Stroke is the fourth leading cause of death in the United States. According to the American Heart Association, 795,000 patients experience a new or recurrent stroke each year in the US, and stroke results in 1 of every 19 deaths.

Current treatments for acute ischemic stroke include intravenous (IV) tissue plasminogen activator (tPA), endovascular mechanical recanalization, and intraarterial thrombolysis. The number needed to treat for IV tPA to benefit 1 patient is about 7. However, less than 5% of patients with acute stroke receive IV tPA. This is largely due to the narrow time window for treatment (3–4.5 hours for IV tPA, 6 hours for intraarterial thrombolysis, and 8 hours for endovascular mechanical recanalization) and delayed presentation to care.

Neuroimaging has become a critical tool in the evaluation and management of stroke. The objectives of imaging include prompt accurate diagnosis, treatment triage, prognosis prediction, and secondary preventative precautions. While capitalizing on the latest treatment options and expanding upon the “time is brain” doctrine, the ultimate goal of imaging is to maximize the number of treated patients and improve the outcome of one of the most costly and morbid diseases. A broad overview of comprehensive multimodal stroke imaging is presented here to affirm its utilization.

**Establishing the Diagnosis of Acute Ischemic Stroke**

**Ruling Out Intracranial Hemorrhage**

The initial step in the evaluation of patients with symptoms of acute stroke is to differentiate between hemorrhagic and ischemic stroke. Since intracranial hemorrhage is an absolute contraindication for reperfusion ther-
Diagnosing Ischemic Stroke

Early ischemic changes in NCHCT include loss of gray-white distinction, indistinct insular cortex and obscured basal ganglia, and hyperattenuated clot in the proximal vessels.\(^1\) The hyperdense vessel sign is most specific but has low sensitivity.\(^2\) Abnormalities on NCHCT are present in 40%–50% of acute ischemic strokes.\(^3,4\) When obvious signs are present, NCHCT allows rapid diagnosis and correlation with presenting symptoms. However, acute ischemic changes are often subtle, with intra- and interobserver variability.\(^6\) Multiple classification systems based on imaging features have been developed to offer reliable, reproducible grading of the extent of ischemic changes on NCHCT. One of them is the Alberta Stroke Program Early CT Score (ASPECTS), a 10-point scoring system\(^1\) (Fig. 2; Table 1). Studies have shown that baseline ASPECTS correlates inversely with severity as assessed by the NIHSS within the first 3 hours of middle cerebral artery (MCA) stroke onset. ASPECTS of 7 or lower has been shown to predict poor functional outcome (78% sensitivity and 96% specificity) and symptomatic hemorrhage (90% sensitivity and 62% specificity).\(^6\)

Diffusion-weighted imaging (DWI) is approximately 4 to 5 times more sensitive in detecting acute stroke than NCHCT\(^5,6\) (Fig. 4). Its sensitivity in detecting ischemia is reported as 99% with a high specificity of 92%.\(^7\) DWI can distinguish acute from chronic ischemia, thereby delineating new lesions even when located in proximity to prior ischemic injury\(^8\) (Table 2). Obscure lesions indiscernible on CT scans, such as lacunar infarcts, particularly those located in the posterior fossa, are better visualized on DWI.\(^9,10\)

Despite strong evidence supporting DWI as superior to NCHCT for confirming diagnosis of acute stroke within the first 24 hours,\(^1\) logistical issues limit its use in emergent setting. Most institutions find it challenging to obtain emergent MRI without delaying treatment.

Of note, restricted diffusion is not exclusively observed in acute ischemic stroke, but can also be seen in some nonischemic entities. These include seizure, encephalitis, abscesses, metabolic derangement (hypoglycemia), Creutzfeldt-Jakob disease, lymphoma, and mucinous adenocarcinoma metastases.\(^11\) Under the guidance of clinical presentation, these entities can be readily differentiated when studies are reviewed in combination with studies using other imaging modalities such as FLAIR. Occasionally, clinical differentiation of seizures from acute stroke may be difficult. Discerning DWI lesions confined to a major vascular territory, a distinctive feature of acute stroke lesions, may be helpful.

