Characterization of Water Diffusion in Gray and White Matter using the Inverse Laplace Transform

I. Ronen[1], S. Moeller[1], K. Ugurbil[1], D-S. Kim[2]

[1]Dept. of Radiology, CMRR/University of Minnesota, Minneapolis, MN, United States, [2]Dept. of Anatomy and Neurobiology, Boston University, Boston, MA, United States

Introduction: water diffusion in living tissue is a complex process that deviates from simple gaussian diffusion process because of the complex microscopic structure of tissue. In particular, the parcellation into different tissue compartments, which are permeable to exchange, and the existence of physical barriers (cell membranes, intracellular organelles etc.) that restrict the motion of water molecules give rise to a non-monoexponential attenuation of the diffusion-weighted signal with respect to b-value. In addition, the anisotropic nature of tissue structures, e.g. axonal fibers in brain, introduces a direction-dependence to the diffusion measurement. One of the most common models used to describe the diffusion-signal as a function of b-value is the biexponential model, which assumes a sum of two *distinct diffusion coefficients*, ADC_{fast} and ADC_{slow} along with their associated volume fractions, f_{fast} and f_{slow}. The biexponential model is a source to much debate. Some of the points of contention regarding the biexponential model are: (a) does the exponential model reflect a realistic distribution of diffusion times in tissue? (b) what is the relation, if at all, between *diffusion components* and *tissue compartments?* (c) what dictates the fractions and the ADCs of the two components in the model? (d) what role does geometry play in dictating the nature of the diffusion curve? We tried to address some of these questions by measuring high SNR diffusion data in cat brain at high field and by analyzing the resulting *diffusograms*[1], i.e. the inverse Laplace transform of the diffusion data. We performed carefully optimized ROI-based diffusometric analyses and compared the results with those obtained by standard biexponential fitting. The resulting diffusograms show a distinct bimodal distribution for both gray matter and white matter. The maxima of these peaks however, and in particular that of the slow diffusion peak deviate considerably from the ADCs, and ADC_{slow} in particular, as measured using the biexponential model. The centers of the diffusogram peaks, on the other hand, did not seem to depend on the type of tissue or on the direction of the diffusion gradients.

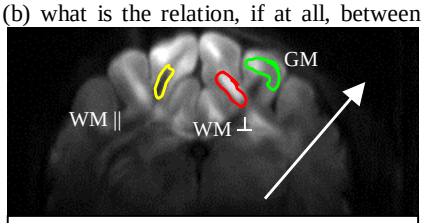

Fig. 1: Diffusion-weighted coronal image of the cat brain. The arrow shows the direction in which the diffusion gradients were applied. Typical ROIs are shown for WM-parallel, WM-perpendicular and GM.

Materials and Methods: Animals: Four cats (800g-1.1kg) were orally intubated and ventilated with 1% isoflurane and 3:7 O_2:N_2O throughout the experiment. Body temperature was controlled via a rectal probe and kept stable around 38.5° by means of a feedback water loop. Experiments were performed on a 9.4T/31cm spectrometer (Varian, CA). Pulse sequence: double spin-echo fully adiabatic echo-planar-imaging sequence (SE-EPI). Bipolar diffusion gradients were positioned before and after the first π pulse. MRI parameters: data matrix 256x256, 4 segments, FOV 5x5x0.2cm^3 (nominal resolution 195×195μm^2 in-plane, denoised with a hanning filter), TE/TR = 34ms/5s, diffusion: δ=8.5ms, Δ=11.5ms. b-values: 40 gradient strength values were used between g = 0.75g/cm and g = 30g/cm, spanning a b-value range between 5 and ~9300 s/mm^2 for a combination of two gradients (X,Y,0). Data Processing: all processing was performed using MATLAB®. A well conditioned finite-dimensional approximation of the Laplace transform is by Gauss-Laguerre quadrature[2]. The Inverse Laplace transformation is an ill-conditioned operator, and the SVD decomposition of the finite-dimensional approximation must be truncated. Using the L-curve criteria as discrepancy principle an 8 dimensional subspace operator (determined by the worst-case scenario of the fast decaying curve of the GM diffusion data) has been determined to be the smallest norm operator that best approximate the inverse Laplace transformation.

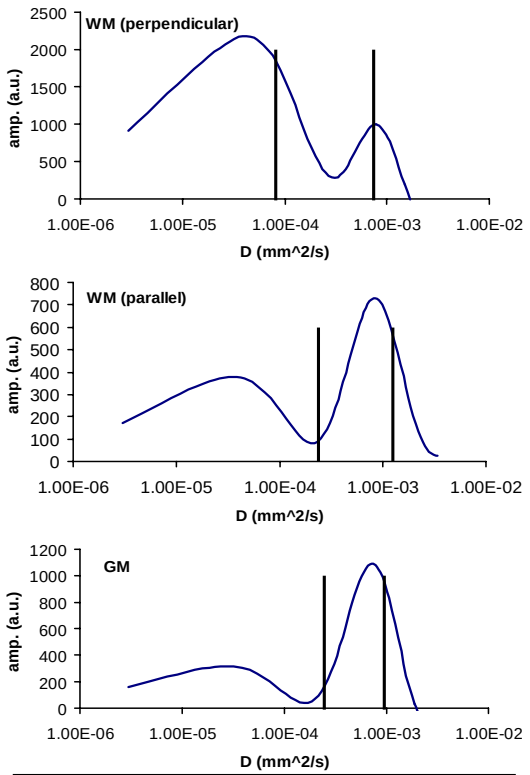

Fig. 2: diffusograms from 3 ROIs: WM where the gradients were applied perpendicular to the fiber direction (top), parallel to the fiber direction (middle) and gray matter (bottom). The bars represent the $ADC_{slow/fast}$ as calculated from the fitting to the biexponential model.

Results and Discussion: three regions of interest were selected for the analysis: white matter (WM) where the gradients are applied perpendicular to the fiber direction, WM with the diffusion gradients in parallel to the fiber direction and gray matter (GM). Initial results of the analysis are shown in fig 1. One striking feature is the relative stability of the centers of the bimodal distribution as observed on the diffusograms, as opposed to the dramatic shift in the ADCs, and in particular the ADC_{slow} as obtained from the biexponential model. This, combined with the sharp difference in peak amplitudes between WM-parallel and WM perpendicular may indicate that the origin of the bimodal distribution is geometric rather than a difference in diffusivity. In WM-perpendicular there is a better agreement between the diffusogram and the biexponential model, seemingly because of the more balanced volumetric ratio between the two distributions. In GM and in WM-parallel, where the "slow" diffusion peak is a small fraction of the total diffusivity distribution (note that the D scale is logarithmic, volumetric analysis not shown), the distribution of diffusion time as measured by the diffusograms can be almost approximated by a unimodal distribution, and the $ADC_{slow/fast}$ are roughly positioned on both sides of the larger peak, in accord with recent findings[3]. In **conclusion**, preliminary analysis of diffusograms of ROIs in cat brain help confirm the geometric source of the non-monoexponential behavior of diffusion curves in living tissue, and can contribute a powerful tool in characterizing diffusion in tissue.

References:

1. Pfeuffer et al., Magma 1999;8(2):98-108. 2. J. M. Varah, SIAM J. Sci. Stat. Comput. 4 (1983), 164-176. 3. Yablonskiy et al., Magn Reson Med 50(4) (2003), 664-9.

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