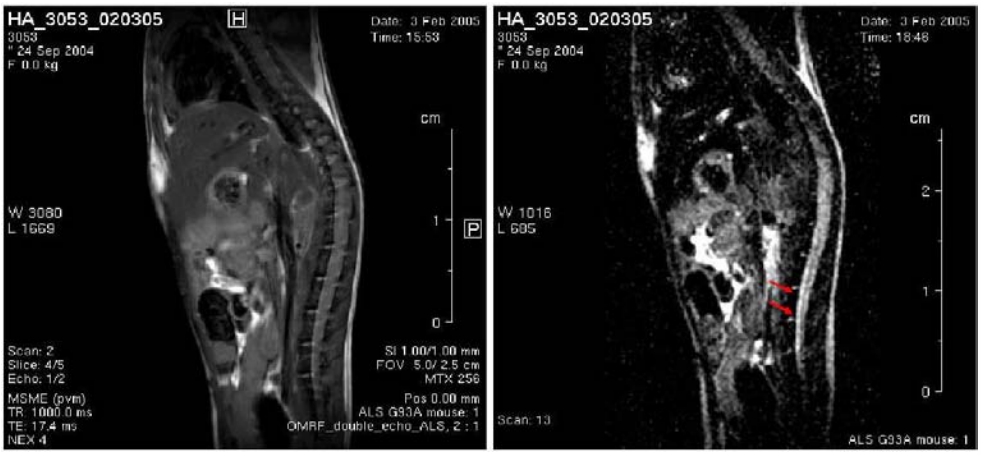
DWI Assessment of a transgenic mouse model for ALS

H. Abdelmoaty[1], M. West[1], Y. Tesiram[1], A. Abbott[1], R. Blindauer[1], K. Hensley[1], R. A. Towner[1]
[1]Free Radical Biology and Aging Research Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, United States

Abstract:
Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disease affecting the upper and lower motor neurons. ALS affects 60,000 to 100,000 individual at any given time [1]. The disease is inexorable with no effective cure with 1-5 years life expectancy following onset [1]. This study examined the spinal cords of G93A-SOD1 mice, a transgenic mouse model for ALS, with diffusion weighted imaging (DWI). Measuring translational diffusion of water with DWI allows the detection of biophysical changes in the spinal cord. Cellular, molecular, and tissue structures act as barriers that restrict diffusion. As these barriers deteriorate, diffusion is expected to increase. A measure of this increase with time can shed light on where and when damage occurs in the spinal cord.

Materials and methods:
DWI largely relies on Brownian motion and phase shift of protons. We used the DWI pulse sequence to probe molecular diffusion in the spinal cord of a G93A-SOD1 mouse model. After preliminary investigations, animal studies were conducted at 85, 105 and 120 days of age. The main study objective was to measure diffusion patterns in G93A mouse spinal cords at different time points during the pathology of the disease, with an of 5 for control (wild-type) and transgenic mice, and to establish whether this method could be used for early diagnosis of disease progression as well as provide a better understanding of underlying mechanisms of the disease. Data analysis was used to measure the apparent diffusion coefficient (ADC) by fitting the equation relating the signal intensity to diffusion ADC= - (1/b)* S(b)/S(0) using approximate b-values of 50, 280, 680, and 2300 s/mm^2. Gradient value strengths were set at 20, 50, 80, and 150 mT/m and a slice thickness of 1 mm was used. For the DWI studies, the spinal cord was divided in 3 regions (cervical, thoracic, and lumbar) where each region was analyzed separately.

Results:
The collected data suggest that early diffusional changes occur in the lumbar region of the spinal cord in G93A-SOD1 mice. Alterations in the spinal cord data took place between 85 days of age and the next two time points at 105 and 120 days. Our data suggest that the mean diffusivity is increased. This increase correlates with the duration and pathological process in ALS progression. An increase in diffusivity represents a more chronic change with neuronal loss. Biophysical alterations may directly correlate to neuronal loss, cell membrane and cytoskeleton damage.



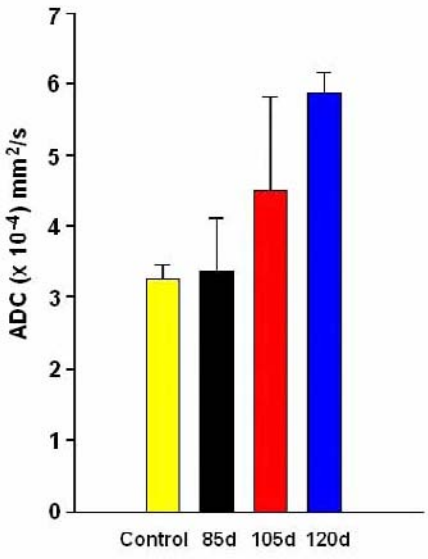


Figure 1: Representative T1w MRI (left) and DWI (center) of a G93A-SOD1 transgenic mouse in the sagittal plane. Calculated ADC values (right) were obtained for control (wild-type) mice and G93A-SOD1 mice at 85, 105 and 120 days of age (n=5 for each).

Conclusion:
This study demonstrates that DWI can provide non-invasive evaluation of ALS pathology without having to obtain invasive histology.

References:
1. Cudkowicz ME *et al*. (1997) Ann. Neurol. 41: 210.