Compartment-specific $q$-space analysis of diffusion-weighted data from isolated rhesus optic and sciatic nerves

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Received 15 April 2008; revised 14 August 2008; accepted 29 August 2008

Abstract

We investigated compartment-specific water diffusion properties in two widely structurally different isolated bovine nerves. Sciatic and optic nerves were immersed in saline containing Gd-DTPA$^{2-}$. Consequently, $T_1$ became non-monoexponential and fit well to a biexponential function. $q$-Space diffusion data were collected for each component. In the sciatic nerve, the slow-decaying component ($T_{1s}$) was considerably more restricted and directional than the fast-decaying component ($T_{1f}$). In the optic nerve, fractional anisotropy of both components was comparable and similar to that of the total H$_2$O signal. The root mean square of the displacement distribution functions of $T_{1s}$ correlated well with the widely different axonal diameters of both nerves. Possibly, the source of $T_{1s}$ is the intra-axonal compartment and that of $T_{1f}$ is associated with the inter-axonal space. The compartment specificity of the method shown makes it useful for the investigation of the contribution of each nerve compartment to diffusion tensor imaging measurements and other diffusion-based methods.

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Keywords: Diffusion-weighted MR; Nerves; $q$-space; Tissue compartments

1. Introduction

The identification and characterization of tissue compartments using nuclear magnetic resonance (NMR) and magnetic resonance imaging (MRI) methods have been for some time one of the central themes in neuroimaging research. The difficulty in devising an MR method for accurate structural characterization of nerves in particular and neural tissue in general stems mostly from lack of a simple one-to-one correspondence between an MR physical measure and a specific tissue compartment: simple MR quantities such as relaxation rates and diffusion coefficients cannot be unequivocally assigned to specific well-defined neuroanatomical compartments. This situation is further exacerbated by the permeability of cell membranes, which introduces mixing between the different compartments. The other major reason is the inadequate spatial resolution of MRI: this severe limitation makes it impossible to spatially distinguish among the different compartments under standard conditions and thus limits the use of MR methods to yielding average structural measures that are susceptible to partial volume effects, heterogeneity of tissue microstructure and more.

Compartment-specific structural investigation of neural tissue becomes particularly relevant in conjunction with diffusion tensor imaging (DTI), in which the parameters associated with the diffusion tensor in each image voxel, such as the fractional anisotropy (FA) and the tensor trace, have been shown to be intimately related to structural parameters of tissue [1–3]. This relationship, although robust, is far from elucidated. A central question is how physical characteristics of the various tissue compartments, such as axonal diameter, axonal packing and permeability, are linked to DTI parameters in both the central and peripheral nervous systems.

Many of the studies aimed at structural elucidation of nerves focused on the non-monoexponential behavior of the transverse relaxation processes in isolated nerves. The results of these studies are extremely diverse, and initial interpretations have been often contradictory. Early $^1$H NMR studies of the frog sciatic nerve revealed that transverse relaxation is
non-monoexponential, and three exponential components were assigned to three water compartments in nerve [4]. These studies, as well as results of later studies [5], assigned the short-lived T2 component to the water contained by the myelin layer, the intermediate-lived component to the axonal water and the long-lived component to the inter-axonal water. However, a later study showed that the first component to be affected by perfusion with the contrast agent Gd-DTPA was the intermediate-lived component, postulating that the previous assignment of the two longer-lived components should be reversed [6]. These results are at least in part supported by the work by Peled et al. [7], which examined the correlation between T2 components in frog sciatic nerves and their diffusion properties and suggested that the intermediate-lived T2 component, which showed no restricted diffusion behavior, can be partly attributed to the inter-axonal space. The longest-lived component, however, did exhibit restriction in the diffusion measurement and thus appeared to have some contribution from the axonal water. Several other studies that correlated diffusion properties with transverse relaxation were performed [8–12], mostly indicating that the long T2 component is at least partly associated with the intra-axonal water. The study of compartment-specific longitudinal relaxation characteristics has been more limited in scope, mostly because the range of proton T1 in neural tissue is considerably more limited than that of T2. Nevertheless, an interesting work that used amphibian sciatic nerve as a model showed that nerve compartments do possess unique T1 and magnetization transfer characteristics [13].

