ProFit-based Quantitation of Cerebral Metabolites using 2D L-COSY at 3T

E. Frias-Martinez[1], N. Rajakumar[1], X. Liu[1], A. Singhal[1], S. Banakar[1], S. Lipnick[1], G. Verma[1], S. Ramadan[1], A. Kumar[2], and M. A. Thomas[1]

[1]Radiological Sciences, UCLA, Los Angeles, CA, United States, [2]Department of Psychiatry, UCLA, Los Angeles, CA, United States

Introduction: The ProFit algorithm has been developed for quantitation of 2D JPRESS (J-resolved spectroscopy) signals [1]. When compared with one-dimensional (1D) MRS data processed using LC Model, the results indicated an increase in the number of metabolites that can be detected (from 8 in LC Model to 17 in ProFit) with decreased Cramer-Rao lower bound (CRLB) values [1,2]. In contrast to JPRESS, localized 2D shift correlated spectroscopy (L-COSY) [3] has improved spectral dispersion along the second spectral dimension, which may offer improved specificity for quantitation. The goal of this work was to adapt ProFit for processing 2D L-COSY spectra and to test if the increased dispersion along the second dimension improves the overall quantitation accuracy.

Methods: A maximum-echo sampling 2D L-COSY sequence containing three slice-selective RF pulses (90^0, 180^0, 90^0) was implemented on a Siemens 3T Trio-Tim scanner (Siemens Medical Systems, Germany) [3]. The following parameters were used: TR/TE=2s/30ms, 3x3x3cm^3 voxel, 8 averages per $\Delta t1$ and 100 $\Delta t1$ increments. A white matter brain phantom containing fifteen metabolites (pH=7.3) was used for processing 10 *in vitro* measurements. Eight healthy volunteers have been investigated so far. The 2D MRS voxel was mainly localized in the occipital white/gray matter. The modified ProFit algorithm uses MATLAB (Mathworks, Natlick, MA, USA, ver. 7.3) and was executed on an Intel 2.8GHz with Windows XP. ProFit algorithm uses prior knowledge constraints and a combined linear and non-linear optimization for fitting concentrations. The algorithm uses a prior knowledge basis-set generated using the GAMMA library [4] in combination with the chemical shift and J-coupling values reported the literature [5]. The main modifications implemented for quantitation of L-COSY include: (1) programming COSY sequence using GAMMA for obtaining prior knowledge metabolite spectra; (2) inclusion of optimal sine bell filters along t1 and t2 dimensions both for display and quantitation, and (3) redefining the size of the region of interest (ROI) used for covering the entire COSY cross peaks along the 2nd dimension. Prior knowledge generated for L-COSY included 20 metabolites: creatine (Cr), N-acetylaspartate (NAA), glycerylphosphocholine (GPC), phosphorylcholine (PCh), free choline (Cho), alanine (Ala), aspartate (Asp), γ-aminobutyric acid (GABA), glucose (Glc), glutamine (Gln), glutamate (Glu), glycine (Gly), glutathione (GSH), lactate (Lac), myo-inositol (mI), N-acetylaspartylglutamate (NAAG), phosphoethanolamine (PE), taurine (Tau), scyllo-inositol (Scy) and ascorbate (Asc). 2D L-COSY spectra were then processed using the modified ProFit code and the measurement accuracy was characterized using CRLB [6].

Results and Discussion: Fig. 1 presents a typical 2D L-COSY spectrum recorded in human brain *in vivo*. Shown in Fig. 2 is the prior knowledge obtained from combining the spectra of the metabolites considered for fitting [4-5], where the cross peaks produced by L-COSY can be clearly seen, and Fig. 3 shows the residual obtained after the fitting process. ProFit quantitation of the 3T L-COSY spectra *in vivo* enabled the quantitation of all the previously enumerated metabolites, with concentrations expressed as ratios to creatine of (mean±SD): 1(Cr), 1.27±0.21(NAA), 0.1±0.02(GPC), 012±0.02(PCh), 0.1±0.02(Cho), 0.12±0.03(Ala), 0.43±0.01(Asp), 0.41±0.2(GABA), 0.31±0.1(Glc), 0.43±0.1(Gln), 1.48±0.3(Glu), 0.12±0.09(Gly), 0.15±0.07(GSH), 0.14±0.05(Lac), 0.83±0.1(mI), 0.33±0.09(NAAG), 0.29±0.07(PE), 0.21±0.08(Tau), 0.05±0.00(Scy), 0.3±0.21(Asc). These concentrations, for the best part, agree with those reported in the literature when using ProFit processed JPRESS [1], but, the CRLBs (mean) reported by L-COSY, for *in vivo* and *in vitro*, are smaller than those reported by ProFit-JPRESS.

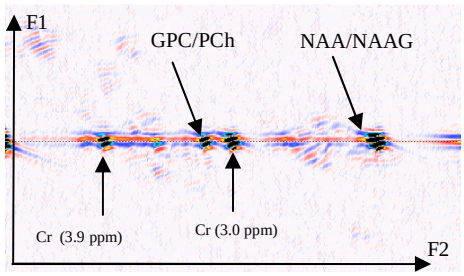

Fig. 1

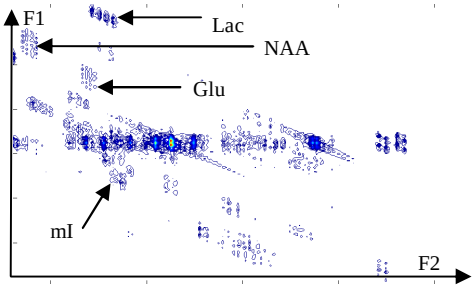

Fig. 2

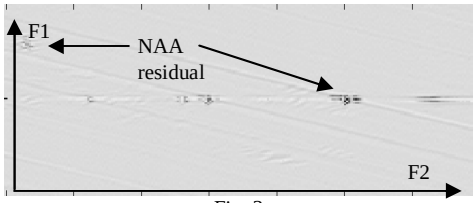

Fig. 3

Conclusion: This work demonstrates the first quantitation of L-COSY spectra using a modified version of ProFit algorithm. Initial results indicate that 20 metabolites can be quantitated successfully with better accuracy than JPRESS. This preliminary study indicates that the initial assumption, that improved dispersion of COSY when compared to JPRESS implies better quantitation, holds true.

References:

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