Assessment of Axonal Fiber Tract Architecture in Rat Spinal Cord by Localized NMR q-Space Imaging: Simulations and Experimental Studies

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Introduction

Q-space imaging [1, 2] has recently been applied to retrieve structural information from biological tissues. However, the complexity of tissue architecture poses challenges to the interpretation of *q*-space data. In this study, *q*-space simulations were carried out on histologic images of rat spinal cord white-matter fiber tracts differing in axonal architecture and the retrieved displacements were correlated with mean axonal size and spacing calculated from segmented optical images. In addition, localized *q*-space imaging data were acquired from the fiber tracts of rat spinal cord specimens studied in the simulations.

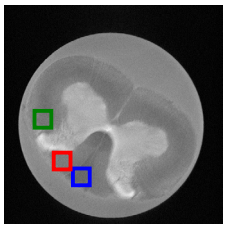
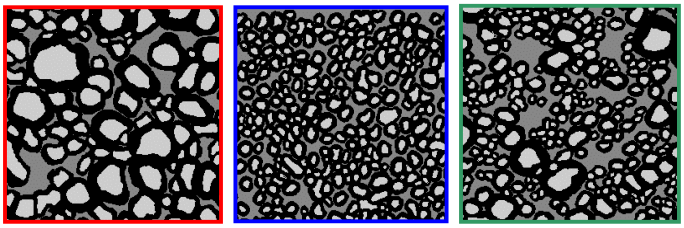


FIG 1 Histologic images of rat spinal cord fiber tract: (left) SE T_2 image showing tract locations: (bottom left) cuneatus; (bottom center) gracilis; (bottom right) rubospinal tract, RST.



Materials and Methods

Simulations were performed using a finite-difference diffusion model developed previously [3]. Segmented histologic image of rat spinal cord fiber tracts (*ECS*/*ICS*/myelin, Fig. 1B-D) served as input for the simulations using the following imaging parameters: TE=105ms, Δ=36 and 100 ms. Diffusion gradient strength was incremented from 0 to 630 G/cm in 10 G/cm steps and δ = 5ms. The permeability of axonal membrane and myelin sheath were set to 0.01 μm/ms, along with T_2 values and water diffusivities of 78/300/19 ms and 1.65/1.12/1.12 μm^2 /ms [3], respectively (*ECS* /*ICS*/ myelin sheath). Structural parameters were calculated from histologic images (Table 1) and compared with those derived from *q*-space analysis. Localized *q*-space spectra of the excised spinal rat spinal cord were acquired at 400 MHz (Bruker DMX 400) at locations where simulations have been performed with a voxel size of 0.3x0.3x3 mm^3, TR/TE=3.3s/18.7 ms, δ=8 ms, Δ=36, 49, 64, and 100 ms, and 32 averages. The diffusion gradient was applied perpendicular to the long axis of the cord and it amplitude increased in equal steps from 0 to 75 G/cm.

Table 1 Structural parameters calculated from images shown in Fig. 1.

Fiber Tract	Cuneatus	Gracilis	RST
Size dist. (μ/σ) [μm]	2.67/1.28	1.06/0.28	1.11/0.46
Spacing dist. (μ/σ) [μm]	3.52/1.03	2.03/0.47	2.00/0.62
Axon counts	78	249	211

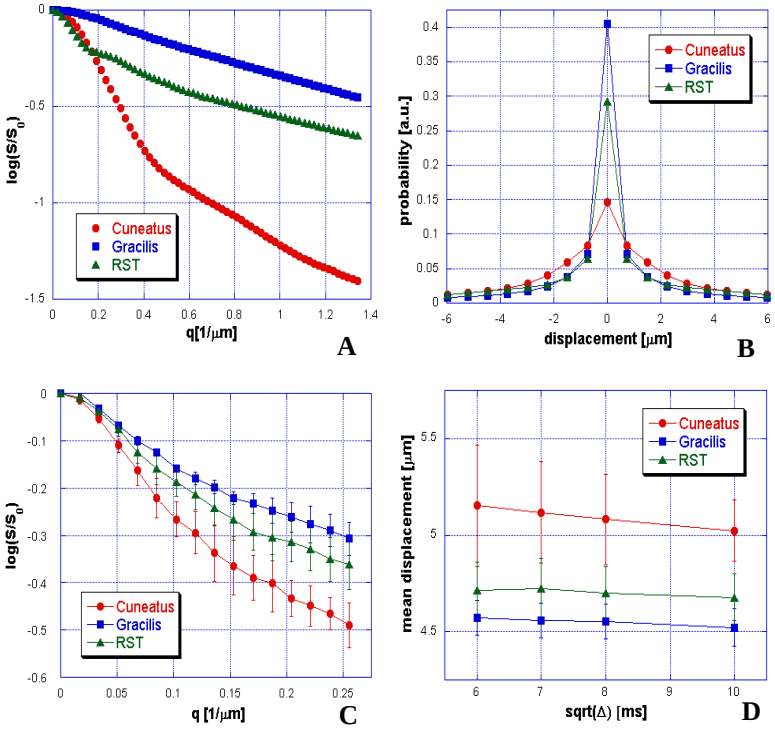


FIG 2 Simulated *q*-space echo attenuation (A) and displacement profiles (B) and experimental *q*-space data (*N*=4) (C) for the three fiber tracts at Δ=100ms. (D) Measured mean displacements at various diffusion times.

Results and Discussion

Both simulated and experimental data in Fig. 2 reflect the differences in axonal architecture: diffusion is more restricted within tracts of smaller axon diameter (Figures 1B-D). The narrowest profile was found for the fiber tract having the smallest axons (and thus highest axon density–gracilis). Table 2 lists the calculated mean displacement (FWHM), probability for zero displacement, and kurtosis [4], indicating the mean displacements to be in fair agreement with the mean axonal size retrieved from optical images. It is noted the mean displacement in the cuneatus region gradually decreases with increasing diffusion time whereas these values remain almost unchanged in the gracilis (Fig. 2D). This finding can be explained by the greater degree of restriction caused by the smaller axonal size (relative to a given diffusion length), which suggests the mean displacements converge toward asymptotic values at very long diffusion times, thus providing an estimate of the relative mean axon diameters. The calculated kurtosis at Δ=100ms from cuneatus, gracilis, and RST is 8.53, 9.51, and 9.23, respectively, which indicates the displacement profiles to significantly deviate from Gaussianity. Nonetheless, unlike the simulated data, the measured mean displacements appear to be larger, and the differences in kurtosis among the three tracts are much smaller than predicted by the simulations. The discrepancy is likely the result of limited resolution in the displacement domain.

Table 2 Structural information retrieved from displacement profiles obtained from rat cord simulations at diffusion times Δ=36/(100)ms

	Cuneatus	Gracilis	RST
Mean disp. [μm]	3.12/(2.01)	0.92/(0.91)	1.04/(0.95)
Prob. of zero disp.	0.09/(0.15)	0.26/(0.41)	0.18/(0.29)
Kurtosis	9.72/(14.16)	48.01/(50.99)	37.51/(46.27)

Conclusions

The simulations and experimental data in this study suggest that *q*-space NMR has potential for providing quantitative information on mean axon size in mammalian spinal cord tissue and is able to distinguish tissues of different axonal density.

References **1**. Callaghan PT. Principles of NMR Microscopy, Oxford University Press, 1993. **2.** Cohen Y et al, NMR BioMed. 2002;15:516. **3.** Hwang SH et al, Magn Reson Med 2003; 50:373 **4**. Latt J et al, Proc. ISMRM 11th Meeting, 2003, 590.