A powerful tool for the investigation of the microscopic structure of biological tissue is q-space analysis of diffusion-weighted MR data. q-Space analysis [14,15] translates the attenuation of the MR signal as a function of \( q = \gamma \delta g / 2\pi \) to a displacement distribution function via the Fourier transformation:

\[
P(\Delta, \Delta \vec{R}) = \int_{0}^{\infty} S(\Delta, \vec{q}) \exp\left(-i\pi \vec{q} \cdot \vec{R}\right) d\vec{q}
\]

where \( \gamma \) is the gyromagnetic ratio for protons, \( \delta \) is the diffusion gradient pulse width, \( \Delta \) is the diffusion time and \( P \) is the probability for displacement \( \Delta \vec{R} \). In the case of unrestricted diffusion, the root mean square (RMS) of the distribution function increases linearly with \( \sqrt{\Delta} \), where \( \Delta \) is the diffusion time in a Stejskal–Tanner diffusion-weighted experiment. When the diffusion process is compartmentally restricted by physical barriers, the displacement RMS at long diffusion times comes to reflect the size of the restricting compartment. The sensitivity of the displacement RMS to compartment size was shown in numerous studies, in which mapping or localized measurements of the displacement RMS in neural tissue were shown to be extremely sensitive to ischemia-like processes [16], maturation of the spinal cord [17] and multiple sclerosis [18]. The lack of compartmental specificity of the water signal, possible transmembrane water exchange and structural heterogeneity of tissue microstructure contribute to the difficulty of obtaining a straightforward interpretation of the displacement distribution functions in q-space analysis. However, a more refined analysis of q-space diffusion data that includes a certain degree of modeling based on the geometric properties of the intra- and extraneous compartments yields accurate estimates of compartment size (e.g., axonal diameter in excised nerves and spinal cord [19–23] and membrane permeability coefficients in erythrocytes [24]).

This work aimed to explore the microstructural geometric properties of nerves using compartment-specific q-space analysis and differentiating between compartments via enhancing the intercompartmental T1 differences using a T1 contrast agent. The two nerves used here are bovine optic and sciatic nerves, which significantly differ in their structure and composition. Compartment specificity is obtained immersion of the specimens in solutions of the contrast agent Gd-DTPA. Previous work [6] and supportive evidence from the results that follow suggest that the contrast agent accumulates mostly in the interstitial space. Resulting from the immersion in the contrast agent, a well-defined bimodal T1 distribution allowed for the selective nulling of each T1 component, while diffusion-weighted data of the other were acquired at multiple b-values. q-Space analysis of the two relaxation components was then separately performed, and the displacement distribution functions of these components in the two nerves were analyzed and interpreted with respect to the possible microstructural differences between the two nerve types.

2. Materials and methods

2.1. Nerve specimen preparation

Rhesus (Macaca mulatta) optic and sciatic nerves (n=3 for each type) were obtained from the pathology laboratory of the New England Primate Research Center. All specimens were freshly collected, put in phosphate-buffered saline (PBS) in 4°C and brought to an NMR scanner within 45 min. Protease inhibitor cocktail (Sigma-Aldrich, St. Louis, MO, USA) was added to the PBS (10 μl of inhibitor per 1 ml of PBS) to further avoid tissue degradation. The nerve specimens were kept under refrigeration (4°C) when not being scanned. All experiments were performed within the same day of the necropsies.

The nerve specimens were either kept in the original PBS or immersed for 8 h in 6 mM solution of Gd-DTPA [0.5 M gadopentetate dimeglumine (Berlex, Montville, NJ, USA)] diluted with PBS to reach the desired concentrations. Before the experiment, the specimen was taken out of the solution, patted dry and put in a short 5-mm NMR tube filled with Fomblin® (Sigma-Aldrich).

2.2. NMR experiments

All NMR experiments were performed on a 500-MHz Bruker Avance spectrometer with an 8.9-cm bore (Bruker...
Spectrospin, Billerica, MA, USA) equipped with a three-axis gradient setup. The maximum gradient strength achievable was 100 g/cm in each axis. RF coil was a solenoid 5 mm in diameter and 1.5 cm in length with the symmetry axis perpendicular to the Z-axis.

2.2.1. T1 measurements

Inversion-recovery experiments were performed with 200 equidistant inversion time (TI) values. The range was determined by the expected T1 value (before and after the addition of the relaxation agent). Maximum and minimum TI values for pre-Gd-DTPA measurements were 10 s and 50 ms, respectively, and those for post-Gd-DTPA were 2 s and 10 ms, respectively. The large number of TI values was necessary for obtaining reliable results from the relaxometric analysis using inverse Laplace transformation (ILT). Pulses used were square pulses (90°=30 μs). The typical SNR for the noninverted spectrum was 20,000.

