A novel method using a single selective editing pulse for in vivo glutathione editing at 3 Tesla

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Introduction Glutathione (GSH) is an important marker of oxidative stress. Its concentration in brain is thought to vary in a variety of brain disorders including schizophrenia and Alzheimer's disease. In vivo detection of GSH in the human brain using MRS has been reported in the literature [1-3]. Here we propose a new method for GSH editing which uses a single selective editing pulse and corrects the transient Bloch-Siegert phase shift with precalibrated postacquisition phase correction. Selective editing pulses affect the free precession of the transverse magnetization outside their selection bandwidth because of the contribution of the selective editing pulse to the effective B_1. This phenomenon has been referred to as the "transient Bloch-Siegert effect" [4]. The phase error caused by the transient Bloch-Siegert effect of an editing pulse can be eliminated using extensive phase cycling at the expense of altered amplitude which requires postacquisition correction of the amplitude of the two-step subtraction editing data [5]. Although the double spin echo strategy [6] cancels the extra phase accumulation caused by the editing pulses, the use of two long 180 degree editing pulses leads to further signal loss due to coherence leakage and the accumulative B_1 inhomogeneity effect. In this study, we incorporated a single inversion pulse into a PRESS sequence to measure GSH in vivo by means of two-step subtraction editing. It is demonstrated here that the transient Bloch-Siegert phase shift can be effectively corrected using phase precalibration.

Methods Fig. 1 shows the phase shift of a transverse magnetization as a function of frequency offset for a 25 ms Gaussian inversion pulse which has a 75 Hz bandwidth at half height. Numerical simulation using Bloch equations was performed to assess the phase shift caused by the transient Bloch-Siegert effect of the Gaussian pulse. The same 25 ms Gaussian pulse was incorporated into the GE PRESS sequence for in vivo glutathione editing using a 3 Tesla GE scanner. The pulse sequence is shown in Fig. 2. The frequency of the Gaussian editing pulse is alternated between 4.56 ppm (cysteinyl α-H) and 5.95 ppm (control) to turn on and off the editing pulse. Based on Fig. 1, this frequency alternation for the purpose of editing gives rise to a phase difference of 0.15 rad for the creatine (Cr) signal at 3.0 ppm. Due to the high intensity of the Cr methyl protons at 3.0 ppm, this slight phase disparity creates a significant Cr subtraction error which contaminates the target GSH signal at 2.95 ppm. However, since the phase shift caused by the transient Bloch-Siegert effect can be accurately predicted as shown in Fig. 1, a postacquisition phase correction can be performed prior to subtraction editing. An echo time of 120 ms was used for all experiments.

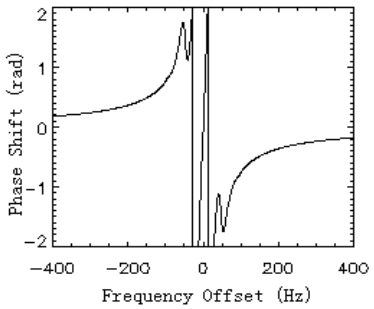

Fig.1 Phase shift vs. frequency offset

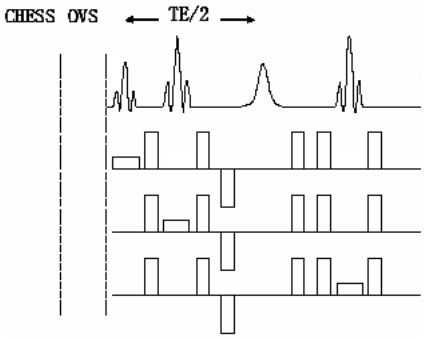

Fig.2 GSH pulse sequence.

Results and Discussion Fig. 3 shows the edited results from a phantom containing 2 mM GSH, 10 mM NAA and 8 mM Cr (a, c) and from a second phantom containing only 2 mM GSH and 10 mM NAA (b, d). Note that contamination due to Cr subtraction error is apparent in (a) where phase correction was not made. After Bloch-Siegert phase correction, the results from the two phantoms are virtually identical (c, d). There are no visible subtraction errors either at 3.0 ppm (Cr methyl) , or 2.0 ppm (NAA methyl), or 3.9 ppm (Cr methylene) in (c, d). The GSH signals at 2.95 ppm edited after phase correction (c, d) are practically identical to each other and to that in (b), indicating completing subtraction of the interfering Cr methyl group at 3.0 ppm. Similar result was obtained in the human study (Fig. 4). The absence of Cho (3.2 ppm) in Fig. 4 also confirms a complete subtraction of Cr at 3.0 ppm. The signals at 2.5-2.6 ppm are predominantly from co-edited NAA β–H_2 which is J-coupled to NAA α-H at 4.4 ppm. The in vivo data were collected from a 3×3×3cm^3 voxel in orbital frontal lobe of a healthy volunteer with a scan number of 256 and TR = 2s.

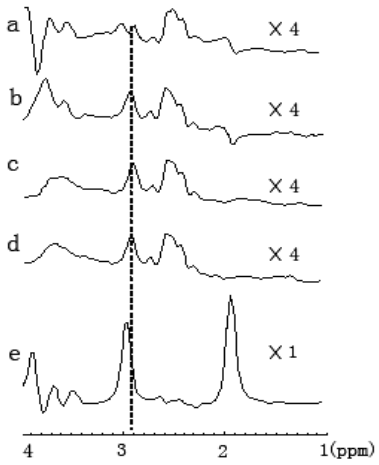

Fig.3 Edited spectra (a,b,c,d) from phantom containing Cr (a, c) and no Cr (b, d). (a) and (b) were processed without Bloch-Siegert phase correction. A large distortion is seen in (a) due to strong residual Cr signal at 3.0 ppm. (c) and (d) were processed after phase correction. No visible Cr (either at 3.9 or 3.0 ppm) or NAA (at 2.0 ppm) was seen in (c) and (d). The frequencies of the Cr and NAA were shown in the unedited spectrum given in (e).

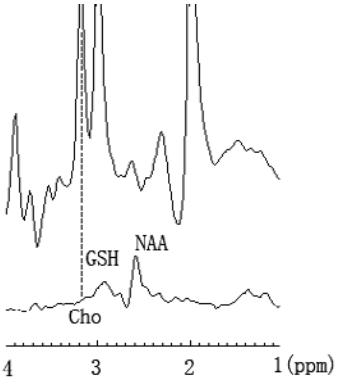

Fig.4 GSH editing in human brain

References [1] Trabesinger et al, *Magn Reson Med* 1999;**42**:283. [2] Terpstra et al, *Magn Reson Med,* 2003;5**0**:19. [3] Choi IY, *ISMRM Abstr* 2004;683. [4] Emsley et al, *Chem Phy Lett* 1990;**168**:297. [5] Rothman et al, *PNAS*, 1993; **90**:5662. [6] Hwang et al, *J. Magn.Reson*, 1995;A**112:**275.