Diffusion Modeling using Bayesian Probability Theory applied to imaging of Multiple Sclerosis

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INTRODUCTION: The diffusion tensor (DT) model introduced by Basser et al. [1] has proven extremely valuable for modeling the diffusion properties of water in the brain. The model incorporates a monoexponential function for the diffusion attenuation curve. Since the introduction of this model studies from several research groups have shown that this function does not fit the data well at high gradient values. As a result many researchers have applied a biexponential function to DT data. Our group has recently explored alternatives to these models using Bayesian probability theory for model selection [2,3]. The simplest modification to the standard DT model that fits the data to the noise is to add a constant offset (CO) to the DT expression. The biological interpretation of this offset remains unclear; though the non-monoexponential character of the signal attenuation curve is likely related to restriction of water diffusion in tissue. Previous studies of the DTCO model focused on baboon brains imaged after formalin fixation [2,3]. We applied the DTCO model to a group of normal subjects and in several patients with relapsing remitting multiple sclerosis (MS).

METHODS: Written informed consent was obtained from all participants according to a protocol approved by the local Institutional Review Board. Five healthy subjects (age range 47-76) and two patients (ages 32 ,36) with MSere scanned on 1.5T Siemens Sonata (Erlangen, Germany). In addition to anatomical imaging the subjects were scanned with a multi-directional DT imaging sequence and with 4 different b-values (max 1200 mm^2/s). The DTCO model that was individually estimated in each pixel is a slight modification of the standard DT model. In equation form the signal S is a function of a gradient vector $\boldsymbol{q} = \gamma \boldsymbol{G} \delta$ ($\boldsymbol{G}$ gradient direction, γ gyromagnetic ratio, δ gradient width) and is defined as: $S(\boldsymbol{q}) = S(0)\exp\left[-\Delta \boldsymbol{q} \cdot \boldsymbol{D} \cdot \boldsymbol{q}^T\right] + C$, in which Δ is the inter-gradient delay (assumed to be much larger than δ), and $\boldsymbol{D}$ is a symmetric 3x3 diffusion matrix. The constant offset C is thought to represent a component of the signal that arises from highly constrained water molecules, and has been found to improve the representation of the data [2,3]. The model parameters were estimated using Bayesian probability theory [4]. The joint posterior probability was sampled using a Metropolis-Hastings Markov chain Monte Carlo simulation with simulated annealing [4,5]. Regions of interest (ROI) were selected in different anatomic structures of the brain in all subjects. In the patients with MS additional ROI were selected in chronic white matter (WM) lesions identified on the T2-weighted images.

RESULTS: The total square residual of the DTCO model is significantly smaller than the traditional DT model and is comparable to the noise in the data. The left figure shows (a) relative anisotropy (RA) image and (b) CO image in a normal subject. The anisotropy image has an appearance similar to that of standard DT processing. The CO image demonstrates contrast between brain structures. The table presents values of the RA and CO in different regions of the normal brain and in MS lesions. A pattern discernable from the table is that normal regions with high RA (e.g. corpus callosum) have a lower CO and vise-versa. The right figure shows (a) T2-weighted image and (b) CO image in MS subject. Arrows point to MS lesions that are decreased in both RA and CO values.

CONCLUSION: The diffusion signal attenuation curve from brain is well described by a monoexponential function plus a constant offset. The inclusion of the additional parameters required by the biexponential model is not justified by the data. Further, the CO term provides anatomical contrast across the normal brain different from that of other diffusion parameters and has abnormal values in chronic MS lesions. Future studies will investigate the possible clinical utility of the CO parameter.

REFERENCES: [1] Basser PJ et al. J Magn Reson B 103:247-254 (1994). [2] Bretthorst GL et al., 24th workshop on Bayesian inference, Garching, Germany, 2004. [3] Kroenke CD, et al., Neuroimage 25:1205-13 (2005). [4] Jaynes ET, Probability Theory, Cambridge Univ. Press, 2003. [5] Metropolis N et al. J Chem Phys 21:1087-1091 (1953).

Brain Region	CorpusCallosum	Internal Capsule	White Matter	Thalamus	Putamen	MS Lesion
Rel Aniostropy	0.78(0.08)	0.60(0.05)	0.33(0.06)	0.25(0.04)	0.14(0.04)	0.15(0.03)
Fractional CO	0.27(0.03)	0.29(0.04)	0.33(0.06)	0.36(0.07)	0.38(0.07)	0.17(0.05)