1D Diffusion Weighted Magnetic Resonance Spectroscopy along the arcuate fasiculus in the human brain at 7T

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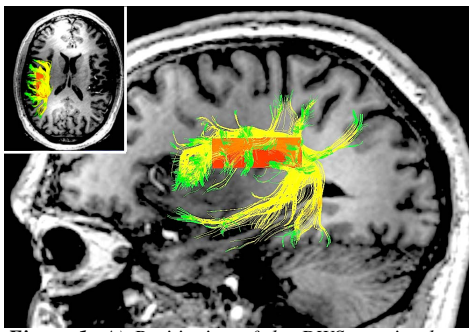
Introduction: Diffusion-weighted spectroscopy (DWS) of brain metabolites offers unique access to compartment-specific microstructural information on neuronal tissue *in vivo* [1]. In this study we combine 1-dimensional chemical shift imaging (CSI) with DWS at 7 T with 'on-the-fly' fiber tracking [2] to place the DWS voxel array along the arcuate fasciculus (AF) - a fiber bundle that is believed to be implicated in many psychiatric diseases. This combined approach allows us to obtain DWS information from a large part of this tract, while increasing the specificity of the DWS measurement to the AF. In this feasibility study we want to determine if this combined approach can be used to measure differences between parallel and perpendicular diffusion of various metabolites in the AF.



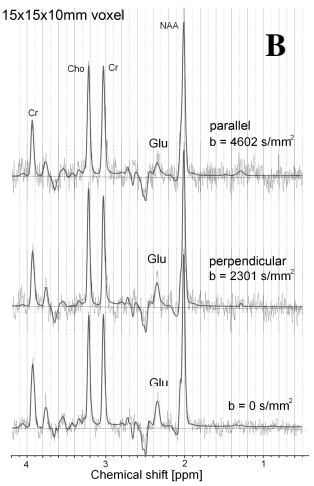


Figure 1: *A) Positioning of the DWS matrix along the fiber track of the left arcuate fasciculus. The PRESS box, (red, 40x15x15mm) contains 4 voxels of 10x15x15mm. B) MR spectra with LCModel fit of the middle voxel of the 1D array with different diffusion weighting, no diffusion (bottom), perpendicular gradients (middle), parallel gradients (top).*

Methods: Five healthy volunteers participated in the study after giving written informed consent. Participants were examined on a 7T MR system (Philips, Cleveland, USA) using quadrature transmit coil (Nova Medical, Wilmington, MA) driven by 2 amplifiers (4 kW each), and a 32 channel receive array. Two single shot echo planar DTI scans were acquired (60 slices; no gap; 104 x 104 acquisition matrix; FOV 231 x 231 mm^2; slice thickness 2 mm; flip angle 90°; TR 9547 ms; TE 68 ms; 30 different diffusion-weighted gradient directions; b 1000 s/mm^2; five diffusion unweighted scans ; SENSE factor 3; scan time per DTI set 273 s. The second DTI scan was identical to the first but was acquired with a reversed k-space readout allowing the application of a susceptibility correction step during post processing[3]. The first DTI set was used to perform on-the-fly reconstruction of the left AF using the FiberTrack software package, part of the Philips acquisition software. These reconstructed tracts were then used to plan the 1D-DWS experiment. For DWS B1-phase shimming was used with maximum B1 amplitude of 20 uT. Up to 2nd order shim gradients were used for B0 shimming of the voxel. The sequence used for the DWS experiment was a point resolved spectroscopy (PRESS) sequence (TE = 125 ms) supplemented with a bipolar diffusion-weighting scheme[4]. Cardiac synchronization on every third cardiac cycle was achieved via a pulse peripheral unit resulting in a TR of about 3 s and was used to avoid strong fluctuations in signal intensity due to cardiac pulsation[5]. The number of complex time-domain points was 1024 with a spectral width of 3000 Hz. Three different diffusion-weighting conditions were used, two semi-parallel to the AF and one perpendicular to the AF. Diffusion weighting parameters were: gradient pulse duration (sum of two bipolar lobes): 42 ms, bipolar gap: 17 ms, diffusion time: 47 ms, gradient amplitude: 25 mT/m, b values: 0–4602 s/mm^2 for g[1,1,0] and g[1,-1,0] and 0-2301 s/mm^2 for g[1,0,0]. Carrier frequency at 2.35 ppm (Glu), VOI 15x15x40 mm, matrix size 1x16 (voxel size 15x15x10mm, 4 voxels within the AF), NSA 64. Partial water suppression was used (2 selective RF pulses followed by dephasing gradients) for subsequent phasing and frequency drift correction for each individual acquisition. Total DWS acquisition time was 26 minutes.

