# Assessment of Longitudinal Blood-Brain Barrier (BBB) Changes Using MR Tracer Kinetics in Human Brain Infarction

**H-S. Liu[1,2], H-W. Chung[1,2], M-C. Chou[1,2], C-Y. Wang[1,2], C-J. Juan[1,2], D-B. Guo[1,2], N-Y. Cho[1], and C-Y. Chen[1,3]**

[1]Radiology, Tri-Service General Hospital, Taipei, Taiwan, Taiwan, [2]Electrical Engineering, National Taiwan University, Taipei, Taiwan, Taiwan, [3]School of Medicine, National Defense Medical Center, Taipei, Taiwan, Taiwan

## Introduction

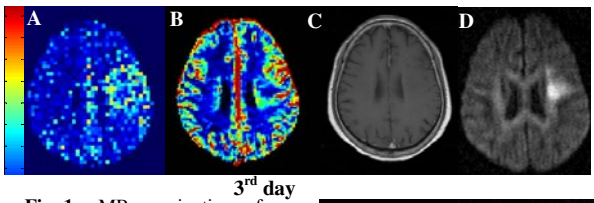
The tracer kinetic models of MR perfusion-weighted images have been widely used in the measurement of the angiogenetic activity in patients with brain tumors, while using the same model in evaluating the pathophysiologic process of ischemic stroke are relatively rare. Since the pathologic evolution of infarct regions may have a close link with blood-brain barrier (BBB) defects [1], we aim to apply the experimental data in this study to investigate whether the infarct growth can be evaluated by the known pharmacokinetic models focusing on contrast leakage profile across the disruptive BBB. It is conceivable to assume that the changes in circulation phase on perfusion-weighted acquisitions may be directly reflected on the status of the endothelial permeability calculations, hence predicting the areas of ischemic brain injury at the earlier stage possible.

## Materials and methods

A longitudinal study in 19 patients with ischemic strokes undergoing at least three times MR follow-up imaging was recruited in this study. All MR conventional and T2* perfusion-weighted MR images (TR/TE=1000/44ms, matrix=128×128, flip angle=90° at 1-second interval with 60-75 dynamic time points) were performed on a 1.5T scanner (Magnetom Vision+; Siemens, Erlangen, Germany). Five of the 19 patients had their MR examinations performed at the acute stage (within 6-48 hours); twelve at the early subacute (within 3-4 days); fourteen at the late subacute (within 7-9days); thirteen at the early chronic (within 10-15 days); and nine at the late chronic stage within 30-31 days after onset of symptoms, were analyzed for vascular permeability maps using the first-pass pharmacokinetic (FPPM) model proposed by Glyn Johnson et., al. [2]. The method used the estimate of vascular contrast medium concentration acquired from normal white matter to allow simultaneous mapping of endothelial permeability ($K^{trans}$) and the fractional plasma volume ($v_p$) of brain tissues. A region of interest was placed in the area of ischemic lesion with significantly elevated values in $K^{trans}$ maps, with contralateral area of normal white matter drawn as the referenced standard to ensure that our calculated values are in reasonable agreement with the literatures. The corresponding calculations of $v_p$ in the same locations were also measured.

## Results

Fig. 1. shows the MR examinations of early onset and late chronic stages together with the calculated $K^{trans}$ and the $v_p$ maps for one patient. $v_p$ values of normal white matter extracted from FPPM model have an approximate value of 0.01 which is consistent with the literature in the previous studies. The $K^{trans}$ map shows better contrast between ischemic lesion and normal brain tissues as compared to that of $v_p$ map and contrast-enhanced T1-weighted images (CET1WIs). It clearly delineates the abnormal area, while the CET1WIs show no significant enhancement at early ischemic stage (Fig. 1A vs. 1C). Both peak values of $K^{trans}$ and $v_p$ occur at the onset of the late subacute state (the 7th day) as shown in Fig. 2.



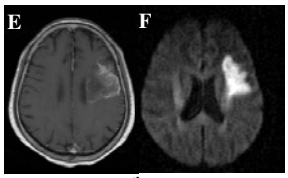




**Fig. 1.** MR examinations of one patient with stroke at two different ischemic phases. Upper (from left to right): $K^{trans}$ map, $v_p$ map, CET1WI and diffusion-weighted image (DWI) at the 3rd day after stroke. Lower (from left to right): CET1WI and DWI at the 30th day after the onset of symptoms.

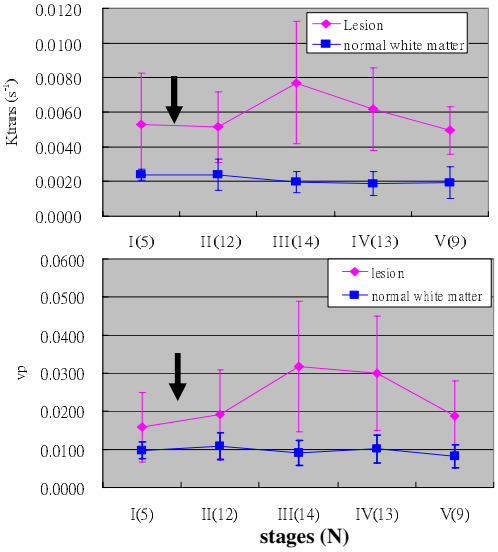



**Fig. 2.** Pattern of longitudinal measurements of FPPM model-derived parameters.Upper: $K^{trans}$ values. Lower: $v_p$ values
N: number of patients being analyzed
I: acute stage
II: early subacute stage
III: late subacute stage
IV: early chronic stage
V: late chronic stage

## Discussion and conclusions

Instead of developing a differential diagnostic tool with a sensitivity superior to the conventional diffusion-weighted MR imaging in detecting acute ischemic stoke, the present study was designed to visualize longitudinal infarct changes by assessing the imaging findings using the tracer kinetics. We applied the patients' data in our institute to confirm that the FPPM model could be an effective means in detecting brain damage in patients with ischemic stroke at the onset of first few days. These data suggest that only at the late ischemic phase can a leakage of contrast medium lead to a parenchymal enhancement such that BBB disruption is severe enough to be monitored in contrast-enhanced T1-weighted images, while the abnormal permeability performance can already be clearly found with a higher sensitivity to the hemodynamic changes of lesion areas at the acute stage for these patients. The progression of ischemic infarction appears to evolve following a similar tendency between the vascular plasma and the permeability calculations with the exception that the opposite sign of slope from the acute stage to the subacute one (arrows in Fig.2). With an increasing pattern from acute to late subacute stage, both $K^{trans}$ and $v_p$ progressively return to a less enhanced contrast at late chronic stage (Fig. 2). It maybe postulated that the reduction of blood flow perfusion at this stage gives rise to a pseudo-repaired BBB phenomenon in brain infarction. The correlation between measurements of $K^{trans}$ and $v_p$ can be predicted because $K^{trans}$ is directly affected not only by endothelial permeability surface area product, but also by blood flow perfusion efficiency. Hemorrhage or large area of cortical necrosis was not included in the ROI calculations because the poorly perfusion-related signal loss would invalidate the computation of hemodynamic analysis.

**References** [1] I-J Huang, et. al., Radiology, 2001. 221: p. 35-42 [2] G. Johnson., et al., MRM, 2004. 51(5): p. 961-8.