Quantification of the Spinal Cord Axon Diameter using an Extension of the PGSE Sequence

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Introduction

It has been previously shown that an idealized version of the two-wave-vector extension of the NMR pulsed-field-gradient spin echo diffusion experiment can be used to determine the apparent radius of geometries with restricted diffusion [1,2]. The feasibility of the sequence is demonstrated in a NMR imaging experiment to determine the apparent radius of axons in white matter tissue non-invasively. The proposed sequence can be used to determine cell radii non-invasively, but the effects of deviations from the idealized experiment must be taken into account for predicting the actual radius.

Theory

The sequence used consists of a double spin echo with two pairs of pulsed gradients $\mathbf{g}_1$ and $\mathbf{g}_2$ around the 180° pulses as shown in Fig.1. All gradient pulses have same duration δ and the same absolute values $|\mathbf{g}_1| = |\mathbf{g}_2|$. The temporal distance between the gradients within a gradient pair is Δ. The second gradient pair is rotated by an angle θ within a pre-defined plane relative to the first gradient pair. τ is the time between the start of the second gradient of the first pair and the first gradient of the second pair. The direction of the first gradient pair $\mathbf{g}_1$ stays the same throughout experiment. The second gradient $\mathbf{g}_2$ is rotated within a plane around the first gradient, i.e. the directions of the two gradient pulse pairs include an angle θ. There is an angular dependence in the signal behaviour in the case of restricted diffusion. The wave vectors $\mathbf{k}_1=\gamma\delta\mathbf{g}_1$ and $\mathbf{k}_2=\gamma\delta\mathbf{g}_2$ are assumed to have the same magnitude $k = |\mathbf{k}_1| = |\mathbf{k}_2|$ with $\mathbf{k}_1 = k\mathbf{e}_1$, $\mathbf{k}_2 = k\mathbf{e}_2$ and $\mathbf{e}_1 \cdot \mathbf{e}_2 = \cos\theta$. The time that particles need to diffuse across the pore is estimated as $\tau_D=a^2/6D$ where a is the pore size and D the diffusion coefficient of the medium. As shown in [3], for the case of $\Delta \gg \tau_D$ and $\tau=0$ (see Fig. 1) and small k, the magnetization can be expressed as

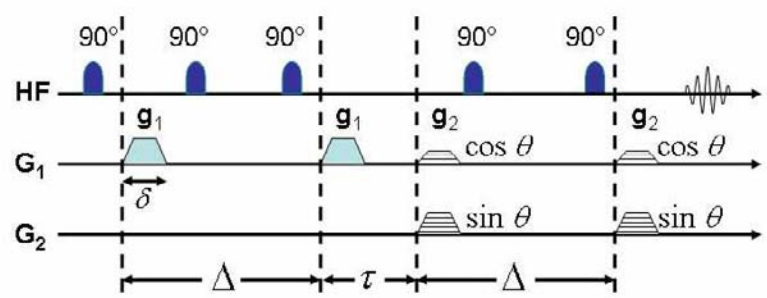

Figure 1: Two-wave vector pulse sequence

$$M(k,\theta) = 1 - k^2 \frac{\langle r^2 \rangle}{2}(2+\cos\theta) \quad . \tag{1}$$

Deviations from the idealized assumptions affect the apparent radius quantified. These effects were studied using numerical simulations. In the narrow pulse limit ($\delta \rightarrow 0$) the magnetization is given by the ensemble average over all spins as $M=\langle \exp\{i\mathbf{k}_1[\mathbf{r}(0)-\mathbf{r}(\Delta)]+i\mathbf{k}_2[\mathbf{r}(2\Delta)-\mathbf{r}(\Delta)]\}\rangle$. A two dimensional random walk simulation was implemented where the starting points of the spins $\mathbf{r}(0)$ were randomly distributed within a circle of radius R.

Experimental and numerical verification

For experimental verification the spinal cord white matter of a Dark Agouti (DA) rat was studied in vitro. Imaging experiments according to the sequence in Fig. 1 were performed on a 17.6T system. For several diffusion times Δ the gradient strength was 0.4 Tm^{-1} for $\mathbf{g}_1$ and $\mathbf{g}_2$ with δ = 3 ms. The angle θ between $\mathbf{g}_1$ und $\mathbf{g}_2$ was increased from 0 to 2π in 16 steps in the *xy*-plane, i.e. perpendicular to the white matter axons of the spinal cord sample. In Fig.2 the signal behaviour can be seen for Δ = 20 ms, 50 ms, 100 ms und 200ms. Fitting the experimental data to Eq.(1) we obtain the apparent radius.

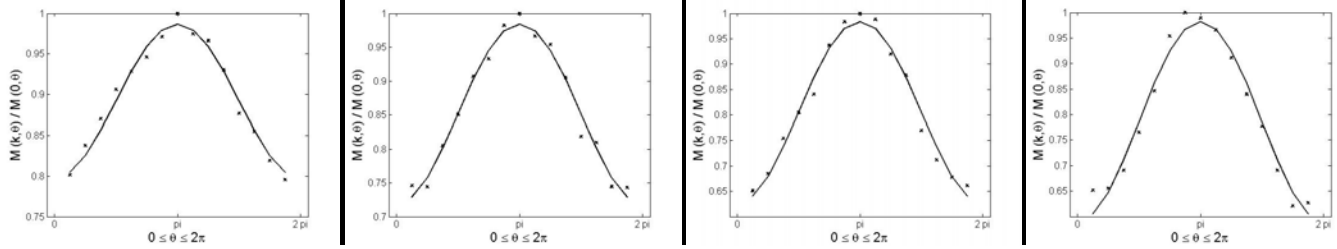

Figure 2: Experimental data for rat spinal cord using Δ= 20 ms, 50 ms, 100ms, and 200ms (from left to right). The NMR imaging data is shown as crosses and the fit to Eq.(1) as solid line.

In the experiment with the longest diffusion time Δ = 200 ms the apparent radius - assuming a circular shape of the axons - was R_{app} = 3.15 µm. In Fig. 3, the simulated signal is shown, including a fit to Eq.(1). The simulated signal can be fitted to the theoretical curve almost perfectly, with the apparent radius of gyration being $\langle r^2_{app} \rangle \approx (1.414\ \mu m)^2$. We obtain an apparent radius of R_{app} = 1.9996 µm. The deviation from the original radius R = 2 µm is therefore less than a factor 10^{-3}. This shows that the simulation describes the model with high accuracy and can be used for studying effects not included in the derivation of Eq. (1).

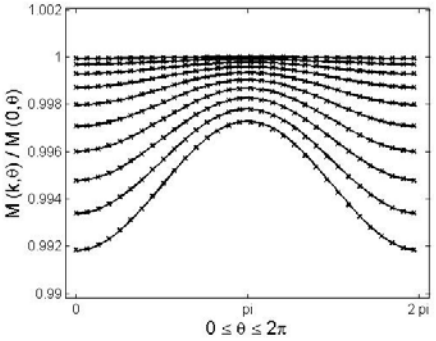

Figure 3: Monte carlo simulation is shown as crosses and the fit of Eq.(1)as a solid line.

Conclusions

The two-wave-vector extension of the PGSE experiment for determination of the apparent radius of restricted geometries has been analyzed with numerical simulations in terms of its applicability in practical experimental situations. The apparent cell radius of rat spinal cord white matter axons obtained in the NMR imaging experiments is close to the compartment size reported by Assaf et al. [4] who used the q-space imaging technique which has the advantage that it is easy to implement, since a standard PGSE is used for data acquisition.

Acknowledgements

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