An Optimized PRESS Sequence for the Detection of Glycine at 9.4 T

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Target Audience: Researchers interested in glycine (Gly) measurement with MRS (Magnetic Resonance Spectroscopy).

Purpose: The levels of Gly, an inhibitory neurotransmitter, are relevant to the study of a number of disorders. Proton MRS can be used to measure Gly levels by quantifying its resonance peak at 3.55 ppm. However, the strong spectral overlap of peaks from myo-inositol (mI), which is present in much higher concentrations than Gly, makes the detection and measurement of Gly difficult even at a high field strength of 9.4 T (1). A long-TE Point RESolved Spectroscopy (PRESS) sequence can be optimized to significantly reduce mI signal in the Gly spectral region by exploiting the J-coupling evolution of mI protons, while retaining signal from the uncoupled spins of Gly at 3.55 ppm. This approach has previously been applied by others at 3 T (2) and 7 T (3); however, the mI protons which resonate in the Gly spectral region are strongly coupled, even at 9.4 T, causing their response to be field strength dependent. The purpose of this work is to investigate the PRESS $\{TE_1, TE_2\}$ signal dependence of the 3.5 -3.6 ppm mI protons at 9.4 T to find an optimal echo time combination that results in sufficient suppression of the mI signal so that the Gly resonance can be resolved and quantified. To our knowledge, PRESS has not been previously optimized for Gly detection at 9.4 T.

Methods: Experiments were performed with a small bore, 9.4 T, animal MRI scanner. A birdcage radiofrequency (RF) coil was employed for phantom experiments while a surface coil was used for rat brain scans. PRESS spectra were acquired from three spherical phantom solutions. One phantom solution consisted of 10 mM creatine (Cr) and 50 mM mI. Another contained 10 mM Cr and 10 mM Gly, while the third phantom solution was composed of 10 mM Cr, 50 mM mI, and 10 mM Gly. Spectra with one hundred and fifty four $\{TE_1, TE_2\}$ combinations were obtained from the mI/Cr phantom, the shortest being {12 ms, 9 ms}. They were acquired as 8192 data points sampled at 10,000 Hz from 5 x 5 x 5 mm^3 voxels in 32 averages, with a repetition time (TR) of 5 s. The optimal $\{TE_1, TE_2\}$ combination for Gly detection was chosen by examining the 3.5-3.6 ppm mI spectral region and selecting the timing set which yielded a spectrum in which the net mI area in the mentioned spectral region was minimal compared to the corresponding mI signal area in the short-TE spectrum. The optimal timing set was verified on the Cr/Gly/mI phantom and on the brains of three Sprague Dawley rats *in vivo*. *In-vivo* spectra were acquired from 5 x 5 x 5 mm^3 voxels placed in the brain as shown in the figure. The short-TE spectra and the optimized-TE spectra were obtained in 128 and 256 averages, respectively, with a TR of 3 s; 2048 data points were collected. *In-vivo* spectra were analyzed with LCModel.

Results: An optimal echo time combination was determined to be {60 ms, 100 ms}, for which the total area and maximum amplitude of mI in the 3.52-3.57 ppm region was -6.1% and 5.2 %, respectively, of the corresponding short-TE spectrum. Phantom results showed that the Gly lineshape was relatively unaffected by the presence of mI at the optimal TE; the Gly/Cr area ratio was altered by about 11 % with the introduction of mI when $\{TE_1, TE_2\}$ = {60 ms, 100 ms}. The three rat brain spectra showed a clear Gly peak at 3.55 ppm. An average CRLB of 18 % was obtained for Gly quantification with LCModel. The average ratio of the concentration of Gly to that of total Cr was 0.170. Assuming a total creatine concentration of 8 mM, this yields an average Gly concentration of 1.36 mM. This is within the range of previously biochemically determined rat brain Gly levels of 1.2 – 1.66 mM (4,5).

Conclusion: We have shown that a PRESS sequence with $\{TE_1, TE_2\}$ equal to {60 ms, 100 ms} is suitable for resolving the Gly signal (~3.55 ppm) from overwhelming, overlapping mI signal at 9.4 T. PRESS has not been previously optimized for resolving the Gly peak at 9.4 T. The presented work has rendered the readily available, commonly employed PRESS sequence a convenient option for isolating and quantifying the Gly resonance and is likely to be of value in animal model studies of brain diseases at 9.4 T.

References: (1) Gambarota et al., Magn Reson Med. **V. 60**, p. 727, 2008

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(4) Cutler et al., J Neurochem. **V. 23**, p. 1005, 1974 (5) Mandel et al., J Neurochem. **V. 12**, p. 987, 1965

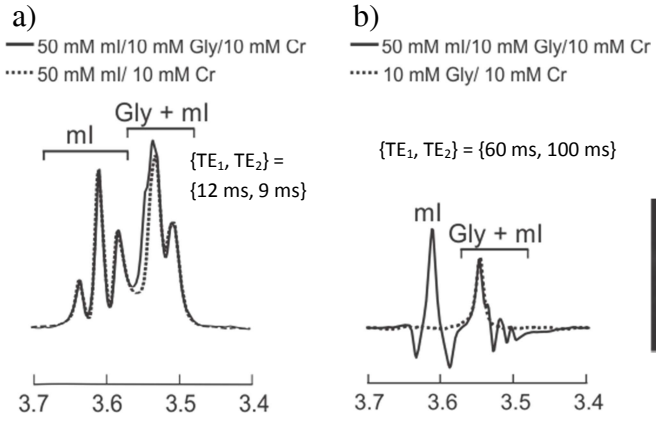
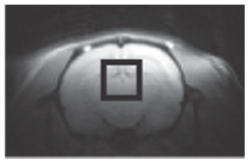


Figure 1: Phantom spectra obtained with PRESS. $\{TE_1, TE_2\}$ combinations are indicated above each spectrum, along with the phantom constituents. In (a), the short-TE mI/Gly spectrum differs only slightly from the mI only spectrum. With the optimized TE combination in (b), the mI/Gly spectrum closely matches that of the Gly only spectrum.



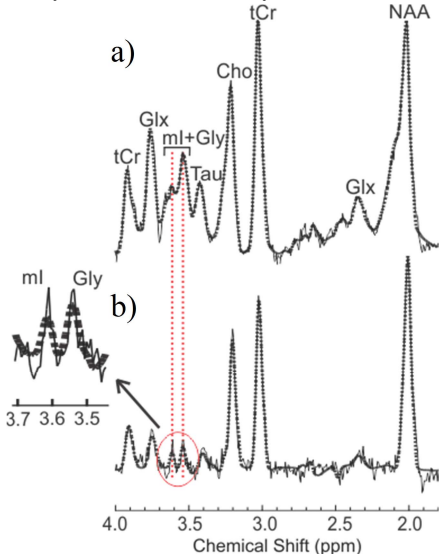


Figure 2: Acquired spectra from one of the rats are displayed, with the corresponding LCmodel fits overlaid. In (a), a spectrum measured with $\{TE_1, TE_2\}$ = {12 ms, 9 ms} shows the overlap between mI and Gly, whereas with the optimized $\{TE_1, TE_2\}$ of {60 ms, 100 ms}, the mI and Gly peaks are clearly separated as shown in panel (b); the vertical dotted lines indicate the centre of each peak.