Compartment-Specific q-space Analysis of Isolated Nerves

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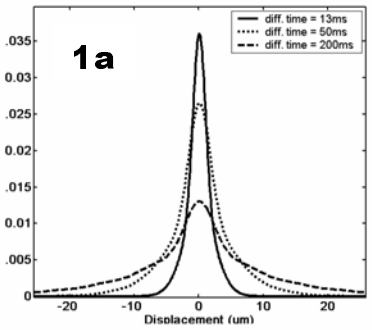
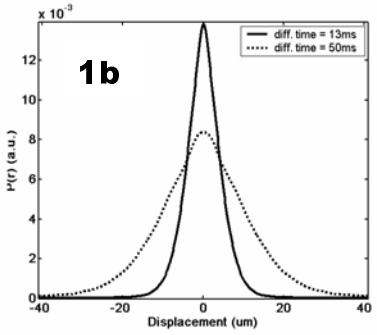
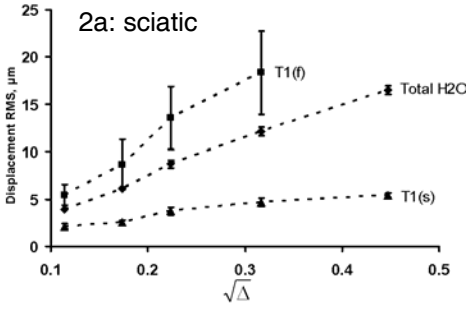
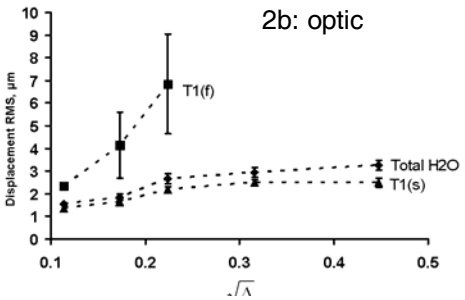
Introduction: Compartment-specific water diffusion properties are herein investigated in isolated bovine nerves. Sciatic and optic nerves were immersed in saline containing $GdDTPA^{2+}$. Following the immersion T_1 became non-monoexponential and fit well to a biexponential function. Using a diffusion-weighted sequence preceded by an inversion-recovery delay matched for selective nulling of each of the T_1 components, q-space data were collected for each component. In the sciatic nerve, the fast-decaying component (T_{1f}) possesses higher diffusivity and has relatively low fractional anisotropy (FA) and that the slow-decaying T_1 component (T_{1s}) is highly restricted and highly directional. In the optic nerve the FA of both components is comparable, and similar to that of the total H_2O signal, whether the ADC of the T_{1f} component remains higher than that of the T_{1s} component. The root mean square values of the displacement distribution functions (DDF) of the restricted component correlate well with the axonal diameters of both nerves. A possible conclusion is that the source of the T_{1s} component is the intra-axonal compartment and that T_{1f} is associated with the interaxonal space. The compartment-specificity of the method shown makes it ideal for the investigation of the contribution of each nerve compartment to DTI measurements and similar DWI-based methods, and thus can contribute to a better understanding of the connection between compartmental tissue structure and DTI parameters such as FA and radial/axial diffusivity.





Methods: Experiments were performed on an 8.9cm bore 500MHz Bruker Avance spectrometer in a 5mm probe. Bovine sciatic and optic nerves (n=3 for each type) were freshly collected, put in phosphate buffer solution (PBS) in 4°C and brought to the NMR scanner within 45 minutes. The nerve specimens were either kept in the original PBS or immersed for 8 hours in 6mM solution of GdDTPA. Following the addition of the contrast agent, the relaxation turned non-monoexponential, and a biexponential fit was used to generate the slow and fast T_1 components T_{1s} and T_{1f} and their volume fractions f_s and f_f respectively. Diffusion experiments: STEAM sequence with TE=12.5ms, δ=6ms, Δ=13, 30, 50, 100, and 200ms. 64 gradient strength values from 0 to 80g/cm (max. q-value = 2043 cm^{-1}). Gradients were applied in parallel ($\parallel$) and perpendicular ($\perp$) to the nerves. Following the addition of GdDTPA, diffusion experiments were performed with an added non-selective inversion pulse that preceded the diffusion module, followed by a variable inversion delay TI. Diffusion experiments were performed using 7 TI values. Of these values, three were set around $TI=T_{1s}\cdot\ln(2)$ for searching the optimal nulling of the T_{1s} component, three around $TI=T_{1f}\cdot\ln(2)$ for nulling of the T_{1f} component, and one at TI=2s, for control repeat of the total H_2O experiment. Data was processed using MATLAB®. The integral values for each data set were used to calculate the DDFs. Displacement RMS values were calculated from the full width at half maximum (FWHM) Fractional anisotropy was calculated using a reduced formula for FA based on the three dimensional definition.





Results: examples of the component-selective displacement distribution functions in the case of the sciatic nerve are given in figure 1. Panel (a) shows DDFs of the T_{1s} component at different Δ values and (b) are the DDFs of the T_{1f} component of the same nerve. In figure 2 the displacement RMS values are plotted as a function of $\sqrt{\Delta}$. The T_{1s} component of both nerves (sciatic nerve on the left (a), optic nerve on the right (b)) shows restricted behavior, and plateau at approximately the axonal diameter of each nerve, respectively. The T_{1f} component in both nerves shows unrestricted behavior, although in the case of the optic nerve the increase in displacement RMS seems more moderate, possibly implying a more hindered diffusion pattern. The ADC and FA for the T_{1s} and T_{1f} components in both nerves were calculated from the measurements with the gradients parallel and perpendicular to the nerve direction, and are shown in figure 3 in panels a and b, respectively. In the sciatic nerve, the directionality of the T_{1s} component is considerably higher than that of the T_{1s} component, and higher than that of the total H_2O present in the nerve. This further supports the hypothesis that the T_{1s} component is associated with the intra-axonal space. The FA of the two T_1 components in optic nerve do not differ much, and only the ADC of the T_{1f} is higher. This may be caused by a tighter axonal packing that increases the directionality of diffusion in the extra-axonal space. **In Conclusion**, it is shown that q-space analysis of DWI data using T_1-selective measurements leads to compartment-selectivity that may allow for an accurate characterization of the geometric properties of each compartment, and aid in the investigation of the water exchange between these compartments.