Magnetic Resonance Imaging of Acute Stroke

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KEYWORDS

• MR imaging • Stroke • Emergency imaging • MR perfusion • MR angiography

KEY POINTS

- Neuroimaging plays a critical role in the management of patients with acute stroke syndrome, with diagnostic, therapeutic, and prognostic implications.
- A multiparametric magnetic resonance (MR) imaging protocol in the emergency setting can address both primary goals of neuroimaging (ie, detection of infarction and exclusion of hemorrhage) and secondary goals of neuroimaging (ie, identifying the site of arterial occlusion, tissue characterization for defining infarct core and penumbra, and determining stroke cause/mechanism).
- MR imaging provides accurate diagnosis of acute ischemic stroke (AIS) and can differentiate AIS from other potential differential diagnoses.

INTRODUCTION

Stroke is a common and serious disorder, with an annual incidence of approximately 795,000 in the United States, of which approximately 85% are ischemic and 15% are hemorrhagic.[1] Neuroimaging plays a critical role in the diagnosis and management of patients with acute stroke. The neuroimaging evaluation of patients with suspected acute stroke has significantly evolved over the past few decades from a simple noncontrast computed tomography (CT) to now frequently including multiparametric data, including vascular and perfusion imaging.

Although the time window of 3.0 to 4.5 hours still applies for intravenous–thrombolytic treatment, recent clinical trials with encouraging results on the potential role of endovascular treatment[2–4] have created new possibilities for advanced stroke treatment, with the potential for treatment of many more patients beyond the 4.5 hours time window. This possibility makes the role of advanced imaging even more crucial, with the potential for expanding the treatment window for patients with acute stroke if carefully screened and selected based on appropriate imaging criteria. The paradigm is changing from "time is brain" to "imaging is brain."

This article reviews the role of magnetic resonance (MR) imaging and multiparametric MR imaging for the evaluation of patients presenting with acute stroke syndrome, such as acute ischemic stroke (AIS), intracranial hemorrhage (ICH), and transient ischemic attack (TIA), and some of the potential challenging differential diagnoses in the acute emergency setting. It also reviews our institutional technical and clinical experience in MR imaging of patients with acute stroke and provides some clinical examples.

ROLE OF MAGNETIC RESONANCE IMAGING IN STROKE IMAGING

The primary goals of neuroimaging are to determine the presence of infarction and to distinguish between hemorrhagic and ischemic stroke. The

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secondary goals of stroke imaging, largely applied to ischemic strokes, are to identify the location and extent of intravascular clot as well as the presence and extent of penumbra (hypoperfused tissue at risk for infarction).[5,6] To be effective, comprehensive stroke protocols should be able to address the aforementioned primary and secondary goals in a timely manner.

Although CT is the most commonly used modality for stroke imaging, partly because of its wide availability and faster acquisition time, some comprehensive stroke centers choose MR imaging rather than CT for 2 major reasons. First, higher sensitivity and specificity of MR imaging for delineation of hyperacute ischemia. Diffusion-weighted imaging (DWI) provides the most specific way to image acute infarction and perfusion imaging can help in delineation of ischemic penumbra. The advent of MR imaging has redefined stroke syndromes such as acute ischemic infarction and TIA from an all-or-none process to a dynamic and evolving process, providing meaningful physiologic and functional information. Second, the absence of radiation. A comprehensive CT stroke protocol delivers a mean effective dose of 16.4 mSv,[7] which is approximately 6 times the dose of an unenhanced CT head. This difference is particularly important for patients who need repeat examinations following treatment or have a change in their neurologic examination, in whom the repeated CT scans can be prohibitive because of the accumulated radiation dose.

HOW I DO IT?

Image Acquisition (Technical Aspects)

At our institution, if there is no contraindication, MR is the default imaging modality for patients presenting with suspicion of AIS. After activation of the stroke code and the patient's arrival at the emergency department, an MR safety questionnaire is administered and MR-compatible electrocardiogram leads are placed as the patient is being evaluated by the neurology team. The patient is then placed on an MR-compatible table and wheeled to the MR magnet for imaging.

We have 2 stroke MR protocols in place: (1) a fast stroke protocol that takes approximately 6 minutes to acquire,[8] and (2) a routine stroke protocol that takes about 20 to 25 minutes. Although many factors contribute to the decision of which protocol to perform, the fast MR protocol is mainly used for patients who are considered strong candidates for an interventional procedure, such as mechanical embolectomy, to minimize the imaging time without delaying treatment. The routine stroke protocol encompasses other imaging components that allow for further detailed evaluation of the brain, taking into account other differential diagnoses and stroke mimics.

Improvements in MR imaging hardware technology, including the introduction of multicoil technology for better signal reception and higher magnetic fields ($\geq$3 T), which afford higher signal/noise ratio, have increased the efficiency with which fast imaging tools can be applied. In addition, fast sequence design such as echo planar imaging (EPI) and rapid imaging tools such as parallel acquisition algorithms[9] have resulted in significant improvements in the efficiency of MR imaging in terms of both spatial and temporal resolution. Taking advantage of these combinations, we have designed and are effectively using a fast MR imaging protocol with total acquisition time of approximately 6 minutes, a 4-fold reduction in scan time compared with conventional MR stroke imaging.[10,11] For comprehensive stroke centers that choose MR imaging as their imaging modality, the described protocol allows a comparable acquisition time and efficiency to that of multimodal CT protocols, and takes advantage of the superior tissue resolution, the higher sensitivity, and the higher specificity for delineation of infarction afforded by MR imaging.[12]

IMAGING COMPONENTS

Comprehensive MR stroke protocols used routinely in major stroke centers have 3 essential components: (1) parenchymal imaging, which identifies the presence and size of an irreversible infarcted core, determines presence of hemorrhage, and helps to age the ischemic event; (2) MR angiogram to determine the location of arterial occlusion and presence of an intravascular thrombus that can be treated with thrombolysis or thrombectomy; (3) perfusion imaging to determine the presence of hypoperfused tissue at risk for subsequent infarction if adequate perfusion is not restored.

Each of these components and their potential clinical applications are reviewed here.

