Identification of abnormalities in the ferret brain following mild brain injury using voxelwise diffusion MRI microimaging

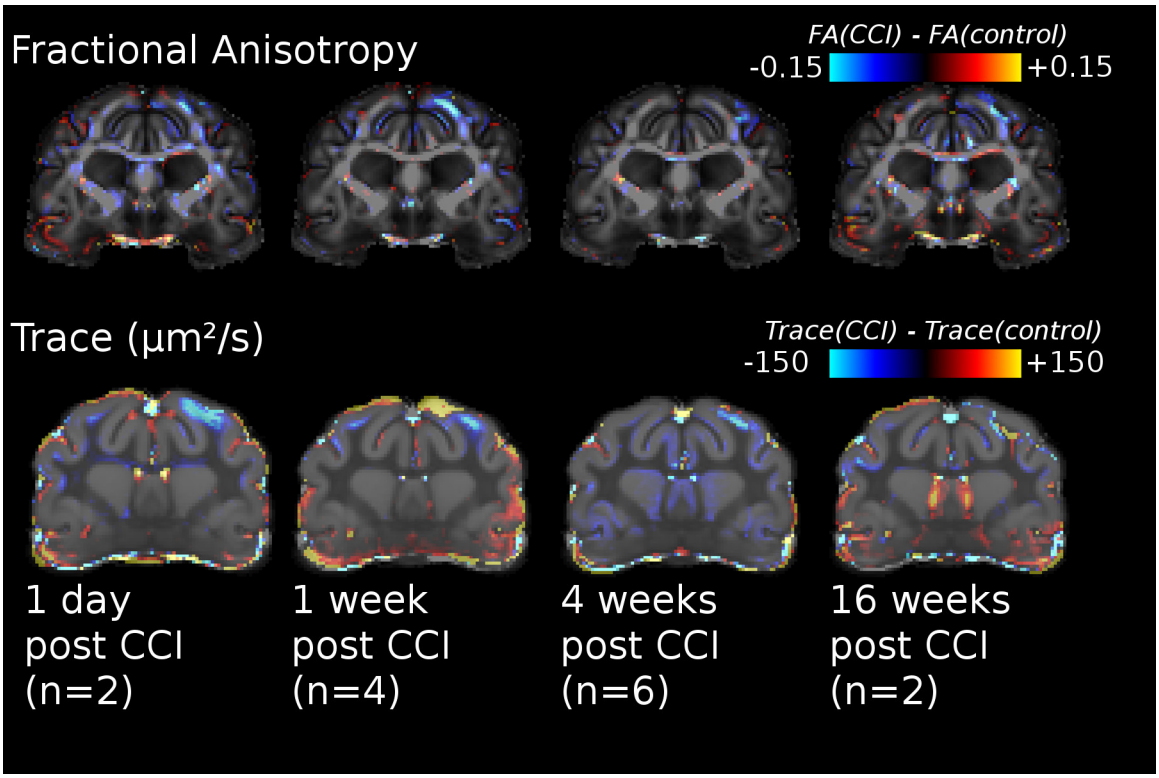
*E. B. HUTCHINSON1, S. C. SCHWERIN2, M. E. KOMLOSH1, K. L. RADOMSKI2, M. O. IRFANOGLU1, S. L. JULIANO2, C. M. PIERPAOLI1;
1NIH, Bethesda, MD; 2USUHS, Bethesda, MD

Introduction.
The combination of high-resolution, quantitative MRI methods with a human-similar experimental model of brain injury is a promising approach to identify and spatially map abnormalities that accompany traumatic brain injury (TBI). We have employed a mild TBI model in the ferret, which has a gyrencephalic cortex and relatively high white matter volume, to examine the ability of diffusion tensor imaging (DTI) to non-invasively detect abnormalities at various times following injury. Voxelwise statistical comparisons of high-resolution ex-vivo DTI maps showed several compelling patterns of brain abnormalities according to time after injury.

Methods. Perfusion fixed brain specimens were taken from 8 uninjured ferrets and 14 ferrets following mild controlled cortical impact for the following times after injury: 1d(n=2), 1w(n=4), 4w(n=6) and 16w(n=2). For each brain, 297 high-resolution (250 μm^2 voxels) DWIs were acquired with b=100-10,000 s/mm^2. The TORTOISE pipeline was used for image corrections and DTI model fitting. Next, diffusion tensor images were warped into a common space using the DRTAMAS registration algorithm. Voxelwise difference maps were generated for Trace and FA to compare groups and individual brains with different time after injury to the control group.

Results. Voxelwise group difference maps for TR and FA examining the effect of time after injury are shown in the included figure. FA was reduced in the white matter near the injury with the greatest change at 1 week after CCI and persistence of this finding out to 16 weeks. TR was decreased in cortex and white matter regions most robustly at one day post-CCI. At 16 weeks TR was increased in the white matter.

Conclusions. The imaging approach shown here provides a high-resolution, whole brain, quantitative and bias-free analysis method for determining anatomical and microstructural abnormalities following TBI. In this study, this approach has enabled the identification of spatial and temporal features of post-traumatic brain changes in a ferret TBI model.


Fractional Anisotropy
FA(CCI) - FA(control)
-0.15
+0.15
Trace (μm²/s)
Trace(CCI) - Trace(control)
-150
+150
1 day post CCI (n=2)
1 week post CCI (n=4)
4 weeks post CCI (n=6)
16 weeks post CCI (n=2)