Transverse relaxation is important when modelling water self diffusion in brain tissue

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INTRODUCTION: Diffusion weighted imaging plays an important role in the detection of acute cerebral ischemia where ADC reductions of up to 40-50% have been observed. The underlying cellular mechanisms responsible for this ADC change are still uncertain, as many factors contribute to the average diffusion weighted signal obtained from various cellular compartments. Factors include compartmental diffusion coefficients and transverse relaxation times as well as restriction and exchange effects caused by cell membranes. Therefore, tissue water diffusion has been modeled analytically and numerically in a number of studies (1-3). The studies have produced realistic ADC reduction in the prediction of the cell swelling, but fail to produce realistic absolute values of ADC, cellular fractions and tortuosity. Most studies have assumed negligible influence of T2 relaxation effects. T2 relaxation may, however, profoundly affect the diffusion signal in cases of slow exchange (and long diffusion time - Δ) when compartmental T2 among compartments are large, the signal become excessively weighted towards the compartment with the longest T2. The assumption of slow or intermediate exchange rates is supported by the existence of two major T2 and diffusion compartments as well as direct studies of water exchange (4).

We hypothesize that absolute ADC values, volume fractions and exchange rates similar to that in experimental studies may be reproduced by incorporating T2 relaxation in a model of human normal gray matter. We will evaluate the predicted dependence of ADC upon T2 (and TE), exchange and volume fractions, We tested the hypothesis by examining possible solutions to the predicted ADC combining experimental data from normal volunteers with generally accepted cell geometries, volume fractions, diffusion coefficients and exchange rates in a fitting procedure.

METHODS: We developed a model very similar to that in (3) with prolate ellipsoids modeling the intra-cellular compartments. Ellipsoids denoted T and S represent glial cells and the neurons, respectively. The intra-cellular compartments are assumed to be parallel, having long axis dimensions denoted $a_T||$ and $a_S||$, and the short axis dimensions $a_T\perp$ and $a_S\perp$, with cellular volume fractions V_T and V_S. We assume identical diffusion coefficients D_i for the intra-cellular compartments, whereas D_E denotes the free diffusion coefficient of the extra-cellular fraction V_E. The three compartments are assumed to have individual T_2 relaxation rates, exchange rates and magnetizations $M_{T,S,E}$. The magnetization change due to diffusion, T2 relaxation and exchange among compartments were described by the shown equations with inspiration from (5). Taking the effect of TE into account in a PGSE experiment where TE>Δ, the equations are integrated in interval: t=[0, Δ] to get the signal from the respective compartments, during application of the diffusion gradients and omitting the first term in interval t=[Δ, TE] where there is no effect from the diffusion gradients, but still T_2 relaxation effects and exchange. Setting the term $(\gamma g\delta)^2 = b/\Delta$ we get the total signal: $S(b)= M_T(b) + M_S(b) + M_E(b)$. The equations are solved for diffusion gradients both parallel and orthogonal to the ellipsoids long axis and angle averaged to model isotropic gray matter. Intra-cellular ADC terms were identified very similar to (3) using a one-dimensional model (6) of restricted diffusion within infinite long parallel membranes as an approximation of the apparent diffusion within the prolate ellipsoids. The extracellular ADC was described as the free diffusion coefficient of the extra-cellular space divided by the tortousity (7) $ADC_E = D_E/\lambda^2$ where λ was calculated using ellipsoids (6). Experimental data was obtained in healthy volunteers using diffusion weighted PGSE EPI with b-factors 0 - 6000 s/mm2 and Δ/TE=56/119 ms. A Powell minimization procedure assuming slow exchange and Di/DE=1.1/3.1E-03mm^2/s was used to fit the model to data from a ROI in gray matter cortex.

$$dM_T/dt = -(\gamma g\delta)^2\, ADC_T\, M_T - k_T\, M_T + k_T\,(V_T / V_E)\, M_E - (1/T_{2T})\, M_T$$

$$dM_S/dt = -(\gamma g\delta)^2\, ADC_S\, M_S - k_S\, M_S + k_S\,(V_S / V_E)\, M_E - (1/T_{2S})\, M_S$$

$$dM_E/dt = -(\gamma g\delta)^2\, ADC_E\, M_E - k_E\, M_E + k_T\, M_T + k_S\, M_S - (1/T_{2E})\, M_E$$

RESULTS: Simulations show strong ADC dependence on the TE as shown - i.e. ADC increases 25% increasing TE from 60 to 90 ms as shown in fig.1. The fitting procedure showed a very good agreement between the model and the data for the solution shown in figure 2. The ADC for the curve is 0.99E-03 mm2/s (calculated at b= 1038 s/mm^2).

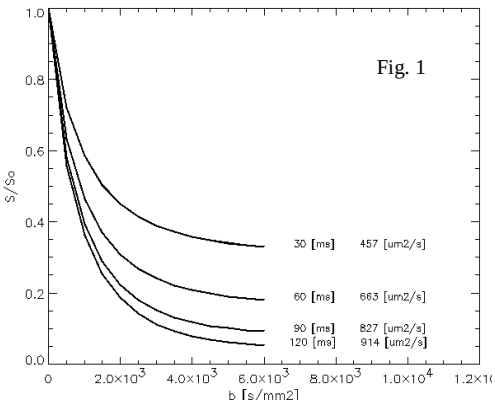

Fig. 1

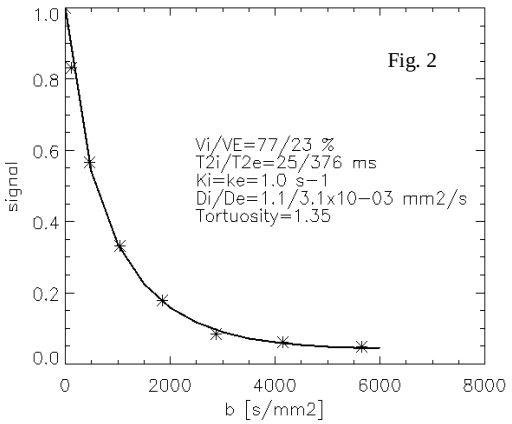

Fig. 2

DISCUSSION: By incorporating T2 relaxation we obtained an extracellular fraction and tortuosity in good agreement with experimental data (7) using TMA+ (V_E=0.18-0.23, λ=1.40-1.65). The estimated ADC is very similar to that found in (8) (ADC=0.92E-03 mm2/s) obtained at almost identical conditions (Δ/TE= 53/120 ms). Based on these results we think that this model, after further validation, seems interesting as a tool to clarify the underlying cellular mechanisms of ADC changes in i.e. ischemia.

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