Towards Quantitative Diffusion-Weighted Chemical Shift Imaging of Brain Metabolites

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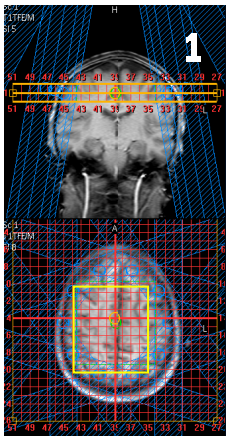
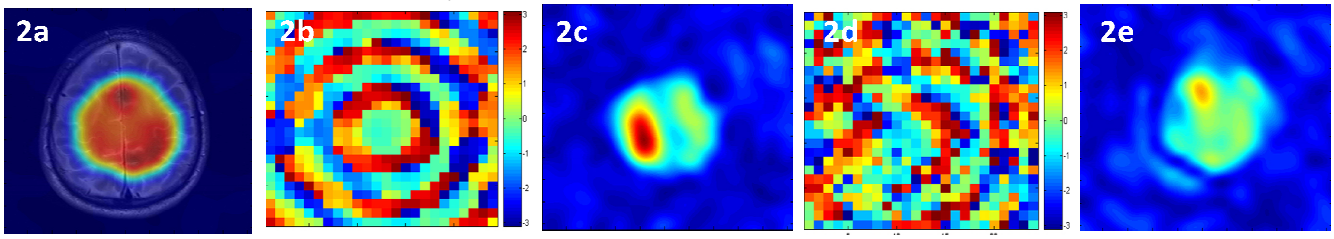
Introduction: Neuronal metabolites such as N-acetyl aspartate (NAA) are endogenous markers for the intracellular medium. As a result, their diffusion properties differ widely from those of water (1), and can help elucidate microstructural geometric properties of the intracellular space that otherwise become diluted when the same type of measurements are performed on water, which is not specific to any cellular compartment in particular. Previous works has shown the possibility and the utility of obtaining diffusion-weighted spectroscopic data from a single volume (e.g. 2,3). In this work the concept of diffusion-weighted spectroscopy is extended to explore the possibility of obtaining diffusion weighted chemical shift imaging (DW-CSI) metabolite maps. The acquisition of this type of data is challenging, since both the phase and the amplitude of the phase-encoded spectra are extremely sensitive to the presence of diffusion gradients, and significant loss of signal and phase errors are introduced by bulk motion and in particular by cardiac pulsation. Here, a strategy for acquisition and processing of DW-CSI data is proposed, based on the following scheme: (a) on the acquisition side, a combination of cardiac gating and a set of parameters that optimizes SNR under the constraint of obtaining stable signal are used; (b) on the processing side, the phase instability problem is approached by applying to each voxel in k-space the phase measured for the same voxel in the absence of diffusion gradient. Here it is assumed that the overall spatial distribution of the signal used for this phase correction procedure (be it the residual water signal or, e.g. the NAA signal) does not change dramatically in the addition of diffusion weighting. A proof of concept for this approach is first demonstrated simply on the water peak in a non-water suppressed DW-CSI experiment, and then is used to generate an initial attempt at diffusion maps of NAA in an axial slice of the brain of a human subject.

