Strategy for Yield Enhancement in Glutathione Double-Quantum Filtering

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INTRODUCTION

Precise measurement of brain glutathione (GSH) by ^{1}H MRS is difficult because of its relatively low concentration and the abundant overlapping signals from N-acetylaspartate (NAA), glutamate, and creatine (Cre). The cysteine moiety is commonly employed in spectral editing approaches [1-3]. The resonances at 2.93 and 2.97 ppm, that are weakly coupled to the 4.56-ppm resonance, are manipulated by means of J difference editing [1] or double-quantum (DQ) filtering [2], to generate a target multiplet at ~2.95 ppm. To date, the theoretical editing yield with respect to a 90°-acquired signal is ~50%, and the practical yield reduces substantially when the bandwidth of the slice-selective RF pulses is not sufficiently large. Here, we have investigated a previously-reported method [2], and a new strategy that includes interchange of DQC and ZQC followed by another encoding step and thereby achieves editing efficiency of 100%. Preliminary results of numerical calculation for sequence time optimization and phantom validation of the yield enhancement of the new GSH DQF are presented.

METHOD and MATERIALS

The responses of the cysteine moiety to three DQF sequences shown in Fig. 1 were investigated with density-matrix simulation, incorporating slice-selective shaped RF and gradient pulses. For all three sequences, double-quantum coherences were prepared using a 10-ms-long single-band 90° RF pulse (S90) tuned to 4.56 ppm, at the end of the antiphase creation period. Sequences B and C included, respectively, a 4.2-ms-long and a 20-ms-long spectrally-selective 180° pulse (S180), tuned to 4.56 ppm, to interchange DQC and ZQC, followed by another DQC encoding gradient within TM. Following DQC-to-antiphase conversion by the second S90, a GSH target multiplet was induced at 2.95 ppm during the single-quantum evolution period. Localization was obtained with a 90° pulse (3 ms; BW = 3.8 kHz) and two 180° pulses (3.4 ms; BW = 1.2 kHz) for sequences A and B. Spatial localization of sequence C included two pairs of adiabatic full passages (AFP) (5 ms; BW = 5 kHz). The RF pulses were all designed at B_1 = 24 μT. Slice thickness was set half the sample dimension along the three orthogonal direction. Optimal sequence times that give maximum peak amplitude were searched for numerically, with TE_1, TM and TE_2 between minimum value and 150 ms, with 1 ms increments. T_1 and T_2 effects were not included in the simulation. The published chemical shift and coupling constants [3] were used. The density-matrix simulation was programmed with Matlab (The MathWorks, Inc.). Single-quantum coherences that were not affected by the S180 were coedited and acquired in a single-shot scan. These signals, including the major contaminant Cre, were eliminated using RF phase cycling of the S180 pulse (i.e., 0 and π/2, and subtraction).

Sequence C was tested on a 25×25×25 mm^3 voxel within a spherical phantom (i.d = 6 cm) with GSH (37 mM), glycine (Gly) (50 mM) and NAA (33 mM). RF phase calibration was not required. Experiments were carried out at 3T in an 80-cm bore magnet, interfaced to a SMIS console. A standard quadrature birdcage head coil was used for RF transmission and reception.

RESULTS and DISCUSSION

Fig. 2 presents the calculated GSH filtered multiplet versus sequence times TE_1, TM and TE_2, for the three DQF sequences. The computer simulation predicts that the GSH edited multiplet at 2.95 ppm from sequence A is maximized at {TE_1, TM, TE_2} = {30, 16, 115} ms, its amplitude being 33% with respect to a 90°-acquired multiplet, see Fig. 3. This low signal return is primarily due to the limited bandwidth of the slice-selective 180° pulses. These sequence times are quite different from those used in a prior study [2], i.e., {10, 16, 70} ms at which the calculated yield is 20%. The signal yield can be enhanced with interchange of DQC and ZQC followed by another encoding (sequence B). The editing yield is then increased to 56% at {64, 17, 41} ms, Fig. 3. The voxel displacement effect, which is the major source of signal loss in sequences A and B, is minimized in sequence C, which utilizes the large bandwidth of AFP pulses. The maximum peak amplitude is predicted at {70, 49, 48} ms, its ratio to the 90°-acquired signal intensity being 105%, Fig. 3. It should be noted that peak area is not maximal at these conditions. In the phantom spectra in Fig. 3, the amplitude ratio of the GSH 2.95-ppm multiplet and the Gly peak is 31% and 24% in the 90°-acquired and DQF spectra, respectively, giving an editing yield of 77% (= 24/31). This is lower than calculated, but much greater than those in prior studies (< 35%). The phantom edited spectrum is devoid of resonances that are not affected by S180, indicating elimination of the major obstacle, Cre 3.03 ppm, in brain. In-vivo application of this yield-enhanced DQF to GSH measure is currently underway.