Parenchymal Imaging

Parenchymal imaging usually encompasses 3 components:

Diffusion-weighted imaging

Diffusion-weighted imaging (DWI) can detect ischemic tissue within minutes of ictus and has emerged as the most sensitive and specific imaging technique for acute ischemia (**Fig. 1**), far beyond nonenhanced CT or any other type of MR imaging sequences.[12] In addition, the pattern of

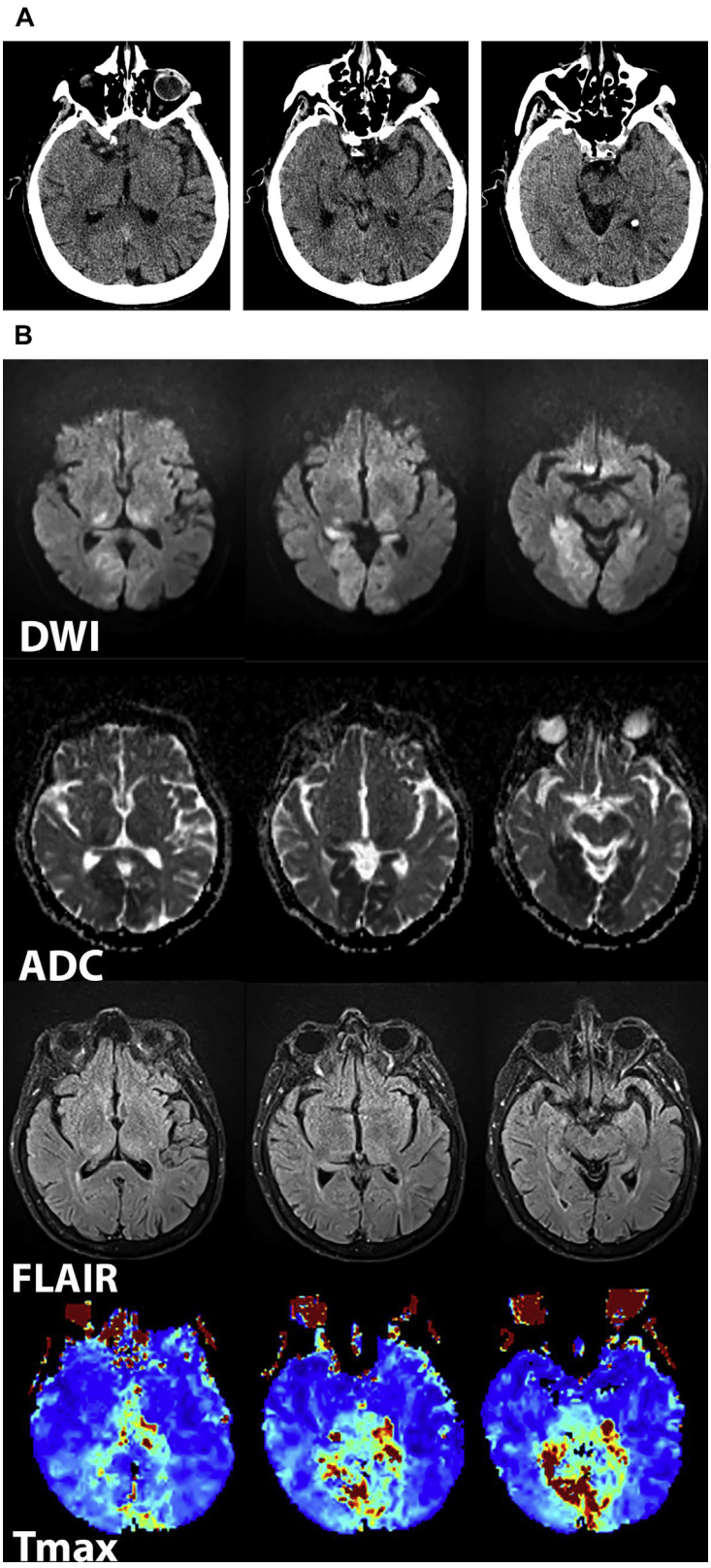

Fig. 1. A 91-year-old woman with history of diabetes, atrial fibrillation, and hypertension presented with acute onset of severe headache and then became unresponsive. Baseline National Institutes of Health Stroke Scale (NIHSS): 26. Time from onset to imaging was approximately 2 hours. Sequential aligned noncontrast CT (*A*) and MR imaging DWI, apparent diffusion coefficient (ADC), fluid-attenuated inversion recovery (FLAIR), and dynamic susceptibility contrast (DSC) time to maximum (T_{max}) (*B*) and a coronal and sagittal maximum intensity projection from the contrast-enhanced magnetic resonance angiography (CE-MRA) image (*C*) are shown. There is a hyperacute infarction seen on DWI-ADC images involving bilateral posterior cerebral artery (PCA) territories, including bilateral thalami and occipital lobes. Note that the infarction is not seen on CT or FLAIR, which is suggestive of hyperacuity. There is matched perfusion deficit on DSC-T_{max}. CE-MRA images show an absence of flow within the left vertebral artery, diminutive flow within the intradural segment of the right vertebral artery and proximal basilar artery, with occlusion and absence of flow within the distal basilar and proximal PCA arteries caused by acute basilar artery thrombosis.

C

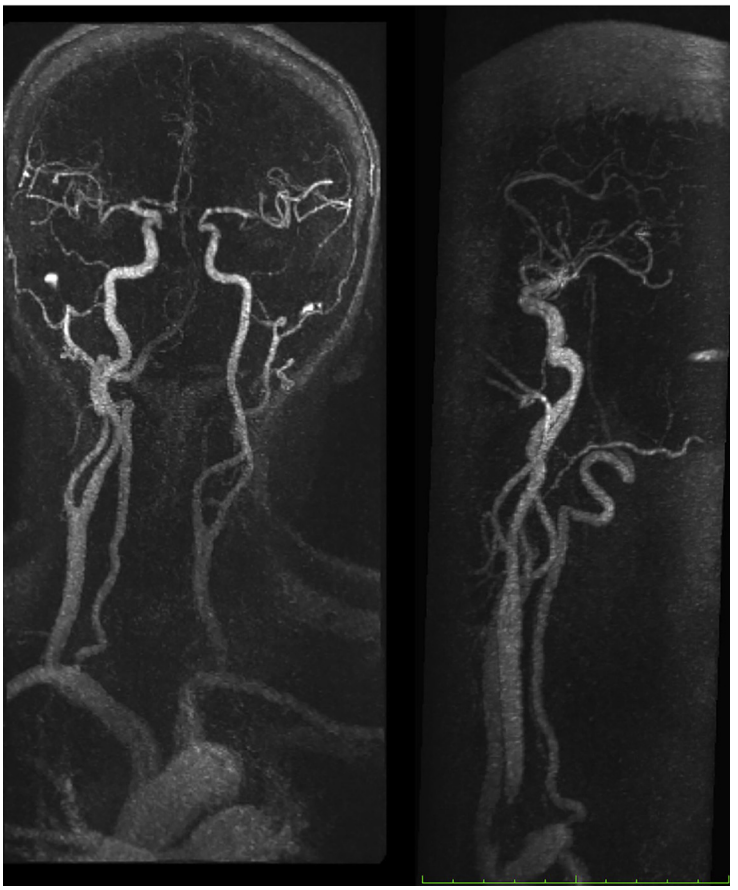

Fig. 1. (*continued*)

the DWI abnormalities provides insight into the underlying cause and stroke subtype. For example, visualization of multiple small bright lesions on DWI sequences within different vascular territories may indicate an embolic stroke mechanism.

