

## Blood-Brain Barrier Permeability Measured by DCE MRI Predicts Perihematomal Edema Diffusivity

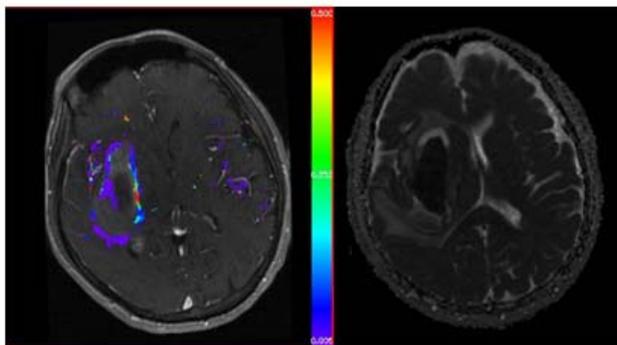
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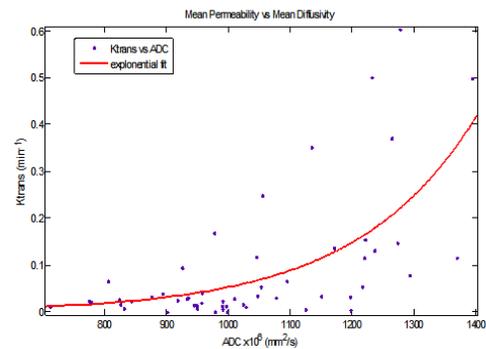
**Introduction:** Spontaneous intracerebral hemorrhage (ICH) is one of the deadliest forms of stroke. Secondary brain injury and edema formation contribute to high morbidity and mortality among ICH patients. Although the exact mechanisms of edema formation are not known, blood-brain barrier (BBB) disruption is potentially an important factor in the formation and progression of perihematomal edema. This study aims to quantify BBB injury by DCE MRI and to examine its relationship with perihematomal diffusivity, as a measure of vasogenic edema severity, utilizing diffusion weighted imaging (DWI).

**Materials and Methods:** Eight prospectively enrolled patients from the Diagnostic Accuracy of MRI in Spontaneous intra-cerebral Hemorrhage (DASH) study were examined using DCE MRI and DWI at approximately one week after symptom onset. All imaging was performed on a 1.5T GE Signa Excite scanner. Proton density weighted (PDW) and DCE MRI scans were used to map the native T<sub>1</sub> times using a double-angle method. Flip angles were 5° for the PDW scan and 30° for the DCE MRI scan. PDW scanning was immediately followed by the DCE time series scans. To obtain PDW and DCE MRI scans, axial spoiled gradient echo sequence were used with scan parameters as follows: TR/TE 7.8/3.4ms, slice thickness 5mm, 12 slices, FOV 220mm, matrix size 256x256, temporal resolution 14 sec/volume). In addition, diffusion-weighted single-shot spin-echo EPI scans were performed with the following parameters: GRAPPA acceleration factor=3, b value=1000 sec/mm<sup>2</sup>, TR/TE=3000ms/60ms, slice thickness=5mm, flip angle=90°, FOV=240mm, matrix size=192x192. For DCE a 0.1 mM/kg Gd-DPTA bolus was administered following by the time resolved SPGR scan. Total acquisition time for DCE MRI images was 420 seconds. An in-house written software developed in MATLAB (Mathworks, Natick, MA) was used for motion-correcting and co-registering PDW and DCE MRI images. Thereafter, CINETool, an investigational pharmacokinetic analysis software package (GE Healthcare, Waukesha, WI), was used for processing the DCE MRI data. Here, contrast agent dynamics in the brain tissue and a two-compartmental general kinetic model were used to estimate the forward leakage rate ( $K^{trans}$ ) at the region of interests. The vascular input function (VIF) was selected semi-automatically at the sagittal sinus. Regions of interests were placed immediately surrounding to the hematoma. To perform the BBB permeability analysis, control ROIs were chosen at the homologous location on the contralateral brain hemisphere. Wilcoxon signed rank test was used to analyze the forward leakage rates obtained from the lesion and control ROIs. Apparent diffusion coefficient (ADC) maps were co-registered with fluid attenuated inversion recovery (FLAIR) images using Medical Image Processing Analysis and Visualization (MIPAV) software. The rim surrounding the hematoma was outlined on FLAIR images and mean ADC values for these ROIs were calculated. EPI-distortions were negligible for the regions analyzed. Correlation between ADC values and BBB permeability values was estimated using Spearman Rank test.

**Results:** Increased BBB permeability was observed at the region immediately surrounding the hematoma at one week after symptom onset. Forward leakage rate at the rim was 0.044 min<sup>-1</sup> (0.016-0.115) compared to 0.004 min<sup>-1</sup> (0-0.012) at the control ROI which can be considered negligible (Figure 1). ADC values in the region surrounding the rim were found to be 1001 (877-1143) x 10<sup>-6</sup> mm<sup>2</sup>/sec. ADC values measured at one week after symptom onset highly correlated with BBB permeability at the ROI (R=0.58, p<0.0001)(Figure 2). Mean ADC values for each patient were also correlated with mean BBB leakage rate measured for each patient (R=0.74, p=0.041).



**Figure 1** Color coded permeability (left) and ADC maps (right) of a patient. Increased permeability surrounding the hematoma and increased diffusivity are clearly visible.



**Figure 2** Correlation between BBB permeability and diffusivity in the region surrounding the hematoma is shown. Increased BBB injury is associated with high ADC values.

**Discussion and Conclusion:** In this study, we showed that BBB permeability assessed by DCE MRI correlates with ADC values in the region surrounding the hematoma at one week after symptom onset. Our findings suggest a strong relationship between BBB injury and severity of the vasogenic edema. A potential explanation would be a common injury process causing both BBB disruption and vasogenic edema. However a more likely interpretation is that severe BBB injury promotes the formation of vasogenic edema. Therapies aimed at limiting BBB injury might provide further insight into the formation and evolution of perihematomal vasogenic edema. DCE MRI and DWI might be used as surrogate markers of BBB injury and edema formation and evolution in spontaneous intracerebral hemorrhage.

**References:** 1. Mayer SA et al., Perilesional blood flow and edema formation in acute intracerebral hemorrhage: a SPECT study. *Stroke*. 1998; 29: 1791–1798  
2. McAuliffe et al., Medical image processing, analysis and visualization in clinical research, *CBMS '01: Proceedings of the Fourteenth IEEE Symposium on Computer-Based Medical Systems*, IEEE Computer Society, Washington, DC, USA (2001), p. 381.

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