Absolute Quantitation of Glutamate, GABA and Glutamine using Localized 2D Constant-time COSY Spectroscopy in Vivo

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Purpose: We propose an absolute quantitation method for metabolites with strongly coupled spin systems using localized 2-dimensional (2D) constant-time correlation spectroscopy (CT-COSY). We also develop two methods for improving the quality of in vivo CT-COSY spectra.

Methods: We substituted an image selected in vivo spectroscopy (ISIS) pulse for a 180° slice pulse in the CT-COSY module to decrease the slice displacement error caused by the chemical shift difference. We measured the slice displacement error due to the differences in the carrier frequency of slice pulse in a phantom experiment to demonstrate this feature. We also developed an asymmetric sampling scheme along the t1 direction to resolve diagonal peaks even in the magnitude mode of 2D spectra. We collected CT-COSY signals of a human brain for a 14% asymmetric sampling scheme. After reconstruction, we obtained a 2D CT-COSY spectrum in magnitude mode and compared a peak of glutamate (Glu) C4H on that spectrum to a peak displayed in absorption mode. In our proposed absolute quantitation method, we developed T2 correction, curve-fitting for computing peak volume and calibration by an internal water reference. We used the method to measure the Glu concentration in 10-mM glutamate phantom experiments. We also attempted to measure concentrations of Glu, γ-aminobutyric acid (GABA) and glutamine (Gln) in a human brain.

Results: Slice displacement error was decreased by a factor of 2.5 using the proposed sequence. Spectra with narrow linewidths could be obtained using the asymmetric sampling scheme in the magnitude mode. Measured Glu concentration in the solution phantom was 9.4 mM. Concentrations of Glu (9.5 mM), GABA (0.61 mM) and Gln (3.6 mM) in a human brain measured by our method agreed well with previously reported values.

Conclusion: Concentrations of metabolites with strongly coupled spin systems can be measured using our proposed absolute quantitation method on 2D CT-COSY spectra.

Keywords: CT-COSY, glutamate, human brain, in vivo, 1H MRS

Introduction

Glutamate (Glu) and γ-aminobutyric acid (GABA), major neurotransmitters in the human brain, are implicated in many psychiatric and neurological disorders. Glutamine (Gln) is a precursor and storage form of Glu that is predominantly synthesized in astrocytes and plays an important role in the Glu and Gln cycle in the brain. Absolute quantitation of these metabolites in vivo is expected to give useful information on the metabolism of Glu and GABA in neurons as well as the metabolism of Gln in astrocytes.

However, these metabolite resonances are overlapped even at 3T due to strongly coupled spin systems that result from the 1H-1H homonuclear coupling (JHH) with small chemical shift differences on the conventional one-dimensional (1D) 1H spectra of the human brain. Although it has been shown that Glu and Gln are resolved at 7T, the resonance of GABA still overlaps with that of Glu.1,2 Several spectral analysis techniques, such as LCModel,3 can be used to estimate the concentrations of these metabolites from the potentially overlapped spectra. Neverthe-
less, the overlapping can cause the estimation errors at low concentrations of the metabolites GABA and Gln.

Constant-time (CT) two-dimensional (2D) methods demonstrate good peak resolution through $^1$H decoupling of $J_{HH}$ along the F1 direction. We have reported the resolution of the 3 diagonal peaks of the C4 protons of Glu (Glu C4H) and Gln (Gln C4H) and C2 proton of GABA (GABA C2H) at around 2.4 ppm on the localized 2D CT-correlation spectroscopy (COSY) spectra in the human brain and on the CT-point resolved spectroscopy (PRESS) in the human brain at 4.7T. This feature of good peak resolution is expected to lead to quantitation of metabolites with strongly coupled spin systems, such as Glu, GABA and Gln.

Still, these CT methods require a considerably long delay of the constant time, $T_{ct}$, of around 100 ms for improving the peak resolution. This long delay causes decay by transverse relaxation, and $T_2$ correction is required for quantitation. The $T_2$ dependency of the singlet peak, such as that of N-acetyl aspartate (NAA) at 2.01 ppm is described only by transverse relaxation. However, complex behaviors caused by strong coupling effects add to that of the peaks of Glu, GABA and Gln, which makes $T_2$ measurement difficult. Calculations of peak volume on 2D spectra and a calibration method for measuring concentrations are also required. Improved quality of the in vivo spectra can assist absolute quantitation.

