Accelerated Multi Echo based Echo-Planar J-Resolved Spectroscopic Imaging: Implementation and Quantitation of Cerebral Metabolites

Manoj Kumar Sarma[1], Rajakumar Nagarajan[1], Neil Wilson[1], Jon Furuyama[1], and M. Albert Thomas[1]
[1]*Radiological Sciences, UCLA School of Medicine, Los Angeles, CA, United States*

Introduction: Three-dimensional (3D) magnetic resonance spectroscopic imaging (MRSI) combining one spectral and 2-3 spatial dimensions has been used clinically in brain studies (1,2). The limitation of this technique is the time needed to acquire large-volume 3D MRSI datasets when using conventional phase encoding in three directions to traverse through k-space. With higher-field MR systems such as 3T MRI scanners becoming widely available and improved coil arrays providing increased signal to noise ratio (SNR), MRSI data can be acquired with higher spatial resolution. Novel MRSI techniques are required to overcome these challenges and to reduce the scan time which would further improve the clinical applicability of this technique. In this study we have implemented a multi-echo (ME) echo planar (EP) based J resolved spectroscopic imaging (ME-EP-JRESI) in brain and quantify the metabolites using prior knowledge fitting (ProFit) algorithm (3). The ME-EP-JPRESS sequence consists of two spatial encodings (read and phase) and two spectral dimensions (t_1 and t_2). Analogous to LC Model (4), ProFit fits the spectra as linear combinations of two-dimensional (2D) basis spectra using a nonlinear least-squares algorithm in combination with a linear least-squares algorithm and incorporates maximum prior knowledge available. In summary, the goals of this study were to implement ME-EP-JRESI in brain at 3T and quantify the cerebral metabolites using the Profit algorithm.

Materials and Methods: A pilot version of the ME-EP-JRESI sequence modified from the multi-echo correlated spectroscopic imaging (ME-EP-COSI) (5) was implemented on the 3T Trio-Tim MRI scanner using the Siemens VB17a compiler. The sequence uses a 90^0-180^0-180^0 scheme for localization with crusher gradients surrounding the last two RF pulses. The crusher gradients ensure magnetization outside of the volume of interest (VOI) that was excited will undergo de-phasing and will not significantly contribute to the acquired signal. A gray matter (GM) brain phantom containing sixteen metabolites (pH=7.3) was used for acquiring 10 *in vitro* measurements. Four healthy volunteers (age = 46±9.9years) have been investigated so far. Water-suppressed four dimensional (4D) ME-EP-JRESI data was recorded and non-water-suppressed 3D ME-EP-JRESI data was recorded only along k_x, k_y and t_2 dimensions. The following parameters were used for ME-EP-JRESI: a) TR/TE = 1.5s/30ms, 1.5x1.5x2cm^3 voxel for VOI localization with the resolution of 4.5cm^3, 64Δt_1 increments, 256 bipolar echoes with each echo sampling 16-32 x-points, 16 y-encoding, FOV= 16x16cm^2, b) TR/TE 1.5s/30ms, 4x5x2cm^3 voxel for VOI localization, 256 bipolar echoes with each echo sampling 16-32 x-points, 16 y-encoding, FOV= 16x16cm^2, $\Delta t1$ =1ms and NEX=1, water reference MR spectrum from the same voxel as the water-suppressed ME-EP-JPRESS. Acquired data were post-processed with a custom MATLAB-based program, which applied spatial Hamming and spectral apodization filters to smoothen the data. Modified Profit algorithm was applied to process the extracted data and to calculate metabolite ratio with respect to the 3.0 ppm creatine peak (S/S_{Cr}). The Cramer-Rao Lower Bound (CRLB) values, a measure of the performance of the fitting technique were also calculated. Prior knowledge generated for ME-EP-JRESI included 20 metabolites icluding, creatine (Cr), N-acetylaspartate (NAA), phosphorylcholine (PCh), free choline (Cho), aspartate (Asp), γ-aminobutyric acid (GABA), glucose (Glc), glutamine (Gln), glutamate (Glu), glutathione (GSH), lactate (Lac), myo-inositol (mI), Nacetylaspartylglutamate (NAAG), phosphoethanolamine (PE), and taurine (Tau).