Determining Eligibility for IV tPA

There is strong evidence supporting the use of IV tPA.
Acute stroke imaging

Fig. 2. Admission NCHCT of patient with ASPECTS 4, calculated at the level of the basal ganglia and at the supraganglionic level. In this scoring system, the MCA territory is divided into 10 regions: the caudate (C), lentiform (L), internal capsule (IC), and 7 cortical regions (insular cortex [I], M1, M2, M3, M4, M5, and M6), based on data from Barber et al.12

as a recanalization therapy to improve clinical outcomes when patients present within the standard 0- to 3-hour time window1,73,155 and the extended 3- to 4.5-hour time window.21,72,125 There is also strong evidence supporting the timely use of imaging to exclude hemorrhage in stroke patients before initiating IV thrombolytic therapy.42,155 Admission NCHCT is recommended prior to thrombolysis, because intracranial hemorrhage is an absolute contraindication to IV thrombolysis. 92,93 Ischemia involving more than one-third of the MCA territory on images obtained within the 0- to 6-hour window constitutes a relative contraindication to IV thrombolysis.73,122,218 Of note, there is disagreement regarding the significance of extensive ischemic signs on admission NCHCT. Early on, the European Cooperative Acute Stroke Studies (ECASS) reported poor outcome with increased incidence of hemorrhage following thrombolysis in patients with early extensive infarctions.218,219 However, the National Institute of Neurological Disorders and Stroke tPA Stroke Trial contested that early extensive infarctions were associated with symptom severity but not with adverse outcome after thrombolysis.266 Results from recent studies recommend withholding IV thrombolysis when more than one-third of the MCA territory is involved.196

Identifying Candidates for Endovascular Revascularization

Detecting Large Artery Occlusion

Imaging of the intracranial and extracranial vessels is needed to determine whether an embolus/thrombus is present and whether it is amenable to endovascular revascularization. The outcome after endovascular therapy depends on the location of the thrombus, with better recanalization rates associated with more proximal thrombus131,144,152,160,192 and poorer outcomes with occlusion of the carotid terminus.190,200

Digital subtraction angiography (DSA) is considered the reference standard for detection of vascular occlusions and stenoses. CTA has reportedly high sensitivity (97%–100%) and specificity (98%–100%) for detecting intracranial occlusions and stenoses.66,79,102,111,157,199,214,222 CTA also performs well in characterizing extracranial occlusions and stenoses, with high sensitivity (95%–97%) and specificity (90%–99%).12 In addition to evaluating the degree of stenosis in the extracranial arteries, CTA provides valuable information of the plaque—such as morphology and composition.224

Magnetic resonance angiography (MRA) can also be used to detect and localize the occlusion.15,42,162 Three-dimensional (3D) time-of-flight (TOF) MRA is the standard MR technique for the examination of intracranial vessels. TOF MRA is, however, especially susceptible to motion artefact and tends to overestimate the degree of stenosis.39 Traditional contrast-enhanced MRA (bolus-chase MRA) is the MR technique of choice for the study

### TABLE 1: Alberta Stroke Program Early CT Score*

<table>
<thead>
<tr>
<th>Region</th>
<th>Value</th>
</tr>
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<tbody>
<tr>
<td>cortical</td>
<td></td>
</tr>
<tr>
<td>M1</td>
<td>−1</td>
</tr>
<tr>
<td>M2</td>
<td>−1</td>
</tr>
<tr>
<td>M3</td>
<td>−1</td>
</tr>
<tr>
<td>M4</td>
<td>−1</td>
</tr>
<tr>
<td>M5</td>
<td>−1</td>
</tr>
<tr>
<td>M6</td>
<td>−1</td>
</tr>
<tr>
<td>insular cortex (I)</td>
<td>−1</td>
</tr>
<tr>
<td>subcortical</td>
<td></td>
</tr>
<tr>
<td>caudate (C)</td>
<td>−1</td>
</tr>
<tr>
<td>lentiform nucleus (L)</td>
<td>−1</td>
</tr>
<tr>
<td>internal capsule (IC)</td>
<td>−1</td>
</tr>
</tbody>
</table>

* A normal CT scan has an ASPECTS of 10 points. One point is subtracted for ischemic changes in each region of the MCA territory. Data obtained from Barber et al.12

Fig. 3. Type PH2 hemorrhagic transformation. Axial NCHCT images obtained 14 hours after initial presentation in a patient with a left MCA infarct, demonstrating hemorrhagic transformation with confluent hematoma (arrows) and surrounding edema causing mass effect (left-to-right midline shift, subfalcine herniation, right lateral ventricle entrapment).

