Proton spectral editing with the PRESS sequence

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Purpose: The purpose of this educational abstract is to describe how the standard single-shot, 3D localization, PRESS (Point RESolved Spectroscopy) spectroscopy pulse sequence can be modified and tailored to measure otherwise difficult to observe metabolites. The PRESS sequence is a double spin echo method characterized by two echo times, namely, TE_1 and TE_2. A number of spectral editing methods can be incorporated into PRESS to enable the observation of protons of interest while simultaneously performing spatial localization.

Outline of content: At clinical field strengths, the proton spectrum exhibits significant overlap of peaks from a number of metabolites due to poor chemical shift spectral resolution resulting in less concentrated target metabolite peaks being obscured by larger overlapping peaks. Furthermore, homonuclear scalar coupling causes the peaks to split into multiplets further complicating the spectrum. Spectral editing methods have been employed to minimize background contaminating peaks while retaining signal from metabolites of interest. Integrating spectral editing techniques into PRESS enables simultaneous spatial localization. Variations of the PRESS sequence have been employed for the improved detection of a number of metabolites *in vivo*, including alanine (Ala), ascorbate (Asc), choline (Cho), citrate (Cit), creatine (Cr), gamma-amino butyric acid (GABA), glutamate (Glu), glutamine(Gln), glutathione (GSH), glycine (Gly), lactate (Lac), myo-inositol (mI), N-acetyl aspartate (NAA), N-acetyl aspartyl glutamate (NAAG), and threonine (Thr). The methods exploit differences in J-coupling evolution between different metabolite spin systems. Some of the editing methods are listed below:

1) ***PRESS with optimized echo times (TEs):*** Long TE spectra are simpler in appearance and are free of baseline signal from macromolecules, which have a short T_2 value [1]. The two PRESS echo times can be optimized numerically or experimentally to yield relatively high signal from desired coupled protons while suppressing signal from background coupled spins. This strategy has been applied for the observation of mI [2], Glu [3], and Cit [4].
2) ***TE-averaged PRESS:*** In this method, several spectra acquired at multiple TEs are summed. It relies on destructive interference of signals from contaminating metabolites and constructive interference of signal from the protons of interest. The sequence has been used for the improved observation of Glu [5], Gly [6], and Cho [7] in breast tumours.
3) ***Constant TE difference PRESS:*** The response of strongly-coupled protons to PRESS depends on both TE_1 and TE_2. In constant-TE PPRESS, two scans acquired with the same total TE but with a different TE_1 and TE_2 are subtracted. The two sets of echo times are selected such that the difference of the two scans yields optimal signal for the strongly-coupled protons of interest. In this manner, signal from the strongly-coupled protons is retained upon subtraction while background signal from uncoupled or weakly-coupled spins is minimized [8]. Constant TE difference spectroscopy with PRESS has been applied to the strongly coupled protons of Cit [8], Glu [9], and GSH [10].
4) ***J-difference editing with PRESS:*** J-difference editing [11] relies on the acquisition of two scans and subtracting them. On alternate scans, selective 180° pulses are applied to the protons that are weakly-coupled to the target protons. The result is that the target proton peaks are upright in one acquisition and inverted in the other. Subtracting them maintains signal from the weakly-coupled protons to be observed while eliminating signal from uncoupled protons. The MEGA (MEscher-Garwood) sequence [12] exploits the concept of J-difference editing and has been integrated into PRESS for measuring GABA [13], GSH [14], Asc [15], NAA and NAAG [16]. J-difference editing with a modified PRESS sequence has also been shown to be effective for separating Lac and Thr [17].
5) ***PRESS multiple quantum filters (MQFs):*** MQFs exploit gradients of appropriate field strengths to pass through spin coherences of a certain order. The body of the PRESS sequence lends itself to the incorporation of MQFs. By optimizing sequence timings and gradient strengths only signal from certain spins can pass through. PRESS MQFs have been used for the *in-vivo* observation of GSH [18], GABA [19], Glu [20], and mI [21].
6) ***PRESS triple refocusing:*** Choi *et al.* [22] designed a method that yields Gly signal with minimal contamination from mI by adding a third refocusing pulse to the basic PRESS sequence and optimizing the three echo times.
7) ***BASING incorporated into PRESS:*** Band selective inversion with gradient dephasing (BASING) refers to frequency selective inversion pulses that are surrounded by two gradients of opposite polarity. PRESS difference editing with BASING has enabled the separation of Lac from overwhelming lipid signals and has also been employed for the measurement of GABA [23].
8) ***Four-pulse PRESS:*** Adding a non-selective 180° pulse between the two PRESS refocusing pulses has been shown to reduce the signal losses associated with the chemical shift displacement effect in weakly-coupled spin systems. Significant increases in signal yield for Lac [24] and GABA [25] have been demonstrated by this technique.
9) ***Polarization transfer PRESS:*** Polarization transfer PRESS involves applying a 90° pulse with orthogonal phase to that of the excitation pulse at the first echo time of a PRESS sequence. The sequence is preceded by a saturation module which dephases signal in the region of interest. Optimizing TE_1 and TE_2 and applying the additional pulse retrieves the desired signal by polarization transfer from spins that are weakly-coupled to the target spins and that lie outside the saturated spectral region. Contaminating background signal remains suppressed. The method has been demonstrated on Lac and GSH *in vitro* [26].
10) ***Narrow-bandwidth PRESS refocusing pulses for rewinding J-coupling:*** The chemical shift displacement effect can be turned to advantage by exploiting PRESS refocusing pulses that have bandwidths less than the chemical shift difference between the target protons and protons to which they are weakly-coupled. The technique rewinds the scalar coupling evolution of the target protons in the selected voxel of interest, thereby enhancing the signal acquired from them [27]. The technique has been applied to enhance signal from the weakly-coupled protons of Glu and Gln [28] and to minimize J-coupling effects on signal from the methyl protons of lipids [29].

Summary:

The PRESS sequence is a versatile sequence for spectral editing [30]. Its structure lends itself to the incorporation of a number of spectral editing techniques that can be employed for the detection of a variety of metabolites *in vivo*. The purpose of the proposed educational e-poster is to describe a number of PRESS based spectral editing methods that have been designed for the detection of a number of key metabolites *in vivo*.

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