In this work, we first show two ways to improve the quality of the localized 2D CT-COSY spectra. One method uses an image-selected in vivo spectroscopy (ISIS) pulse for one direction to minimize the displacement error due to the chemical shift differences. The other uses a sampling scheme along the $t_1$ direction to improve the peak resolution. We propose an absolute quantitation method on the localized CT-COSY spectra and demonstrate to measure concentration of Glu in the phantom experiments. We also measure concentrations of Glu, GABA and Gln in a human brain.

**Materials and Methods**

We present a modified localized CT-COSY sequence and a sampling scheme along the $t_1$ direction and then, show our $T_2$ measurement and absolute quantitation methods.

**ISIS CT-COSY sequence**

Figure 1 shows a modified localized 2D CT-COSY sequence with an ISIS pulse. This sequence consists of four modules: water suppression of variable power radio frequency (RF) pulses with optimized relaxation delays (VAPOR), outer volume suppression (OVS), ISIS localization for one dimension, and CT-COSY for localization for two dimensions. The delay of $T_{ct}$ between the first and third RF pulses in the CT-COSY module is kept constant during the entire measurement. The temporal position of the 180° pulse in the CT-COSY module and crusher gradient pulses are shifted by $\Delta t_1/2$ for every $t_1$ increment. These pulses are shown as a crosshatched area. As the $^1$H chemical shift is refocused by this 180° pulse, the chemical shift evolution depends on the $t_1$ increment. In contrast, the evolution of $^1$H-$^1$H homonuclear coupling ($J_{HH}$) is kept constant because this pulse does not affect $J_{HH}$. Then, 2D spectra can be obtained with $^1$H decoupling along the $F_1$ direction. When $t_{delay}$ is a positive value, the data are collected by an asymmetric sampling scheme along the $t_1$ direction (see Fig. 2).
spatially 2D localized column selected by two slice selective pulses in the CT-COSY module is suppressed by VAPOR. Thus, the water signal is more suppressed compared to the 3D localization when using three ISIS pulses for all 3D axes. Because an ISIS pulse is a preparation pulse, long pulse duration can be used. Thus, an adiabatic pulse with a wide bandwidth can be used, which improves the slice displacement and slice profile compared to the results using the previously reported method. Use of a non-selective 180° pulse in the CT-COSY module may also improve the refocus and inversion features. A hyperbolic secant pulse of 7-ms duration was used for the ISIS pulse and in the CT-COSY module, the 90° pulses were 2-ms asymmetric pulses\(^1\)\(^4\) and the 180° pulse was a 3-ms rectangular pulse.

Asymmetric sampling scheme along \(t_1\) direction

In the localized CT-COSY sequence with the ISIS pulse as shown in Fig. 1, no refocusing pulses are used after the third RF pulse in the CT-COSY module to minimize the number of RF pulses for reducing coherence loss. Reconstructed spectra are displayed only in magnitude mode. Even in this condition, an absorption shape and narrow linewidth are expected along the \(F_1\) direction by using a symmetric sampling scheme between the positive and negative regions in the \(t_1\) domain similar to the sampling scheme in spin echo (SE).

Under the condition of \(in\ vivo\) inhomogeneous \(B_0\) field, a coherence transfer echo\(^6\) appears along the \(t_2\) direction. Figure 2d shows the coherence transfer echo of the lowest free induction decay (FID). After the temporal position of the 180° pulse is shifted every \(t_1\) increment in the CT-COSY module (Fig. 2a), the FID is collected along the \(t_2\) direction as shown in Fig. 2d. Figure 2b shows the signal profile at \(t_2 = 0\) along the \(t_1\) direction on the accumulated 2D time domain data on the \(t_1\) and \(t_2\) axes (shown in Fig. 2c). Here, the coherence transfer echo is generated in the negative region on the \(t_1\) domain. Then, the collection of signals in only this region can maximize sensitivity. However, linewidth along the \(F_1\) direction will be widened. To compromise this issue, we used an asymmetric sampling scheme along the \(t_1\) direction where the number of \(t_1\) increments in the negative region is a little larger than that in the positive region. This negative region is marked by white dashed lines in Fig. 2c. When the delay of \(t_{\text{delay}}\) in the CT-COSY sequence shown in Fig. 1 is positive, data are collected using this asymmetric sampling scheme along the \(t_1\) direction.