2.2.2. Diffusion experiments

The pulse sequence used was diffusion-weighted pulse gradient stimulated-echo sequence with TE=12.5 ms, δ=6 ms and Δ=13, 30, 50, 100 and 200 ms. There were 64 gradient strength values from 0 to 80 g/cm (maximum q-value=2043 cm⁻¹), with two averages at each gradient strength and TR=4 s. Gaussian RF pulses of duration=250 μs were used (transmit gain was adjusted to obtain the desired tilt angle). Gradients were applied in parallel with (||) and perpendicular (┴) to the nerves. Following the addition of Gd-DTPA, diffusion experiments were repeated, this time with a nonselective inversion pulse that preceded the diffusion module, followed by a variable inversion delay TI. Diffusion experiments were performed using seven TI values. Among these values, three were set around TI=T1f (2) for searching the optimal nulling of the T1f component, three were set around TI=T1r-ln(2) for nulling of the T1r component and one was set at TI=2 s for control repeat of the total H2O experiment. Acquisition time per TI value was 8.5 min. With seven TI values and two gradient directions, the total acquisition time per specimen was about 2 h. SNR varied according to TI. SNR_{max} (q=0 at nulling of the T1f component) was about 10,000. SNR_{min} (q=q_{max} at nulling of the T1s component) was about 10 for Δ=50 ms. Measurements in which the SNR was lower than 10 for a significant part of the diffusion experiment were discarded.

2.3. Data processing and analysis

Data were processed using MATLAB® (Mathworks, Natick, MA, USA).

2.3.1. Relaxometry

A well-conditioned finite-dimensional approximation of the Laplace transform was applied using the Gauss–Laguerre quadrature. A nine-dimensional subspace operator has been determined to be the smallest norm operator that best approximates the ILT for all the cases that were analyzed. To ensure positivity of the solution, we subse-

quently used an iterative restoration algorithm [25]. The combination of two algorithms was used to ensure (1) a solution that has a large degree of flexibility with good stability and (2) a solution that is consistent with the physical assumptions (nonnegativity).

2.3.2. Diffusion data q-space analysis

At first, each two-dimensional data set was phase/baseline corrected. The integral of the water signal was then taken for each diffusion gradient value, avoiding the contribution of the lipid peaks. The integral values for each data set were used to calculate the displacement distribution function according to: 

\[
P(\Delta, \Delta R) = \int_0^\infty S(\Delta, q) \exp(-i\pi q \cdot \Delta) \, dq,
\]

where \(S\) is the integrated H2O signal at a given q-value (\(q=\gamma \delta g/2\pi\)), \(\gamma\)=gyromagnetic ratio for protons, \(\delta\)=diffusion gradient pulse width) and a specific diffusion time \(\Delta\) and \(P\) is the probability for displacement \(\Delta R\). Displacement RMS values were calculated from the full width at half maximum (FWHM), according to the relation RMS=0.425-FWHM [15,26]. FA was calculated using a reduced formula for FA based on the three-dimensional definition: 

\[
FA = \sqrt{\left(\frac{D_{||}-D_{\perp}}{D_{||}+D_{\perp}}\right)^2 + D_{\perp}}.
\]

\(D_{||}\) and \(D_{\perp}\) are the diffusion coefficients measured with the gradients perpendicular to the nerve fibers and parallel with them, respectively. Diffusion coefficients for both gradient directions were calculated from the relation given in the paragraph above, for \(\Delta=50\) ms as a representative value.

In order to avoid truncation effects, particularly in the low-diffusion-time experiments, we used triexponential fitting for extrapolation of the data to higher q-values (up to twice the maximal acquired value). It should be emphasized that the bulk of the energy was contained in the acquired q-space regime. This analytic extrapolation had some effect at short diffusion times. At the longer diffusion times, when the signal almost completely disappeared at the high b-values, there was no apparent difference between the displacement distribution functions obtained with and those obtained without the extrapolation.

