Diffusion kurtosis imaging quantifies the effects of mild traumatic brain injury in football players

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Target Audience: Clinicians and researchers interested in MRI biomarkers for mild traumatic brain injury.

Purpose: Mild traumatic brain injury (mTBI) is a prevalent injury for athletes in contact sports. Behavioral tests indirectly estimate injury, but objective imaging biomarkers that reflect the extent and severity of brain tissue damage and ensuing changes would be crucial in informing treatment and recovery. In order to study changes in brain tissue microstructure after mTBI, we used Diffusion Kurtosis Imaging (DKI), an extension of DTI. DKI complements DTI by estimating non-Gaussianity of the molecular diffusion in complex tissue microstructures; therefore, it is hypothesized to be more sensitive and specific to subtle microstructural changes due to mild concussion. The kurtosis tensor model produces the maps of mean kurtosis (MK), radial kurtosis (Krad), and axial kurtosis (Kax), in addition to the DTI metrics of mean diffusivity (MD) and fractional anisotropy (FA). Observed changes in DKI metrics in football players with mTBI were validated using simulations.

Methods: DKI data were acquired from 13 high school and college football players using a GE MR750 3T scanner. The study was approved by the IRB and written consent was obtained from participants. Subjects with concussion were administered the SCAT3 postconcussion symptom checklist after the injury and scanned within 12 hours of injury and at 8 days post injury. The SCAT3 symptom checklist has a score range of 0-132; high scores indicate more severe symptom burden. 4 control subjects with no history of concussion were also scanned twice. Single-shot SE-EPI sequence was used with 3x3x3mm voxels, four b=0 (reference images) and 60 diffusion-weighted images with b=1000s/mm^2 and 2000s/mm^2 (30 diffusion directions for each shell). Images were processed through software developed in-house to estimate DKI tensors based on the algorithm by Jensen et al[1]. The kurtosis tensor is fitted via unconstrained singular value decomposition. High resolution T1-weighted images were segmented to generate a white matter mask and average kurtosis metrics were calculated in the whole brain white matter for each subject. A repeated measures ANOVA was performed on the mean Krad value within the whole-brain WM mask.

Results: Fig.1 shows results from repeated measures ANOVA comparing subjects with: 1) no mTBI; 2) mTBI with mean SCAT3=25.75; and 3) mTBI with mean SCAT3=37.0. Fig.2 illustrates representative Krad maps from 12 hours post-injury (A-C) and 8 days post-injury (D-F) scans. Healthy control (A,D), low SCAT3 (B,E), and high SCAT3 (C,F). All images are windowed and leveled according to the provided colorbar.

Discussion: Our results indicate that radial kurtosis is a promising biomarker to quantify mTBI severity and longitudinal evaluation of recovery. The mean Krad value in whole-brain WM is significantly lower in more severe mTBI, with severity measured by a standardized self-report symptom checklist. Statistically significant differences between groups persisted in both initial and follow-up scans. Interestingly, subjects with higher SCAT scores had lower Krad in the follow-up scans. While this could be due to some bias in this relatively small subject population, it could also be due to persisting widespread physicochemical changes that lasted 8 days or longer. Of note, MD, FA, and Kax did not show significant differences between groups. Our study does not rely on ROI analysis, so it is independent from the location of the concussion. This also indicated that the injury-related changes could be relatively widespread in the brain. While these preliminary findings support our hypothesis, we continue to enroll subjects for more conclusive and generalizable results. It is worth noting that a recent DKI study on mTBI subjects (with various causes of head trauma) reported similar findings, although their first scan was 10 days after injury[2]. Our study focused only on football players and included a scan obtained shortly after the injury, enabling us to observe early changes after trauma.

References: 1. Jensen et al. MRM 53: 1432-1440; 2. Stokum et al, Brain Inj. 2014 Sep 26:1-11. [Epub ahead of print]

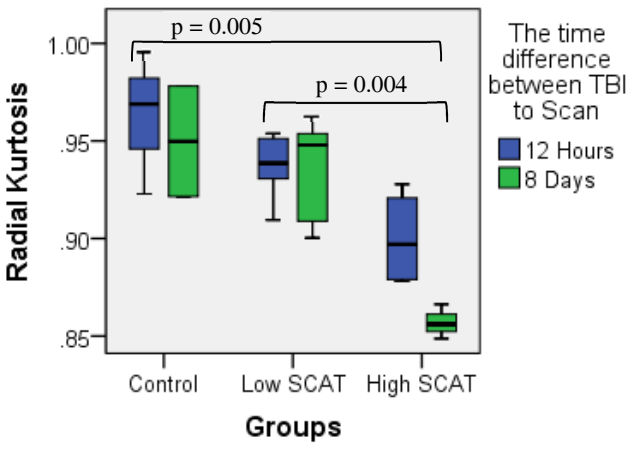

Fig. 1: Repeated measures ANOVA

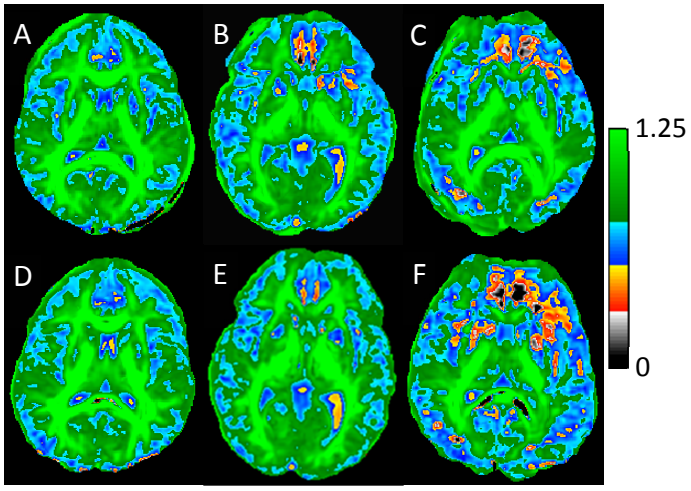

Fig. 2: Radial kurtosis maps