In-Vivo Measurement of Serine in Human Brain by Constant-TE PRESS Difference Editing at 7.0 Tesla

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INTRODUCTION: Serine (Ser), a co-agonist at N-methyl-D-aspartate receptors, has three coupled spins resonating at 3.98, 3.94 and 3.83 ppm [1]. Because of its low concentration (~0.5 mM) and the overlap with primarily the creatine (Cr) 3.92 ppm singlet, detection of Ser in human brain by ^{1}H-MRS remains as a challenge. A spectrally-selective refocusing approach, that is the first attempt to measure this experimentally-challenging metabolite, was reported a year ago [2], which employed a narrow-band 180° RF pulse to refocus the Ser 3.83-ppm resonance and to dephase the Cr signal and other neighboring resonances. The clinical utility of this method may not be very promising because the signal intensity and lineshape are both sensitive to the potential frequency drift, arising from subject motion during the long measurement time required to achieve an acceptable SNR *in vivo*. Here, we propose a constant-TE PRESS difference editing strategy for detection of Ser, which utilizes difference in spectral pattern of strongly-coupled spins at unequal subecho times (TE_1 and TE_2) with a single (total) TE. A preliminary *in vivo* result at 7T is presented.

METHODS: Due to the coherence proliferation between coupled resonances and the imperfect excitation profile of volume selective RF pulses, the signal from strongly coupled spins is not fully described by the total echo time (TE) but also depend on the subecho times of a PRESS sequence. A difference in spectral patterns of Ser between unequal pairs of subecho times with an identical total TE can be utilized to reveal a Ser signal and cancel out the Cr 3.92-ppm singlet which depends on TE only. Subecho time dependence of the Ser multiplet at 7T was investigated for TE_1 and TE_2 between 20 – 200 ms with 1 ms increments, using density-matrix simulation incorporating the slice-selective shaped RF and gradient pulses. Spatial localization was obtained with an 8.8-ms 90° RF pulse (BW = 4.7 kHz) and two 11.9-ms 180° RF pulses (BW = 1.4 kHz). *In vivo* validation of the simulation result was conducted at 7T (Philips Medical Systems, Cleveland, OH, USA), using a quadrature birdcage head RF coil with 16 reception channels for RF transmission and reception. A 40×40×40 mm^3 voxel was positioned in the medial prefrontal cortex of a healthy volunteer (see Fig. 3).

RESULTS and DISCUSSION: Fig. 1 presents the dependence of the Ser multiplet on PRESS TE_1 and TE_2. For a given TE, the Ser signal intensity and lineshape differ between various pairs of TE_1 and TE_2. Two spectra within circles indicate the possibility of Ser difference editing. Further refinement of TE_1 and TE_2 was conducted in such a way that, for a given TE, the difference edited Ser peak amplitude was calculated for all possible pairs to obtain two pairs of TE_1 and TE_2 that give maximum difference-edited peak amplitude. This amplitude is plotted vs. TE in Fig. 2. For T_2 = 130 ms (which is a mean value of experimental T_2,s of Cr and NAA in human brain at 7T), the maximum edited peak amplitude is predicted at TE = 188 ms, namely, from (TE_1, TE_2) = (108, 80) and (49, 139) ms. Fig. 3 displays calculated difference-edited spectra of Ser and several contaminants from these subecho times and an *in vivo* brain edited spectrum at the bottom. A peak is clearly discernible at ~3.96 ppm, in agreement with calculation. The area of this peak was estimated to be 1.5% with respect to a Cr "3.03-ppm" signal, giving 0.4 mM with reference to Cr at 8 mM. Further *in vivo* studies are currently underway.

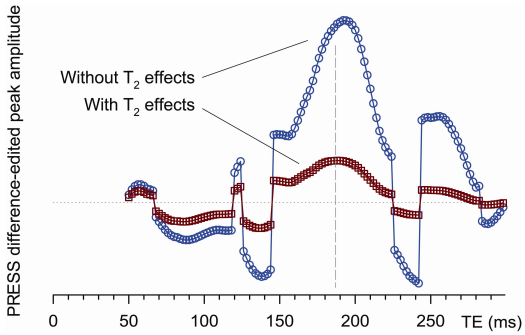

FIG. 2. Maximum constant-TE-PRESS-difference-edited peak amplitude of serine (obtained from various TE_1-TE_2 pairs for a given TE) is plotted versus TE (= TE_1+TE_2). When T_2 of 130 ms is incorporated, the peak amplitude is maximum at TE = 188 ms. The peak amplitude was obtained from spectra broadened to 12 Hz. A horizontal dotted line indicates zero amplitude.