Fluid-attenuated inversion recovery

Fluid-attenuated inversion recovery (FLAIR) helps to determine the age of the infarction,[13,14] permits detection of subtle cerebral subarachnoid hemorrhage, and can add diagnostic value to gradient-echo (GRE) images for detecting intra-arterial clot.[15–17] The most important use of FLAIR imaging in the setting of acute stroke is to identify acute ischemic infarcts that lie within the thrombolytic time window in patients with symptoms first noted on awakening (wake-up stroke),[18] or patients with unwitnessed onset who are unable to provide an accurate history. As a rule, lesion visibility on FLAIR increases as time passes from the stroke onset and up to 93% of acute stroke lesions can have positive FLAIR findings at greater than 6 hours.[13,18,19] FLAIR sequences may also show hyperintense vessels following a proximal occlusion even in the absence of parenchymal signal changes. These findings may indicate slow flow in the collateral circulation. In our 6-minute stroke protocol we have replaced conventional FLAIR with EPI-FLAIR.[8] We have shown that EPI-FLAIR has similar diagnostic performance and quantitative and qualitative results to conventional FLAIR (**Fig. 2**), but only requires one-third of the acquisition time.[20] Because of the shorter acquisition time, EPI-FLAIR may provide better image quality with less motion artifact, particularly in uncooperative patients (**Fig. 3**).

Gradient-echo imaging

GRE imaging is used to detect intracranial hemorrhage and intraluminal thrombus formation (**Fig. 4**). Although CT is the standard method used to rule out intracranial hemorrhage, GRE has been shown to be at least as accurate as CT for the detection of acute intraparenchymal hemorrhage.[21] Both FLAIR and GRE images have been used to detect intra-arterial clot with variable sensitivity and

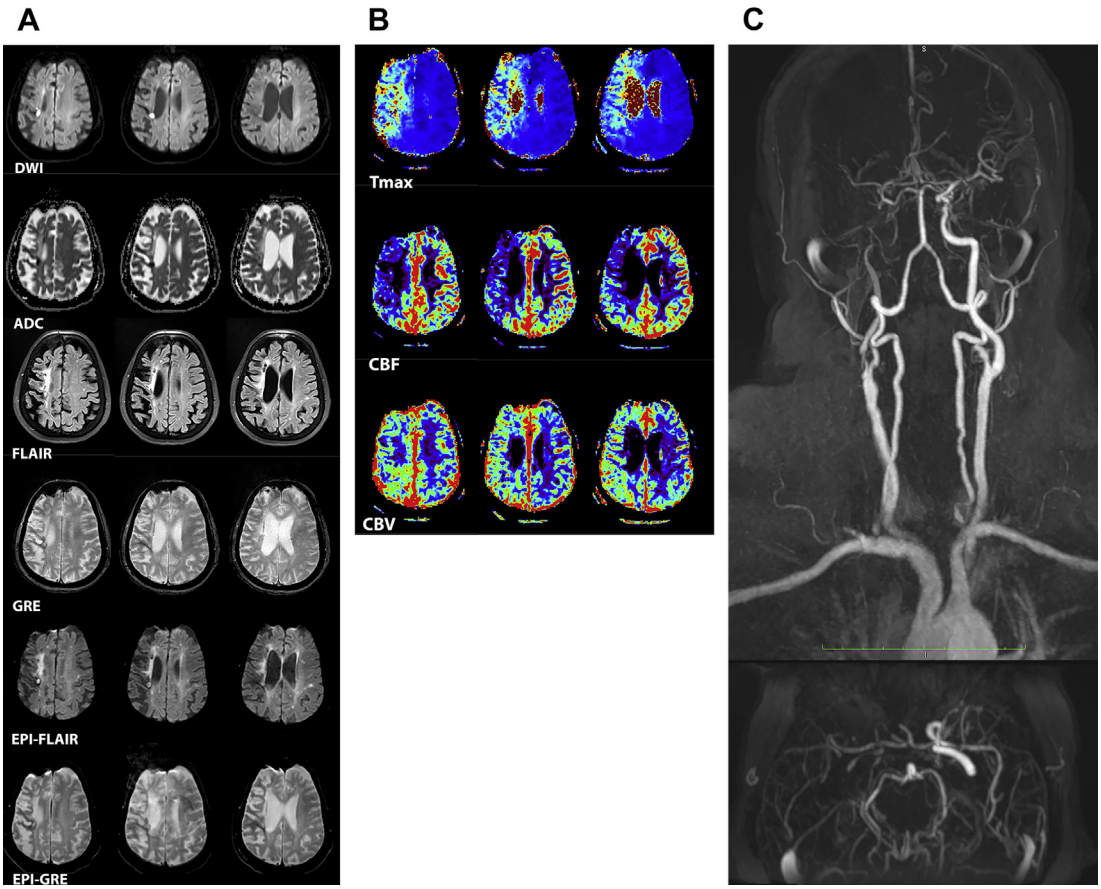

Fig. 2. A 68-year-old woman with a history of stroke approximately 1 year earlier that left her with residual left-sided deficits now presents with a new onset of left-sided weakness. NIHSS: 7. Sequentially aligned DWI, ADC, FLAIR, GRE, EPI-FLAIR, and EPI-GRE (*A*) are shown. There is a small acute infarction in the right posterior centrum semiovale on the background of chronic infarction in the right cerebral deep white matter seen on FLAIR images. There are chronic blood products and hemosiderin staining within the chronic infarction seen on GRE images. EPI-FLAIR and EPI-GRE, used in our 6-minute stroke protocol, are acquired in a fraction (one-third) of the time compared with conventional FLAIR and GRE, but with identical image quality and diagnostic information. CE-MRA (*C*) shows diminutive flow signal in the high cervical segment and occlusion of the petrous segment of the right internal carotid artery. There is reconstitution of flow signal in the cavernous and supraclinoid segment and proximal anterior cerebral artery and middle cerebral artery branches with less signal intensity compared with the normal left side, likely through collateral flow. On DSC-T_{max} and CBF (*B*), there is a large perfusion deficit that indicates delayed perfusion and hypoperfusion respectively. In contrast, CBV has significantly increased, suggesting collateralization in this patient with a history of chronic infraction.

specificity.[15,16] Again, in our 6-minute stroke protocol, EPI-GRE has replaced conventional GRE with similar diagnostic performance but only a fraction of the acquisition time[8] (see **Fig. 2**).