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of the extracranial arteries. It is relatively independent of flow dynamics and is less susceptible to motion artifacts (Fig. 5). Peak arterial enhancement is obtained by estimating the arrival of the contrast bolus. This technique is often limited by inaccurate timing of the bolus, which causes venous contamination.133 Newer time-resolved contrast-enhanced MRA repeatedly acquires images of a volume during the passage of the contrast material. De-lineation of arterial vasculature from venous vasculature is more accurate.114,133 Additionally, the dynamic acquisition allows visualization of complex flow patterns.114,133

The combined use of 3D TOF and contrast-enhanced MRA can improve diagnostic ability.203 However, CTA has been shown to be slightly superior to MRA for this purpose, typically for distal vascular lesions68,107 (Fig. 6).

Assessing Viable Ischemic Brain Tissue

Following an arterial occlusion, brain tissue that cannot sustain the sudden drop in perfusion rapidly undergoes infarction. The surrounding hypoperfused tissue that can autoregulate to sustain metabolic needs remains viable.77,223,226 The former is labeled “ischemic infarct core,” and the injury to this tissue is irreversible. The latter is known as “ischemic penumbra.” Differentiation of the ischemic core and ischemic penumbra relies on the tissue’s ability to carry out vascular autoregulation.77,223,225,226 The penumbra is in danger of proceeding to infarction, but represents potentially salvageable tissue if recanalization is achieved quickly57,62,86,90 (Fig. 7). The evolution of the penumbra is a dynamic process and can be indirectly visualized by various advanced imaging techniques.

Perfusion-CT (PCT) can characterize cerebral perfusion by dynamically tracing an iodinated contrast bolus from its arrival to its departure.50 PCT allows quantitative assessment of cerebral blood flow (CBF), cerebral blood volume (CBV), and mean transit time (MTT).50 PCT delineation of the ischemic core and penumbra is typically based on the concept of cerebral vascular autoregulation. In the penumbra, where autoregulation is preserved, MTT is prolonged, but CBV is maintained.223 Quantitatively, a relative increase in MTT of 145% most accurately represents the penumbra.223 Within the ischemic core, where autoregulation is lost, there is a matched reduction in CBF and CBV with prolonged MTT.223 A prospective multicenter study reported an absolute CBV < 2 mL/100 g optimally best delineated the ischemic core.106 However, more recent studies found relative CBF to be more predictive of the ischemic core.6,17–19,99,110,147,168,202

MRI delineation of the ischemic core and penumbra relies on DWI and perfusion-weighted imaging (PWI) techniques.67 Characterization of the ischemic core and penumbra on MRI is based on the assumption that the DWI abnormality reflects the ischemic core, whereas the PWI abnormality reflects the overall area of ischemia.96 The PWI/DWI-mismatch is often thought to represent the ischemic penumbra56,64 (Table 3; Fig. 8). However, users should be cautious of the spontaneous resolution of

| TABLE 2: Temporal changes of MRI findings in ischemic stroke* |
|---|---|---|---|---|---|---|
| Time Frame | Etiology | DWI | ADC | T1 | T2 | FLAIR |
| hyperacute (0–6 hrs) | cytotoxic edema | hyperintense | hypointense | hypointense | hypointense | hyperintense |
| acute (6–24 hrs) | vasogenic edema | hyperintense | hypointense | hypointense | hyperintense | hyperintense |
| subacute (1–7 days) | edema resolved; infarction, complete | variable | hyperintense | hypointense | hyperintense | variable |
| chronic (>1 mo) | gliosis; encephalomalacia | | | | | |

