Spontaneous Recovery Following Spinal Cord Injury: In vivo longitudinal Diffusion Tensor Imaging Studies

P. A. Narayana[1], I. Elshafiey[2], B. Mehmet[3]

[1]Radiology, University of Texas at Houston, Houston, Texas, United States, [2]Cairo University, Cairo, Cairo, Egypt, [3]Kansas University Medical Center, Kansas City, Kansas, United States

Introduction: Compromised fiber tract integrity is mainly responsible for the neurologic deficit in spinal cord injured subjects. Diffusion tensor imaging (DTI)-based anisotropic estimates, such as fractional anisotropy (FA), reflect the fiber integrity. However, *in vivo* longitudinal DTI studies of injured spinal cord are technically challenging. In this abstract we report, what we believe to be the first time, in vivo longitudinal studies of DTI in rats. The results of these studies along with neurobehavioral assessment and histology demonstrate the spontaneous recovery in these animals as a result of endogenous tissue repair.

Methods: Ten male Sprague Dawley rats weighing between 320-400 grams were used in these studies. Six animals were injured while the other four animals served as controls. Following laminectomy at the T7 level, a moderately severe contusive spinal cord injury (SCI) was produced using an in-house fabricated injury device. Following injury, a rectangular RF coil of dimensions 12 X 30 mm was surgically implanted subcutaneously above the T7 level and inductively coupled to an external coil of dimensions 15 X 30 mm for improved SNR [1]. All MR scans were performed on days 0, 3, 7, 14, 28, 42, and 60 on a 7T, 30 cm horizontal bore BioSpec MR Scanner (Bruker, Billerica, MA) equipped with a 116 mm diameter gradient coil system that is capable of generating a maximum gradient amplitude of 200 mT/m. All surgical procedures and MR scans were performed with animals under isoflurane anesthesia (a mixture of 1.5% isoflurane, 30% oxygen, and air), ventilated through a rodent ventilator that was modified to provide the necessary trigger signal for respiratory gated acquisition. Multi-shot, blipped EPI sequence was used to acquire diffusion-weighted images with the MR scanner triggered on every other respiratory cycle. The acquisition parameters were: number of shots = 8, TR = 2000 ms, TE = 40.2 ms, NEX =4, FOV = 25 mm, image matrix = 128 X 128, slice thickness=1 mm with 0.25 mm inter-slice gap, diffusion gradient width (δ) = 12 ms, and diffusion gradient separation (Δ)=18.9 ms. Diffusion gradients were applied along seven independent directions: read, phase, slice, read-phase, read-slice, phase-slice, and read-phase-slice. Gradient amplitudes were incremented linearly in 16 steps from 0 up to maximum of 200 mT/m. The maximum b-value was 6200 s/mm^2. The amplitudes of diffusion and imaging gradients were determined numerically from the gradient waveforms sampled at the amplifier output with a four channel digital storage for computing the b matrix to include contributions from imaging and diffusion gradients. EPI image reconstruction was performed using the procedure described by Fenyes et al. [2]. Eddy current induced distortions were corrected with an iterative cross-correlation technique [3]. Neurobehavioral assessment was performed based on the open field locomotion on the same days as the DTI scans, but prior to administration of anesthesia, and the scores were expressed using the modified Tralov scale. End point histology was performed on all the injured cords.

Results Typical density-weighted spin echo images of a spinal cord at and 5 mm caudal to the epicenter on different days are shown in Fig. 1. The increased pathology on day 3 can be seen on these images. The FA maps of a normal and injured cord on days 3 and 14 are shown in Fig. 2. The normal estimated FA value of the white matter is 0.88 ± 0.098. The temporal stability of the normal FA value is well within 10% of the mean value. The FA maps of a normal cord and injured cord that is 5 mm away from the epicenter are shown in Fig.2. The temporal changes of FA from tissue located at 5 mm from the epicenter along with the Tarlov score is shown in Fig. 3. All the post-injury FA values of cord are statistically different from the normal control. Both the FA values and Tarlov score show sharp decline immediately after injury, but slowly recover, reaching their maximum values around 3 weeks and 4 weeks respectively. End point histology shows that the caudal sections close to the epicenter are filled with tissue. While this tissue is not replete with fully functional tissue, some of the neurons were lucid in their shape and appear to be functional.

Discussion: These studies, based on longitudinal in vivo DTI and neurobehavioral studies suggest spontaneous recovery in spinal cord injured rats. This is consistent with histology. Our studies are consistent with reports, based on histology that documented spontaneous recovery [4]. These in vivo studies have demonstrate that the state of cord tissue that is not directly affected by the mechanical trauma, but affected by the subsequent pathophysiological changes, can be followed noninvasively and quantitatively with DTI.

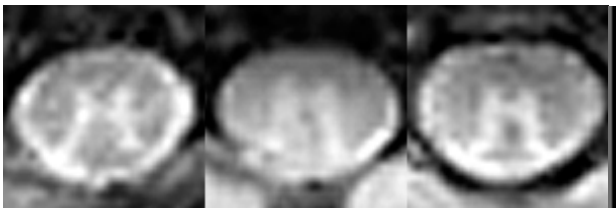

Fig.1 Density weighted images of injured cord

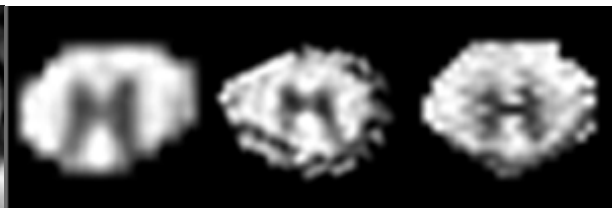

Fig. 2 FA maps of normal and injured cord on days 3 and 14

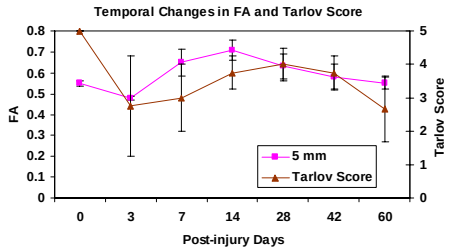

Fig. 3. Tempral changes in FA and Tarlov score

References:

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