Data analysis: DTI processing and fiber reconstruction was done using in house software[2]. The tracts that are part of the left AF were selected utilizing a multi-ROI approach and used for visual inspection of the overlap between the DWS voxels and the reconstructed left AF. DWS data processing was performed using custom written Matlab software as described previously[4]. Briefly, the main steps in the data processing included: weighted summation and phasing of the individual outputs of the 32 receive coils based on the reference water signal, eddy current correction, zero-order phase correction, frequency drift correction and subsequent averaging. The resulting spectra were analyzed using LCModel[6] with a simulated set of 21 basis spectra.

Results and Discussion: A reconstructed left AF (yellow) with the PRESS box position along it (red) is shown in Fig. 1. The parallel and perpendicular apparent diffusion coefficient (ADC) for Glu, Cr+PCr and NAA+NAAG were computed for each of the 4 voxels within the AF and for each of the 5 healthy volunteers (**Fig. 2**) The max CRLB of the fits of Glu was 20%, (mean 11%), for NAA+NAAG and Cr+PCr the max CRLB was 5%. For Glu the mean parallel ADC was significantly higher than the mean perpendicular ADC ($p < 0.0001$). No differences were found between mean parallel and mean perpendicular ADC for Cr+PCr ($p = 0.14$) and NAA+NAAG ($p = 0.36$). These preliminary results indicate that even with such a small group size (n=5) differences in diffusion profiles can be detected between the various metabolites. Future work includes incorporation of information on gray/white matter segmentation as well as directional information of the AF tracts to refine the ADC computation.

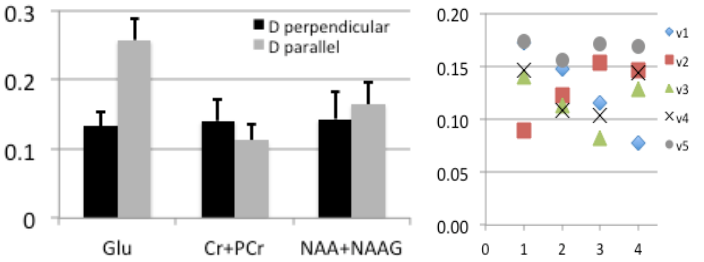


Figure 2: *Left: Metabolite ADC levels in the entire PRESS box (average of 4 voxels). Mean and standard deviation of perpendicular and parallel ADC computed over of 5 subjects. Right: D perpendicular of all volunteers in each voxel of the PRESS box.*

Conclusion: 1D-diffusion weighted spectroscopy of glutamate in a specific fiber bundle has been demonstrated at 7 Tesla. This method can be used to study the compartmentalization of glutamate and other metabolites in the brain both in health and disease.

***References*:** [1] Nicolay K et al. 2001, NBM Apr;14 (2):94; [2] Mandl RC et.al, 2012, Hum Brain Mapp Jul 33 (7):1503; [3] Andersson JL et al., 2003, Neuroimage 20:870.; [4] Kan HE et al., 2012 MRM 67(5):1203 [5]; Upadhyay J et al., 2007, MRM 58(5):1045; [6] Provencher SW et al., 1993, MRM 30 (6):672