

Oxygen Metabolic Index as a Predictor of Tissue Viability in Acute Ischemic Stroke Patients

H. An¹, A. L. Ford², K. Vo³, W. J. Powers⁴, J-M. Lee², and W. Lin¹

¹Radiology, University of North Carolina at Chapel Hill, Chapel Hill, NC, United States, ²Neurology, Washington University in St. Louis, St. Louis, MO, United States, ³Radiology, Washington University in St. Louis, St. Louis, MO, United States, ⁴Neurology, University of North Carolina at Chapel Hill, Chapel Hill, NC, United States

Introduction

During an acute ischemic stroke, alterations in cerebral blood flow and metabolism are highly complex and dynamic. Approaches capable of delineating viable tissue from irreversibly injured tissue will likely have clinical utility for acute stroke management, allowing patients with potentially viable tissue to receive therapy beyond the current thrombolytic window. Magnetic resonance diffusion and perfusion imaging have been studied extensively for this purpose, however one limitation of perfusion-based thresholds for tissue injury is its dependence on elapsing time from stroke onset¹. Several lines of evidence derived from PET studies suggest that measures of cerebral metabolic rate of oxygen utilization (CMRO₂) may identify viable tissue at risk for infarction in a time-invariant manner^{2,3}. The need for an onsite cyclotron has limited PET's clinical utility in acute stroke. In this study, an MR derived cerebral oxygen metabolic index (MR_OMI), an analogue to PET CMRO₂, was acquired in acute ischemic stroke patients at two early timepoints (< 3.5 hours and 6 hours) to assess tissue viability either with or without early reperfusion.

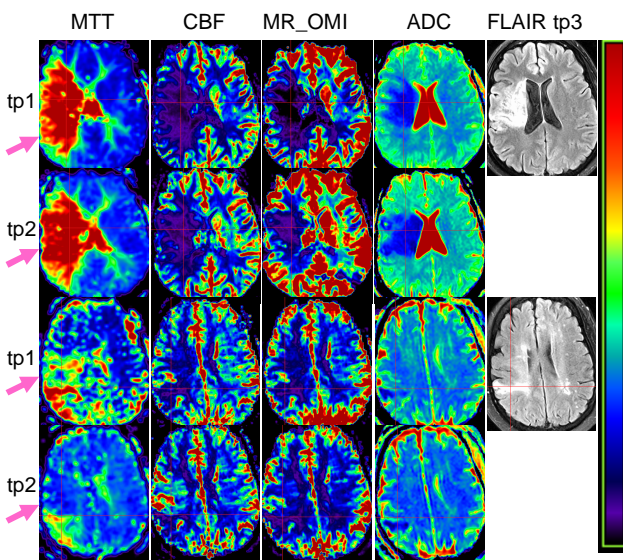


Figure 1. Representative MTT, CBF, MR_OMI, ADC tp1 and tp2 and tp3 FLAIR from two patients with minimal reperfusion (first two rows) and moderate reperfusion (lower two rows). The range of the colorbar is from 0 to 20 seconds for MTT, 0 to 150 ml/100g/min for CBF, 0 to 60 for MR_OMI, and 20 to 220×10⁻⁵ mm²/s for ADC.

because little tissue infarcted after reperfusion in 4 patients. Figure 2 shows the histograms of tp1 nMR_OMI in dead and alive tissue without reperfusion (Figure 2, upper row) and with reperfusion (Figure 2, lower row). Regardless of reperfusion status, dead tissue (red) always showed considerably lower values of nMR_OMI compared to viable tissue (green), suggesting that nMR_OMI can be used to separate irreversibly injured tissue from viable irrespective of reperfusion status.

