Trace ADC of Metabolites in Human Brain using Diffusion Weighted MRS

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Introduction – The micro-structural organization of white matter in brain tissue leads to directional-dependence (i.e. anisotropy) of the apparent diffusion coefficient (ADC) of water and metabolites. However, the trace of the diffusion tensor provides an accurate method of determining a rotationally invariant measure of molecular diffusion in tissue. There are only two published studies which have examined the diffusion of N-acetyl aspartate (NAA), creatine (Cr), and choline (Cho) in the human brain, but only one diffusion direction was measured in the periventricular white matter in either case (1, 2). Quantification of the trace ADC values in different brain regions of these metabolites have been examined in rat brain (3), but have never been measured in human brain. The purpose of this study was to quantify the trace ADC values of the major singlet metabolites (NAA, Cre, and Cho) in two different regions of the human brain.

Methods – Three healthy volunteers (ages 23-30) were scanned on an SMIS 3T MRI equipped with a maximum gradient strength of 20mT/m. An in-house single-voxel, diffusion-weighted STEAM (STimulated Echo Acquisition Mode) sequence was used to measure the diffusion of the metabolites NAA, creatine, and choline. The diffusion sequence parameters were: δ=20ms, Δ=124.6ms, TM=30ms, TE=180ms, TR=3s, 4 sets of 128 averages per spectrum, 2.5x2.5x2.5cm^3 voxel. The diffusion gradients along X, Y, and Z were temperature calibrated on the water signal and validated using a 100mL spherical phantom (N=3) containing creatine (30mM) and choline (10mM) **(Table 1)**. Three different levels of diffusion sensitivity (i.e. b-values ~ 18, 632, and 1602 s/mm^2) were acquired with the diffusion gradients applied individually in three orthogonal directions (X, Y, and Z) to yield nine spectra per voxel in each individual. The ADC values were calculated from the slope of ln(peak intensity) versus b-value. The Trace ADC values were derived subsequently by taking the average of the ADCs obtained from the three orthogonal diffusion directions. Spectra from two different voxels were measured: (a) a predominantly white matter region in the corona radiata / centrum semiovale **(Figure 1)** and (b) a predominantly gray matter region in the occipital cortex. The in-vivo water line widths were ~3-6 Hz.

Results and Discussion – Phantom Study: The ADC values of creatine and choline in the X, Y, and Z directions are very similar in the water phantom because of the isotropic micro-environment **(Table 1)**. The measured ADC in the phantom agrees with the literature values of 0.8x10^{-3}mm^2/s and 0.9-1.3x10^{-3}mm^2/s for creatine and choline, respectively (4). In Vivo Study: Typical diffusion-weighted spectra of human brain are shown in **Figure 2**. Unlike the phantom, the diffusion coefficients of the metabolites in human brain varied significantly with the direction of the diffusion gradients which is indicative of the underlying tissue micro-structure **(Table 1)**. Diffusion in the X direction (i.e. left-right) was hindered to a greater extent, as evident by the lower ADC, which is consistent with the fact that the fibre tracts in this volume run primarily along Z (i.e. inferior-superior). The Trace ADC values were comparable for all three metabolites in the corona radiata / centrum semiovale of the human brain and were reduced by ~ 45-60% relative to the Trace ADC of the metabolites in pure water. Consistent values of the Trace ADC were also measured in the occipital gray matter, namely (0.35±0.05), (0.34±0.08), and (0.34±0.06) x 10^{-3}mm^2/s for NAA, creatine, and choline, respectively. The Trace ADC of the metabolites in human brain are greater than those in rodent brain (~0.13-0.15x10^{-3}mm^2/s) (3). In summary, diffusion-weighted MRS of metabolites in the human brain has demonstrated marked anisotropic effects and thus the importance of measuring a rotationally invariant measure such as the Trace ADC when characterizing metabolite diffusion in-vivo.

References: (1) Posse et al. *Radiology*, 1993; 188:719-725. (2) Harada et al. *NMR Biomed*, 2002; 15:69-74. (3) de Graaf et al. *MRM*, 2001; 45:741-748. (4) Nicolay et al. *NMR Biomed*, 1995; 8:365-374. **Acknowledgements:** CIHR, AHFMR, CFI, ASRA, UHF, Province of Alberta.

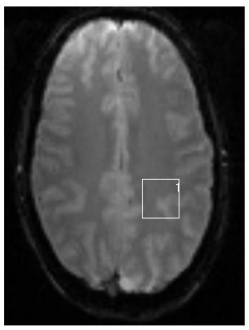

Figure 1 – Spectroscopy voxel-of-interest in a primarily white matter region (corona radiata / centrum semiovale).

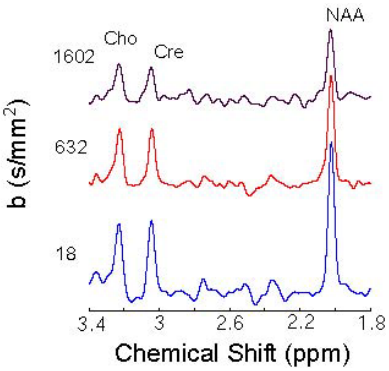

Figure 2 – Diffusion-weighted spectra obtained from occipital gray matter in a healthy volunteer with the diffusion gradients applied along Y (A/P) direction.

	ADC (10^{-3}mm^2/s)			Trace ADC (10^{-3}mm^2/s)
	X	Y	Z	
Phantom (N=3)				
Water	2.04 ± 0.03	2.00 ± 0.01	2.01 ± 0.01	**2.02 ± 0.01**
Cre	0.79 ± 0.02	0.76 ± 0.01	0.78 ± 0.01	**0.78 ± 0.01**
Cho	0.96 ± 0.02	0.91± 0.03	0.92 ± 0.01	**0.93 ± 0.02**
In Vivo (N=3) (corona radiata / centrum semiovale)				
NAA	0.21 ± 0.11	0.45 ± 0.06	0.53 ± 0.06	**0.39 ± 0.04**
Cre	0.23 ± 0.16	0.49 ± 0.10	0.53 ± 0.11	**0.42 ± 0.07**
Cho	0.23 ± 0.13	0.43 ± 0.08	0.45 ± 0.09	**0.37 ± 0.04**

Table 1 – ADC values in the orthogonal X, Y, and Z directions and Trace ADC obtained in a phantom and the periventricular white matter (see Fig. 1 for VOI) of the brain in three healthy volunteers.