Factors Affecting the Detection of Permeability Derangements in Perfusion Imaging of Stroke Patients

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Background: In acute ischemic stroke (AIS) patients, damage to the blood-brain barrier (BBB) can ultimately lead to the most feared complication of thrombolytic therapy, intracranial hemorrhage (ICH). MRI evidence of breakdown in the BBB has been linked to subsequent ICH in animals and in humans. Recent studies have demonstrated that leakage of contrast during PWI of AIS patients due to increased permeability may be a sensitive predictor of subsequent hemorrhagic transformation.(1;2) Currently, however, no technique using perfusion-based permeability imaging (PPI) in stroke patients has been able to quantify permeability. Furthermore published methods for PPI in AIS have been poorly described and not rigorously tested with basic MR principles.
Hypothesis: The signal change caused by contrast leakage through the BBB is dependent on the parameters of the acquisition which need be corrected for in order to quantify permeability.
Methods:
PPI algorithm: Damage to the BBB results in contrast extravasation into the parenchyma during the course of a PWI acquisition. This affects the recorded signal by introducing a T_1 component to what is primarily a T_2* weighted signal. In the absence of BBB derangements, changes in tissue contrast agent concentration are measured as changes in relaxivity with the equation:(3)

1) $\Delta R2^*(t) = (-1/TE)\ln(S(t)/S_0)$

Where TE is the time to echo, S(t) is the signal intensity in the voxel at time t, and S_0 is the baseline signal intensity prior to delivery of the contrast bolus. When taking into consideration the effects of extravasation, the measured signal is more accurately characterized by adding a term to equation (1) to account for T_1 effects:(3)

2) $$\Delta R2^*(t)_{measured} = \Delta R2^*(t) - \frac{TRe^{(\frac{-TR}{T_1})}}{TE(1-e^{(\frac{-TR}{T_1})})} R_1 C_{tissue}(t)$$

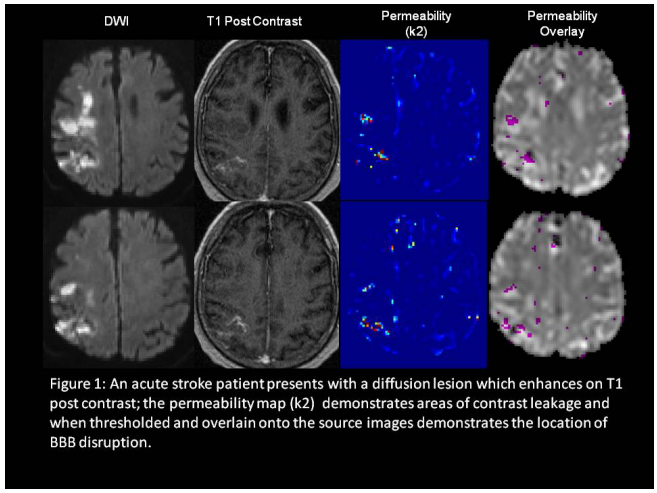

Figure 1: An acute stroke patient presents with a diffusion lesion which enhances on T1 post contrast; the permeability map (k2) demonstrates areas of contrast leakage and when thresholded and overlain onto the source images demonstrates the location of BBB disruption.

Patient	TR (msec)	TE (msec)	Field (Tesla)	K_2 Measured	Correction factor WM	Correction factor GM	K_2 WM Corrected	K_2 GM Corrected
1	1500	40	3	0.09	41.4	96.7	0.002264	0.000969
2	2000	60	1.5	0.10	15.1	26.4	0.006962	0.003985
3	3350	62	1.5	0.24	4.87	11.3	0.050784	0.021959
4	1500	40	3	0.10	41.4	96.7	0.002521	0.001079
5	3350	62	1.5	0.02	4.87	11.3	0.004087	0.001767
6	1460	52	1.5	0.06	25.9	41.1	0.002379	0.001504
7	1330	45	1.5	0.03	32.9	50.9	0.001017	0.000658
8	1500	40	3	0.02	41.4	96.7	0.000595	0.000255
9	1670	60	1.5	0.05	19.3	31.8	0.002652	0.001615

Where TR is the time to repetition, R_1 is molar T_1 relaxivity of the contrast agent, and $C_{tissue}(t)$ is the concentration of contrast in the tissue at time t. This T_1 affect can be modeled as a percent of the CBV over time as described by Boxerman et al.(4) referred to as K_2. Thus the K_2 values measured are relative to the T_1 properties of the sequence acquired.
Imaging: Nine patients were identified from our stroke imaging database who underwent perfusion MRI followed by post contrast-T_1 imaging who demonstrated parenchymal enhancement. K_2 permeability maps were generated from the perfusion source data (figure 1). Regions of interest (ROIs) were drawn around areas of contrast leakage. Mirror ROIs were then reflected into the contralateral hemisphere to establish control K_2 values.

Using equation (2) a correction factor was generated for each patient based on the TR, TE, T_1 and R_1 of the scan. T_1 varies by tissue type and since T_2* images are generally not of sufficient quality to reliably segment grey and white matter, a correction factor was calculated for both grey and white matter using published norms.(5) All patients received Gd-DTPA and thus R_1 varied only by field strength.(6) This correction factor was then divided into the K_2 values to make them comparable between scans.
Results: The uncorrected K_2 values had a mean of 8.2%±13.7 for the enhancing hemispheres and a mean of 0.8%±1.0 for the control hemispheres. Comparing the two hemispheres across the patient cohort with a paired t-test revealed a statistically significant difference (p=0.006). The correction values, displayed in the table, varied considerably with the exception of the three patients who were scanned under a uniform research protocol. Even within patients, the difference between the expected signal change in white vs. grey matter was substantial.
Conclusions: While PPI offers a novel and potentially quantifiable method for measuring damage to the BBB, application of this method must account for basic MR principles. Choice of scan parameters may enhance or degrade our ability to detect BBB derangements from PWI.

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