GRE is significantly more sensitive for detection of chronic intracerebral microhemorrhages, which may be the sequelae of amyloid angiopathy or chronic hypertension. The clinical importance of these microbleeds is unknown. At present, there is no statistically significant increased risk of ICH when patients with a small number of chronic microhemorrhages (<5) are treated with thrombolysis.[22,23] However, the risk of hemorrhage in patients with more than 5 chronic microhemorrhages is unknown.[24]

Hemorrhagic transformation (HT) of an ischemic infarction is a common occurrence, and can be seen in 30% to 74% of patients, particularly in patients with embolic strokes and those treated with thrombolytic or mechanical revascularization therapies. Although CT is equally sensitive for detection of parenchymal hematomas, petechial hemorrhages on the more subtle spectrum of HT are detected by GRE with significantly higher

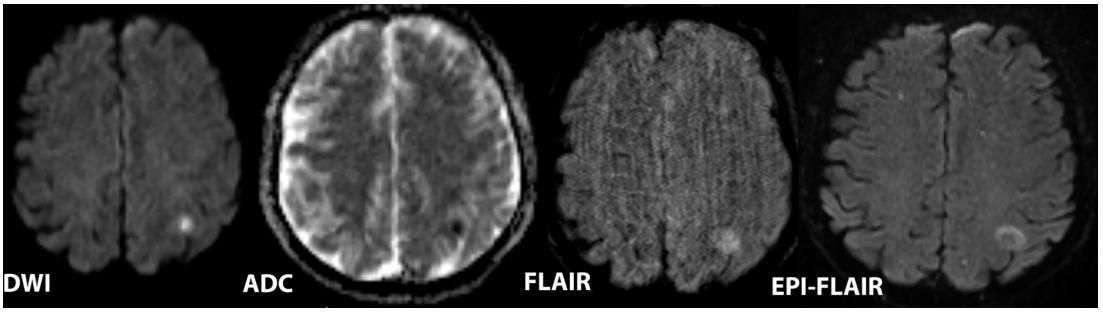

Fig. 3. A 28-year-old man with past medical history of intravenous drug abuse and infective endocarditis presented with right-sided weakness 6 hours before imaging. Baseline NIHSS: 5. The patient was uncooperative and could not hold still. There is an acute infarction in the left postcentral gyrus with associated FLAIR hyperintensity, presumably caused by septic embolism in this patient who had positive blood culture (methicillin-resistant *Staphylococcus aureus*) and positive echocardiography with vegetations. Note the significantly better image quality on EPI-FLAIR image compared with conventional FLAIR, which is degraded by motion artifact. This difference is a clear advantage of the EPI-FLAIR technique used in our 6-minute MR stroke protocol because of the shorter acquisition time (52 seconds in EPI-FLAIR compared with 3 minutes in conventional FLAIR), in particular in uncooperative patients.

sensitivity. The clinical significance of petechial hemorrhage is unknown.

Magnetic Resonance Angiogram

An important aspect of the work-up of patients with AIS or TIA is the imaging of both the intracranial and extracranial vasculature. Intravenous thrombolysis has been shown to be more effective in reperfusing small distal vessels than larger proximal vessels.[25] Larger vessel occlusion may be more effectively treated with intra-arterial thrombolysis or mechanical thrombectomy, which are associated with fewer complications.[26,27] Precise imaging of the vascular tree is required during the initial assessment of patients with acute stroke, not only to accurately detect the site of the arterial disease but also to identify the underlying stroke cause, such as carotid atherosclerotic disease; vascular dissection with or without intraluminal thrombosis (see **Fig. 1**); vasculopathy, such as fibromuscular dysplasia; and other treatable structural causes.

The magnetic resonance angiography (MRA) techniques often used in stroke imaging include the noncontrast time-of-flight (TOF) technique and contrast-enhanced MRA (CE-MRA). Limitations of TOF-MRA include long acquisition times and overestimation of arterial stenosis caused by spin saturation and phase dispersion secondary to slow, in-plane, turbulent, or complex flow.[28,29] An improved CE-MRA technique with higher spatial resolution and faster acquisition time afforded by advances in technology such as multicoil technology and parallel imaging can now be used in acute stroke imaging for complete evaluation of both the extracranial and intracranial (see **Figs. 2** and **4**) supra-aortic arteries,[30,31] resulting in significant improvement in the performance of stroke protocols in terms of image quality and speed.[8,32]

Magnetic Resonance Perfusion

Bolus dynamic susceptibility contrast (DSC) and arterial spin labeling are two methods of measuring cerebral perfusion using MR imaging, each with different strengths and limitations.[33–35] Faster image acquisition and the ability to generate perfusion maps in a few minutes have made DSC a more robust and widely accepted technique to measure cerebral perfusion in patients with acute stroke. The gadolinium contrast dose is approximately 0.1 mmol/kg. Perfusion imaging in patients with presentation of acute stroke syndromes can be used in the following scenarios:

Defining ischemic penumbra

Following a cerebral arterial occlusion, there is a developing infarction core and surrounding hypoperfused brain tissue that is potentially at risk of infarction if blood flow is not restored in a timely manner. This potentially salvageable tissue is called the ischemic penumbra. The rate of change in the extent of infarction core and penumbra is a dynamic process that depends on the recanalization of the occlusion and presence of collateral flow. In the absence of effective revascularization, the infarction core is likely to grow and progressively replace the penumbra (**Fig. 5**). In the case of early revascularization, either spontaneously or resulting from thrombolysis, the penumbra may be salvaged from infarction.[36]