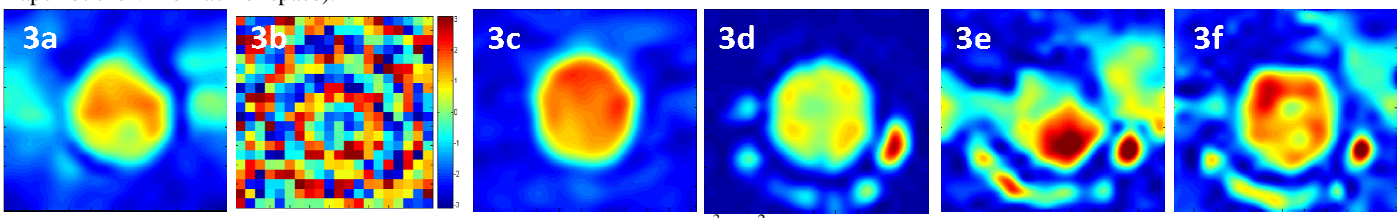


Materials and Methods: Scans were performed on a 3T Philips Intera. RF coil used for this work was a 6-channel synergy coil. A single-slice T2W-TSE (RARE) was acquired in axial plane and used to plan the DW-CSI experiment, as shown in fig. 1. In-plane FOV for the CSI experiments was kept identical to the RARE image (230x230 mm2), with a slice thickness of 2cm. Typical parameters: CSI matrix: 24x24, 10 conically arranged saturation slabs, TR/TE = 2000/120 msec with half-echo acquisition; n(points)=2048, SW=2000Hz. Diffusion weighting was applied in 3 directions: d1=[1 1 0], d2=[1 0 1], d3=[0 1 1]. Flip angle used was of 60˚, which yields M_{xy}=0.87·M(eq.), M_z=0.5·M(eq.) and assuming T_1(metabolite)=1sec, a TR=2s allows for recovery of about 95% of the equilibrium magnetization. Diffusion parameters: Δ=65 msec, δ=30 msec and g=1.6 g/cm (b=1806 s/mm^2). Cardiac gating based on pulse-oxymeter peak, and a delay of 300ms to start of acquisition. Processing was done using a home-written Matlab program. Phase correction of the (i,j) voxel in the DW-CSI k-space data set was performed according to the following scheme: $S_{i,j}$,(DW, corrected)=$S_{i,j}$(DW)·[$\varphi_{i,j}$(non-DW)/ $\varphi_{i,j}$(DW)] where the phase $\varphi_{i,j}$ was calculated from the real and imaginary spectral regions of the resonance of interest at the k-space point i,j: $\varphi_{i,j}=\tan^{-1}(\mathrm{im}(S_{ij})/\mathrm{re}(S_{i,j}))$

Results and discussion: Figure 2a shows the CSI map of water without diffusion weighting, and figure 2b shows the phase φ for this experiment. The degradation in phase and its effect on the diffusion weighted CSI water map can be seen in figures 2c and 2d (diffusion weighting given in [1,0,1]). Phase correction using the scheme mentioned earlier corrects for some of the spatial distortions, but does not compensate for the overall loss of signal. The "phase-corrected" CSI map is shown in figure 2e. Average ADC calculated for water from these results (using the other diffusion directions as well) was markedly overestimated, about 1.5×10^{-3}mm^2/s, for both the corrected and non-corrected images.



The effect of addition of cardiac gating can be appreciated in figure 3a, where the CSI water map is shown next to the phase map (figure 3b), which is less noisy than the map in 2d. Although artifacts are still visible (such as strong signal outside the brain), the geometric properties are significantly improved. Ulterior phase correction using the proposed scheme yields an artifact-free DW image (3c). The same procedure is applied to the NAA peak, where the CSI map is at 3d, the non phase-corrected DW-CSI is shown in 3d and in 3e is the NAA DW-CSI map after phase correction (ADC maps not shown for lack of space).



Average ADC for water using the three directions was about 0.9×10^{-3}mm^2/s, a more realistic assessment than in the case without the phase correction. For NAA the ADC values calculated from the images are still overestimated (about 0.2×10^{-3}mm^2/s), and we attribute this partly to the rather crude integration method we used to calculate the peak areas. In ***conclusion***, we show preliminary data for a method that paves the way for an accurate estimate of intracellular diffusion, which together with standard DTI may shed more light on tissue microstructure in health and disease.

Selected References: (1) Assaf, Y, Cohen, Y., J. Magn. Reson. 131(1) 69-85 (1998); (2) Ellegood, J. et al., Magn. Reson. Med. 53(5): 1025-32 (2005); Upadhyay, J., et al, Magn. Reson. Med. 58(3) 1045-1053 (2007).