Discussion and Conclusions

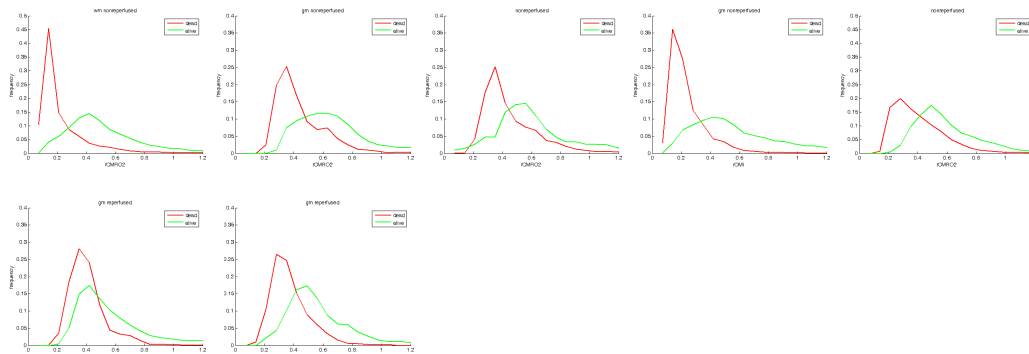


Figure 2. Histograms of nMR_OMI in the dead (red) and alive (green) tissue without reperfusion (upper row) and with reperfusion (lower row) from six different patients. (One patient had both reperfusion and non-reperfusion ROIs and has two representative histograms.) The first histogram in the upper row corresponds to the patient from Figure 1, Patient 1. The first graph in the lower row corresponds to the patient from Figure 1, Patient 2.

Reference

1. Jones et al, J Neurosurg, 1981, 773-782; 2. Powers et al, JCBFM, 1985, 600-608; 3. Frykholm et al, Acta Neurol Scand, 2000, 18-26.

Methods

Six acute ischemic stroke patients were prospectively studied. Two sequential MR scans were acquired within 3.5 hours (tp1) and at 6 hours (tp2). At tp1 and tp2, the following sequences were obtained: diffusion weighted imaging (DWI), T1, T2, FLAIR, asymmetric spin echo sequence (ASE), and perfusion weighted images (PWI) using dynamic susceptibility contrast (DSC). At one month after the stroke, FLAIR images were acquired to delineate the final infarct region. Five patients received intravenous tPA while one patient did not due to contraindications. Mean transit time (MTT) and cerebral blood flow (CBF) were computed from PWI. Oxygen extraction fraction (MR_OEF) and apparent diffusion coefficient (ADC) maps were obtained from the ASE and DWI images, respectively. MR_OMI was then computed as a product of MR_OEF and CBF. A rigid image registration was performed to align all images across all tps for each patient. A voxel with MTT > 4 seconds of the mean contralateral MTT was defined as "hypoperfused". A "reperfusion" voxel was defined as a voxel which was hypoperfused at tp1 but not at tp2. Final infarcted tissue was manually delineated from new hyperintense regions on FLAIR images at tp3. Based on reperfusion and final infarct status, four ROIs were defined: reperfusion dead, reperfusion alive, non-reperfusion dead, and non-reperfusion alive. To minimize the effects of noise, only ROIs greater than 3ml were analyzed. CBF and MR_OMI were normalized (nCBF and nMR_OMI) to the contralateral hemisphere in gray matter and white matter separately, based on tissue segmentation obtained from T1 and T2 images. Histograms of nMR_OMI at tp1 were used to compare dead and alive tissue in the presence and absence of reperfusion seen at tp2.

Results

Reperfusion status varied per patient as shown in Figure 1. Regardless of reperfusion status, lesions defined by PWI (MTT and CBF) at the hyperacute time-point (tp1) tended to be larger than the final lesion. Frequently, ADC at tp1 did not precisely represent the final infarct, and was either larger (Figure 1, Patient 1) or smaller (Figure 1, Patient 2) than the final infarct. The region of reduced MR_OMI on tp1, however, corresponded well to the final infarct. Including ROIs of size 3 ml or greater, non-reperfusion dead and alive ROIs were detected in 5 out of 6 patients, while reperfusion dead and alive ROIs were observed in only 2 out of 6 patients

In this study, we examined the ability of MR_OMI (as a marker of cerebral oxygen metabolism) to predict tissue outcome in six hyper-acute ischemic stroke patients. By using reperfusion at tp2 and final infarct status at 1 month, tissue with different outcomes (alive or dead) was examined in regions with or without reperfusion. We found that tissue destined to die had much lower MR_OMI values than tissue that remained alive, suggesting that MR_OMI is capable of predicting tissue outcome early in acute ischemic stroke. Moreover, MR_OMI predicted tissue outcome in both areas of non-reperfusion and reperfusion. Larger numbers of patients are needed to determine thresholds for core, penumbra, oligemic, and normal tissue. In summary, MR_OMI provides a complementary modality to the existing methods. A multi-modal approach to assess tissue viability non-invasively will likely have profound clinical implications for acute stroke management.