Assesment of Blood-Brain Barrier Injury Following Acute Intracerebral Hemorrhage by DCE MRI

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Introduction: Blood-brain barrier (BBB) disruption as well as perihematomal injury and edema are commonly observed as a result of spontaneous intracerebral hemorrhage (ICH). BBB injury is potentially an important pathophysiological factor in secondary brain injury caused by ICH [1]. The aim of this study was to detect changes in BBB permeability and quantify BBB injury following acute ICH by using dynamic contrast-enhanced (DCE) MRI.

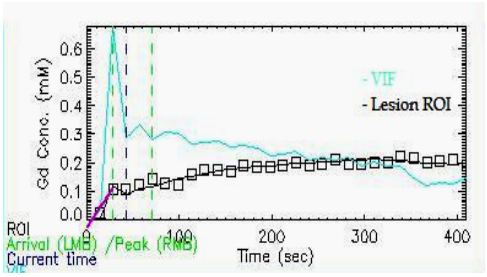

***Figure 1**. Gd concentration vs. time graph. The change of Gd concentration with time is used to derive the estimates of forward leakage, leakage space volume and fractional plasma volume. VIF plot (blue), data and model fit for the lesion ROI (black) are shown.*

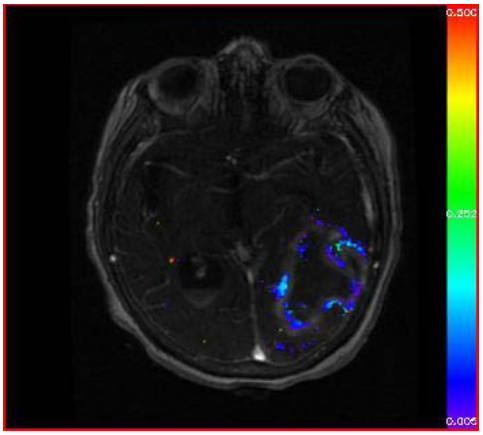

***Figure 2**. Color-coded forward leakage (Ktrans) map showing increased BBB permeability surrounding the hematoma.*

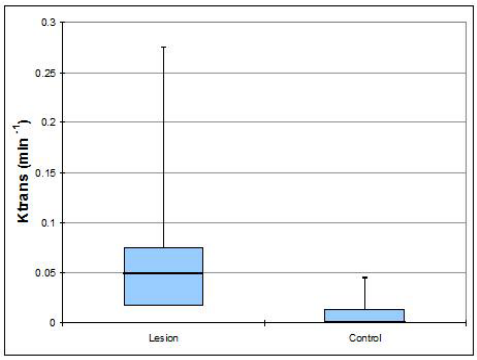

***Figure 3**. Median forward leakage (Ktrans) values (black) and interquartile ranges(blue) for lesion ROIs and control ROIs ($p<0.001$)*

Material and Methods: Sixteen patients (9 females aged 66.0±9.5 years, and 7 males aged 70.7±13.0 years) with intracerebral hemorrhage were examined approximately one week (7.6±1.6 days) after symptom onset. Subjects were imaged on a 1.5T GE Signa Excite scanner. Low flip angle (5º) proton density weighted (PDW) images together with the matching baseline scans (i.e. prior to contrast arrival) from the DCE-MRI scan (flip angle 30º) served to map the native T_1 times using a double-angle method. Scan parameters were identical for the PDW and DCE-MRI scans except for the flip angle and were as follows: axial spoiled gradient echo sequence (TR/TE 7.8/3.4ms, slice thickness 5mm, 12 slices, FOV 220mm, matrix size 256x256, temporal resolution 14 sec/vol). Following the PDW scan, 0.1 mM/kg Gd-DPTA was administered and DCE MRI images were obtained over a 420sec period. Thereafter, motion correction and coregistration were performed using in-house software developped in MATLAB (Mathworks, Natick, MA). Data were processed using CINETool, an investigational pharmacokinetic analysis software (GE Healthcare, Waukesha, WI). Two-compartment pharmacokinetic model parameters (forward leakage rate Ktrans, leakage space volume v_e and fractional plasma volume f_{pv}) were derived using the dynamics of Gd-DTPA in the brain tissue (Fig 1) [2]. Vascular input function (VIF) was measured by semiautomatic selection of a region of interest in the sagittal sinus. The lesion region of interest (ROI) was selected to cover the entire rim surrounding the hematoma. A control ROI was placed on the homologous location on the contralateral side. Parameter values obtained from the lesion and control ROIs were analyzed using Wilcoxon signed rank test.

Results: Areas of increased permability were identifiable on the color-coded K_{trans} maps (Fig 2). Comparison of the model parameters K_{trans} and v_e revealed a significant difference between the lesion and control ROIs. The median(IQR) forward leakage rate for the lesion ROI was 0.049 min^{-1} (0.016-0.075) and median(IQR) forward leakage rate for the control ROI was 0.003 min^{-1} (0-0.013) ($p<0.001$) (Fig. 3). Half of the patients had no BBB leakage (K_{trans}=0 min^{-1}) in their control ROI and the others had some increase in BBB permeability in their control ROIs, which was significantly less than in their lesion ROIs ($p=0.008$).

Discussion and Conclusion: This study shows that DCE MRI may be used to assess BBB permeability following ICH. BBB permeability is significantly increased in the region immediately surrounding the hematoma 1 week after ICH onset. The relationships between loss of BBB integrity measured by DCE MRI, perihematomal injury and clinical outcome following ICH need further study.

References: 1. Yang GY, et al. J Neurosurg, 1994, 81(1): p.93-102.
2. Ferrier MC, et al., Neoplasia, 2007, 9(7): p.546-555

Acknowledgements: This work was supported by the NIH (ROI NS034866-08, 2R01EB002711, 1R21EB006860) and the Neurocritical Care Society Career Development Fellowship in Cerebrovascular Disease and Neurotrauma.