\(T_{ct}\) dependency in strongly coupled spin systems

Signals of the peak of strongly coupled spin systems decay by the transverse relaxation with a rate of \(T_2\) and change by \(J_{HH}\) during \(T_{ct}\) in the localized CT-COSY. We thought that the signal could be described by a model of \(e^{-T_{ct}/T_2}f_{\text{inh}}(T_{ct})\) in which \(T_{ct}\) dependency by \(J_{HH}\) is defined as a function of \(f_{\text{inh}}(T_{ct})\). To calculate this dependency function of \(f_{\text{inh}}(T_{ct})\), we computed the peak volume on CT-COSY spectra with varied values of \(T_{ct}\). These spectra were simulated by magnetic resonance experiments of a general approach to magnetic resonance mathematical analysis (GAMMA). We used the previously reported values of chemical shifts and coupling constants. We validated this model by curve-fitting the spectra of a glutamate solution measured by the localized CT-COSY sequence.
describe measurement conditions in the section entitled “Experimental” below.

**Absolute quantitation protocol**

Figure 3 shows the protocol we developed for absolute quantitation. First, we obtain at least two localized CT-COSY spectra from a subject for $T_2$ correction, collecting each spectrum with a different $T_{ct}$ value.

Next, we extract the rectangular area that contains the diagonal peaks of the targeted metabolites to calculate the peak volume. The area marked by a yellow rectangle in Fig. 4 shows the diagonal peaks of Glu C4H on the CT-COSY spectrum. Figure 4 also shows the surface plots of these diagonal peaks. We then compute the peak volumes of those diagonal peaks using the spectral analysis software that we developed on MATLAB 7.4. In this tool, the diagonal peak is curve-fitted with a linear combination model of basis CT-COSY spectra. A basis spectrum of each metabolite was calculated by the software of GAMMA with the value of $T_{ct}$ corresponding to that in the measurement. The peak volume of the targeted metabolite is calculated as the ratio to the peak volume on the basis spectrum after minimization using a simplex algorithm.

Because the simulated basis spectra comprise the $T_{ct}$ dependency due to $J_{HH}$, the calculated ratio of the peak volume, $PV_{ratio}(T_{ct})$, on the measured spectrum decays only at a rate of $T_2$. $T_2$ decay during the $T_{ct}$ delay can then be corrected by curve-fitting using a model of $M_0 e^{-T_{ct}/T_2}$ and the $PV_{ratio}(T_{ct} = 0)$, without transverse relaxation effects, can be calculated in the $T_2$ correction step.

Concentration of the target metabolite is calculated by the internal water reference method in the final step. We measured the water signal inside the same voxel of the CT-COSY spectra. The number of $^1H$ spins of the targeted metabolite is proportional to the concentration of the metabolite, $C_{metab}$ and the voxel volume, $Vol_{metab}$. While the induced voltage on the RF coil is proportional to the number of $^1H$ spins, that voltage is proportional to the product of $C_{metab}$ and $Vol_{metab}$. The peak volume without transverse relaxation is proportional to the induced voltage. Then, the value of $PV_{ratio}(T_{ct} = 0)$ can be given by:

$$PV_{ratio}(T_{ct} = 0) = Coef_{2Dmetab} Coef_{RFcoil} C_{metab} V_{ol_{metab}}$$

Fig. 4. In our absolute quantitation protocol, constant-time correlation spectroscopy (CT-COSY) spectra are obtained from a voxel in the human brain (a) with varied values of $T_{ct}$, and water spectra with varied values of echo time (TE) are obtained (b). In the measurement of the concentration of glutamate (Glu), the region around the diagonal peak of Glu C4H is extracted. This peak is curve-fitted with a simulated Glu spectrum computed by general approach to magnetic resonance mathematical analysis (GAMMA). To calculate the concentrations of metabolites, the water signal in the same voxel is obtained (c).
\[
PA_{\text{water}}(TE = 0) = \text{Coef}_{1D}\text{Coef}_{\text{RFcoil}}C_{\text{water}}V_{\text{water}}
\]

where \(C_{\text{water}}\) denotes the concentration of water, \(V_{\text{water}}\) denotes the voxel volume for water signal and \(\text{Coef}_{1D}\) denotes the factor in the transformation to a 1D spectrum. Then, the concentration of the target metabolite is described as:

\[
C_{\text{metab}} = \frac{\text{Coef}_{\text{metab}}P_{\text{ratio}}(T_{\text{ct}} = 0) V_{\text{water}}}{PA_{\text{water}}(TE = 0) V_{\text{metab}}C_{\text{water}}}
\]

where \(\text{Coef}_{\text{metab}} = \frac{\text{Coef}_{1D}}{\text{Coef}_{2D\text{metab}}}.\)

The value of \(\text{Coef}_{\text{metab}}\) that depends only on the metabolite can be measured in phantom experiments. We can measure the concentration of the target metabolite of a subject.

