Localized In Vivo Human ^{1}H MRS at Very Short Echo Times

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A new point-resolved spectroscopy (PRESS) sequence was developed that allows localized human proton MR spectra to be acquired at echo times (TEs) of 10 ms or less. The method was implemented on a 4 Tesla Varian research console and a clinical 3 Tesla Siemens Trio scanner. Human brain spectra acquired in vivo from the prefrontal cortex at TE = 8 ms showed improved signals from coupled resonances (such as glutamate, glutamine, and myo-inositol) compared to spectra acquired at TE = 30 ms. These improvements should result in more accurate quantitation of these metabolites. Magn Reson Med 52: 898–901, 2004. © 2004 Wiley-Liss, Inc.

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Localized proton magnetic resonance spectroscopy (MRS) studies in humans are typically carried out at echo times (TEs) between 20 ms and up to a few hundred milliseconds. However, shorter TEs are desirable to minimize spin dephasing due to J–coupling and associated signal losses. Shorter TEs would also be advantageous for precise quantitation of macromolecules in vivo (1). The two most commonly used single-voxel MRS sequences are the stimulated echo acquisition method (STEAM) (2) and the point resolved spectroscopy (PRESS) technique (3). With STEAM, a TE as short as 1 ms has been achieved in rats (4). Previous human in vivo studies employing STEAM have reported TEs < 10 ms on 1.5 Tesla (5–7) and 3 Tesla (8) scanners. For PRESS, the shortest TE reported is 6.0 ms, in the rat brain (9). Although a PRESS sequence with such short TEs has not been demonstrated in human studies, such a sequence is desirable because PRESS has an inherently twofold higher signal intensity compared to STEAM.

Therefore, the goal of this work was to develop a PRESS sequence for very short TEs (≤10 ms). One of the major challenges in performing such studies in vivo is to achieve sufficient gradient (crusher) areas to dephase unwanted coherences. Therefore, the proposed method eliminated crusher gradients between the 90° excitation pulse and the first 180° refocusing pulse. The slice-selection gradients were extended, and they additionally functioned as crusher gradients between the 180° pulses. The first 90° slice gradient also served as a crusher gradient, which

eliminated the need for an extra refocusing gradient pulse. At 4 Tesla, where susceptibility artifacts were more pronounced, oblique gradients were used for voxel selection to maximize the gradient area for dephasing of unwanted coherences. Together, these measures made it possible to reduce the TE to <10 ms.

MATERIALS AND METHODS

Two sets of experiments were performed separately on a Siemens AG (Erlangen, Germany) Trio 3 Tesla Scanner and a Varian (Palo Alto, CA) Unity-Inova console equipped with a 4 Tesla magnet. Both systems were equipped with a self-shielded Siemens Sonata gradient set (40 mT/m, slew rate = 160 T/m/s). The 3T Siemens console was equipped with a transmission/receiver circularly polarized (CP) head coil. The Varian console was equipped with a quadrature head coil. A 2-L spherical glass bottle containing an aqueous solution of lactate (Lac, 5 mM), N-acetyl-aspartate (NAA, 12.5 mM), glutamate (Glu, 12.5 mM), creatine (Cr, 10 mM), choline (Cho, 3 mM), and myo-inositol (mI, 7.5 mM) was used to simulate a spectrum from the human brain. Two other phantoms containing only Glu or mI were also used. Phantom spectra were collected at both TE = 5 ms and TE = 30 ms on the 4 Tesla system to evaluate the performance of the new sequence, as well as to quantitate the improvement in signal line shape and intensity.

The pulse sequence on the Varian scanner consisted of three modules: outer-volume suppression (Fig. 1a), water suppression (Fig. 1b), and the new PRESS module (Fig. 1c). On the Siemens 3 Tesla scanner, we were able to obtain artifact-free spectra with modules b and c only. The 3 Tesla PRESS module used a Hamming-filtered 90° sinc pulse (1.2 ms, bandwidth = 8.75 kHz), two Mao4 180° refocusing pulses (2 ms, bandwidth = 6 kHz), and trapezoidal gradient pulses (15 mT/m). At 4 Tesla, the RF pulses for PRESS voxel selection were 1.5-ms sinc pulses with a 4.1 KHz bandwidth. A double 45° rotation (coronal → sagittal → transverse) oblique voxel was used for improved artifact suppression. Additionally, a pair of crusher gradients (half-sine shape, 25 mT/m, 1.5 ms) was positioned symmetrically around the second 180° refocusing pulse.

