Diffusion Tensor Spectroscopic Imaging in Human Brain

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INTRODUCTION: Metabolite diffusion can provide unique information on intracellular properties, such as viscosity, cell swelling, restriction in subcellular structures, and cytoplasmic streaming that may help to characterize possible inflammatory processes in ischemia and multiple sclerosis, and brain tumors[1,2]. Intracellular metabolite mobility provides complementary information to DTI, which represents an average of water diffusion across the intra- and extracellular compartments. All human studies thus far investigating metabolite diffusion have used single voxel localization methods[3-7] due to overwhelming motion sensitivity of conventional MR spectroscopic imaging (MRSI) techniques[11]. However, it is desirable to map metabolite diffusion across extended brain areas to correlate with DTI.

In this study we demonstrate the feasibility of diffusion tensor spectroscopic imaging (DTSI) in human brain using high-speed proton-echo-planar-spectroscopic-imaging (PEPSI)[8] with ECG gating, correction of movement-related phase errors using navigator signal acquisition[9] and compensation of the variability in T_1-saturation, which results from heart-rate variability with cardiac gating.

METHOD: The PEPSI-based DTSI pulse sequence employed PRESS volume pre-localization and diffusion gradients with 25 ms duration and 23 mT/m maximum amplitude. Spatial localization along the edges of the PRESS box and suppression of regions with subcutaneous fat was enhanced using 8 outer volume suppression slices (Fig. 1a). ECG gating using a time delay of 250 msec between the systolic wave and the beginning of the pulse sequence was used to compensate for cardiac-related brain and cerebrospinal fluid pulsations. Correction of movement-related phase instability in individual acquisitions was performed on a coil-by-coil basis following the approach described in[9], using a navigator acquisition immediately before the phase encoding gradients and the echo-planar readout train. The navigator acquisition was spatially localized using a pair of echo-planar gradients oriented perpendicular to the PEPSI slice and employed automatic detection of the center of the PEPSI slice across the multi-coil data by enforcing consistency between multi-coil data. Navigator correction, spatial-spectral reconstruction with multi-coil combination and phase correction based on the residual water signal was performed online on the scanner as described in[8].

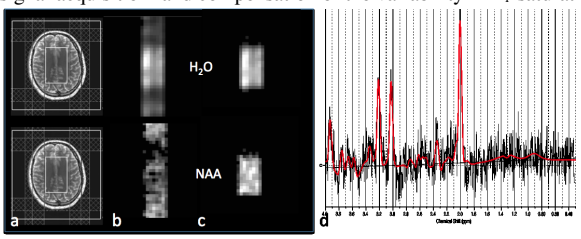

Figure 1: (a) PRESS volume selection with outer volume suppression slices. Diffusion weighted spectroscopic images of (top) tissue water (bottom) and NAA reconstructed (b) without and (c) with navigator correction, which strongly reduces ghosting along the phase encoding direction. (d) Localized spectrum at b: 1734 s/mm^2 with LCModel fit.

Three healthy subjects participated after giving institutionally reviewed informed consent. Data were collected on clinical 3T TIM Trio scanners (Siemens Medical Solutions, Inc) equipped with a 32-channel head array coil. 2D DTSI data were collected from a supraventricular 20 mm thick slice in AC/PC orientation using: TE: 90 ms, TR: 2 s, b-values: 0 and 1734 s/mm^2, 6 gradient directions, FOV: 226x226 mm^2, spatial matrix: 32x32 voxels, nominal voxel size: 1 cm^3, nominal scan times: 2:16 min for water-suppressed scans with 2 averages and 1:12 min for non-water-suppressed scans with single average. The total scan time to collect 7 water-suppressed and 7 non-water-suppressed data sets was approximately 30 minutes. A single 3D DTSI data set with b-value: 1734 s/mm^2 was acquired in one subject using TR: 1.75 s, spatial matrix: 32x32x8 with elliptical sampling, voxel size: 0.6 cc and nominal scan time of 4:07 min. Spectral quantification of Choline (Cho), Creatine (Cr) and NAA was performed using LCModel fitting[10] with an analytically modeled basis set. Non-water-suppressed data were quantified using spectral integration of the water resonance. Relaxation correction was applied to account for differences in scan time between individual data sets as a result of heart rate related variability in TR. The diffusion tensor, the apparent diffusion coefficient (ADC), the Trace/3 ADC (mean diffusivity), the fractional anisotropy (FA) and relative anisotropy (RA) were computed using MedINRIA software. Thresholds were used to remove outliers at the edges of the PRESS box.