Before validating the absolute quantitation method, we measured the values of \(\text{Coef}_{\text{metab}}\) for Glu, GABA and Gln in three types of phantom measurements using a solution phantom of 50 mM L-glutamic acid, 50 mM L-glutamine (Wako Pure Chemical Industries, Ltd., Osaka, Japan), or 50 mM GABA (Sigma-Aldrich Co., St. Louis, MO, USA).

**Experimental**

We performed all measurements using a 4.7T whole-body MR scanner interfaced to an INOV A console (Agilent, Palo Alto, CA, USA) with a gradient system with maximum strength of 35 mT/m at a rise time of 350 µs and with first and second-order shim coils. We used a quadrature volume transverse electromagnetic (TEM) coil of 300-mm diameter for both transmission and reception. The internal review board of the National Institute for Environmental Studies approved the protocol, and we obtained informed consent from all volunteers to conduct these measurements.

First, we performed phantom measurements to demonstrate the decrease in the slice displacement error due to the chemical shift difference and the improvement in the slice profile. We used a spherical phantom of 130-mm diameter filled with saline. Volume size was set to \(30 \times 30 \times 30\) mm\(^3\). To measure slice profiles, we applied read gradient pulses in the conventional localized CT-COSY sequence and in the proposed CT-COSY sequence with an ISIS pulse. Each slice profile was measured using water signal without water suppression pulse. In both measurements, carrier frequencies of the RF pulses in the CT-COSY modules were first set to water resonance and the frequency of the 180° pulse in the conventional CT-COSY sequence or that of the ISIS pulse in the ISIS CT-COSY sequence was then shifted upfield by 200 Hz, which is equal to the difference between creatine (Cr) resonance of 3 ppm and NAA resonance of 2 ppm at 4.7T. A hyperbolic secant pulse with duration of 7 ms was used for the ISIS pulse. The bandwidth was 2800 Hz. A universal rotator pulse with duration of 4 ms was used for the slice selective pulse of 180° in the conventional sequence. The bandwidth was 1240 Hz.

To evaluate the peak resolution by the asymmetric sampling scheme, we simulated SE signal, 14% asymmetric SE signal and FID signal. We compared two spectra calculated by 1D Fourier transform (FT) of these signals. We also evaluated the localized CT-COSY spectra obtained from a human brain with a 14% asymmetric sampling along the \(t_1\) direction. A volume of interest (VOI) of \(30 \times 30 \times 30\) mm\(^3\) was defined inside the parieto-occipital region on the gradient echo images. After shining inside the VOI with fast automatic shimming technique by mapping along projections (FASTMAP), RF power was adjusted for both the slice and water suppression pulses. A simultaneous quadrature detection was used to acquire 512 complex data points in \(t_2\) (number of points \(np = 1024\)) with 150 increments in \(t_1\) (number of \(t_1\) increments \(ni = 150\)). The spectral width for \(F_1\) was 1 kHz and that for \(F_2\) was 2 kHz. Relaxation delay was 3 s and \(T_{\text{ct}}\) was 110 ms.

We performed phantom experiments to validate a model of \(T_{\text{ct}}\) dependency in strongly coupled spin system. We filled a 200-mL bottle with a solution of 50 mM L-glutamic acid, placed the bottle in a water bath containing 0.9% dissolved NaCl for mimicking an \textit{in vivo} load, and acquired 9 sets of localized CT-COSY signals with varied values of \(T_{\text{ct}}\) from a VOI of \(30 \times 30 \times 30\) mm\(^3\) in the bottle. The values of \(T_{\text{ct}}\) were 110, 130, 150, 250, 270, 290, 380, 400, and 420 ms. Relaxation delay was 1.87 s for all spectra. Other measurement parameters were the same as those of measurements of the human brain spectra.