On the 3 Tesla system, an eight-step phase cycle proved sufficient to suppress artifacts in the spectra without outer volume suppression. In comparison, the implementation of the sequence on the 4 Tesla required additional measures to eliminate artifacts that could have originated from small amounts of water or lipid in the nasal cavities and mouth (10). An outer-volume suppression module was implemented for this purpose, with the use of dual-band RF suppression pulses (8 ms, 2 KHz/2 KHz bandwidth/

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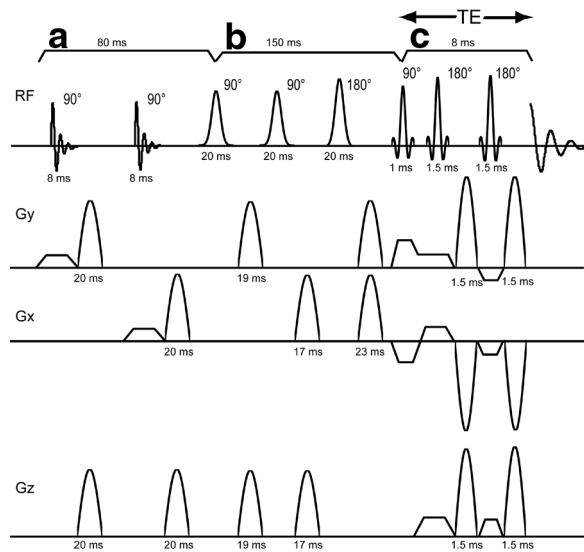
FIG. 1. The pulse sequence diagram of the localized spectroscopy sequence for very short TEs involves three stages: outer-volume suppression (**a**), water suppression (**b**), and the new PRESS module (**c**).

bandgap) that were optimized with the Shinnar-Le Roux algorithm (11). Outer-volume suppression was performed only in the *x-y* plane, and not along the *z*-axis. This avoided the excitation of spins from the neck, which may give rise to other artifacts.

On the Varian, a modified CHESS-type water suppression module (using 20-ms Gaussian pulses) was used for water suppression (10). On the Siemens console, the water suppression followed the method prescribed in Ref. 12, and a 25.6-ms Gaussian pulse was used (bandwidth for water suppression = 35 Hz).

A group of eight healthy volunteers (five males and three females) were recruited and scanned on separate dates (five on the 3 T scanner, and three on the 4 T system). Oral and written consent was obtained prior to the MR scan, following the guidelines of the respective institutional review boards. On both scanners, multislice spin-echo images were acquired as localizer images, on which a $1.5 \times 1.5 \times 1.5$ cm³ voxel was prescribed. Two spectra were acquired in each subject at TE = 10 ms and 30 ms on the 3T Siemens scanner, and at TE = 8 ms and 30 ms on the 4T Varian scanner. The repetition time (TR) was 3 s, with 64 averages for each scan on both systems. In one of the subjects, an extra set of metabolite-nulled spectra was obtained (4T) to quantitate macromolecule signals (inversion time (TI) = 920 ms). All postprocessing was performed with software written in-house in IDL (Research System Inc., Boulder, CO) and Matlab (Mathworks, Natick, MA).

RESULTS

The results from the phantom studies at 4 Tesla are shown in Fig. 2. The top spectrum was acquired from the mixed phantom at TE = 5 ms. The spectrum shows essentially no

dephasing due to J-coupling. The effect of the TE on the multiplet patterns is exemplified in Fig. 2b and c, which show the mI and Glu spectra at TE = 8 and 30 ms. The phases of the Glu and mI multiplets are clearly improved at the shorter TE (8 ms), and there is some signal loss at TE = 30 ms. Furthermore, the phantom studies demonstrated that there is little difference between spectra acquired at TE = 8 ms and 10 ms (not shown).

Figure 3 shows in vivo spectra from the 4 T scanner, which were acquired in the right prefrontal lobe white matter of a human brain. The major metabolite peaks (NAA = 2.0 ppm; total creatine (tCr) = 3.0, 3.9 ppm; Cho = 3.25 ppm; and mI = 3.55 ppm) are clearly visible at both TEs (Fig. 3a and b). Compared to TE = 30 ms, the major improvement at TE = 8 ms is the elevation of the glutamate plus glutamine (Glx) and mI resonances, and the broad baseline signals from macromolecules. The increase in the Glx and mI signal areas at TE = 8 ms was close to 20%. The elevation in the macromolecule resonances can be estimated from the peak areas at 0.9 and 1.4 ppm, which increased by approximately 110% and 50%.

