Acute Basilar Artery Occlusion
Diffusion-Perfusion MRI Characterization of Tissue Salvage in Patients Receiving Intra-Arterial Stroke Therapies

Jill L. Ostrem, MD; Jeffrey L. Saver, MD; Jeffry R. Alger, PhD; Sidney Starkman, MD; Megan C. Leary, MD; Gary Duckwiler, MD; Reza Jahan, MD; Paul Vespa, MD; J. Pablo Villablanca, MD; Y. Pierre Gobin, MD; Fernando Vinuela, MD; Chelsea S. Kidwell, MD

Background and Purpose—Diffusion-perfusion MRI in patients with anterior circulation occlusions has demonstrated salvage of threatened tissue after thrombolytic therapy. Similar studies have not been reported with posterior circulation occlusions.

Methods—Patients with acute basilar artery occlusion treated with intra-arterial thrombolytics were studied with multimodal MRI before treatment, several hours after treatment, and at day 7.

Results—Ten patients were studied (9 men, 1 woman). Mean age was 70 years, and median pretreatment National Institutes of Health Stroke Scale (NIHSS) score was 14. In 6 patients imaged before treatment and at day 7, mean pretreatment diffusion-weighted imaging (DWI) lesion volume was 11 cm³, and day 7, lesion volume was 2.6 cm³. Significant mismatch was visualized in all 5 patients with pretreatment perfusion-diffusion imaging (mean, 73%; range, 49% to 99%). Late imaging obtained in 4 of these 5 patients demonstrated that mean posttreatment DWI lesion volume (21 cm³) was less than the mean initial perfusion lesion volume (62 cm³). Although there was no direct correlation between pretreatment DWI volume and initial NIHSS ($r = -0.113$), there was good correlation between pretreatment perfusion-weighted imaging volume and initial NIHSS ($r = 0.72$).

Conclusions—In this first report of diffusion-perfusion MRI in patients with acute basilar artery occlusions treated with intra-arterial thrombolysis, significant mismatch was visualized on pretreatment studies, suggesting that large volumes of salvageable tissue were present. Final infarct volumes were smaller than pretreatment perfusion volumes, suggesting that substantial volumes of tissue were salvaged by thrombolytic reperfusion. (Stroke. 2004;35:e30-e34.)

Key Words: magnetic resonance imaging, diffusion-weighted ■ magnetic resonance imaging, perfusion-weighted ■ penumbra ■ stroke, ischemic ■ thrombolytic therapy

Acute basilar artery occlusion can lead to substantial morbidity and mortality, estimated to be 80% to 90% in patients treated with standard medical care by prior clinical studies.1,2 The advent of thrombolytic therapy has provided one of the first opportunities to substantially improve outcome in patients with otherwise devastating posterior circulation strokes.

Diffusion-weighted imaging (DWI) and perfusion weighted imaging (PWI) are useful tools for assessing patients with acute ischemic stroke.3,4 The region of diffusion-perfusion mismatch is a good and easily operationalized proxy for the penumbral zone.5 In patients with anterior circulation ischemia, salvage of the mismatch region has been demonstrated after recanalization with thrombolytic therapy.6–8

The objectives of our study were to determine the pattern of diffusion-perfusion MRI lesions in patients with acute basilar artery occlusion, to determine whether thrombolytic therapy can salvage at-risk tissue in the posterior circulation, and to correlate the MRI abnormalities with clinical outcome.

Patients and Methods
This analysis was performed as part of an ongoing, prospective study of MRI changes in patients receiving intra-arterial thrombolytic therapy and was approved by the UCLA Institutional Review Board. Patients were included in the current analysis if (1) they presented with symptoms of posterior circulation ischemia, (2) acute basilar artery occlusion was identified at angiography, (3) intra-arterial thrombolytic therapy was administered, and (4) an MRI, including a DWI sequence, was performed before treatment. Thrombolytic regimens included combined intravenous/intra-arterial tissue plas-
minogen activator (tPA) in patients treated within <3 hours or pure intra-arterial tPA or urokinase in those treated >3 hours.\textsuperscript{6}

MRI scans were performed on a 1.5-T scanner (Siemens Vision System) equipped with echo-planar imaging data acquisition capability. Image acquisition, postprocessing, and analysis were performed according to a previously described protocol.\textsuperscript{6}

**Statistical Analysis**

Correlations between clinical outcome (National Institutes of Health Stroke Scale [NIHSS] scores) and MRI lesion volumes are reported as Spearman’s rank correlation coefficients.