After reconstruction of 2D spectra in magnitude mode, each peak volume of the diagonal peak of Glu C4H was calculated by integrating the rectangular area containing the diagonal peak. We curve-fitted those data by a model of \(e^{-T_{\text{ct}}/T_2}f_{\text{inn}}(T_{\text{ct}})\), where the function of \(f_{\text{inn}}(T_{\text{ct}})\) was calculated by simulating Glu spectra using GAMMA software with reported chemical shift values and coupling constants.

To validate the absolute quantitation method, we performed phantom experiments of a solution with 10 mM L-glutamic acid. We obtained three sets of the localized CT-COSY spectra from a volume of \(30 \times 30 \times 30\) mm\(^3\) with a relaxation delay of 8 s. The values of \(T_{\text{ct}}\) were 130, 270, and 400 ms. Water signal was obtained in the same voxel. Other measurement parameters were the same as those for meas-
measurements of human brain spectra.

We also tried absolute quantitation of metabolites with strongly coupled spin systems in human brain. We selected a VOI of a $30 \times 30 \times 30$ mm$^3$ in the parieto-occipital region on a scout image and obtained two localized CT-COSY spectra of the human brain after the same procedure described above. Relaxation delay was 4 s, and values of $T_{ct}$ were 135 and 275 ms. With $ni = 150$ and number of excitations ($nt) = 4$, each measurement took 40 min. Water signal was collected in the same voxel by the localized CT-COSY sequence without modules of water suppression and OVS and with a fixed $t_1/2$ of 10 ms. The values of $T_{ct}$ were 30, 45, 55, 65, 75, 85, 95, 105, 155, 205, 255, 305, 355, and 405 ms. To discriminate water in the brain tissue from that in CSF, the values of the peak area of all spectra were curve-fitted by a model of $M_{\text{brain tissue}}e^{-t_1/T_{2\text{brain}}} + M_{\text{CSF}}e^{-t_1/T_{2\text{CSF}}}$, in which $M$ denotes the signal amplitude of the brain tissue or CSF. The concentration of water in the voxel was calculated by measured fractions of the gray and white matter (GM, WM) and reported concentrations of water in the GM and WM.11 Those fractions of GM and WM were determined by segmentation of a 3D $T_1$ weighted image.

Results

Figure 5 shows the slice profiles of the phantom obtained by the original localized CT-COSY sequence (a) and by the proposed ISIS CT-COSY sequence (b). The slice profile of the proposed method is better than that of the original. In both plots, solid lines show the slice profiles when the carrier frequency of the slice pulse was tuned to the resonant frequency. Dashed lines show them when the carrier frequency is shifted upfield by 200 Hz, which is equal to the difference between Cr resonance of 3 ppm and NAA resonance of 2 ppm at 4.7T. The slice displacement of the proposed method is about 2 mm due to the frequency shift of 200 Hz compared to that of about 5 mm with the original method. These displacement values were equivalent to the computed values with bandwidths of 2800 and 1240 Hz.

Figure 6a-c shows simulated SE and FID signals and spectra. In the case of SE signal, only the absorption curve appeared, and the magnitude spectrum was equal to the absorption spectrum (Fig. 6a). In the case of 14% asymmetric SE signal, the linewidth of the magnitude spectrum was equivalent to that of the absorption spectrum although the dispersion curve arose (Fig. 6b). However, in the case of the FID signal, the linewidth of the magnitude spectrum was wider than that of the absorption spectrum (Fig. 6c). Figure 6d shows a magnitude mode display of a CT-COSY spectrum of a human brain. Diagonal peaks of glutamate, GABA, and glutamine are clearly resolved. Diagonal peaks of Glu C4H on this spectrum are viewed from the $F_1$ axis in magnitude mode (Fig. 6e) and in absorption mode (Fig. 6f). The linewidth in magnitude mode is around 10 Hz, which is equivalent to that in absorption mode. This indicates that narrow linewidth can be obtained even in magnitude mode under the asymmetric $t_1$ sampling scheme.

