Localized Spectroscopy Without J-modulation at Ultra High Field

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Target Audience - Scientists interested in spectroscopy of coupled metabolites (e.g., GABA, glutamate, glutamine, etc.).

Introduction - Short echo-time (1-20 ms) *in vivo* spectra suffer from baseline contamination arising from lipids and macromolecules[1]. This can lead to significant errors in metabolite quantification – especially with gamma-aminobutyric acid (GABA)[2]. One solution is to use longer echo times (TE) as macromolecules have shorter T_1 and T_2 relaxation times than metabolites[3] thereby effectively removing macromolecule signal. However, at long TE J-modulation eliminates the signal from coupled metabolites such as GABA, glutamate (Glu), glutamine (Gln) and lactate (Lac). There are a variety of techniques that attempt to accurately measure these metabolites but they are generally only able to quantify a small number of metabolites accurately at a time[4]. Here we present a method to refocus J-modulation for all weakly coupled metabolites at long TE in order to acquire fully refocused spectra without baseline contamination. The method is entitled PRESS with J-Refocusing (PRESS-JR).

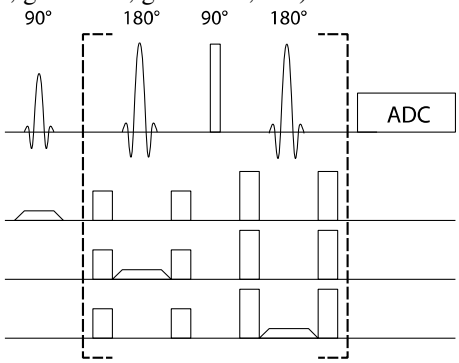

Figure 1: PRESS-JR pulse sequence diagram.

Methods - Van Zijl et al. showed a simple pulse scheme to refocus scalar coupling in NMR spectrometers[5] by inserting a 90° pulse at the midpoint of a double spin echo. This effectively exchanges coherence between spins and refocuses J-modulation caused during the first half of the sequence leading to complete refocusing of J-modulation at the end of the sequence for an AX spin system. For complex spin systems (AX_n) there remains one important constraint: the TE must be less than 1/4J for the relevant structure. Lee et al. demonstrated this concept for localized spectroscopy showing J-refocused spectra of glutamate and glutamine up to 40 ms TE[6]. Recently Aguilar et al. proposed an elegant and simple extension by showing that looping "refocusing units" can circumvent the aforementioned 1/4J constraint[7]. We extend the concepts outlined by Lee et al. and Aguilar et al. as illustrated by the pulse sequence in Fig. 1. The area inside the dashed line shows a "refocusing unit". Immediately after each refocusing unit the J-modulation is refocused - assuming each unit is shorter than 1/4J.

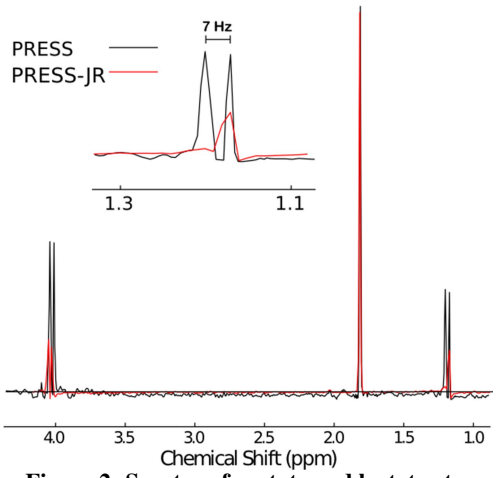

Figure 2: Spectra of acetate and lactate at 100 ms for PRESS (above) and PRESS-JR with 3 refocusing units.

Experimental - PRESS-JR was performed on a 7 T whole body scanner (SIEMENS Medical Solutions) using a single channel surface coil on a spherical phantom (diameter 17 cm) containing acetate and lactate (TE/TR = 100/8000ms, Averages=16). A 20 x 20 x 20 mm voxel at the center of the phantom was selected with removal of unwanted coherences generated by the hard 90° pulses accomplished with outer volume suppression and a 4 step phase cycle. S-BREBOP[8] slice-selective refocusing pulses were used due to their large bandwidth (BW = 2792 Hz, 7500 ms duration) and their ability to reduce the effects of pulse imperfections.

Results - A comparison between conventional PRESS and PRESS-JR spectra is illustrated in Figure 2. As expected, with PRESS-JR the lactate peaks are completely upright indicating refocusing of J-modulation whereas PRESS shows severe signal loss (35% less signal) due to J-modulation.

Discussion and Conclusion - Due to the number of refocusing pulses, pulse imperfections can lead to signal loss and degradation. As well, the inclusion of hard 90° pulses introduces global excitation which requires careful removal. If these difficulties can be overcome, this technique has potential to accurately measure coupled metabolites (GABA, Glu, Gln, Lac). This technique is especially suited for ultra high field, as the increased spectral dispersion will facilitate more accurate and reliable measurements. It also may be advantageous to replace the conventional refocusing pulses with adiabatic pulses as in semi-LASER – though specific absorption rate (SAR) may be a problem. Future experiments will include *in vivo* validation as well as more complicated phantom studies and comparison with other techniques (J-resolved spectroscopy, MEGA-PRESS) as with the method outlined by Henry et al. [4].

References – 1. Behar, K.L. et al. (1994). Magn. Reson. Med., 32, 294–302. 2. Cudalbu, C. et al. (2012). J. Alzheimers Dis., 31 Suppl 3, S101–115. 3. De Graaf, R.A. et al. (2006). Magn. Reson. Med., 56, 386–394. 4. Henry, M.E. et al. (2011). J. Magn. Reson. 1997, 208, 210–218. 5. Van Zijl, P.C.. et al. (1990). J. Magn. Reson. 1969, 89, 28–40. 6. Lee, H.K. et al. (1995). Magn. Reson. Med., 34, 253–259. 7. Aguilar, J.A. et al. (2012). Chem. Commun., 48, 811. 8. Janich, M.A. et al. (2012). J. Magn. Reson. 1997, 223, 129–137.