* T1 = T1-weighted sequences; T2 = T2-weighted sequences.
Acute stroke imaging

some DWI hyperintense lesions\textsuperscript{119} (Fig. 9), and the inclusion of benign oligemia within the PWI abnormalities that are not at risk for infarction.\textsuperscript{104} The extent of mismatched tissue varies depending on the perfusion parameter selected and the threshold selected to represent the PWI abnormality.\textsuperscript{60,70,71,104,119,170} In a post hoc analysis of the DEFUSE trial,\textsuperscript{4} defining penumbra by using Tmax of 4–6 seconds provided the most accurate estimate of the penumbra.\textsuperscript{162} Other studies recommended using Tmax > 6 seconds.\textsuperscript{120,150,162} There is no consensus on the optimal perfusion parameter for the definition of infarct core and penumbra. Further studies to standardize perfusion imaging are needed.

The clinical utility of penumbral imaging has not been proven. The utilization of penumbral imaging in the decision for mechanical embolectomy has generated mixed results in recent clinical trials.\textsuperscript{107,207} Trials such as Diffusion-Weighted Imaging Evaluation For Understanding Stroke Evolution (DEFUSE), DEFUSE-2, and Echo-planar Imaging Thrombolysis Evaluation Trial (EPI-THET) showed promising results by using a combination of diffusion and perfusion imaging as selection criteria for revascularization therapy beyond 3 hours.\textsuperscript{4,41,121} However, the MR and Recanalization of Stroke Clots Using Embolectomy (MR RESCUE) trial, a multicenter, blinded randomized-controlled trial, failed to show benefits in using penumbral imaging, and was also unable to show superiority of endovascular mechanical thrombectomy over medical treatment.\textsuperscript{207} The Desmoteplase in Acute Ischemic Stroke–phase II (DIAS-II) trial used MR diffusion/perfusion mismatch and a perfusion-CT mismatch as selection criteria to administer IV desmoteplase in patients presenting up to 9 hours since symptom onset.\textsuperscript{21} This trial also failed to demonstrate superiority of treatment over placebo.

Further randomized-controlled trials are needed to support the accuracy and usefulness of perfusion imaging in the selection of patients for acute reperfusion therapy. One of the ongoing trials is the EXTEND trial, in which patients with mismatch on diffusion/perfusion-weighted MRI or PCT in the 4.5- to 9-hour time window are randomly assigned to receive IV tPA or placebo.\textsuperscript{140}

Assessing Cerebral Collateral Circulation

Cerebral collateral circulation designates the alternate vascular pathways that allow ischemic brain tissue to receive its blood supply despite the occlusion of the primary supplying artery. Collateral vessels are divided into 1) primary collaterals at the circle of Willis and 2) secondary collaterals by recruitment of leptomeningeal vessels to perfuse adjacent cerebral and cerebellar territories in a retrograde fashion.\textsuperscript{128} Anatomical variation in the circle of Willis is common,\textsuperscript{128} and its appearance may change dynamically, from hypoplastic to ectatic, based on fluctuating demand.\textsuperscript{132} Collaterals have been shown to enhance recanalization and reperfusion, reduce the size of the final infarct core, slow ischemic lesion growth, decrease the risk of hemorrhagic transformation, and improve the outcome of IV thrombolytic therapy and endovascular recanalization.\textsuperscript{181,205} A poor pattern of collateral circulation has a high specificity for poor tissue and clinical outcome.\textsuperscript{10}

Currently, there is no established standard imaging technique to quantify and qualify the extent of collateral circulation. The Technology Assessment Committees of the American Society of Interventional and Therapeutic

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**Fig. 5.** MRA of the extracranial carotid artery. **Left:** 3D-TOF MR angiogram. This modality is more susceptible to motion artifact and overestimates the degree of stenosis at the internal carotid artery at the bifurcation of the common carotid artery (arrow). **Right:** Gadolinium-enhanced MR angiogram showing the true caliber of the right ICA bulb and also unmasking an ulceration (arrow) that could not be detected on the TOF MRA because of the absence of rapid flow within it.