Figure 7 shows $T_{ct}$ dependency of the diagonal peak of Glu C4H measured in the 50 mM glutamate phantom experiments. The dashed line shows the $T_{ct}$ dependency function of $f_{in}(T_{ct})$ calculated by GAMMA. The solid line shows a curve of $A e^{-t_1/T_2} f_{in}(T_{ct})$. The measured peak volumes of

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Fig. 5. Comparison of the slice profile of the phantom obtained by the conventional localized constant-time correlation spectroscopy (CT-COSY) sequence (a) to that by the proposed image-selected in vivo spectroscopy (ISIS) CT-COSY sequence (b). In both plots, solid lines indicate the slice profiles when the carrier frequency of the slice pulse was tuned to the resonant frequency. Dashed lines show that when the frequency is shifted upfield by 200 Hz, the slice displacement is 5 mm in the conventional sequence, compared to 2 mm in the proposed sequence. In addition, a better slice profile can be obtained in the proposed sequence.
In validating the absolute quantitation, we calculated the concentration of the 10 mM Glu phantom as 9.4 mM. In the trial of the absolute quantitation of metabolites with strongly coupled spin systems in the human brain, we calculated concentrations of Glu, GABA and Gln as 9.5, 0.61, and 3.6 mM.

Discussion

In this work, we have developed an absolute quantitation method for in vivo 2D MRS. Diagonal peaks of Glu, GABA, and Gln with strongly coupled spin systems can be resolved on human brain spectra obtained by CT-COSY (Fig. 6c) or CT-PRESS through 1H decoupling along the F1 direction. 2,4 While overlapped peaks are curve-fitted by a model of absorption and dispersion spectra are drawn as bold lines on the F1 axis. In the case of the SE signal, only the absorption curve appears, and the magnitude spectrum is equal to the absorption spectrum (a). For the 14% asymmetric SE signal, the linewidth of the magnitude spectrum is equivalent to that of the observation spectrum although a dispersion curve appears (b). However, for the FID signal, the linewidth of the magnitude spectrum is wider than that of the observation spectrum (c). A localized constant-time correlation spectroscopy (CT-COSY) spectrum obtained from a 27-mL voxel in the parieto-occipital lobe of a human brain is displayed in magnitude mode (d). Peaks of Glu C4H in magnitude mode (e) and in absorption mode (f) are viewed from the F1 axis. Absorption peak shape of glutamate (Glu) C4H was computed by correction of the phase of this peak only. Both full widths at half maximum are around 10 Hz. This means that the peak with narrow linewidth could be obtained in a magnitude mode even under the 14% asymmetric t1 sampling scheme.

Glu C4H, indicated by rhombus symbols in the figure were well fitted by this curve where the calculated T2 value was 580 ms.

In validating the absolute quantitation, we calculated the concentration of the 10 mM Glu phantom as 9.4 mM. In the trial of the absolute quantitation of
ment and correction, calculation of peak volume, and calibration by the internal water reference. The ratio of peak volumes could be computed by the basis set calculated by GAMMA. We validated the method in the 10-mM Glu phantom experiments. As a result, measured concentration was 9.4 mM. This result shows that our absolute quantitation method is useful for measuring concentrations of metabolites with strongly coupled spin systems.

In testing the absolute quantitation of metabolites in the human brain, concentrations of Glu, GABA, and Gln were calculated as 9.5, 0.61, and 3.6 mM, which agreed well with reported values. This result suggests that those metabolites can be quantitated by our method. Long total measurement time of 80 min does not permit multiple volunteer measurements for validation. Such measurements can be performed in future studies after reducing the measurement time with achieving higher sensitivity by phased array coils or by CT-PRESS.

Displacement error due to chemical shift differences is one of problems at higher magnetic fields. This error is caused among the peaks of the same metabolite. Voxel positions for Glu differ among three peaks of C4H at around 2.35 ppm, C3H at around 2.1 ppm, and C2H at around 3.75 ppm. Even in our proposed ISIS CT-COSY method for reducing this displacement error, the computed displacement value between C4H and C2H is approximately 3 mm. Because we used only one peak of Glu C4H for absolute quantitation on the 2D CT spectra, the displacement error does not reduce the accuracy of quantitation.

Conclusions

We can reduce the displacement error due to chemical shift difference by the ISIS CT COSY sequence. Using an asymmetric sampling scheme along the t1 direction, we can obtain peaks of narrow linewidths for better peak resolution along the F1 direction on the CT-COSY spectra. These two methods can improve the quality of the CT-COSY spectra. We can measure concentrations of metabolites with strongly coupled spins, such as Glu, GABA and Gln using our proposed absolute quantitation method on the CT-COSY spectra.

References