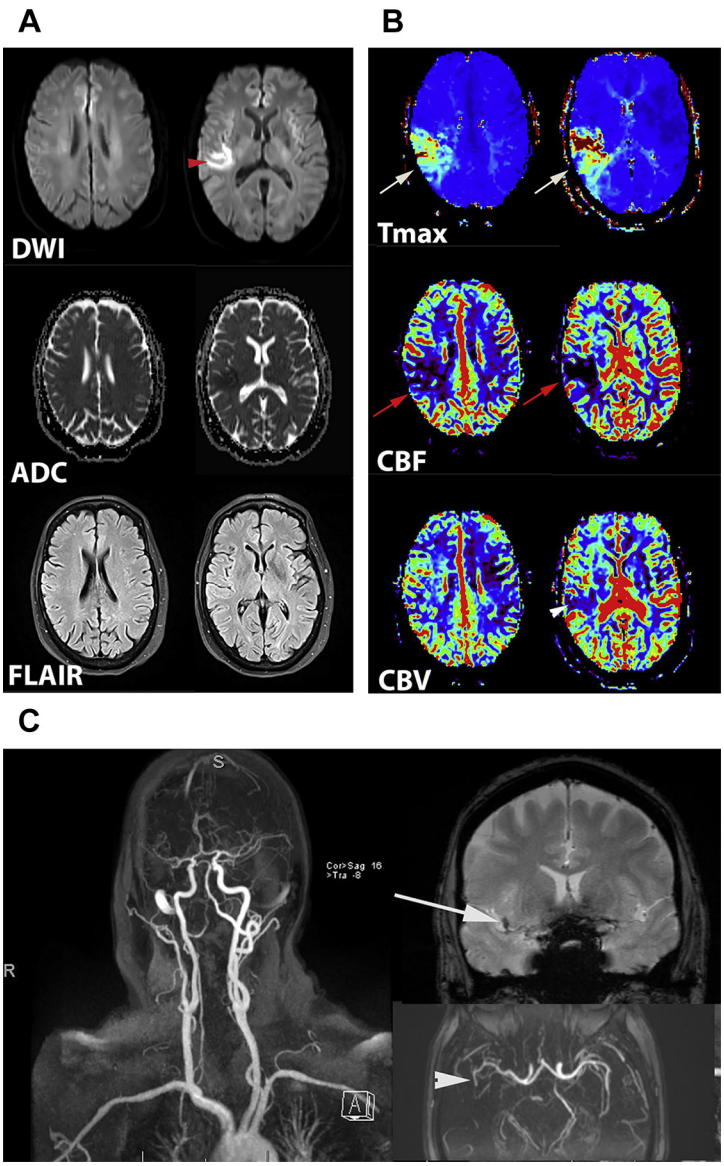

Fig. 4. A 71-year-old woman with past medical history of hypertension and coronary artery disease with cardiomyopathy presented with sudden onset of left-sided facial, upper extremity, and lower extremity weakness. Baseline NIHSS: 4. Time from onset to imaging: 110 minutes. Sequentially aligned DWI, ADC, FLAIR, DSC-T_{max}, CBF, and CBV (*A*) and a coronal and axial maximum intensity projection from CE-MRA in addition to coronal GRE image (*B*) are shown. There is an acute infarction involving the right opercular region (*arrowhead on DWI*). Note that there is no corresponding FLAIR hyperintensity, which indicates the hyperacute nature of the infarction (time from onset to imaging was 110 minutes). On perfusion images (*B*), the T_{max} lesion (delayed perfusion) (*white arrows*) and CBF lesion (hypoperfusion) (*red arrows*) are both larger than acute infarcted tissue seen on DWI (*arrowhead in A*), a representation of ischemic penumbra (so called diffusion-perfusion mismatch). The CBV lesion (*white arrowhead*) is significantly smaller, closely mimicking the infarction core, as expected. CE-MRA (*C*) shows normal appearance of the cervical arteries. There is occlusion of the right M2 posterior division (*arrowhead*). GRE (*C*) shows increased blooming, indicating a thrombus (*arrow*).

Perfusion imaging can be used to determine the extent of ischemic penumbra. Although the clinical utility of ischemic penumbra defined by perfusion imaging and its effect on patient outcomes remains controversial,[37,38] it has been used with some success to identify patients who may respond favorably to revascularization therapies and in the identification of potentially salvageable tissue.[3,10,11,39]

DSC perfusion can provide various maps showing regions of hemodynamic compromise. These maps often include a measure of time such as mean transit time (MTT) or time to maximum (T_{max}), cerebral blood flow (CBF), and cerebral blood volume (CBV). Following an arterial occlusion, regions of irreversible infarction show low CBV, low CBF, and increased MTT/T_{max}. The ischemic penumbra is expected to have CBV within normal ranges, moderate reduction in CBF, and moderately increased MTT/T_{max}. Modest changes in these values can be seen in regions of benign oligemia: tissue with modest hemodynamic compromise that does not reach the level of being at risk of infarction, regardless of reperfusion status. Differentiation of penumbra and benign oligemia remains a diagnostic challenge because absolute thresholds have not been fully validated.