3. Results and discussion

Fig. 1 shows the results of the relaxometric analysis on the two nerve specimens — one optic nerve and one sciatic nerve. In the left panel are shown the results for the pre-Gd-DTPA samples. A narrow distribution consisting of one peak is seen for both nerves, in accordance with the monoexponential behavior of the temporal relaxation data for both nerves. The right panel shows the relaxometric analysis results for the post-Gd-DTPA samples. For both nerves, a bimodal distribution is obtained and similar results were obtained from the remaining specimens. The maxima of the peaks in the distribution corresponded well to two T1 values (“slow” and “fast”) obtained from biexponential fitting of the data. It is important to emphasize that although the ILT is biased in that it assumes the target function to be a continuous sum of exponential functions, it is not biased.
with respect to the distribution of the exponential coefficients. Since $T_1$ components are expected to be exponential, the ILT analysis is a reasonably unbiased tool for relaxation analysis. The peaks in the distribution shown in Fig. 1B are relatively broad, mostly as a result of the regularization applied to the ILT results. The regularization or the use of a limited subspace ensures stability to the ill-conditioned ILT, at the cost of broadening the distributions in the resulting relaxogram.

The ratio between the slow-relaxing fraction ($f_s$) and the fast-relaxing one ($f_f$) in the case of the optic nerve is 1.94:1. Assuming that the contribution to $f_s$ is mostly from the intra-axonal space and the myelin water and that $f_f$ consists mostly of extra-axonal water, it is possible to roughly evaluate this ratio from histological evaluation of the optic nerve in the rhesus monkey [27]. When assuming a myelin water fraction of about 15% [28], the ratio between axonal water (intra-axonal+myelin water) and extra-axonal water (extracellular matrix+glia) is approximately 3:1, which is higher than the measured $f_s/f_f$ ratio: No precise histological information was available for a similar evaluation for the sciatic nerve. The histological results are based on local population analysis in which the axonal density is rather constant (i.e., areas that do not include the dura mater, pia mater and arachnoid, all of which are suspected to contribute significantly to the fraction of tissue accessible to the contrast agent).

Table 1 summarizes the results of the $T_1$ measurements performed on the nerve samples before the addition of the contrast agent and following 8 h of infusion in the PBS/Gd-DTPA solution. After the addition of the contrast agent, a single exponential did not properly fit the $T_1$ data and a biexponential function fit was applied. Both $T_1s$ and $T_1f$ are considerably shorter than the $T_1$ value prior to the addition of the relaxation agent. There are two possible explanations for this: either (1) the contrast agent Gd-DTPA resides almost exclusively in the extra-axonal space and the apparent shortening of the $T_1$ occurs by fast exchange with the intra-axonal space or (2) the contrast agent reaches both spaces but the final concentration in the extra-axonal space is higher than that in the axonal cytoplasm. In this case, the transmembrane water exchange rate can be slow and the total shortening of $T_1$ will still occur. In all samples, the fraction of $T_1f$ in the sciatic nerve was considerably higher than that in the optic nerve.

Fig. 2 shows semilogarithmic plots of the normalized signal as a function of $q$ (panels A–C) and the resulting displacement distribution functions (panels D–F) for one specimen of the sciatic nerve. The vertical scale of the diffusion data plots and the horizontal scale of the displacement function plots were varied for optimal display. It can be seen in panel E that the
Fig. 2. \(q\)-Space diffusion data (panels A–C) and the resulting displacement distribution functions (panels D–F) for a sciatic nerve. Measurements shown here were performed with the diffusion gradient perpendicular to the nerve axis. Panels A and D were obtained from the total \(H_2O\) signal; panels B and E, from the \(T_{1s}\) component; and panels C and F, from the \(T_{1f}\) component. Symbols on the left panels reflect extrapolated points using triexponential fitting.
broad component was significantly reduced, albeit not completely so. Similarly, in panel F, in which the distribution functions are much broader, one can observe the residual contribution of a narrower distribution at a diffusion time of 50 ms. Fig. 3 shows the same plots for a specimen of the optic nerve. The differences between the displacement distribution function of the total H2O signal (panel D) and that of the T1s (panel E) are less conspicuous. However, when two of these functions are plotted together and scaled to intensity (panel G), it is readily visible that the displacement distribution function of the total H2O signal (dotted line) contains a broad component that is absent from the T1s function.

The displacement RMS for each measurement was derived from the FWHM as mentioned in Section 2. These values were calculated for all displacement distribution functions and averaged across samples. The displacement RMS values are shown as a function of $\sqrt{D}$ in Fig. 4 for the sciatic nerve and in Fig. 5 for the optic nerve. It is evident from Fig. 4 that in the case of the sciatic nerve, the displacement distribution function width for the total H2O signal increases with $\sqrt{D}$ for the entire range of diffusion times used, suggesting a dominating presence of a nonrestricted water compartment. However, the same plot for the optic nerve (Fig. 4) reveals a different situation, in which the increase in displacement RMS at high $\sqrt{D}$ is very shallow, possibly indicating a smaller fraction of the nonrestricted compartment in the optic nerve, as subsequently corroborated, following the assignment of the two T1 components.