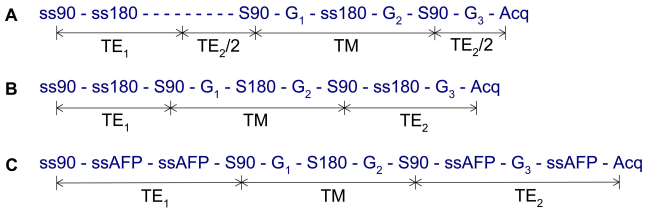

FIG. 1. Double-quantum filters for detection of the ~2.95-ppm resonances of the GSH cysteine moiety. The symbols ss, S and AFP denote slice-selective, spectrally-selective and adiabatic-full-passage RF pulses. Decoding and encoding gradients were $G_1 = -G_2 = G_3/4$ in A, and $G_1 = G_2 = G_3/2$ in B and C. Sequence A was reported by Zhao *et al.* [2].

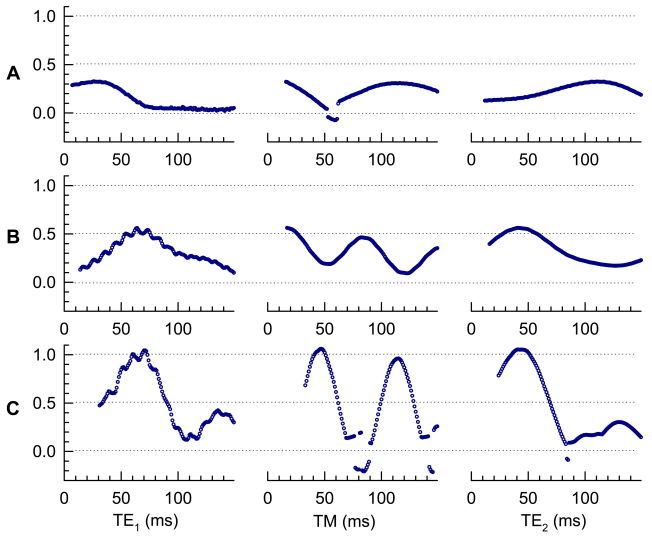

FIG. 2. For the three sequences in Fig. 1, the calculated GSH edited peak amplitude is plotted versus TE_1, TM, or TE_2, with other two variable fixed at {TE_1, TM, TE_2} = {30, 16, 115}, {64, 17, 41} and {70, 49, 48} ms for sequences A, B and C. The peak amplitude is normalized with respect to a 90°-acquired multiplet of the voxel.

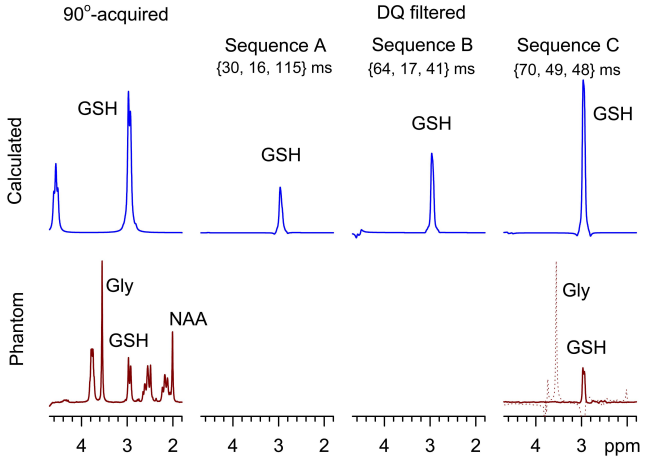

FIG. 3. Calculated and phantom spectra from 90°-acquisition and DQ filters. Calculated and phantom spectra are normalized with respect to the 90°-acquired GSH multiplet and a Gly peak, respectively. A dotted line on the right is a spectrum obtained without S180 phase cycling, which gave a co-edited Gly singlet used as a reference for estimating the GSH editing yield.

REFERENCES

1. Terpstra M *et al.* Magn Reson Med 2003;50:19-23.
2. Zhao T *et al.* Magn Reson Med 2006;55:676-680.
3. Govindaraju V *et. al.* NMR Biomed 2000;13:129-153.

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