**Results**

**Patients and Clinical Outcome**

Ten patients (9 men, 1 woman) with acute basilar artery occlusion meeting inclusion criteria were treated with intra-arterial thrombolysis at our institution between November 1998 and January 2001 (see Table). Mean age was 70 years (range, 39 to 88 years). Median entry NIHSS was 14 (range, 4 to 28). Two subjects had proximal, 5 had mid, and 3 had distal basilar occlusion. The median time interval from symptom onset to pretreatment MRI was 4 hours 10 minutes (range, 2 hours 30 minutes to 30 hours 5 minutes), and median time from recanalization to early posttreatment MRI was 5 hours 55 minutes (range, 3 hours 5 minutes to 18 hours 30 minutes).

Recanalization results showed 1 patient with no (Thrombolysis in Myocardial Infarction [TIMI] 0), 1 with minimal (TIMI 1), 7 with partial (TIMI 2), and 1 with complete (TIMI 3) recanalization.\textsuperscript{9} Two patients developed asymptomatic hemorrhagic transformation, 2 had symptomatic hemorrhagic transformations, and 6 had no hemorrhage. Three patients died within 7 days of treatment, including 1 with failure to recanalize and 1 with symptomatic hemorrhagic transformation. Median NIHSS among survivors showed an improvement from 13 pretreatment to 10 early after treatment, to 7 at day 7. Among the 6 survivors at day 90, median modified Rankin Scale was 2 (range, 0 to 5).

**Imaging Patterns**

Substantial diffusion-perfusion mismatch was visualized in all 5 patients who underwent pretreatment PWI. Mismatch was seen in the brain stem (100%), cerebellum (100%), and posterior cerebral hemispheres (60%).

Mean pretreatment DWI lesion volume was 8 cm\(^3\); mean PWI lesion volume was 51 cm\(^3\). In individual patients, the mismatch volume ranged from 49% to 99% (mean, 73%) of the perfusion abnormality volume. Four patients had pretreatment PWI and early posttreatment DWI studies. The post-treatment DWI mean lesion volume (22 cm\(^3\)) was smaller than the preperfusion mean lesion volume (62 cm\(^3\)), suggesting salvage of penumbral territories at risk as a result of thrombolysis (Figures 1 and 2). In the 6 patients imaged before treatment and at day 7, the mean DWI lesion volume did not enlarge but remained relatively unchanged (mean pretreatment volume, 3.1 cm\(^3\); mean day 7 volume, 2.6 cm\(^3\)). No instances of reversal of a region of initial diffusion abnormality were noted in this sample.

**Clinicoradiological Correlations**

Across the whole cohort, pretreatment DWI lesion volume did not correlate with pretreatment NIHSS score (n=10, \(r=-0.113, P=0.756\)). There was a suggestion of moderate correlation between pretreatment PWI lesion volume and baseline NIHSS (n=5, \(r=0.72, P=0.172\)). In the 6 patients in whom late imaging was preformed, there was not a strong correlation between day 7 DWI lesion volume and day 7 NIHSS (n=6, \(r=0.29, P=0.577\)).

**Discussion**

Treatment of acute basilar artery occlusion remains clinically challenging. In this preliminary study of diffusion-perfusion MRI changes in patients treated with intra-arterial thrombolysis and studied serially with multimodal MRI, we found that diffusion-perfusion mismatch can be visualized clearly in the posterior circulation, including the brain stem, and can be seen in some patients well beyond 6 hours from symptom onset. Moreover, we were able to demonstrate improvement of this mismatch region after basilar artery recanalization with intra-arterial thrombolytic therapy. This improvement may represent therapeutic salvage of the mismatch region; however, a controlled study is required to confirm this.