Figs. 4 and 5 show that in both nerve types, the displacement RMS of the T1s component deviates most significantly from linearity with $\sqrt{D}$ and that in both cases the displacement RMS at long diffusion times approximately reaches a constant value of $3.2\pm0.1$ $\mu$m for the sciatic nerve and that of $1.44\pm0.07$ $\mu$m for the optic nerve. These values are close to the literature value of the axonal internal diameter for both nerve types. The total diameter, including the myelin sheath, is $5–7$ $\mu$m for the sciatic nerve [29] and is $1–2$ $\mu$m for the optic nerve [30]. The T1f component appears to be more Gaussian in behavior, exhibiting an almost-linear increase with $\sqrt{D}$. The attenuation of the T1f component at diffusion times greater than 50 ms due to the loss of echo signal during the pulse gradient stimulated-echo mixing time prevented the evaluation of the FWHM for the longer diffusion times. It should be noted that the apparent overestimation of the displacement RMS at the lowest diffusion time value of 13 ms is probably attributable to the violation of the $q$-space condition ($\Delta \gg \delta$) for this particular combination of parameters (see, for example, Ref. [31]).

Complete elimination of the T1s and T1f components using the inversion-recovery method is possible only if there are two distinct values for T1s and T1f. This is most probably not the case, in particular for T1f. The inhomogeneous distribution of Gd-DTPA along with the heterogeneous structure of the nerves gives rise to a distribution of T1 values upon addition of the contrast agent, rather than a single value per compartment. As mentioned earlier, the fact that the elimination is not complete is mostly reflected in the presence of a broad component in the displacement distribution function of the T1s component and that of a narrower component in the T1f functions. This admixture of components could not be easily eliminated by variation of the TI value around the expected Tnull for each component, affecting also the FWHM measurements. In particular, the challenging situation for measuring the T1f functions led to a rather large variance in the estimation of the displacement RMS for this component.

Based on these results, it is possible to tentatively attribute the T1 components to tissue compartments, based on their geometric characterization: the T1s component appears to be generated by the intra-axonal space of both nerves, whereas the T1f, which is less restricted in character, can be attributed to the inter-axonal matrix, which in the peripheral nerve (in this case, the sciatic nerve) would coincide with either the endoneurium or the epineurium and in the central nervous system nerve (e.g., the optic nerve) would be the pia and dura mater.

Several studies have identified another major source of water proton signal in neural tissue, that is, the intramyelinic water [32,33]. The myelin water, despite its relatively short TE, can significantly contribute to the diffusion measurement. Andrews et al. [34] carefully measured the diffusion properties of myelin water in frog sciatic nerve and found a relatively high degree of anisotropy and diffusion coefficients that indicate a restricted diffusion perpendicular to the axonal direction. It is difficult to estimate the exact contribution of myelin water to the experiments shown here. An approximate evaluation of the contribution of the myelin water that assumes that the myelin water T1 is included in the long T1 component in the T1 relaxograms and a T2 of about 15 ms indicate that the contribution of the myelin water to the measured signal at the short TI can be up to 25%. This is a nonnegligible contribution, and elimination of the myelin signal using methods similar to those used by Andrews et al. [34] should be considered.

Further support for the relationship between the T1 components and nerve compartments comes from comparing the behavior of the total H2O signal with that of the T1s, in both nerves. In the sciatic nerve, where $f_2$, the fraction of T1f is relatively high (about 61%; see Table 1), the nulling of this...
component has a dramatic effect on the way the displacement RMS changes with $\sqrt{\Delta}$. In the optic nerve, where $f_i$ is significantly lower (about 34%), the displacement of the total H$_2$O signal is more similar to that of the $T_{1s}$ and only at the largest diffusion time value can any difference be observed. To emphasize this point, we show in Fig. 3G the displacement distribution functions for the total H$_2$O signal and the $T_{1s}$ of the optic nerve at $\Delta=50$ ms. For emphasis, in this figure, the intensity of both functions is normalized to their maximum intensity. It can be seen that although the total H$_2$O function contains a broad component that is much lower in intensity or absent from the $T_{1s}$ function, the FWHM values of both functions are almost identical. This is clearly not the case in the sciatic nerve, as can be directly seen in panels D and E in Fig. 2.

