Simulation and experimental verification of the diffusion in the interstitial space

E. Fieremans[1], S. Delputte[1], Y. De Deene[2], Y. D'Asseler[1], E. Achten[3], and I. Lemahieu[1]

[1]Department of Electronics and Information Systems, Ghent university, Ghent, Belgium, [2]Department of radiotherapy, Ghent university hospital, Ghent, Belgium, [3]Department of neuroradiology, Ghent university hospital, Ghent, Belgium

Introduction

The diffusion in porous media can be considered as the analogue of diffusion in the extra cellular space *in vivo* [1] and can be studied *ex vivo* by fiber phantoms [2] (fig.1). Based on phantom studies and Monte Carlo simulations, the diffusion coefficient and diffusional kurtosis in the interstitial space were studied in the short and long time limit, whereby the effect of the fiber geometry and density was evaluated.

Materials and methods

A fiber phantom consists of parallel Dyneema® fibers tightly held together by a shrinking tube (fig. 1). To determine the fiber packing geometry, a fiber bundle phantom with an external diameter of 3 mm was manufactured and scanned with an X-ray micro-CT with an isotropic resolution of 3.4 µm.

Experiments:

1. To evaluate the effect of the packing density experimentally, 54 straight fiber bundles (Ø 1 cm) with varying fiber density were fabricated. Proton density (PD) and fractional anisotropy (FA) were measured on a Siemens Trio scanner equipped with an 8-element head coil at 20°C. PD was measured with a multiple spin echo sequence with 32 contrasts, ΔTE= 40 ms and a TR of 10s. DW EPI-imaging was performed in 60 directions with b-factors of 0 and 700 s/mm² and Δ = 36 ms.

2. Consequently, one fiber phantom with a measured proton density of 0.45 ± 0.5 was used to determine the time-dependent apparent diffusion coefficient (D_{app}) and kurtosis (K_{app}) with a diffusion weighted stimulated echo (PFG-STEAM) and a spin echo (SE) sequence on a Brüker Minispec mq20 benchtop NMR system (0.5T) equipped with a pulsed gradient unit. Varying diffusion weighted gradients (0 up to 2T/m) were applied perpendicular to the fiber directions for increasing diffusion times (Δ = 20 ms up to 100 ms for PFG-STEAM, Δ = 4 ms up to 50 ms for SE, δ = 0.7 ms). The temperature was kept constant at 40°C. $D_{app}(\Delta)$ and $K_{app}(\Delta)$ were obtained by fitting the $\ln\left(\frac{S(b)}{S(0)}\right)$-curve to the following formula [3]: $\ln\left(\frac{S(b)}{S(0)}\right) = -bD_{app} + \frac{1}{6}b^2 D_{app}^2 K_{app} + O(b^3)$

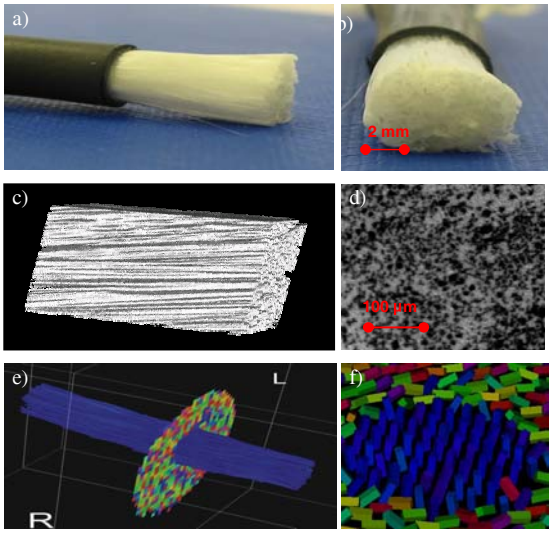

Figure 1:
Longitudinal (a) and transversal (b) view of a fiber phantom Micro-CTimage: 3D reconstruction (c) and cross section (d) fiber tracking result (e) and color coded DT boxoids (f)

Simulations: Random water molecule displacement was simulated in Matlab via 3D Monte Carlo (MC) simulations of 100.000 random walkers in a cubic raster (1mm³) filled with parallel aligned impermeable cylinders (Ø 20 µm). The trajectory of one spin particle was generated by moving the particle during each time step *t* over a distance of $\sqrt{6Dt}$ (with D the diffusion coefficient of water in a free medium) in a randomly chosen direction, whereby the particles were allowed to bounce elastically with the cylinders. D_{app} was computed along and perpendicular to the cylinder direction, as well as the excess kurtosis K_{app}, quantifying the deviation from a Gaussian diffusion profile. Simulations were performed at a temperature of 20°C (D = 1.98.10^{-3} mm²/s) for a hexagonal and random cylinder packing whereby increasing fiber densities (0.1 up to the closest packing) and diffusion times were considered. Subsequently, the simulation of diffusion in a random packing with a density of 0.54 was repeated for a higher number of particles (500.000) at a temperature of 40°C (D = 3.28. 10^{-3} mm²/s) to compare this result with the second experiment.

Results

In figure 2a, the experimental FA-data of the first experiment are compared with the simulated FA-values for random and hexagonal packing geometries. Simulated FA-values are plotted for Δ = 36 ms and for the long time diffusion limit. For the second experiment, a Levenberg-Marquardt algorithm was used to fit D_{app} and K_{app} with all correlation coefficients > 0.9998. Figure 2b shows the measured D_{app} and the simulated D_{app} for a random packing with a density of 0.54. K_{app} becomes constant in the MC-simulation (K_{app} = 0.63 ± 0.04), as well as in the experimental setup (K_{app} = 0.61 ± 0.02) for Δ > 20 ms.

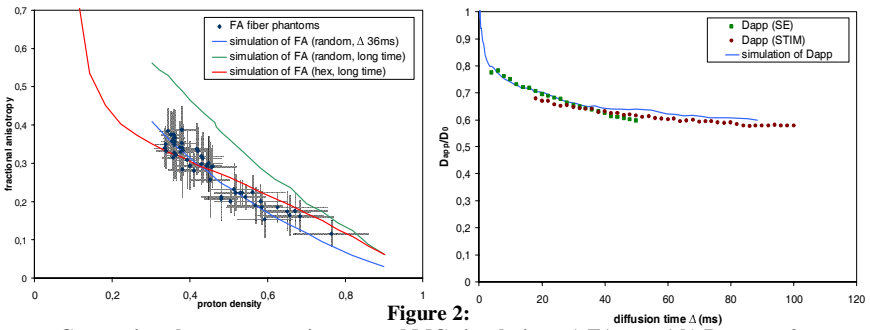

Figure 2:
Comparison between experiments and MC-simulations a) FA exp. 1 b) D_{app} exp. 2

Discussion and conclusion

The simulation results in fig. 2a show that for a random packing, in contrast with an ordered packing, the long time diffusion limit is not reached for Δ = 36 ms. In the long time limit, the tortuosity depends on the packing density, as well as the packing geometry. In the short time diffusion limit, the MC-simulations correspond well with the theory of diffusion in porous media [4,5,6] and are therefore a useful tool for diffusion modeling.

Figure 2a and 2b show a good agreement between the data of experiment 1 and 2 and the MC-simulations for random cylinder packing geometries with the corresponding packing densities (obtained by 1-PD). The random packing geometry was also observed on the micro-CT image (fig. 1d). The observed and simulated K_{app} have similar values.

To conclude, dyneema® fiber phantoms can be used for the quantitative validation of DWI and calibration of diffusion parameters on clinical MRI-scanners.

References

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