Several prior reports have begun to assess the role of advanced MRI techniques in acute posterior circulation stroke.\textsuperscript{10,11} Du Mesnil de Rochement and colleagues\textsuperscript{10} studied 4 patients with acute basilar artery occlusions with DWI and MR angiography sequences. They found variable patterns of DWI lesions and clear evidence of basilar occlusion on MR angiography. In our larger series of patients, we additionally report PWI results and correlate these DWI-PWI patterns with clinical outcome.

These findings have important implications for the future of thrombolytic therapy for basilar artery occlusions. The time window for thrombolysis in the posterior circulation may be longer than that in the anterior circulation because of lower risk of hemorrhagic transformation (as a result of smaller infarct volumes), worse outcomes with conventional therapy, and additional pathophysiological differences (including collateral flow patterns) that lead to a slower evolution of irreversible ischemia within this region. Successful thrombolysis with improved clinical outcome has been reported up to 24 hours or longer.\textsuperscript{1,12,13} However, it is also likely that some patients, even when treated within 6 hours of onset, will not benefit from therapy. Multimodal MRI may provide a means to identify those patients who may benefit from both early and late therapy.

We did not identify reversal of diffusion abnormalities in either the brain stem or cerebellum in this initial series of patients. This may reflect in part the later timing of recanalization in these patients compared with anterior circulation cohorts, because diffusion abnormality reversibility is likely a time-dependent phenomenon. Also, our study is limited by small sample size and incomplete imaging data for all patients at all time points. A larger series of patients is required to determine whether reversal can occur in the posterior circulation as in the anterior circulation and, if so, how frequently. In addition, future larger studies are needed.
to determine whether multimodal MRI signatures for penumbral tissue, infarct core, and tissue at heightened risk of hemorrhagic transformation in the brain stem, cerebellum, and posterior cerebral artery territory are similar to those being identified in the anterior circulation.

Our analyses of clinicoradiological correlations confirm and extend previously reported findings that DWI lesion volumes do not significantly correlate with NIHSS scores in patients with posterior circulation ischemia. These results contrast with the more robust correlations of lesions volumes
with clinical outcome measures demonstrated in the anterior circulation. In the posterior circulation, small strategic brainstem infarcts can lead to devastating clinical syndromes, whereas large cerebellar infarcts may cause minimal symptomatology, attenuating the strength of the relationship between lesion volume and clinical functional status. In addition, NIHSS scores may be more weighted toward anterior circulation symptoms (eg, neglect and aphasia).

We did, however, find a suggestion that pretreatment PWI lesion volumes correlate moderately well with pretreatment NIHSS score. This finding suggests that the region of acute synaptic transmission failure (producing clinical deficits) correlates more closely with the region of pretreatment perfusion than diffusion abnormalities. This further supports the role of combined diffusion-perfusion imaging in the hyperacute time window (even in patients with basilar artery occlusions) and its ability to identify patients with large perfusion-diffusion mismatch who may benefit from thrombolysis.

We conclude that in basilar artery occlusion, diffusion-perfusion mismatch on MRI can be visualized clearly throughout the posterior circulation, including the brain stem,
and improvement in this mismatch region can be documented after vessel recanalization.

Acknowledgments
This study was supported in part from grants from the American Heart Association (0170033N, C.S.K.), by a fellowship grant from the National Stroke Association (C.S.K.), and by grants K23 NS 02088 (C.S.K.), NS 39498 (J.R.A.), and K24 NS 02092 (J.L.S.) from the National Institute of Neurological Disorders and Stroke.

References
Acute Basilar Artery Occlusion: Diffusion-Perfusion MRI Characterization of Tissue Salvage in Patients Receiving Intra-Arterial Stroke Therapies


Stroke. 2004;35:e30-e34; originally published online January 22, 2004; doi: 10.1161/01.STR.0000113783.45745.BE

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2004 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/35/2/e30

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Stroke can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Stroke is online at:
http://stroke.ahajournals.org//subscriptions/