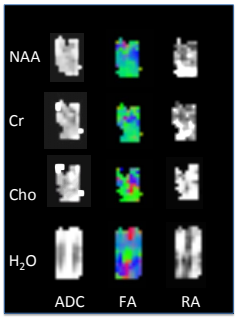

Figure 2: Trace/3 ADC, FA and RA maps of Cho, Cr, NAA and water in subject 1.

RESULTS: Phase encoding ghosting and eddy current artifacts were negligible in the phantom. Mean Trace/3 ADC values of NAA ($0.73+/-0.7*10^{-3}$ mm^2/s) and water ($1.84+/-0.07*10^{-3}$ mm^2/s) in the phantom at 20^0 C were consistent with our previous study[3]. The FA values measured in the phantom (NAA: 0.11+/- 0.05, water: 0.04+/-0.02) represent the experimental threshold for detecting diffusion anisotropy. In vivo, phase encoding ghosting in non-navigator corrected DTSI data (Fig. 1b) was most prominent for diffusion sensitization along the z-axis, consistent with a recent DTI study using interleaved EPI. Navigator correction was effective in reducing the ghosting (Fig. 1c), resulting in spectral quality comparable to that in non-diffusion-weighted data (Fig. 1d). TR variability with ECG gating was associated with scan time variability up to 17 % between scans, resulting in up to 7 % differences in metabolite signal saturation, before correction. Water Trace/3 ADC, FA and RA maps show distinction between gray and white matter. Metabolite Trace/3 ADC, FA and RA maps were less spatially distinct in gray and white matter, in part due to limitations in SNR and phase correction using the small residual water signal (Fig. 2). Slice averaged Trace/3 ADC and FA values of Cho, Cr, NAA and tissue water measured in subjects 1 and 2, and of tissue water measured in subject 3 were in the ranges reported in previous studies using single voxel methods[4-6] and using diffusion tensor MRI (Table 1). Diffusion sensitive 3D-PEPSI data demonstrated excellent spatial localization and spectral quality consistent with that in Fig.1d.

DISCUSSION AND CONCLUSION: This study demonstrates feasibility of 2D-DTSI in human brain with slice-averaged Trace/3 ADC and FA values that are consistent with previous studies. Further work is required to improve the spatial uniformity of DTSI. We are investigating reduced water suppression to improve phase correction based on the residual water peak. We are also investigating single-shot 2D spatial - 1D spectral encoding using interleaved phase encoding and parallel imaging[11] to further reduce motion sensitivity. Spectral sparsity at the long echo times used in DTSI motivates the use of compressed sensing combined with parallel imaging, which as we have recently demonstrated accelerates PEPSI and increases the spatial resolution and the narrow spectral width in single-shot DTSI[12]. DTSI is a new technique to map metabolite diffusion that in conjunction with DTI may provide an improved understanding of regional differences in tissue microstructure properties.

		Subject 1		Subject 2		Subject 3	
		mean	SD	mean	SD	mean	SD
NAA	Trace/3 ADC *10-3 mm2/s	0.17	0.04	0.17	0.05	0.24	0.06
	FA	0.67	0.13	0.61	0.15	0.57	0.15
	RA	0.32	0.07	0.37	0.12	0.27	0.08
Cr	Trace/3 ADC *10-3 mm2/s	0.20	0.05	0.19	0.05	0.28	0.15
	FA	0.57	0.15	0.70	0.10	0.60	0.15
	RA	0.28	0.07	0.48	0.16	0.31	0.11
Cho	Trace/3 ADC *10-3 mm2/s	0.19	0.04	0.17	0.05	0.23	0.06
	FA	0.56	0.18	0.64	0.16	0.62	0.13
	RA	0.26	0.09	0.40	0.14	0.31	0.08
Water	Trace/3 ADC *10-3 mm2/s	0.75	0.09	0.79	0.14	0.60	0.11
	FA	0.19	0.07	0.42	0.15	0.28	0.18
	RA	0.17	0.06	0.38	0.14	0.22	0.09

Table 1: Mean and standard deviation (SD) of Trace/3 ADC, FA and RA across the PEPSI slice in the 3 subjects.

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