To further characterize the macromolecule resonances, a metabolite-nulled spectrum (TI = 920 ms) was acquired (Fig. 3d). In agreement with previous measurements (1), the metabolite-nulled spectrum shows macromolecule peaks at 0.9 ppm and 1.4 ppm, and two broad peaks at about 2 and 3 ppm.

For the in vivo measurements at 3 Tesla, voxels from the right prefrontal, right occipital, and right parietal lobes were selected. Spectra from right prefrontal (Fig. 4a and b) and occipital white matter (Fig. 4c and d) are shown in Fig. 4, acquired with a single CP coil. The major metabolite peaks (NAA = 2.0 ppm; tCr = 3.0, 3.9 ppm; Cho = 3.25 ppm; and mI = 3.55 ppm) are well resolved in all spectra acquired at TE = 10 ms (Fig. 4a and c) and 30 ms (Fig. 4b and d). The Glx and mI profiles are different from
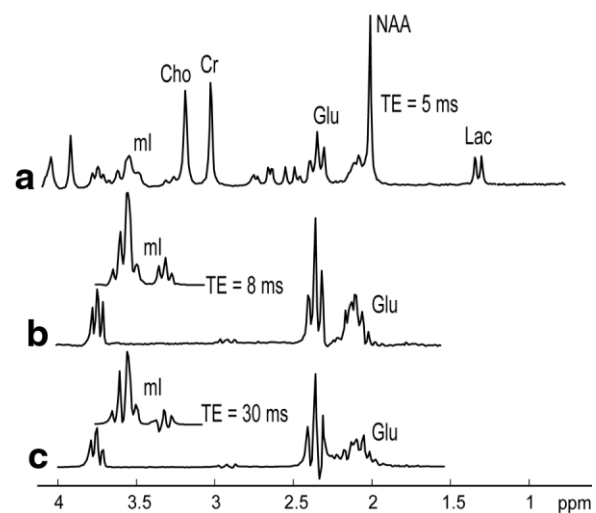

FIG. 2. **a:** Spectra acquired at 4 Tesla from a 2-L phantom containing Lac, NAA, Glu, Cr, Cho, and mI. Spectra acquired separately from Glu and mI solutions are shown with TE = (**b**) 8 ms and (**c**) 30 ms. All spectra demonstrate significantly more spin dephasing due to J-coupling at TE = 30 ms compared to TE = 8 ms.
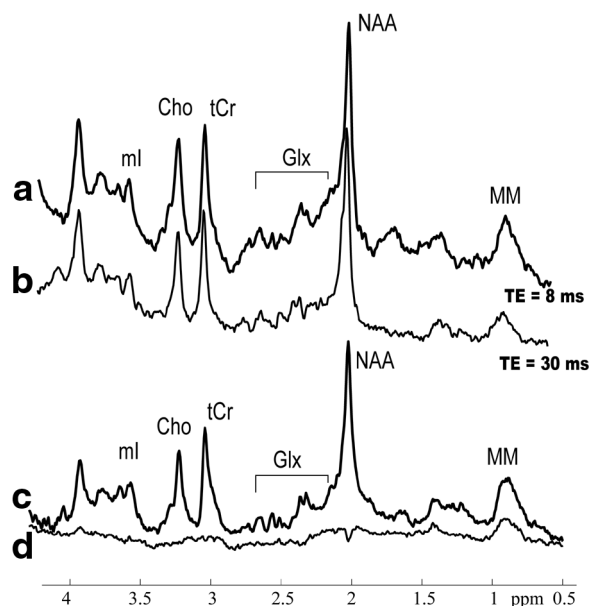
FIG. 3. In vivo spectra at 4 Tesla from the right prefrontal white matter. Relative to the spectra acquired at TE = 30 ms (**b**), the Glu/Gln and macromolecule signals are increased at TE = 8 ms (**a** and **c**). **d**: A metabolite-nulled spectrum shows predominantly the macromolecule signals at 0.9 and 1.4 ppm, as well as two broad resonances between 2 ppm and 3 ppm. The small inverted peak at 2 ppm is the residual NAA signal.

the 4 Tesla spectra due to the lower field strength used. However, the spectral baseline is much improved. This may be due to 1) the improved performance of the Hamming-filtered RF pulses, 2) more effective phasing cycling (e.g., more stable RF amplifier and receivers), or 3) the analog-digital converter (ADC) oversampling scheme applied on the Siemens scanner. Improvements in the Glx and mI signals were also observed for TE = 10 ms compared to TE = 30 ms; likewise, the macromolecule resonances at 0.9 and 1.4 ppm were enhanced in the TE = 10 ms spectra. No major artifacts were observed in the spectra.