**Fig. 6.** Vascular occlusion detected by CTA, MR 3D-TOF, and DSA. **A:** CTA maximum intensity projection demonstrating severe stenosis in the M\textsubscript{1} segment of the right MCA (arrow). There is retrograde filling of the distal portions of the right MCA by collaterals. **B:** MR 3D-TOF image demonstrating overestimation of the stenosis and showing absence of antegrade flow in the right MCA distal to the stenosis. **C:** DS angiogram demonstrating a short segment of tight stenosis in the proximal right MCA (arrow) with collaterals.
Neuroradiology and the Society of Interventional Radiology recently proposed a standardized classification scheme for leptomeningeal collaterals⁷⁸ (Table 4). Several imaging approaches have been explored, including DSA,⁸ CTA,¹⁴ arterial spin-labeling (ASL),³⁴,²¹⁵ PWI,⁸,¹⁵ and PCT.¹⁰

Primary and secondary collateral vessels can be directly characterized with conventional angiography utilizing DSA. Angiography illustrates collaterals in real time with good spatial and temporal resolution.¹² Angiography also has the unique ability to isolate each major vascular territory by selective injection.¹³

CTA has been proposed as a surrogate for DSA in the assessment of collateral circulation. However, CTA only offers a snapshot of the cerebral vessels without dynamic information and can only provide an approximation of the maximum extent of collaterals.¹² The dynamic nature of collaterals is better appreciated on PCT, which follows the dispersion of a contrast bolus by performing a repeated series of images at predefined slice locations.

Perfusion imaging techniques provide estimates of collateral flow through measurement of the contrast arrival delay, typically featuring prolonged time-to-peak (TTP) or mean transit time (MTT) with relative preservation of cerebral blood flow (CBF).¹²⁹,¹³⁰ ASL is a method for describing brain perfusion based on MRI without the need of a contrast medium. The blood in a region of interest is magnetically labeled. As the labeled blood flows, its paramagnetic effect alters the image intensity.³² ASL technique can be applied selectively to individual artery, thereby delineating the regions each vessel supplies. This technique can show collaterals, arising from one artery, supplementing another occluded or stenotic artery.³⁴

### Table 3: Perfusion-weighted imaging/diffusion-weighted imaging in acute ischemic stroke

<table>
<thead>
<tr>
<th>Finding</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>PWI &gt; DWI</td>
<td>mismatched regions likely represent penumbra</td>
</tr>
<tr>
<td>PWI = DWI</td>
<td>infarcted lesion, no penumbra</td>
</tr>
<tr>
<td>PWI &lt; DWI</td>
<td>early reperfusion of the ischemic tissue</td>
</tr>
</tbody>
</table>

Determined Eligibility for Endovascular Revascularization

Mechanical thrombectomy devices received FDA approval for use in patients presenting up to 8 hours after symptom onset because of early recanalization being associated with a 4- to 5-fold improvement in clinical outcome.¹⁷

Three imaging strategies for selecting patients for endovascular revascularization were proposed. In the first strategy, the patient proceeds to the angiography suite immediately after the initial NCHCT, thus minimizing the door-to-recanalization time. The patency of the vessels and collaterals are assessed by DSA. However, infarct volume can only be indirectly assessed by attention to flow, parenchymal blush, and arterial-to-venous transit times. The second strategy utilizes multimodal CT (NCHCT and CTA) to assess ischemic core and vascular patency (with optional PCT for penumbra assessment) for making decisions regarding endovascular therapy. The rationale for this approach is to limit catheterization studies to those patients with a vascular clot amenable to endovascular treatment. The third strategy uses multimodal MRI for information gathering, which includes DWI, the...
Acute stroke imaging

most accurate method, to assess the extent of the ischemic core. Several studies have demonstrated that the extra time required for MRI/DWI did not adversely affect the outcome.\textsuperscript{26,113,195} To date, there is no definitive evidence to favor one strategy over the other.

**Other Settings**

For the remaining patients not falling under the broad categories described above, imaging still plays a crucial role. This is a conglomerate group including those with wake-up strokes (in which patients awaken with neurological deficits), transient ischemic attack (TIA), and posterior fossa strokes.

