# Magnetic Resonance Imaging in Acute Ischemic Stroke Patients with Mild Symptoms: An Opportunity to Standardize Intravenous Thrombolysis

Tyler A. Brown, BS, Marie Luby, PhD, Jignesh Shah, MD,
Dimitrios Giannakidis, MD, and Lawrence L. Latour, PhD

*Background:* Patients presenting with mild stroke symptoms are excluded inconsistently from intravenous (IV) thrombolysis. We aimed to compare acute magnetic resonance imaging findings in patients with mild symptoms to those with more severe deficits to identify clinically mild patients who might benefit from IV thrombolysis. *Methods:* We retrospectively studied consecutive stroke patients presenting with perfusion deficit who underwent time-of-flight magnetic resonance angiography within 24 hours of time last seen normal. Two raters measured the lesion volumes on diffusion-weighted imaging (DWI) and perfusion-weighted imaging (PWI) with mismatch (MM) calculated as PWI minus DWI. Occlusion site was categorized as "proximal," "distal," or "magnetic resonance angiography-negative" by consensus review. Stroke with mild symptoms was defined as admit National Institutes of Health Stroke Scale score of 4 or less. Values were reported as n (%). *Results:* Ninety-one patients were included; 56 (61.5%) with nonmild and 35 (38.5%) with mild symptoms. After stratifying for occlusion site, there were no differences in PWI and MM lesion volumes for the nonmild versus mild patients ($P = .34$-$.98$ and $P = .54$-$1$, respectively). Furthermore, there was a trend for thrombolyzed mild stroke patients (88%, n = 7 of 8) to more likely have a favorable clinical outcome (discharge modified Rankin score $\leq 2$) versus untreated patients (70%, n = 16 of 23). *Conclusions:* When present, conspicuous vessel occlusions in clinically mild stroke patients are concomitant with similar perfusion deficit and MM volumes in more clinically severe stroke patients. Coupled with a trend toward better outcomes in mild stroke patients who were treated with IV tissue plasminogen activator (t-PA), this could indicate that advanced imaging may be used in standardizing the way these patients are selected for IV t-PA therapy. **Key Words:** Mild stroke—minor stroke—PWI—infarction—volumetric MRI—DWI.
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## Introduction

Stroke patients presenting within the 4.5-hour treatment window determined to have mild symptoms are excluded from thrombolysis in both clinical practice and randomized clinical trials.[1-4] Furthermore, the variability in treatment with thrombolysis of mild stroke patients has been demonstrated in a large Specialized Program of Translational Research in Acute Stroke study.[5] This is in spite of growing evidence that a significant proportion of these patients go on to deteriorate neurologically and experience poor clinical outcomes.[2,6-8] In the few studies that have reported magnetic resonance angiography (MRA) findings for this group, proximal vessel occlusion has been one of the strongest predictors of poor outcome,[7,9,10] with the largest and most recent reporting nearly 50%-75% of patients with significant neurologic deterioration consistent with vessel occlusion.[7]

In addition to occlusion site, diffusion-weighted (DWI) and perfusion-weighted (PWI) magnetic resonance imaging (MRI) can be invaluable in the work-up of stroke. Not only can lesion visualization be useful for excluding stroke mimics,[11] but the presence of significant ischemic penumbra, as estimated by a mismatch (MM) between hypoperfused regions on PWI and ischemic core on DWI has been shown to predict poor outcomes if early reperfusion is not achieved.[12-14] Recent evidence of a similar association specifically in patients with mild symptoms has also been described.[15] However, a complete understanding of how patients with mild symptoms differ from nonmild stroke patients is lacking. Standardization of thrombolysis decision making in mild stroke patients is also warranted.[5]

As such, using multimodal MRI, our purpose was to better characterize the findings of acute ischemic stroke patients with perfusion deficit presenting with mild symptoms to identify a clinically mild subpopulation that might benefit from intravenous (IV) thrombolysis.

## Methods

### Patients

This study is a retrospective analysis of data collected from patients who consented to an ongoing natural history study by the stroke section at the National Institute of Neurological Diseases and Stroke (NINDS). All eligible patients receive multimodal MRI. The appropriate ethics and institutional review boards approved the study. Consecutive patients presenting to Suburban Hospital in Bethesda, MD within 24 hours of time last seen normal between September 2003 and April 2008 were considered for inclusion in the study. Patients were included if they had discharge diagnosis of ischemic stroke; screening MRI containing evaluable DWI, PWI, and time-of-flight (TOF) MRA performed before standard intravenous tissue plasminogen activator (IV t-PA); perfusion deficit in middle cerebral artery territory based on visual imaging confirmation; and admit National Institutes of Health Stroke Scale (NIHSS). Patients deemed to have stenosis without occlusion were excluded. Stroke with mild symptoms was defined as admit NIHSS score of 4 or less and those with nonmild symptoms as admit NIHSS score more than 4.

### Imaging Acquisition

Imaging was performed using a 1.5-T (Twinspeed; General Electric) clinical MRI scanner. DWI and PWI series were acquired colocalized over the entire brain with a superior-to-inferior coverage of 14 cm. Typical imaging parameters for the spin-echo DWI echo-planar series included either 40–3.5-mm- or 20–7-mm-thick contiguous axial oblique sections with $b = 0$ and $b = 1000$ seconds/mm$^2$, trace or isotropically weighted, TR/TE (repetition time/echo time) = 6000-7000/72-90 ms, acquisition matrix of $64 \times 64$-$128 \times 128$, and field of view (FOV) = 22 cm. Typical imaging parameters for the gradient-recalled PWI echoplanar series included 20 contiguous axial oblique slices with single-dose gadolinium contrast injection of .1 mmol/kg through a power injector using 25-40 phase measurements TR/TE = 2000-2200/45 ms, acquisition matrix of $64 \times 64$-$128 \times 128$, 20-7-mm slice thickness, and FOV = 22 cm. The intracranial three-dimensional TOF MRA was acquired in the region of the Circle of Willis with parameters as follows: TR/TE = 39/6.9 ms, flip-angle = 25°; FOV = $24 \times 18$ cm; matrix of $224 \times 160$ for an in-plane resolution of approximately 1 mm, reconstructed to 92 axial images, 1.6-mm thick with a .8-mm overlap.

### Imaging Analysis

DWI and PWI volumes were measured by 2 blinded, independent raters; one (M.L.) having years of experience and previously validated reliability[16,17] and the other (T.B.) trained over a month-long period reading multiple rounds of practice images and receiving detailed feedback. Readers were blinded to data from the clinical presentation including lateralization of the ischemic lesion and any other series from the screening MRI. Measurements were performed using Medical Imaging Processing and Visualization (MIPAV), image analysis software with visualization, segmentation, and editing tools designed specifically for quantitative lesion measurement. Lesions were segmented on a slice-by-slice basis after optimally adjusting the window and level of the image without thresholding. DWI and PWI lesions were identified as hyperintense areas after excluding bilateral and susceptibility artifacts and chronic lesions. The mean transit time maps were calculated as the first moment of the time concentration curves divided by the zeroth moment with no arterial input correction or deconvolution. The volumes were automatically calculated using the