DISCUSSION

We demonstrate a PRESS sequence that makes it possible to acquire high-quality ^{1}H MR spectra from the human brain at TE ≤ 10 ms. As a result of the short TE, the resonances of Glu and mI show virtually no dephasing due to J-coupling. Thus, these improvements increase the signal-to-noise ratios (SNRs) of these resonances and should ultimately improve the quantitation.

The increased macromolecule signals at TE < 10 ms (compared to 30 ms) reflect the fact that macromolecule signals have very short T_2 values. In fact, the intensity of the macromolecule peak at 0.9 ppm doubled at TE = 8 ms compared to 30 ms, which should enable more accurate quantitation of these peaks.

Previous efforts have been made to reduce the TE in PRESS sequences. In one approach, optimized asymmetric RF pulses were used to reduce the TE of a PRESS sequence

(TE = 6 ms) (9) and a STEAM sequence (4). However, those studies were carried out on animal scanners. In contrast, our approach allows marked reductions in TE for human in vivo studies simply by redesigning the gradient sequence. If one were to combine the two methods, it might be possible to achieve a TE of approximately 5 ms for the PRESS sequence. It should be possible to reduce the TE in small-animal studies, which are typically performed on systems with much stronger and faster gradients. Alternately, the use of asymmetric RF pulses (9) would allow increased time for crusher gradient widths.

However, our new method also has limitations. The removal of the crusher gradient between the 90° excitation pulse and the first 180° refocusing pulse requires a more effective phase cycling scheme or outer-volume suppression to eliminate artifacts. Furthermore, the crusher gradient amplitudes for oblique voxels are limited by the nerve stimulation threshold, and may be insufficient to suppress spurious signals. Additionally, the performance of the new method may be reduced somewhat with large voxels, where weaker slice gradients are applied. Oblique voxel selection is another potential concern for older scanners such as the Varian system employed in this study. However, this is not a problem for newer systems such as the Siemens Trio, where double-rotating voxels can be prescribed easily with the system software (13).

A modified PRESS sequence is described that allows TEs of 10 ms or less for in vivo human examinations at 3 and 4 Tesla. The shorter TEs promise more accurate quan-
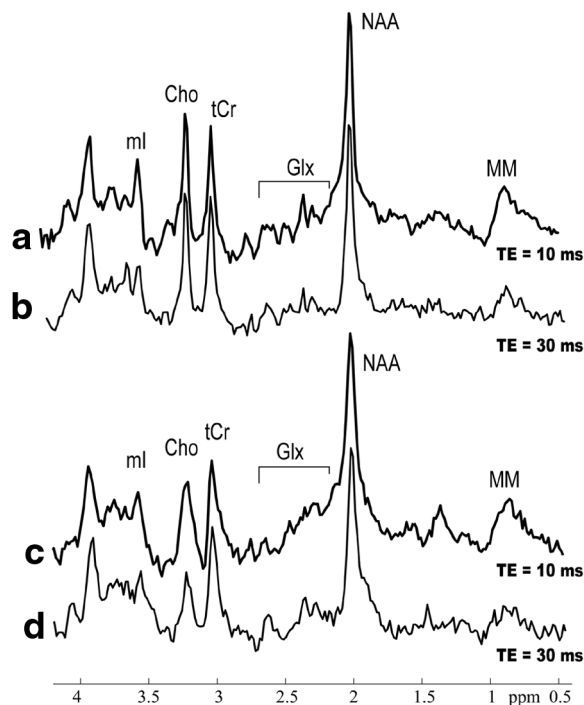

FIG. 4. In vivo spectra at 3 Tesla from the right prefrontal (**a** and **b**) and right occipital (**c** and **d**) white matter. The improvements in spectral quality between TE = 10 and 30 ms were similar to those observed at 4 Tesla (cf., Fig. 3). No major artifacts were present in the spectra.

titation of coupled metabolite signals (Glu or mI) and macromolecules.

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