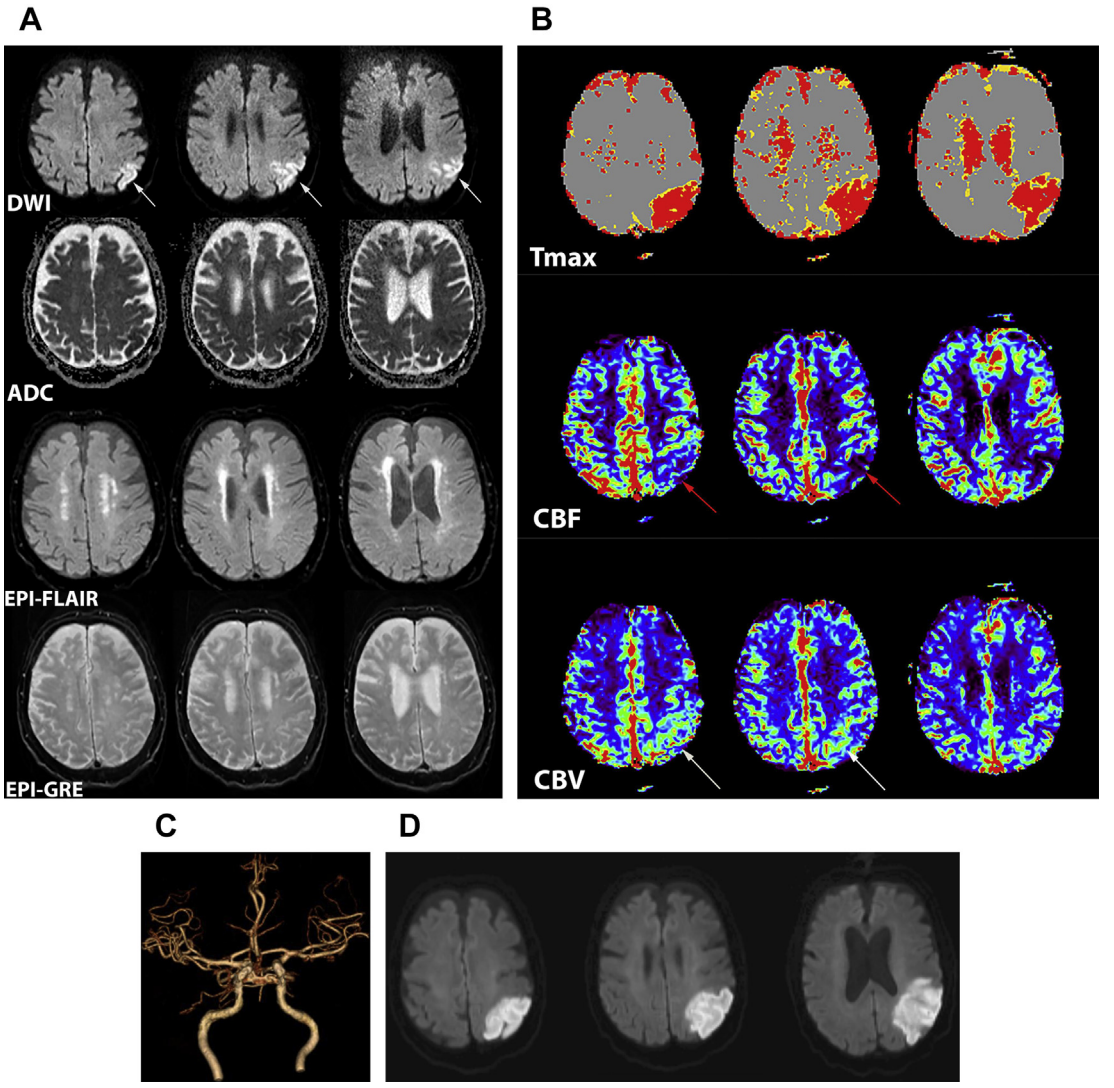

Fig. 5. A 58-year-old man with past medical history of atrial fibrillation hypertension, presents with right-sided weakness. Baseline NIHSS: 6. Time of onset to first MR imaging was approximately 90 minutes. Using the 6-minute MR stroke protocol, there is a hyperacute infarction involving left posterior frontal and parietal lobes (*A*) (*white arrows on DWI images*). Note the absence of FLAIR hyperintense signal, which is suggestive of hyperacuity. There is no hemorrhage on EPI-GRE images. There is a larger perfusion deficit (so-called diffusion-perfusion mismatch) best seen on DSC-T_{max} greater than 6 seconds (*B*), which is suggestive of critical delayed perfusion. There is regional increased CBV (*white arrows*) caused by increased autoregulation, which seems inadequate because there is decreased CBF (*red arrows*). MRA (*C*) shows no proximal arterial stenosis. On follow-up MR imaging (*D*) obtained 12 hours later, there is progression and growth of infarction now encompassing the entire hypoperfused region detected on the initial MR imaging.

Collateral flow status

Perfusion imaging can provide an indirect measure of collateral flow.[10,40,41]

Several investigators have shown reverse correlation between the degree of collateral flow and the extent and severity of hypoperfusion defined on MR perfusion data.[39,42–44]

Collateral flow is often directly evaluated with vascular imaging such as catheter angiography, CT angiography (CTA), or MRA. Because of inherent limited spatial and temporal resolution of cross-sectional vascular imaging such as CTA or MRA to evaluate the full extent of collateral flow, catheter angiography remains the gold standard method for imaging collateral vasculature. Because multivessel conventional angiography is impractical for all patients in routine practice, the development of noninvasive approaches that

combine angiographic information with perfusion data can significantly enhance understanding of the collateral circulation.

Perfusion deficit noted on MR perfusion time maps (such as T_{max}) encompasses both delayed perfusion caused by underlying arterial occlusion and delayed flow through collateral circulation, without the ability to distinguish antegrade from collateral flow. In contrast, CBF and CBV maps provide information regarding the amount of blood flow to specific regions of the brain, although the arterial source of sustained perfusion may not be evident, some of which may be from collateral flow. Therefore a mismatch between the volume of brain with time delay on T_{max} and the volume of brain with hypoperfusion on CBF/CBV may in part be a good representation of collateral flow (see **Figs. 2** and **4**).

Furthermore, MR perfusion data, as an indirect measure of collateral flow, have been used as a marker of successful recanalization, which in turn can improve therapeutic decision making, tailoring patient selection and enrollment to those who will most benefit from recanalization procedures.[3,42,45] A further imaging-driven collateral flow index has been developed, enabling risk stratification for

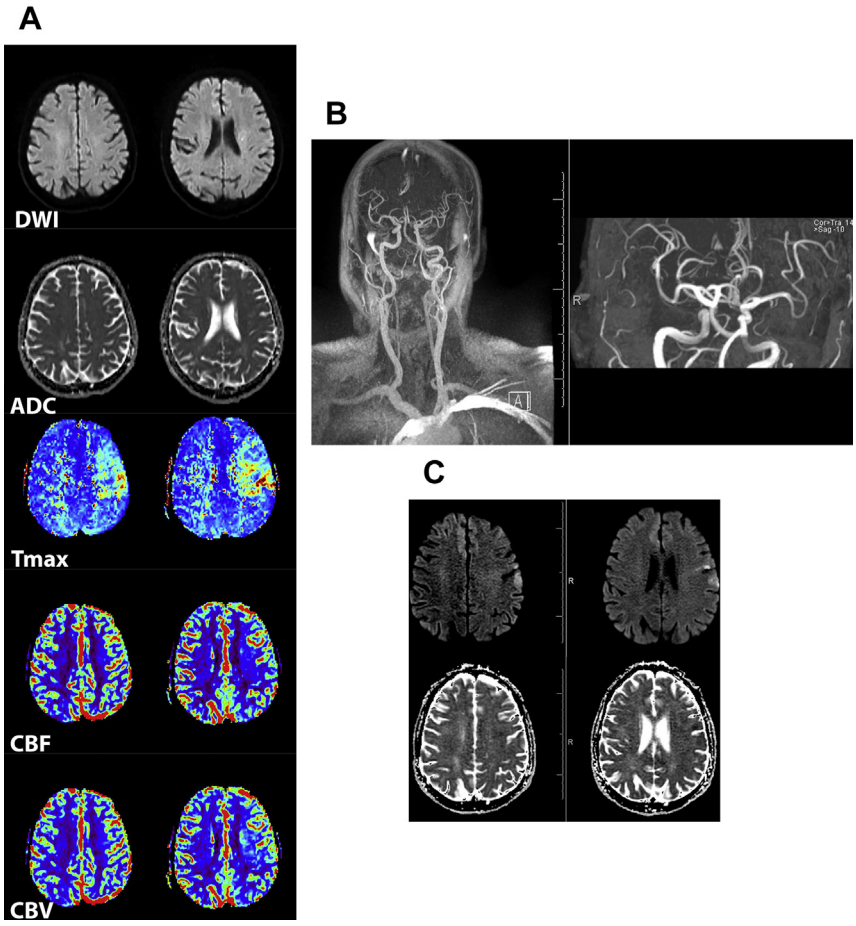

Fig. 6. A 67-year-old man with past medical history of atrial fibrillation and prior TIAs presents with complaints of garbled speech for 10 minutes before it resolved. Time of onset to first MR imaging was approximately 2 hours. On initial MR images (*A*), there is no acute infarction on the DWI-ADC images. Perfusion imaging (*A*) reveals a regional perfusion deficit evident by increased T_{max} involving the left operculum and Broca area. Note compensatory increased in CBV suggestive of autoregulation and luxury perfusion to maintain the CBF. MRA (*B*) shows a normal proximal arterial tree without evidence of hemodynamically significant stenosis. The patient was discharged from the emergency department with the diagnosis of TIA; however, 14 hours later his garbled speech returned and was noted to be persistent. He also complained of a patch of right-sided upper lip numbness. He was able to follow commands and communicate by writing, but was noted to have a severe expressive aphasia. Second MR imaging (*C*) reveals restricted diffusion and acute infarction involving the frontal operculum and Broca area, in the region of previously identified delayed perfusion.

individual treatment decision making, expanding treatment options for patients with AIS.

