Diffusion diffraction patterns in different cells

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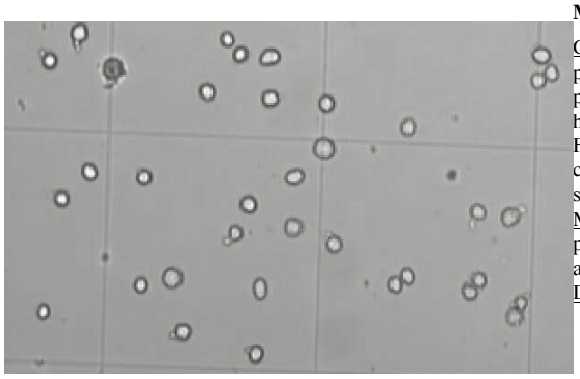
Introduction

Diffusion imaging enables microscopic assessment of tissue micro-structures by measuring the displacement of water protons. Different methods were proposed to couple the features of MR diffusion signal decay with the underlying structure of tissue on a microscopic scale. One of the most common approaches is based on the diffusion diffraction effect of bounded diffusion (Kuchel et al. 1997). When spin phase coherence is disrupted using increasing diffusion sensitisation, the decay presents pattern typical of the bounding structure. The MR decay of fluid diffusing in spherical or cylindrical compartments gives rise to a set of peaks and valleys with semi-periodic pattern. The pattern corresponds to the zeros of a Bessel function scaled by the size of the compartments. In cylinders, the intensity of this periodic structure is influenced by the orientation of the major axis of the cylinder with respect to the applied gradient (Avram et al. 2004, Bar-Shir et al. 2007). In this study we use different cell preparates evaluate the feasibility of diffusion-based cell size distribution measurements of biological tissue. The experiments were carried out to validate preliminary results (Imperati et al. 2007) and to asses reproducibility of the measures.. The results obtained by spectral analysis of the (pre-processed) data (Kuchel et al. 2004) were in good agreement with the parameters estimated using standard microscopy, and repeated measures on different preparates of the same cell type produce comparable results.



Methods

Cell cultures: 10×10^6 of the cell line were cultured in 10% fetal calf serum containing medium supplemented with penicillin, streptomycin, L-glutamine and 4.5 g/l glucose in T75 bottles coated with poly(2-hydroxyethylmetacrilate) (Sigma-Aldrich), preventing attachment to the surface for 5 days in a humidified atmosphere (5% CO_2). For the first experiment we used cell of the cell lines Monomacs and FDCP-Mix and cultured 1.8 million cells. In the second experiment we used the cell line HeLa and cultured about 150 million cells. The cells in a suspension with the total volume of 500 µl, were inserted into a susceptibility-matched MR tube and allowed for equilibration at 37°C.

MR experiments: A sets of high *b*-value diffusion-weighted spectra were acquired with the following parameters: (1) TR/TE = 5000/27 ms, pulse separation Δ =20 ms. Both sets were acquired 8 times for averaging, each with δ = 500 µs at G_{max} varying from 0 to 18 T/m in 36 steps linearly spaced.

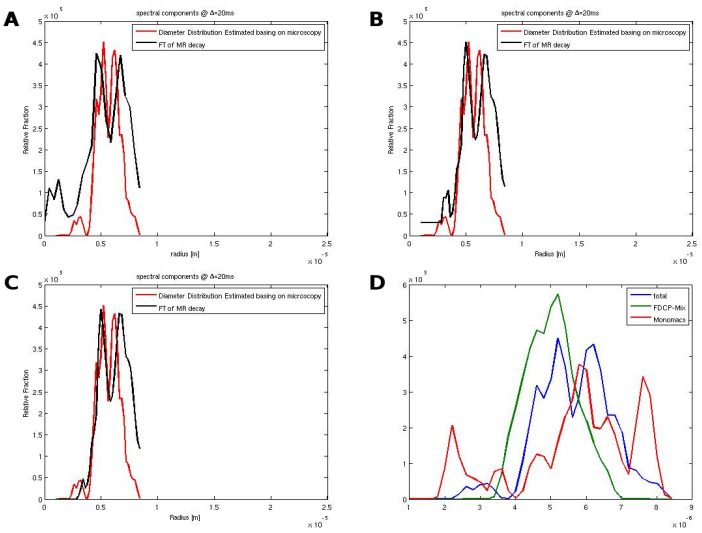
Data Analysis:

Analysis of data was performed according to (Kuchel et al. 2004): data were filtered by applying a Blackman- Harris filter to reduce noise, and were then scaled up by a factor 4 and interpolated (b-spline) to increase resolution. The second (numerical) derivative of the pre-processed data was Fourier-transformed to reveal the density of (semi)-periodic spectral components as in (Imperati et al. 2008). The resulting histogram was corrected for narrow pulse violation using an approximate scheme derived from (Mitra et al. 1995).

Result and discussion.

MR data: The histograms produced by the raw spectral analysis presented an apparent shrinkage of the cell diameter and bias in the relative component, which was more pronounced in the smaller cells. This effect is due to a violation of the narrow pulse approximation and was corrected using an approximation derived as in (Mitra et al. 1995). in the first experiment the estimated histogram does fit well with the reference and the two peaks in the size distribution are resolved (Fig. 1). The second experiment showed that the results are reproducible and have a good correlation with the reference data, r>0.86, p<1e-4 and with each other r>.97, p<1e-4

Discussion: By spectral analysis we identified the distribution of compartment sizes in MR diffusion data. Its features are well correlated with the underlying structure of the probed biological sample. The size measured with MR underestimates the size of the compartments assessed by conventional microscopy and requires a correction; The corrected histograms presents components of higher size which are probabli related to diffraction effects in the extracellular compartments (data not shown).



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