Measurement of Cell Size in Biological Tissue Using Diffusion-Weighted MRI

Olaf DIETRICH[1], Sabine HEILAND[1], Klaus SARTOR[1]
[1]University of Heidelberg Medical School, Department of Neuroradiology, Heidelberg, Germany;

Introduction

In diffusion-weighted MRI (DWI), the random motion of molecules during a diffusion time ô causes a signal attenuation from which the apparent diffusion coefficient (ADC) can be calculated. For unrestricted diffusion, the displacement of molecules can be described by a Gauss function and the average diffusion distance of a particle is proportional to the square root of ô. If diffusion is restricted, e. g., by cell membranes in biological tissue, the mean displacement is smaller than in the case of free diffusion and the calculated ADC will decrease with increasing diffusion time in a characteristic way depending on the confining geometry.

This dependence can be used to determine (locally) the cell size in biological tissue by acquiring a series of diffusion-weighted images with different diffusion times and fitting the data to a model of restricted diffusion.

Methods

We used a model of diffusion in a one-dimensional system of equally spaced, permeable membranes [1] to study the exact dependence of the ADC on both the diffusion time ô and the three model parameters: the free diffusivity D_0, the distance L, and the permeability P of the membranes. Extensive computer simulations of such systems over a wide range of parameters were performed. The results of these simulations were used to develop an efficient method to derive the parameters D_0, L, and P from measurements of ADCs at an appropriate range of diffusion times. Key feature of this method is the fit of a simple function f to the data points in order to obtain intermediate quantities from which the model parameters can be calculated.

This method was evaluated in measurements of a transversal slice of a carrot. The measurements were performed on a 2.4 T scanner (Biospec 24/40, Bruker Medical Systems, Ettlingen, Germany) using diffusion-weighted stimulated echo sequences with EPI readout. 18 different diffusion times between 11.25 ms and 1024 ms were used; the diffusion gradient duration was 4 ms, diffusion weighting was applied in read-out direction with 9 different b values between 0 and 400 s/mm². Other imaging parameters were: TE/TR = 45 ms/3000 ms, resolution 128×64, FOV 5×5 cm², slice thickness 4 mm. Cell sizes were determined in three regions of interest (ROIs) and pixel-by-pixel, thus creating a parameter map for L. The calculated cell sizes were compared to results obtained by conventional microscopy.

Results

Figure 1 shows an example of the acquired diffusion-weighted images and the position of the three ROIs used for the determination of cell sizes. The dependence of the ADC on the diffusion time ô in each of these ROIs is shown in Figure 2. The most important parameter obtained from these curves in order to determine the cell size is its slope in the range of short diffusion times. This slope increases with decreasing cell size. To determine this slope and the other parameters used for the cell size determination, a function f was fitted to the data points; this function is shown in Figure 2 as well. The calculated cell sizes are: 67 ìm in ROI 1, 28 ìm in ROI 2, and 40 ìm in ROI 3. Similar values are displayed in the parameter map (Figure 3): the cell sizes are large in the center of the carrot, very small in a ring of about half the object's radius, and medium-sized near the border. The determined cell sizes agree well with the microscopical data, that is about 84 ìm in the center, about 55 ìm near the border, and about 30 ìm in between.

Discussion

The results show that cell sizes in biological tissue can be successfully determined by DWI methods. The current method provides only an estimation of the cell size, because the underlying mathematical model is one-dimensional and hence ignores the three-dimensional shape of the cells; therefore, systematically too small cell sizes should be expected. Further restrictions of the current model will become evident in the presence of considerable amounts of extracellular water or a strong variation of cell sizes in the region of one voxel. We hope to overcome some of these problems with improved mathematical models in the future.

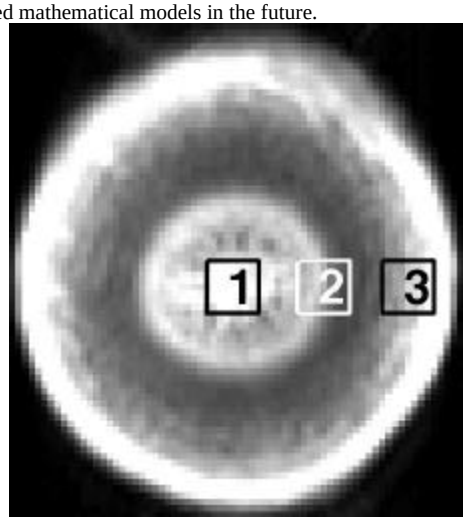

Figure 1: Position of ROIs in the transversal image of a carrot.

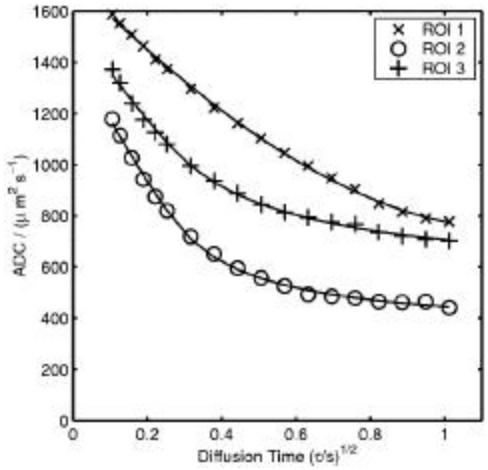

Figure 2: Dependence of the ADC on the diffusion time shown for the three different ROIs and model function f fitted to the datapoints.

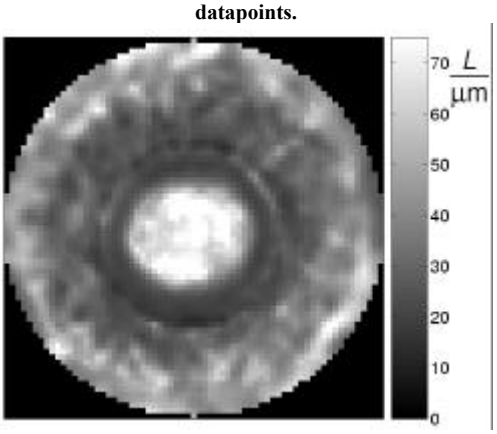

Figure 3: Parameter map showing the cell size L in the imaged slice of a carrot.

References

[1] Powles JG, Mallett MJD, Rickayzen G, Evans WAB (1992) *Proc. R. Soc. Lond.* A **436**:391-403