REFERENCES: **1.** Govindaraju V *et. al.*, NMR Biomed 2000;13:129-153. **2.** Theberge J, Renshaw PF. Proceedings ISMRM 2007, Toronto. p. 1373.

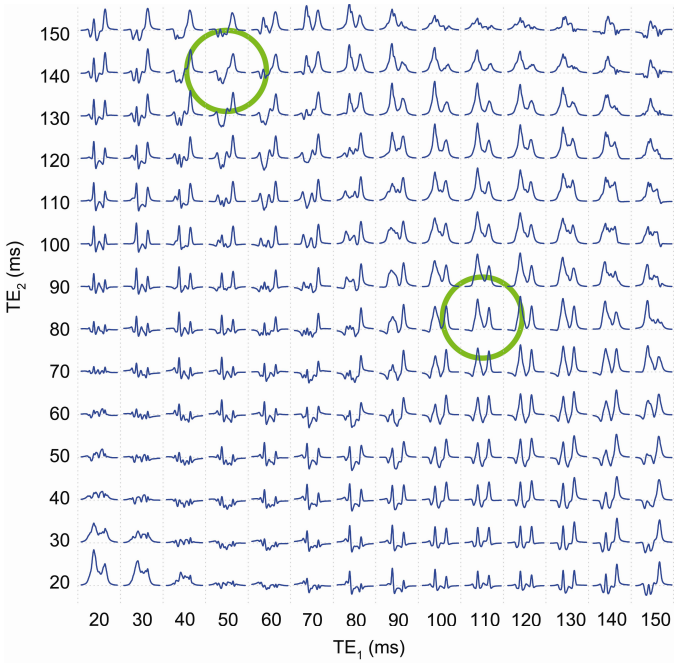

FIG. 1. Numerically-calculated PRESS spectra of serine at 7T are plotted vs. TE_1 and TE_2. Spectra are shown between 3.7 – 4.1 ppm. Spectra are broadened to 0.04 ppm (12 Hz). Two circles indicate potential pairs of spectra for difference editing.

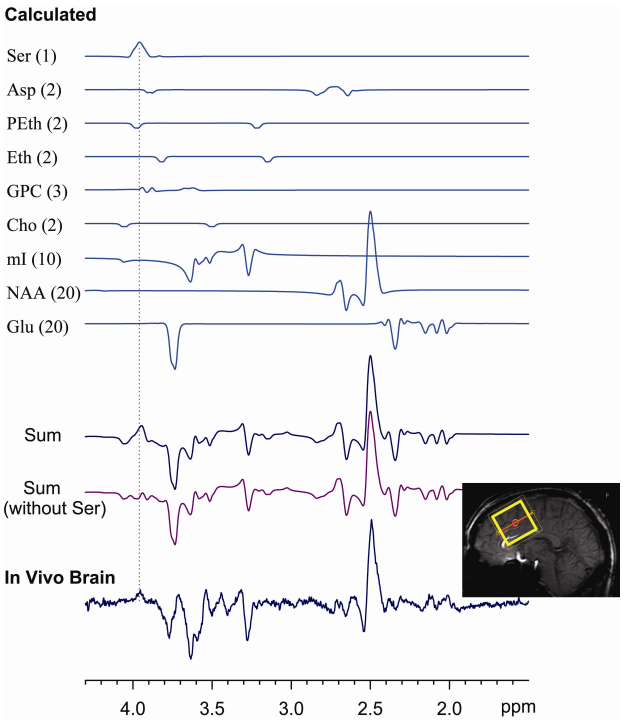

FIG. 3. (Top) Spectra of serine and several metabolites, calculated for PRESS difference editing using (TE_1, TE_2) = (108, 80) and (49, 139) ms are shown for concentrations in brackets. (Bottom) An *in vivo* edited spectrum from the medial frontal brain (40×40×40 mm^3). The total measurement time for two PRESS scans was 32 min (TR = 2.5 s. NEX = 768).