Dynamic Contrast Enhanced MRI to Detect Vascular Injury in a Rat Model of Traumatic Brain Injury
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Introduction
Traumatic brain injury (TBI) is an important public health problem, with 1.4 million incidents annually in the US1. While computed tomography remains the standard of care for acute TBI management, MRI-based measures are being investigated as potential markers of injury and as specific markers for a variety of therapeutic interventions. Direct brain trauma causes injury to both the brain tissue as well as the related vasculature. We sought to investigate whether interferon-Beta 1, a drug that stabilizes the blood brain barrier (BBB) and has anti-inflammatory properties2, would be effective in a rat model of TBI and whether dynamic contrast enhanced (DCE) MRI could be used to monitor its effect on BBB disruption3.

Materials and Methods
Rats were exposed to a controlled cortical impact (CCI) centered over the left motor cortex (1.1 mm Bregma, 2.5 mm lateral) at a depth of 2 mm, and underwent in vivo MRI within 30 minutes of injury. A multi-echo spin echo sequence was used for T2 mapping at a resolution of 118 μm2 and slice thickness of 0.5 mm. T1 was measured from a series of T1-weighted gradient echo images with variable flip angles. DCE was performed using a T1-weighted gradient echo sequence at a temporal resolution of 10 s and a spatial resolution of 234 μm2 and 0.5 mm slice thickness centered over the lesion before and during a intravenous bolus injection of Gd-DTPA (Magnevist). A post-contrast T1-weighted spin echo was acquired at the completion of the DCE assessment at the same resolution as the T2 image. DCE was analyzed using the reference region model3, assuming a \( k^{trans} \) of 0.1 min\(^{-1}\) and \( V_e \) of 0.1 for muscle. A cohort of rats (n=8) were administered interferon beta-1b (Betaseron; 1 μl/g body weight i.v.) within 6 hours post injury for 3 consecutive days. Saline was administered similarly to control rats (n=9). Rats underwent MRI again at 3, 7, and 30 days post-injury. All images were registered to a common space using ANTS software and quantified with a region of interest analysis. The fractional injured volume (greater than 2 s.d. of the contralateral hemisphere) was quantified for T2, post-contrast T1(Gd), \( k^{trans} \), and \( V_e \).

Results
Within 30 minutes of injury, extensive BBB disruption was the most striking feature in the lesioned cortex, with less visible edema. Spatially, Gd leakage coincided with the periphery of the lesion, suggesting greater vascular shearing in these areas. By day 28 post-injury, the lesion consisted of a fluid-filled cavity. Interferon-Beta treated animals were not significantly different than control animals in any of the measures at any time point. In saline-treated animals, T2 in the acute phase was a greater predictor of eventual lesion volume than either semi-quantitative (enhancing volume) or quantitative (\( k^{trans} \) and \( V_e \)) indicators of BBB disruption. On the other hand, acute neuroimaging markers were poor predictors of sub-chronic to chronic functional abnormalities (foot faults), although the lesion volume at the endpoint (day 28) had a significant correlation with foot faults at the same time point.

Discussion and Conclusions
Although the BBB was severely disrupted in the hyperacute and acute phases of injury, it was uncorrelated with either the T2 lesion volume at day 28 or foot faults, and interferon beta-1b did not alter the course of injury. It is possible that the vascular shearing in this model is too great for pharmacological intervention. Moreover, compared to conventional contrast-enhanced T1-weighted imaging, DCE MRI did not seem to offer significantly greater pathological insight or sensitivity. In severe TBI, conventional T2 weighted imaging and post-contrast T1-weighted imaging may be sufficient to determine tissue and vascular injury severity, respectively.