Pathophysiological changes in pericontusional tissue post traumatic brain injury: a diffusion tensor imaging study.

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Introduction: Perilesional tissue is a major component of the traumatic penumbra, where physiology is deranged, but clinical interventions may enhance tissue survival.[1] The time course of imaging changes in such target tissue is not well described. We have used diffusion tensor imaging (DTI) to understand temporal changes in pathophysiology around contusions and traumatic intracerebral haematomas, and identify possible biomarkers.

Methods: 6 patients (mean age 39 (SD±14) years, median Glasgow Coma Score 6 (range 3 to 14)) with TBI who required sedation and mechanical ventilation underwent magnetic resonance (MR) imaging twice in the acute injury period; the first at a median of 28 hours (range 20 to 44) post injury and the second at a median of 182 hours (range 68 to 283 hours). Ethical approval was obtained from the Local Research Ethics Committee and assent from next-of-kin was obtained in all cases. MR imaging was performed using a 3 Tesla Total Imaging Matrix Siemens Tim Trio. The imaging protocol included a 3D T1-weighted structural sequence (MP-RAGE) as well as spin echo planar diffusion weighted imaging which was acquired using 12 non-collinear directions, 5 b values equally spaced from 300 to 1500 s/mm^2 with 4 b = 0 images. The diffusion weighted parameters were: 20 x 20 cm field of view, 100 x 100 matrix size, 63 axial slices, 2 mm slice thickness, TR = 6000ms, TE = 100ms, diffusion sensitizing duration = 23.5ms (δ); with separation (leading edge to leading edge) = 60ms (Δ). FMRIB's Diffusion Toolbox was used to fit a tensor at each voxel and create ADC maps.[2] Four regions of interest (ROI) were manually drawn based on the ADC map of the first scan using Analyze:[3] a hypointense core, a hyperintense region surrounding the core, a hypointense rim of tissue beyond and an area of normal appearing brain away from the contusion (see Figure 1). To assess how the initially contused tissue may change over time the second ADC map was coregistered to the first using the vtkCISG normalised mutual information algorithm[4] and histogram analysis was performed to calculate the mean ADC in the ROIs on both scans. In order to determine the volumetric evolution of the lesions the same areas were identified on non-coregistered images and the volumes calculated.

Results: The median ADC (interquartile range(x10^{-3}mm^2/s)) in normal appearing brain did not change overtime (0.80 (0.7 to 0.9) Vs 0.86 (0.8 to 1.0) p=0.7).The three pericontusional regions were consistently present except in one patient where the hypotintense rim was no longer visible on the second scan. In all patients the ADC values increased in both the core and rim regions. The median ADC in the rim significantly increased from 0.61 (0.5 to 0.7) to 0.82 (0.7 to 0.9)(p=0.02). The core ADC also increased from 0.46 (0.2 to 0.6) to 0.76 (0.6 to 1.0)(p=0.02). The hyperintense region decreased in all but one patient with an overall significant decrease of 1.27 (1.1to1.5) to 1.19 (1.0 to 1.4)(p=0.02). The volume (median, interquartile range) of hypointense rim decreased in all but one patient but overall the change was non significant (scan1 280(72 to 570), scan 2 80(48 to 304)p=0.313). In comparison the volume of core of the lesions increased in all but one (scan1 340(52 to 690), scan2 224(58 to 1392)p=0.313). In all patients the volume of hyperintense rim increased (scan1, 804(280 to 1270), scan 2, 4036(718 to 7478)p=0.031).

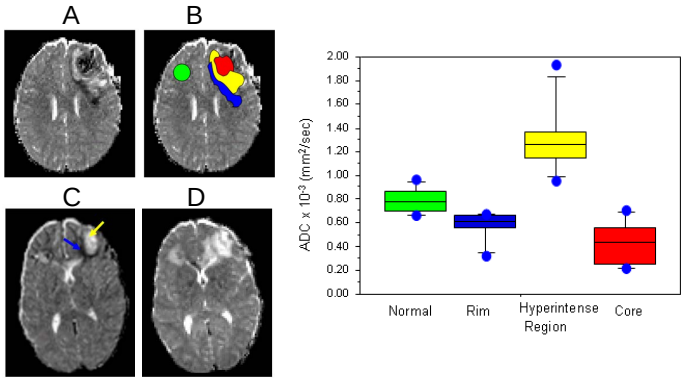

Figure 1: The top ADC map (A and B) shows a left frontal contusion demonstrating normal appearing brain (green), a contusional core (red), pericontusional hyperintensity (yellow) and a hypointense rim (blue). The box plots corresponds to the median ADC for all patients in scan 1 for these regions. The lower ADC maps are from a patient imaged approximately 44 hours (C) and the 142 hours (D) post injury. They show a left frontal contusion with pericontusional hyperintensity (yellow arrow) and a hypointense rim (blue arrow). The hypointense rim can no longer be seen by the second scan and the hyperintense region appears to be enlarged.

Discussion: This study describes the heterogeneity within contusions and their evolution following acute TBI. The changes seen around focal lesions within the first 48 hours post injury appear to be characteristic with all lesions showing three regions; a core, an area of raised ADC around the core and a thin rim of hypointensity. While some lesions showed these regions more clearly than others this pattern was consistently in patients in the first scan. Over time, the increase in ADC in the hypointense core is likely to represent the changing stages of haematomas. The early reduction in ADC in the hypointense rim may represent cytotoxic oedema, indicating the tissue that may be experiencing critical energy failure, perhaps due to microvascular changes.[5] The hyperintense region, which may represent vasogenic oedema, enlarges over time, pushing into and incorporating the hypointense region.

Conclusions: This study describes the heterogeneity within lesions and their evolution following acute TBI. More frequent imaging might demonstrate an advancing low ADC region of spatially progressive perilesional energy failure.

References

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