Figs. 6 and 7 summarize the equivalent of the tensor characteristics of the total H$_2$O and of the $T_{1s}$ and $T_{1f}$ components at a representative diffusion time value of 50 ms. FA (Fig. 6) and ADC (Fig. 7) values are calculated from the FWHM measurements as explained in Section 2. In the case of the sciatic nerve, the $T_{1s}$ component is highly directional, with an FA value that is higher than that of the total H$_2$O signal. The $T_{1f}$ component in the sciatic nerve is markedly less directional, in accordance with its attribution to the less restricted, but still hindered, endoneurial and epineurial spaces. In the optic nerve, interestingly, the FA value of the total H$_2$O signal and those of the $T_{1s}$ and $T_{1f}$ components are not statistically different. This can be attributed to a difference in axonal packing, which may be higher in the optic nerve than it is in the sciatic nerve. This has to be further verified by histological examination and simulations derived from histology (e.g., Ref. [35]). ADC$_{fast}$ for the optic nerve, attributed here to the diffusivity of inter-axonal water, is lower than ADC$_{fast}$ for the sciatic nerve, possibly because of a difference in axonal packing. If this is indeed the case, this is in accordance with the higher FA$_{fast}$ in the optic nerve that also suggests a higher axonal density in the optic nerve than that in the sciatic nerve.

It is not clear how water exchange between the intra and inter-axonal spaces impacts the displacement profiles for the

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Fig. 4. Displacement RMS values obtained from the displacement distribution functions measured for the sciatic nerve.

Fig. 5. Displacement RMS values obtained from the displacement distribution functions measured for the optic nerve.

Fig. 6. FA values calculated for the total H$_2$O signal and for the $T_{1s}$ and $T_{1f}$ components measured for the two nerve types at a diffusion time of 50 ms.

Fig. 7. ADC values calculated for the total H$_2$O signal and for the $T_{1s}$ and $T_{1f}$ components measured for the two nerve types at a diffusion time of 50 ms.
various nerve compartments. For example, one may intuitively assume that the fact that the displacement RMS of the T$_1$ changes very little, if at all, for both nerves at high $\Delta$ values may indicate a rather slow exchange between the compartments. This assessment has yet to be verified, and at this time, there is no comprehensive model that binds the shape of $q$-space displacement distribution functions with parameters such as permeability and exchange rates. An initial treatment of the problem under specific conditions has been proposed [36], but a more comprehensive model that will allow the extraction of cross-membrane exchange rates from compartment-specific $q$-space measurements has yet to be devised. The experimental framework shown here may serve as a starting point for providing compartment-specific data for future models that include exchange characteristics and can be expanded to include nonmyelinated nerve models, degeneration models and alteration of the intra-axonal space characteristics using, for example, the collage-nase model for degradation of the endoneurial collagen.

Compartment-specific measurement of diffusion properties is important in the frame of evaluation of tissue properties via such tools as DTI. There is no question that parameters such as FA, radial/axial diffusivities and trace tensor are all intimately related to microscopic tissue structure and provide a sensitive set of noninvasive tools for the evaluation of tissue integrity. However, the relation between the geometry of tissue compartments and the impact they have on the properties of water diffusion in each compartment has yet to be fully characterized. Admirable computational efforts to characterize tissue structure have been made based on modeling the water diffusivity in various compartments [e.g., in the work of Assaf and Basser [37]). There is an ongoing effort to develop compartment-specific NMR and MRI methods, based on the different characteristics of tissue compartments, whether it is T$_2$ [e.g., [32]) or macromolecular content [38]. Lacking is a link between the various compartment-preferential acquisition methods and a full geometric characterization of these compartments. Such characterization is crucial for the verification of the compartment specificity of the acquisition methods on one hand and for more informed modeling of the postprocessing methods on the other.

4. Conclusions

Compartment-specific $q$-space diffusion-weighted MR in the presence of a relaxation agent has been shown to provide realistic geometric characterization of the intra-axonal and inter-axonal spaces in isolated bovine optic and sciatic nerves. The characterization, which included the estimation of directionality of diffusion as well as the size and character of the geometric restrictions imposed on water self-diffusion, is well correlated with the structural parameters of these nerves (e.g., typical axonal diameter). Such compartment-specific analysis can prove to be particularly useful for the verification of the specificity of several suggested methods, in the investigation of the microscopic correlates of such measures as DTI FA and in the accurate evaluation of the structural changes in neural tissue following changes in myelination and membrane permeability.

Acknowledgments

We thank Ms. Alkystis Phinikaridou and Dr. Kevin Hallock for helping with the experiments and Dr. James Hamilton for making the MR spectrometer available for these experiments.

References


