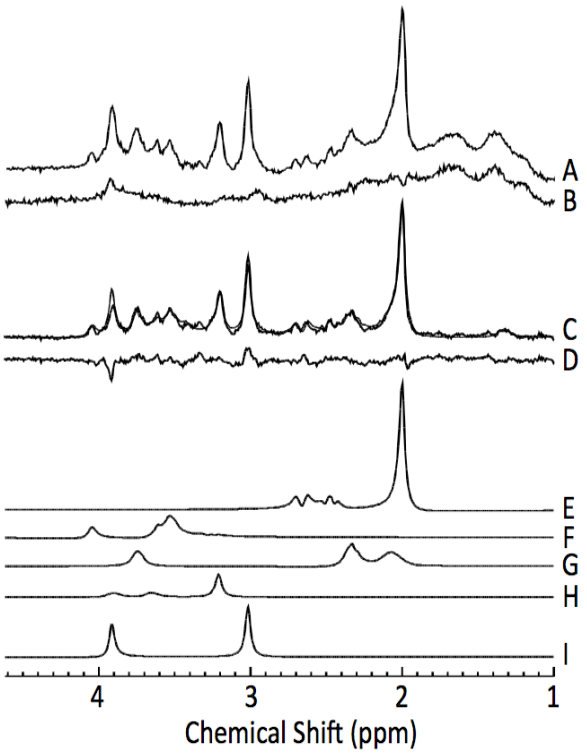

Figure 1: (A) full, (B) macromolecule, (C) difference spectra with the fitting result superimposed, and (D) is the residual between the data and the fit. Below the data are 5 of the 19 individual metabolite components (E) NAA, (F) Myo, (G) Glu, (H) Cr, and (I) Cho.

Results and Discussion: The T_1 values for NAA, Glu, Cr, and Cho were found to be 1.34 ± 0.08 s, 1.04 ± 0.09 s, 1.48 ± 0.05 s, and 1.22 ± 0.05 s, respectively. From these T_1 values, the double inversion recovery times TI1/TI2 for optimal metabolite suppression leading to macromolecule detection were calculated to be 3.14/0.70 s. Figure 1 (A) is a representative in-vivo full spectrum without metabolite suppression, and (B) is the macromolecule spectrum acquired with metabolite suppression. NAA, myo-inositol (Myo), Glu, Cr, and Cho are 5 of the 19 metabolites fitted and their prior knowledge lineshapes are shown in Figure 1 (E - I). The least squares fit of the 19 individual metabolite basis curves to the metabolite only spectrum (Figure 1 (C)) produced a small residual (Figure 1 (D)) illustrating the effectiveness of the macromolecule removal. Future work will involve using this method to measure metabolite changes over time in Alzheimer's disease clinical studies.

References:

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