Metabolite	Expected Ratios	Determined Ratios	
		Mean	SD
Cr303	1.00	1.00	0.00
Cr391	1.00	1.01	0.01
NAA	1.27	1.38	0.10
PCh	0.09	0.13	0.01
Cho	0.13	0.14	0.01
Asp	0.30	0.29	0.07
GABA	0.10	0.09	0.05
Glc	0.14	0.28	0.15
Glu	1.79	1.97	0.13
GSH	0.61	0.20	0.02
mI	0.63	1.02	0.14
NAAG	0.07	0.20	0.07
PE	0.14	0.17	0.06
Tau	0.26	0.25	0.07
tNAA	1.34	1.58	0.04
Glx	2.14	2.02	0.14
tCho	0.21	0.27	0.02

Table 1: Comparison of metabolite ratios (S/S_{Cr}) in same voxel across 10 gray matter phantom measurements with expected ratios. tNAA = NAA +NAAG, Glx = Glu + Gln, tCho = Cho + PCh.

Results and Discussion: Fig. 1 shows a typical ME-EP-JRESI spectrum extracted from the occipital region of 42 years old healthy brain *in vivo*. Table 1 shows the mean value of various metabolite ratios with respect to creatine over the gray matter phantom across the 10 studies in the same location. Fig. 2 shows the coefficient of variation (CV) for various metabolites across eight voxels in a single measurement of the gray matter phantom. Table 2 shows the mean metabolite ratios of four healthy control in a voxel extracted from the occipito-parietal GM/WM regions. Metabolites with higher physiological concentrations including glutamate/glutamine (Glx), N-acetylaspartate (NAA), myo-inositol (mI), which all show cross peaks due to J-coupling (6), all had acceptable CRLBs < 6.3 and CVs between 2–10%. ProFit consistently overestimated the concentration of mI, yet maintained a low CRLB, suggesting it may have been influenced from terrible water suppression in the in-vivo data. Lactate and GABA, whose physiological concentrations are low, and were observed to have the poorest fit, as indicated by the CRLBs.

Metabolite	Mean (S/S_{Cr})	SD	Mean CRLB
Cre303	1.000	0.000	2.63
Cre391	1.105	0.218	3.32
NAA	1.835	0.222	1.78
PCh	0.158	0.092	7.98
Cho	0.273	0.128	6.85
Asp	0.592	0.337	6.10
GABA	0.230	0.069	29.35
Glu	1.317	0.255	7.30
GSH	0.468	0.105	6.54
Lac	0.618	0.113	22.45
mI	1.574	0.278	4.55
NAAG	0.381	0.239	9.17
Tau	0.448	0.117	13.67
tNAA	2.217	0.229	1.10
Glx	1.562	0.201	6.30
tCho	0.374	0.072	9.82

Table 2: Metabolite ratios and CRLBs in the occipito-parietal GM/WM regions in healthy subjects.

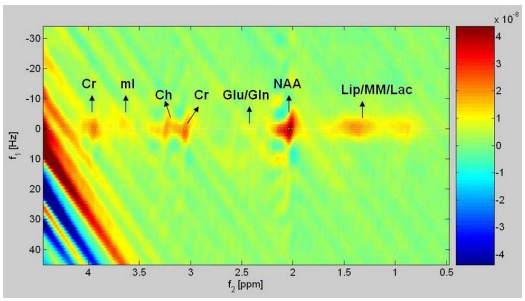

Fig.1: A ME-EP-JRESI spectrum recorded in the occipital region of a healthy human brain in vivo.

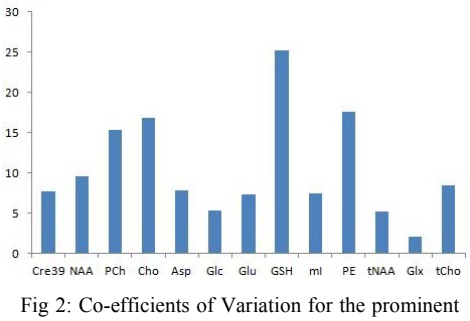

Fig 2: Co-efficients of Variation for the prominent metabolites observed across eight voxels of one measurment of the gray matter phantom.

Conclusion: This is an exploratory, validation, and feasibility study for ME-EP-JRESI in human brain at 3T. We demonstrates the implementation of ME-EP-JRESI in the brain and also the quantitation of the spectra using a modified version of ProFit algorithm. Initial results indicate that 20 metabolites can be quantified successfully with better accuracy than 1D MRS.

References: 1. Kurhanewicz J, Vigneron DB, Nelson SJ. Neoplasia 2000; 2:166–89. 2. Chmelík M, Schmid AI, Gruber S, et al. Magn Reson Med 2008; 60:796-802. 3. Schulte, RF and Boesiger, P. NMR Biomed 2006; 19: 225-263. 4. Provencher SW.. Mag. Reson. Med. 1993; 30: 672-679. 5. Furuyama J, Thomas MA. ISMRM 2011 # 1435. 6. Velan S, Lemieux R, Raylman W, Boling G, Magn Reson Med 2007; 265:409.