Differential diagnosis: transient ischemic attack, seizure

Transient ischemic attack With the introduction of DWI into routine clinical practice, studies have shown that up to 40% of patients with clinically defined TIA have evidence of restricted diffusion that indicates ischemic infarction. This finding has led to a recent American Stroke Association–endorsed proposal to revise the definition of TIA from time-based to tissue-based criteria.[46] However, DWI-negative patients remain a source of uncertainty and a great clinical challenge. Many of these patients may have transient cerebral ischemia in which the degree of hemodynamic compromise did not reach the threshold for tissue injury. Acknowledging this challenge, several investigators used perfusion imaging to further stratify patients with TIA.[47–50] In our experience, perfusion imaging, when incorporating both T_{max} and CBF parametric maps, has added diagnostic value to the detection of regions of hypoperfusion or postischemic hyperperfusion in approximately one-quarter of patients with DWI-negative TIA (**Fig. 6**), thus providing additional evidence to confirm a footprint of ischemia that would otherwise go undetected.[51]

Seizure Prolonged seizures or status epilepticus can lead to restricted diffusion on DWI.[52] These changes often do not respect the margins of vascular territories and are associated with increased, not decreased, perfusion.[53] Another helpful imaging finding to differentiate seizure from AIS is the pulvinar sign, which is restricted diffusion and increased CBF in the ipsilateral thalamic pulvinar. This finding may be caused by extensive neuronal connections between the thalamus and parietotemporal regions, which are often involved in seizure activity.[53]

SUMMARY

MR imaging can be used effectively for the diagnosis and evaluation of patients presenting with acute stroke syndrome in emergency settings. Recent advances in MR imaging technology have allowed fast and efficient multimodal MR imaging, such as the described 6-minute MR stroke protocol that can be used for the evaluation of patients with AIS, with resultant significant reduction in scan times, rivaling those multimodal CT protocols.

Because recent clinical trials have established endovascular procedures as effective treatment strategies for patients with acute stroke, multimodal neuroimaging will continue to play an increasingly important role in the evaluation and management of patients with stroke. Advanced imaging techniques provide important insights into individual patient pathophysiology, stroke cause, and prognosis. This information may be used by clinicians to make treatment decisions for both acute therapies and long-term secondary prevention approaches.

REFERENCES

1. Lloyd-Jones D, Adams RJ, Brown TM, et al. Heart disease and stroke statistics–2010 update: a report from the American Heart Association. Circulation 2010;121:e46–215.
2. Goyal M, Demchuk AM, Menon BK, et al. Randomized assessment of rapid endovascular treatment of ischemic stroke. N Engl J Med 2015;372:1019–30.
3. Campbell BCV, Mitchell PJ, Kleinig TJ, et al. Endovascular therapy for ischemic stroke with perfusion-imaging selection. N Engl J Med 2015; 372:1009–18.
4. Berkhemer OA, Fransen PSS, Beumer D, et al. A randomized trial of intraarterial treatment for acute ischemic stroke. N Engl J Med 2015;372:11–20.
5. Schellinger PD. The evolving role of advanced MR imaging as a management tool for adult ischemic stroke: a western-European perspective. Neuroimaging Clin North Am 2005;15:245–58, ix.
6. Rowley HA. Extending the time window for thrombolysis: evidence from acute stroke trials. Neuroimaging Clin North Am 2005;15:575–87, x.
7. Mnyusiwalla A, Aviv RI, Symons SP. Radiation dose from multidetector row ct imaging for acute stroke. Neuroradiology 2009;51:635–40.
8. Nael K, Khan R, Choudhary G, et al. Six-minute magnetic resonance imaging protocol for evaluation of acute ischemic stroke: pushing the boundaries. Stroke 2014;45:1985–91.
9. Griswold MA, Jakob PM, Heidemann RM, et al. Generalized autocalibrating partially parallel acquisitions (GRAPPA). Magn Reson Med 2002;47: 1202–10.
10. Albers GW, Thijs VN, Wechsler L, et al. Magnetic resonance imaging profiles predict clinical response to early reperfusion: the Diffusion and Perfusion Imaging Evaluation for Understanding Stroke Evolution (DEFUSE) study. Ann Neurol 2006;60:508–17.
11. Davis SM, Donnan GA, Parsons MW, et al. Effects of alteplase beyond 3 h after stroke in the echoplanar imaging thrombolytic evaluation trial (epithet): a placebo-controlled randomised trial. Lancet Neurol 2008;7:299–309.
12. Fiebach JB, Schellinger PD, Jansen O, et al. CT and diffusion-weighted MR imaging in randomized order: diffusion-weighted imaging results in higher

