Tracking the Evolution of Experimental Spinal Cord Injury by *in-vivo* MRI Microscopy

U. Nevo[1,2], A. Gothilf[2], S. Akselrod[1], M. Neeman[3], M. Schwartz[2]

[1]Abramson Center for Medical Physics, Tel Aviv University, Tel Aviv, Israel, [2]Department of Neurobiology, Weizmann Institute of Science, Rehovot, Israel, [3]Department of Biological Regulation, Weizmann Institute of Science, Rehovot, Israel

Introduction

Quantification of the severity of spinal cord injuries, and of the path of degeneration that follows it is a challenge that complicates clinical diagnosis as well as experimental and pharmaceutical studies of possible treatments. MRI and especially Diffusion tensor imaging (DTI) can differentiate between damaged and normal neuronal tissue and are expected to be critical for future quantification of spinal cord damage [see reviews in 1,2]. Nevertheless, currently this is not achieved routinely due to various factors such as motion artifacts in the vicinity of the spinal cord (due to breathing, swallowing and various non-voluntary movements), the small dimensions of the spinal cord requiring high spatial resolution, bone-to-tissue proximity that creates susceptibility artifacts, etc. Despite these difficulties a few important studies have demonstrated the potential of microimaging MRI & DTI in diagnosis following spinal cord injury [1,2]. This study aimed to perform in-vivo microimaging of experimental controlled spinal cord injury over time and to facilitate future quantitative follow up of the secondary loss or the recovery that follow spinal cord trauma.

Materials and Methods

Animals - Adult female Lewis rats (n=10) were contused by NYU's Impactor device to create a controlled insult. One group of rats was treated with an immune-modulating therapy, by the use of dendritic cells, to minimize the degree of secondary degeneration.

T2 weighted & Diffusion tensor MRI - T2 weighted and DTI scans were performed for 10 weeks using a 4.7 Bruker Biospec scanner with a 2cm diameter surface coil. To minimize motion, rats were laid supine inside a restricting halved cylinder cradle, with the surface coil attached to its bottom. T2 weighted scans had TR/TE of 3000/60 msec and used 6cm FOV sagittal sections. DTI scans were performed with 2.5 cm axial sections. This small FOV 'allowed' aliasing as long as there was no overlap of image components onto the spinal cord. Matrix size was 128x128 pixels and was later doubled by zero-filling, yielding voxel sizes of 100x100x500 μm. To reduce susceptibility artifacts, sequences that are less sensitive to field inhomogeneity were used: Spin-echo pulse sequence for the T2 measurements, and PGSE for the DTI measurements. DTI scans were performed in 8 non-collinear directions, where one of them was along the estimated spinal cord's axis. Diffusion weighting parameters were: Gd=0,200 mT/m, Δ=20 msec, δ=4 msec, TR/TE = 34.4/1000 msec. Scans were respiratory gated. No averaging repetitions were used in either case.

Analysis - Denoising of the DTI data, prior to tensor derivation, was performed by the use of a novel Complex GCV Wavelet denoising scheme [3]. Following this pre-processing, the diffusion tensor eigenvalues and the characteristic measures (Trace and Anisotropy) were calculated.

Results

Technical Results - The resulting T2 weighted and DTI images obtained are depicted in Figures 1 & 2. (Multicolor-code is used in images characterized by a wide dynamic range of intensities). The outcome of 'denoising' is demonstrated in Figure 1a and 1b, with 'zooming' in Figure 1c. It is possible to differentiate between gray and white matter in the diffusion- weighted images (with longitudinally oriented diffusion gradients). The applied denoising significantly improved the reliability of the derived DT-MRI parameters. Despite this, while in some cases the DTI images were informative and the tensor data was successfully derived, in others it was impossible to differentiate white matter from gray matter or to resolve structure.

Neurobiological Results - The evolution of the insult, as revealed by sagittal T2 weighted MR image is depicted in Figure 2. The intensity in these images is mostly weighted by non-neuronal changes in the tissue. Nevertheless, the effect of the progressing morphological longitudinal changes is evident, and so is the effect of treatment. In accordance, the immune-treated group showed significantly improved functional outcome.

Discussion

This study demonstrates the feasibility of microimaging MRI for *in-vivo* characterization of spinal cord injury. **Technically**, as expected, the less demanding T2 weighted images may easily provide some of the required information. Nevertheless, in our view, despite the difficulty in obtaining reproducible DTI results in this model, the DTI data yields more quantitative results. The use of our novel Complex GCV wavelet-denoising technique was found very efficient and improved DTI analysis. **From the neurobiological point of view** these results demonstrate the importance of tracking the progress of morphological changes in injured spinal cord and the effect of immune-based therapy. The observed changes in the images evolve from multiple sources, neuronal (demyelination, cavitation, fibers loss) or non-neuronal (edema, scar, angiogenesis, etc). A major task still not addressed is thus the ability to define and differentiate between the contributions of these physiological components.

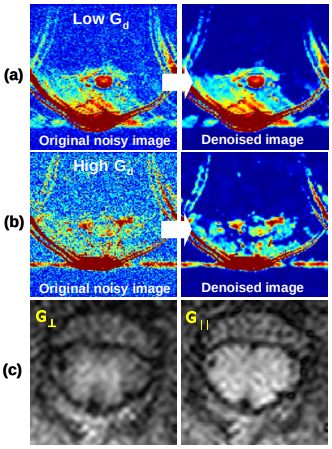

Figure 1: the effect of denoising of DT-MRI images. (a-b) denoising of low & high diffusion gradients, respectively. (c) The denoised spinal cord region.

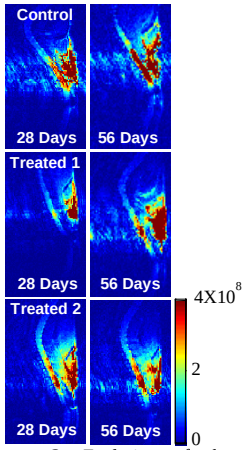

Figure 2: Evolution of the contused spinal cord. T2 weighted sagittal sections. Wound epi-center is presented.

1. Schwartz E.D., Hackney D.B. Exp Neurol. 2003
2. Bammer R., Fazekas F. Top Magn Reson Imaging. 2003
3. Nevo et. al. Proc. of the 11th ISMRM meeting.