Multiexponential Diffusion Imaging of Normal Rat Spinal Cords *In Vivo*

EL Bossart, XS Silver, E Mercer, BA Inglis and TH Mareci
Departments of Physics, Neuroscience, Biochemistry, the UF Brain Institute and the Center for Structural Biology at the University of Florida, Gainesville, FL 32610, USA and the National High Magnetic Field Laboratory

Introduction. The availability of very large magnetic field gradients allows an extended range of diffusion rates to be measured. Such measurements have shown that diffusion-weighted signal loss in tissues occurs by a multiexponential process (1, 2). To the limits of the gradients we have available here, two unique diffusion regimes have been seen in excised, fixed spinal cord tissue: a fast and a slow component (3, 4). Others have speculated that the fast and slow components of diffusion in tissue are equivalent to diffusion in the extracellular and intracellular spaces, respectively (1, 2).

In the work reported here, the rate and direction of water diffusion in living rat spinal cord tissue were measured and compared to the results in excised, fixed normal rat spinal cord tissue taken at the same vertebral level. We have observed biexponential diffusion in the rat spinal cord for the first time.

Method. In this work, apparent diffusion coefficient (ADC) measurements were performed *in vivo* along the three principal axes (along the length of the spinal cord, z; and in two orthogonal directions in the plane of the spinal cord, x and y). These ADC measurements were performed to high gradient weightings (b ~ 7000 s/mm^2) in order to look for multiple component diffusion. The *in vivo* measurements were performed on a 4.7 T, 33 cm bore magnet utilizing inductively coupled implanted coils to image the rat spine (6). The diffusion images were taken using a pulsed-gradient spin-echo imaging sequence triggered off of the animal ventilator in order to reduce motion artifacts. The total measurement time was approximately 4 ½hours.

These measurements were compared to measurements taken at 600 MHz on excised, fixed normal rat spinal cord (3, 4). All data was processed using a multiexponential ADC model to calculate the fast and slow component of diffusion in each of three orthogonal directions. The excised, fixed spinal cord data (taken at 20^{o}C) was temperature corrected to 37^{o}C in order to make a more direct comparison (7).

Results and Discussion. Only two unique components of diffusion were observed in rat spinal cord gray matter (GM) and white matter (WM) *in vivo* for the limits of the gradients utilized (Figure 1). The imaging data was fit pixelwise to a biexponential ADC model. The diffusion rate for regions of interest (ROIs) in the GM and WM were measured. Table 1 shows the *in vivo* and excised, fixed cord diffusion rates for the three ADC directions. Note that the diffusion rates are very similar for both cases, indicating that animal respiratory motion has been effectively removed. The fast diffusion rate is fairly isotropic in the GM, and biased along the length of the cord in the WM. That WM bias is less evident in the slow diffusion component, following previous observations for excised, fixed spinal cords (3, 4).

The small amount diffusion-rate anisotropy in the white matter for the slow diffusion component seems to support the proposal that the slow diffusion component is associated with intracellular water. Cyto-skeletal features would greatly restrict the intracellular water diffusion in all directions resulting in a reduction in diffusion rate and anisotropy. Likewise the large amount of anisotropy for the fast diffusion component supports its association with extracellular water. Water in the extracellular space would move more freely through the extracellular matrix with mainly only cells as boundaries.

These results illustrate the potential for multiple rate diffusion measurements in spinal cords of living systems, which has the potential to provide detailed structural information on these tissue in normal and pathological states.

Acknowledgements: The respiratory gating system was designed and built by Barbara Beck. This work was supported in part by NIH Grants RO1-NS29362 and PO1-NS35702

References

1. KG Helmer, et al. *NMR in Biomed* **8**, 297 (1995)
2. T Niendorf, et al., *Mag Reson Med* **36**, 847 (1996).
3. EL Bossart, et al. *ISMRM Philadelphia*, p. 328 (1999).
4. EL Bossart, et al. *ISMRM Philadelphia*, p. 991 (1999).
5. J Karger, et al., *Adv in Mag Reson* **12**, 1 (1988).
6. X Silver, et al., *ISMRM Philadelphia*, p. 2065 (1999).
7. Mills, *J Phys Chem* **77**, 685 (1973).

Figure 1. Graphs of the Signal Intensity vs. b value for GM and WM *in vivo*. Curves are shown for the directions of x/y and z.

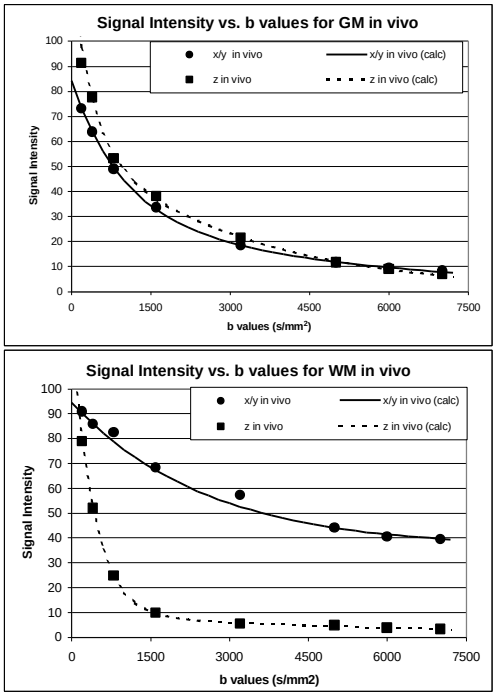

Table 1. Comparison of *in vivo* and *in vitro* ADCs. In vitro data corrected to 37^{o}C.

ADC	*in vivo*		*in vitro*	
$\mu m^2/s$	GM	WM	GM	WM
x (fast)	1290	710	1231	748
y (fast)	880	550	960	554
z (fast)	1890	2110	1849	2186
x (slow)	150	150	147	156
y (slow)	170	120	190	99
z (slow)	230	170	207	202