A Finite Difference Model of Diffusion Applied to Ischemia

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Introduction

Diffusion-weighted MRI (DWMRI) is commonly used in the clinical diagnosis and evaluation of ischemic stroke. The apparent diffusion coefficient (ADC) of tissue water drops significantly following cerebral ischemia, enabling easy identification of ischemic tissue in diffusion-weighted images. Although this observation has been clinically useful over the last several years, the biophysical mechanisms underlying the reduction of tissue ADC are still unknown. To help elucidate these mechanisms, we have developed a finite difference (FD) model of diffusion that simulates water movement within a two-dimensional (2D) array of semi-permeable cells separated by extracellular space. The FD model enables the evaluation of the effect of several biophysical parameters on MRI signal decay including cell size, cell volume fraction, membrane permeability as well as the intrinsic T2-relaxation and diffusion coefficients in the intra- and extracellular spaces. In this report, the effect of cellular swelling is modeled and compared to experimental results obtained from clinical stroke and ischemia experiments performed in cell cultures [1].

Methods

The FD diffusion model calculates the motion of water by evaluating an explicit Euler approximation of diffusion in two dimensions to determine time-dependent probability distributions of water starting from discrete locations (grid points) inside and outside square cells. Cell size, intracellular volume fraction, and cell membrane permeability are input parameters into the model as well as intrinsic diffusion coefficients and T2-relaxation of water in the intra and extracellular spaces. At specified diffusion times (Δ), two dimensional probability distributions from all starting locations are spatially averaged to produce an effective diffusion propagator [2] which is projected in the direction perpendicular to the applied diffusion gradient and converted into MR signal decay curves through the Fourier transform. Signal decay curves can then be analyzed in terms of experimental observables such as the ADC. Signal decay of water in intracellular and extracellular spaces can be individually determined by simply zeroing the component of the probability distribution in the unwanted space prior to calculating the effective propagator. The simulation and fitting shown here were calculated with a membrane permeability, $P = 5.0 \times 10^{-4}$, intracellular diffusion coefficients, $D_{int} = 1.0$ μm²/ms and extracellular diffusion coefficient, $D_{ext} = 3.0$ μm²/ms. Identical T2 was assumed for the intra- and extracellular spaces. Non-ischemic 'normal' tissue was modeled as 18 μm square cells with an intracellular volume fraction, IVF = 0.8. Ischemic tissue was modeled as 19 μm cells and an IVF = 0.9.

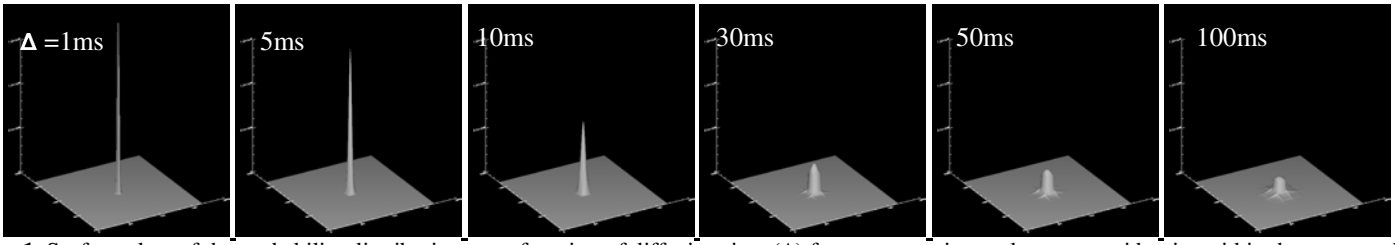

Fig. 1. Surface plots of the probability distributions as a function of diffusion time (Δ) for water starting at the center grid point within the center cell.

Results and Discussion

Probability distributions calculated from parameters similar to 'normal' tissue are shown in **Fig. 1**. The effect of restriction by the cell membrane is seen within 10 ms and the appearance of exchange is noticeable by 30 ms. At longer diffusion times (> 50 ms) a significant portion of water starting in the intracellular space has made its way out of the cell and into the extracellular space as well as into adjacent cells. From such distributions, the MRI signal decay can be calculated as shown in **Fig. 2**. The signal decay over the large b-value range shown (0 - 20,000 s/mm²) is clearly non-monoexponential in nature, consistent with other models. However, the signal decay over a low, clinically relevant range, b = 0 – 1000 s/mm², can be adequately fit by a single exponential decay. **Fig. 3** shows ADC values determined from single exponential fits to the simulated signal decay over this range. The FD model predicts a decrease in ADC of the total water signal as cells swell, consistent with numerous experimental observations. Also, the ADC of water in the intracellular space increases upon cell swelling which is consistent with experimental data obtained in bioreactor cell cultures where intracellular water can be monitored independently [1]. The magnitude of the calculated ADC is somewhat different from values experimentally measured, which may be explained by differences in membrane permeability and intrinsic diffusion coefficients.

The FD model allows the effect of physiologically relevant parameters of water motion to be visualized and evaluated and will be a useful tool to interpret DWMRI results.

Fig. 2

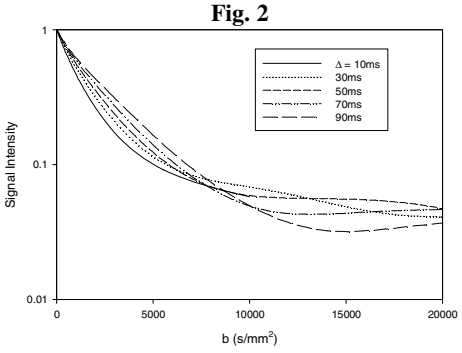

Fig. 3

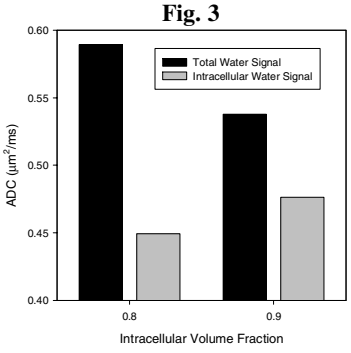

Fig. 2. MRI signal decay versus b-value for 'normal' cells at Δ = 10, 30, 50, 70, and 90ms.
Fig. 3. Calculated ADC values at Δ=50ms from mono-exponential fits to low b-values (0 < b < 1000 s/mm²) from the total water signal.

References

1. Trouard et al. Proc. ISMRM 2005, P.827
2. Hagslätt et al. JMR 2003, 161:138

Acknowledgments

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