**Wake-Up Stroke**

Currently, patients with unknown onset of symptoms, such as those who suffer wake-up stroke, are often denied treatment. Multimodal MRI (using DWI-PWI mismatch or DWI-FLAIR mismatch) or multimodal CT (NCHCT, CTA, and PCT) may be used to assess the “tissue clock.”\textsuperscript{100,209,210} A recent study has shown that a DWI-positive lesion in a patient with a concomitant normal FLAIR image suggests that less than 3 hours has elapsed, with > 90\% specificity and positive predictive value (Fig. 10). Therefore, if acute reperfusion therapy is considered, distinguishing a matched DWI-FLAIR lesion from a mismatched DWI-FLAIR lesion may be a plausible way to estimate the elapsed time since onset and identify patients.
who are likely to benefit from thrombolysis. However, there is no prospective evidence supporting imaging selection for treatment in this patient population.

Transient Ischemic Attacks

Patients with TIsA are a very diverse group in terms of their symptoms, risk factors, prognosis, and future stroke risk. As the presenting symptoms can be diverse, imaging can potentially help to improve the accuracy of TIA diagnosis. DWI abnormalities are found in approximately 40% of patients with TIsA.

After establishing the diagnosis of TIA, triage begins with identifying patients who require admission, which depends on their imminent stroke risk. Several scoring systems have been proposed to predict stroke risk in patients with TIsA. The ABCD2 score is one of the more widely used systems. This score represents the summation of points associated with 5 clinical factors independently predictive of stroke risk—age, blood pressure, clinical features such as unilateral weakness or speech impairment, symptom duration, and the presence of diabetes (Table 5). The ABCD2 score has been shown to accurately predict the risk of stroke at 2, 7, and 90 days following a TIA.

Studies have shown imaging, MRI, or CT can further enhance the prediction of stroke risk. Abnormalities on DWI are associated with a higher risk of additional vascular events. Other imaging features associated with stroke risk include occlusion of large cervicocerebral arteries and embolic signals on transcranial Doppler sonography.

![Fig. 9. Reversible DWI lesions. Axial DW (upper) and ADC (lower) images. The DW image obtained 1 hour (h) after presentation shows a hyperintense lesion in the right basal ganglia. The DW image obtained 4 hours after presentation shows a hyperintense lesion at the right inferolateral frontal lobe. The abnormality previously seen in the right basal ganglia has resolved. The DW image obtained 24 hours after presentation shows the hyperintense lesion at the right inferior frontal lateral lobe and reappearance of the lesion in the right basal ganglia.]

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>no collaterals visible to the ischemic site</td>
</tr>
<tr>
<td>1</td>
<td>slow collaterals to the periphery of the ischemic site, w/ persistence of some of the defect</td>
</tr>
<tr>
<td>2</td>
<td>rapid collaterals to the periphery of the ischemic site, w/ persistence of some of the defect, but only to a portion of the ischemic territory</td>
</tr>
<tr>
<td>3</td>
<td>collaterals w/ slow but complete angiographic blood flow of the ischemic bed occurring by the late venous phase</td>
</tr>
<tr>
<td>4</td>
<td>complete &amp; rapid collateral blood flow to the vascular bed of the entire ischemic territory, by retrograde perfusion</td>
</tr>
</tbody>
</table>

* Data obtained from Higashida et al.
Acute stroke imaging

![Axial DW image and Axial FLAIR image](image)

**Fig. 10.** Use of DWI-FLAIR mismatch to estimate the elapsed time since onset. **Left:** Axial DW image obtained in patient presenting with acute right-side weakness. There is restricted diffusion in the left basal ganglia, consistent with acute infarction. **Right:** Axial FLAIR image obtained in the same patient, showing no matching abnormality suggests an elapsed time of less than 3 hours.

Treatment of TIA is for secondary stroke prevention and is broadly divided into medical and/or surgical. The detailed recommendations for the treatment of TIA are beyond the scope of this review. (Please refer to the latest guidelines from the American Heart Association and American Stroke Association.) In brief, the current recommendations include antiplatelet therapy with rigorous lipid control. Surgical options include endarterectomy and carotid artery angioplasty with stent placement.