accuracy and lower interrater variability in the diagnosis of hyperacute ischemic stroke. Stroke 2002; 33:2206–10.
13. Thomalla G, Cheng B, Ebinger M, et al. DWI-FLAIR mismatch for the identification of patients with acute ischaemic stroke within 4.5 h of symptom onset (pre-FLAIR): a multicentre observational study. Lancet Neurol 2011;10:978–86.
14. Aoki J, Kimura K, Iguchi Y, et al. FLAIR can estimate the onset time in acute ischemic stroke patients. J Neurol Sci 2010;293:39–44.
15. Flacke S, Urbach H, Keller E, et al. Middle cerebral artery (MCA) susceptibility sign at susceptibility-based perfusion MR imaging: clinical importance and comparison with hyperdense MCA sign at CT. Radiology 2000;215:476–82.
16. Assouline E, Benziane K, Reizine D, et al. Intra-arterial thrombus visualized on T2* gradient echo imaging in acute ischemic stroke. Cerebrovasc Dis 2005; 20:6–11.
17. Noguchi K, Ogawa T, Seto H, et al. Subacute and chronic subarachnoid hemorrhage: diagnosis with fluid-attenuated inversion-recovery MR imaging. Radiology 1997;203:257–62.
18. Thomalla G, Rossbach P, Rosenkranz M, et al. Negative fluid-attenuated inversion recovery imaging identifies acute ischemic stroke at 3 hours or less. Ann Neurol 2009;65:724–32.
19. Petkova M, Rodrigo S, Lamy C, et al. MR imaging helps predict time from symptom onset in patients with acute stroke: implications for patients with unknown onset time. Radiology 2010;257:782–92.
20. Meshksar A, Villablanca JP, Khan R, et al. Role of EPI-FLAIR in patients with acute stroke: a comparative analysis with FLAIR. AJNR Am J Neuroradiol 2014;35(5):878–83.
21. Kidwell CS, Chalela JA, Saver JL, et al. Comparison of MRI and CT for detection of acute intracerebral hemorrhage. JAMA 2004;292:1823–30.
22. Kakuda W, Thijs VN, Lansberg MG, et al. Clinical importance of microbleeds in patients receiving IV thrombolysis. Neurology 2005;65:1175–8.
23. Lee SH, Kang BS, Kim N, et al. Does microbleed predict haemorrhagic transformation after acute atherothrombotic or cardioembolic stroke? J Neurol Neurosurg Psychiatry 2008;79:913–6.
24. Wintermark M, Sanelli PC, Albers GW, et al. Imaging recommendations for acute stroke and transient ischemic attack patients: a joint statement by the American Society of Neuroradiology, the American College of Radiology and the Society of Neurointerventional Surgery. J Am Coll Radiol 2013;10:828–32.
25. del Zoppo GJ, Poeck K, Pessin MS, et al. Recombinant tissue plasminogen activator in acute thrombotic and embolic stroke. Ann Neurol 1992;32:78–86.
26. Furlan A, Higashida R, Wechsler L, et al. Intra-arterial prourokinase for acute ischemic stroke. The PROACT II study: a randomized controlled trial. Prolyse in Acute Cerebral Thromboembolism. JAMA 1999;282:2003–11.
27. Becker KJ, Brott TG. Approval of the MERCI clot retriever: a critical view. Stroke 2005;36:400–3.
28. Lin W, Tkach JA, Haacke EM, et al. Intracranial MR angiography: application of magnetization transfer contrast and fat saturation to short gradient-echo, velocity-compensated sequences. Radiology 1993; 186:753–61.
29. Isoda H, Takehara Y, Isogai S, et al. MRA of intracranial aneurysm models: a comparison of contrast-enhanced three-dimensional MRA with time-of-flight MRA. J Comput Assist Tomogr 2000;24:308–15.
30. Nael K, Villablanca JP, Pope WB, et al. Supraaortic arteries: contrast-enhanced MR angiography at 3.0 T–highly accelerated parallel acquisition for improved spatial resolution over an extended field of view. Radiology 2007;242:600–9.
31. Phan T, Huston J 3rd, Bernstein MA, et al. Contrast-enhanced magnetic resonance angiography of the cervical vessels: experience with 422 patients. Stroke 2001;32:2282–6.
32. Nael K, Meshksar A, Ellingson B, et al. Combined low-dose contrast-enhanced MR angiography and perfusion for acute ischemic stroke at 3T: a more efficient stroke protocol. AJNR Am J Neuroradiol 2014;35:1078–84.
33. Detre JA, Leigh JS, Williams DS, et al. Perfusion imaging. Magn Reson Med 1992;23:37–45.
34. Wolf RL, Alsop DC, McGarvey ML, et al. Susceptibility contrast and arterial spin labeled perfusion MRI in cerebrovascular disease. J Neuroimaging 2003;13: 17–27.
35. Smith AM, Grandin CB, Duprez T, et al. Whole brain quantitative CBF and CBV measurements using MRI bolus tracking: comparison of methodologies. Magn Reson Med 2000;43:559–64.
36. Read SJ, Hirano T, Abbott DF, et al. The fate of hypoxic tissue on 18F-fluoromisonidazole positron emission tomography after ischemic stroke. Ann Neurol 2000;48:228–35.
37. Hacke W, Furlan AJ, Al-Rawi Y, et al. Intravenous desmoteplase in patients with acute ischaemic stroke selected by MRI perfusion-diffusion weighted imaging or perfusion CT (DIAS-2): a prospective, randomised, double-blind, placebo-controlled study. Lancet Neurol 2009;8:141–50.
38. Kidwell CS, Jahan R, Gornbein J, et al. A trial of imaging selection and endovascular treatment for ischemic stroke. N Engl J Med 2013;368:914–23.
39. Lansberg MG, Straka M, Kemp S, et al. MRI profile and response to endovascular reperfusion after stroke (DEFUSE 2): a prospective cohort study. Lancet Neurol 2012;11:860–7.
40. Olivot JM, Mlynash M, Thijs VN, et al. Geography, structure, and evolution of diffusion and perfusion

lesions in Diffusion and Perfusion Imaging Evaluation for Understanding Stroke Evolution (DEFUSE). Stroke 2009;40:3245–51.
41. Soares BP, Tong E, Hom J, et al. Reperfusion is a more accurate predictor of follow-up infarct volume than recanalization: a proof of concept using CT in acute ischemic stroke patients. Stroke 2010;41: e34–40.
42. Nicoli F, Lafaye de Micheaux P, Girard N. Perfusion-weighted imaging-derived collateral flow index is a predictor of MCA M1 recanalization after I.V. thrombolysis. AJNR Am J Neuroradiol 2013;34:107–14.
43. Bang OY, Saver JL, Alger JR, et al. Determinants of the distribution and severity of hypoperfusion in patients with ischemic stroke. Neurology 2008;71: 1804–11.
44. Olivot JM, Mlynash M, Inoue M, et al. Hypoperfusion intensity ratio predicts infarct progression and functional outcome in the DEFUSE 2 cohort. Stroke 2014; 45:1018–23.
45. Nicoli F, Scalzo F, Saver JL, et al. The combination of baseline magnetic resonance perfusion-weighted imaging-derived tissue volume with severely prolonged arterial-tissue delay and diffusion-weighted imaging lesion volume is predictive of MCA-M1 recanalization in patients treated with endovascular thrombectomy. Neuroradiology 2014;56:117–27.
46. Easton JD, Saver JL, Albers GW, et al. Definition and evaluation of transient ischemic attack: a scientific statement for healthcare professionals from the American Heart Association/American Stroke Association Stroke Council; Council on Cardiovascular Surgery and Anesthesia; Council on Cardiovascular Radiology and Intervention; Council on Cardiovascular Nursing; and the Interdisciplinary Council on Peripheral Vascular Disease. The American Academy of Neurology affirms the value of this statement as an educational tool for neurologists. Stroke 2009; 40:2276–93.
47. Restrepo L, Jacobs MA, Barker PB, et al. Assessment of transient ischemic attack with diffusion- and perfusion-weighted imaging. AJNR Am J Neuroradiol 2004;25:1645–52.
48. Krol AL, Coutts SB, Simon JE, et al. Perfusion MRI abnormalities in speech or motor transient ischemic attack patients. Stroke 2005;36:2487–9.
49. Mlynash M, Olivot JM, Tong DC, et al. Yield of combined perfusion and diffusion MR imaging in hemispheric TIA. Neurology 2009;72:1127–33.
50. Kleinman JT, Zaharchuk G, Mlynash M, et al. Automated perfusion imaging for the evaluation of transient ischemic attack. Stroke 2012;43:1556–60.
51. Grams R, Kidwell C, Shroff S, et al. Tissue negative-transient ischemic attack: is there a role for MR perfusion? Paper presented at the ASNR 52nd Annual Meeting. Montréal, Canada, May 22, 2014.
52. Londono A, Castillo M, Lee YZ, et al. Apparent diffusion coefficient measurements in the hippocampi in patients with temporal lobe seizures. AJNR Am J Neuroradiol 2003;24:1582–6.
53. Szabo K, Poepel A, Pohlmann-Eden B, et al. Diffusion-weighted and perfusion MRI demonstrates parenchymal changes in complex partial status epilepticus. Brain 2005;128:1369–76.