T_2 correction and quantitation method on highly resolved 2D constant time ^{1}H spectra in human brain using 2D FT of shared time domain data

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Introduction

Constant time two dimensional methods have a feature of good peak resolution through ^{1}H decoupling along F_1. We have reported *in vivo* detection of glutamate (Glu), γ-amino butyric acid (GABA) and glutamine (Gln) in human brain using two kinds of 2D localized constant time methods, CT-COSY (1) and CT-PRESS (2). Furthermore, we have developed a quantitation method on 2D CT-COSY spectra and demonstrated quantitation of glutamate and GABA in human brain (3). This method required at least two sets of spectra for T_2 correction and a long total measurement time of 80 min. Since CT-PRESS is the spin echo type, SNR of glutamate C4H was improved by a factor of 1.7 in the human brain (2) and a shorter measurement time is expected. In addition to this feature of high sensitivity, we will propose T_2 correction and quantitation method on CT-PRESS spectra using 2D FT of shared time domain (TD) data within a shortened measurement time and demonstrate phantom experiments and human studies.

Methods

In ISIS version of CT-PRESS sequence (2), water suppression and outer volume suppression are followed by a module for localization; ISIS pulse (x-direction) – 90° slice pulse (y-direction) – 1/2*TE1 – 180° non-slice pulse – 1/2*(TE1+TE2)+Δt_1/2 – 180° slice pulse (z-direction) – {data acquisition}. To meet the constant time condition, a suitable amount of zeroes were filled in front of the acquisition data (4). After N_1 increments by Δt_1 along t_1, 2D TD data defined by $N_1 \times n_2$ matrices are accumulated where n_2 is number of sampling points in FID. A part of the total TD data defined by $n_1 \times n_2$ shown as a dotted area in Fig. 1 is extracted. Reconstruction of this partial TD data generates a CT-PRESS spectrum weighted by $\exp(-T_{ct}/T_2)$. The value of T_{ct} can be expressed as TE1+TE2+(n_{1start}+n_1/2)Δt_1 by applying a window where intensity is maximized at the center along t_1 axis on the partial TD data. Since T_{ct} is varied with n_{1start}, series of ^{1}H decoupled spectra along F_1 weighted with varied T_{ct} can be obtained by reconstruction of other parts of TD data where n_{1start} is incremented along t_1. By curve-fitting of peak volumes on these series of spectra, T_2 can be obtained. These peak volumes calculated using basis spectra obtained by GAMMA simulation are proportional to a model function of $A*\exp(-T_{ct}/T_2)$ even for metabolites having J coupled spin systems. By long waiting delay after the second 180° slice pulse, saturation effect due to T_1 can be ignored. Difference of coil-loading factors between the human brain and the reference phantom can be corrected using an internal water reference method (3). Then, absolute concentrations of metabolites can be calculated.

All experiments were performed using a 4.7 T whole-body NMR spectrometer (*INOVA*, Varian). A volume TEM coil was used both for transmission and reception. In phantom experiments, we used a reference phantom containing a brain metabolite mixture of 10 mM NAA, 8 mM Cr, 9 mM Glu, 3 mM Gln and 2 mM GABA. A 200-mL bottle containing this solution was placed in a water bath containing 0.9 % dissolved NaCl for mimicking an *in vivo* load and ISIS CT-PRESS signals were acquired inside a voxel within that bottle. First, T_2 of a Cr singlet was calculated by our proposed T_2 measurement method on 2D CT-PRESS data. These 2D TD data consist of series of 1D PRESS signals with varied TE. T_2 of a Cr singlet without J coupling can be calculated by the conventional 1D method which performs fitting on peak area in 1D PRESS spectra. Then, T_2 of a Cr singlet by the proposed method was compared to the value by the conventional 1D method. Next, T_2 of glutamate was calculated by this method and $M_{0\_phantom}$ was obtained by T_2 correction for absolute quantitation of glutamate in human brain. In volunteer studies, ISIS CT-PRESS signals were acquired in a 30x30x30 mm^3 voxel in a parieto-occipital region with a measurement time of 24 min. After T_2 of glutamate in the human brain was calculated and M_{0_vivo} was obtained by T_2 correction, the concentration of glutamate in the human brain was obtained by comparison between M_{0_vivo} and $M_{0\_phantom}$ with correction of difference between coil loading factors via water signals. In all measurements, TE1 was 15 ms and TE2 was 17 ms. Spectral widths along F_1 and F_2 were 1 kHz and 2 kHz, respectively. N_1 and n_1 were 180 and 150, respectively in volunteer studies. Relaxation delay was 4 s for volunteer studies.

Results & Discussion

The proposed method in 2D gave T_2 value of 582 ms for a Cr peak, which was in good agreement with the value of 574 ms obtained by a conventional 1D method (Fig. 2). Figure 3 shows a result of quantitation on glutamate in the human brain. After quantitation protocol with T_2 correction and the internal water reference method, the concentration of glutamate was calculated as 8.0 mM which is also in good agreement with reported values.

Conclusions

Glutamate in the human brain can be quantitated with measurement time of 24 min on highly resolved CT-PRESS spectra at 4.7 T. This proposed method will be useful to quantitation of other metabolites having J_{HH} coupled spin systems such as GABA and glutamine.

References

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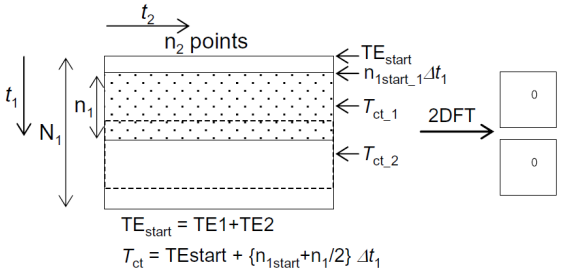

Fig. 1. A schematic of a proposed T_2 measurement method on highly resolved CT-PRESS spectra.

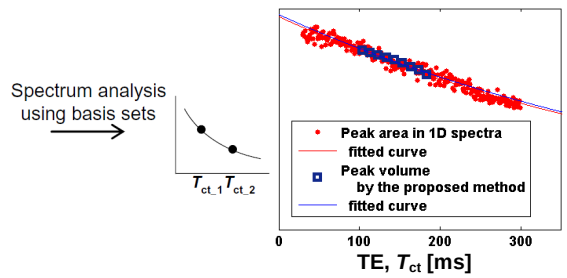

Fig. 2. Comparison between proposed T_2 measurement method on CT-PRESS spectra and the conventional method on 1D spectra. T_2 of Cr peak was calculated.

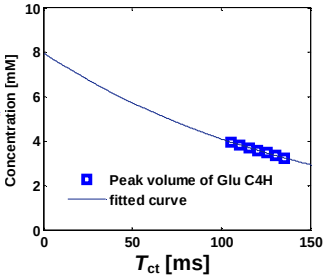

Fig. 3. Quantitation of glutamate in the human brain. Concentration is calculated as 8 mM.