**TABLE 5: ABCD2 score to assess the risk of stroke after TIA***

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>age ≥60 yrs</td>
<td>1</td>
</tr>
<tr>
<td>SBP ≥140 mm Hg or DBP ≥90 mm Hg</td>
<td>1</td>
</tr>
<tr>
<td>clinical features</td>
<td></td>
</tr>
<tr>
<td>speech impairment</td>
<td>1</td>
</tr>
<tr>
<td>unilateral weakness</td>
<td>2</td>
</tr>
<tr>
<td>duration</td>
<td></td>
</tr>
<tr>
<td>10–59 min</td>
<td>1</td>
</tr>
<tr>
<td>≥60 min</td>
<td>2</td>
</tr>
<tr>
<td>diabetes</td>
<td>1</td>
</tr>
</tbody>
</table>

* Data obtained from Naghavi et al. DBP = diastolic blood pressure; SBP = systolic blood pressure.

Also used to identify stenosis. Overall, these noninvasive techniques have shown good agreement with DSA in approximately 90% of cases. Concordant results of two noninvasive techniques (DUS, CTA, and/or MRA) can be used to determine revascularization procedures, thus circumventing catheterization risks.

Assessment of atherosclerosis, an important risk factor for cerebrovascular ischemic events, has recently shifted from lumen measurement to the evaluation of the plaque structure and composition. Several features have been shown to increase the risk of cerebrovascular events, including plaque ulceration, intraplaque hemorrhage, and a ruptured or fissured fibrous cap. Ulceration within plaques is best imaged on CTA. Intraplaque hemorrhage is best evaluated with MRI, which can determine the chronicity of the hemorrhage by distinguishing signal intensities on T1-weighted, T2-weighted, proton density weighted, and TOF images. Protective features such as fibrous cap are best assessed on MRI.

Plaque composition can be evaluated on ultrasound, CT, or MRI. CT measures the density in Hounsfield units. The Gray-Weale classification is commonly used to evaluate the composition of ultrasonography, based on the echogenicity of the plaque. This classification has been shown to correspond to the fatty, mixed, and calcified plaques on CT. Plaque volume is easily calculated using CTA-based software. Plaque neovascularization, a hallmark of advanced atherosclerotic lesions, can be evaluated on contrast-enhanced ultrasonography, CT, and dynamic contrast-enhanced MRI.

**Posterior Fossa Stroke**

There are a few imaging aspects specific to posterior fossa infarction due to its unique location and dire prognosis. Poor image quality secondary to beam-hardening artifacts limits the sensitivity of NCHCT and PCT to posterior fossa ischemia. DWI is the optimal imaging technique to assess the presence of ischemia in the posterior fossa. DWI can also assess the degree of brainstem infarction before proceeding with endovascular treatment.

CTA and DSA are the preferred imaging techniques to assess for basilar artery thrombosis. In one study, the detection of basilar artery occlusion on CTA was equivalent to detection on DSA, with accurate location of the thrombosis, and equivalent capability of detecting stenosis > 50%. The extent of the thrombosis could be more precisely measured on CTA. However, CTA failed to detect occlusion in the vertebral artery in about one-half of cases. The differentiation between high-grade stenosis and hypoplasia on CTA was most disparate from DSA. MRA is an acceptable alternative.

Leniency regarding the treatment time window is often granted in cases of basilar occlusion due to its dismal prognosis.

**Stroke Complications**

Malignant edema and hemorrhagic transformation are the most feared complications of ischemic stroke. Hemorrhagic transformation, a common complication...
of severe stroke (Fig. 3), is likely caused by a synergistic combination of reperfusion and a disrupted blood brain barrier. The clinical presentation of hemorrhagic transformation is widely variable, ranging from subtle neurological findings to sudden rapid decline and death.

The spectrum of imaging findings is wide, ranging from petechial hemorrhage to confluent hemorrhage. Studies on thrombolytic treatment have categorized the findings into 4 groups: HI1, characterized by small petechiae along the margins of the infarct; HI2, characterized by more confluent petechiae within the infarcted area; PH1, characterized by hematoma involving 30% of the infarcted area or less, with slight mass effect; and PH2, characterized by dense hematoma involving more than 30% of the infarcted area, with substantial mass effect, or any hemorrhagic lesion outside the infarcted area. HI1 and HI2, often asymptomatic, occur more frequently than the more symptomatic PH2. Hemorrhagic transformation can occur in untreated patients, with a mildly increased incidence in patients receiving anti-thrombotic treatment and a significantly higher incidence after thrombolysis.

Different risk factors for hemorrhagic transformation have been identified: stroke severity,161 hyperglycemia/diabetes,83,84 and cardioembolic stroke.5,31,83,164 Radiographic risk factors include large infarct area,16,83,84,156,161,212 and early ischemic signs at the first NCHCT scan. It has been proposed that the incidence of hemorrhagic transformation depends on the underlying etiology. Specifically, cardioembolic stroke is widely accepted as a risk factor. Radiographic risk factors include large infarct area,16,83,84,156,161,212 and early ischemic signs at the first NCHCT scan. It has been proposed that the incidence of hemorrhagic transformation depends on the underlying etiology. Specifically, cardioembolic stroke is widely accepted as a risk factor. Some have postulated that the softer consistency of the embolus yields higher rates of recanalization, which subsequently leads to hemorrhagic transformation. Others have observed that cardioembolic strokes frequently cause large-vessel occlusion, resulting in large infarcted area, which in turn is a risk factor for hemorrhagic transformation.

Malignant edema, which is associated with a 40%–80% risk of death, occurs in 10%–15% of all MCA territory ischemic strokes.76,81 A “T occlusion” of the distal internal carotid artery is frequently associated with malignant edema.91,117 Solitary infarction from MCA branch occlusions typically do not result in swelling with clinically significant mass effect.74 Additional vascular territory infarctions, an incomplete circle of Willis, and poor collateral circulation are additional risk factors for the development of malignant edema. There is no reliable way to predict the course of brain swelling.

NCHCT is the follow-up imaging modality of choice for patients with cerebral infarcts with swelling. The degree of midline shift on NCHCT is the most commonly used benchmark for monitoring deterioration. NCHCT findings that predict malignant edema and poor prognosis include frank hypodensity on NCHCT within the first 6 hours and involvement of one-third of the MCA territory or more. The presence of a dense MCA sign or midline shift of 5 mm or more within the first 2 days are also associated with neurological deterioration and early mortality. Blood-brain barrier permeability measurement on admission PCT have been shown to be highly sensitive in predicting malignant edema and hemorrhagic transformation (100% sensitivity and 79% specificity).

Measurement of DWI volume has been studied as a method of predicting neurological deterioration from cerebral edema. A DWI volume of more than 80 ml within 6 hours of stroke onset is predictive of a rapid fulminant course. Results from PWI are inconsistent. Transcranial Doppler sonography, a noninvasive method for monitoring intracranial pressure, has been used for the detection of cerebral herniation and for therapy decision. High pulsatility indices correlated with increased midline shift and poor outcome. Near-infrared spectroscopy remains an investigational modality for nonin-
Acute stroke imaging

vasively obtaining information on intracranial oxygenation in patients with infarctions and swelling.⁴⁰

Conclusions

Neuroimaging has become a crucial component in acute stroke care. While capitalizing on the latest treatment options and expanding upon the “time is brain” doctrine, the ultimate goal of neuroimaging is to maximize the number of patients treated and improve the outcome of one the most costly and morbid diseases. Definitive validation of various aspects of stroke imaging awaits more research and further studies.

Disclosure

Dr. Wintermark reports receiving funding from GE Healthcare and Philips Healthcare and having a consultant relationship with Biogen Idec.

Author contributions to the study and manuscript preparation include the following. Conception and design: Wintermark, Tong. Acquisition of data: Fiebach. Drafting the article: all authors. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Wintermark. Study supervision: Wintermark.

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Neurosurg Focus / Volume 36 / January 2014

11
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Please include this information when citing this paper: DOI: 10.3171/2013.10.FOCUS13396

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