

# Imaging in Stroke Diagnosis and Treatment: An Update

## Description

As thrombectomy has become the standard of care for large vessel/arterial occlusions, the indications are initiated by proper imaging and understanding of the brain blood flow physiology. This two-part series examines the standard of care for acute stroke imaging and the latest techniques. The second part of this activity on stroke intervention will appear in the November-December issue of *Applied Radiology*.

## Learning Objectives

Upon completing this activity, the reader should be able to:

- Understand the concept of “time is brain” and the importance of prompt diagnosis of acute ischemic stroke;
- Select the imaging modalities that can be employed for the evaluation of acute ischemic stroke; and,
- Identify which patients are likely to have a good outcome after thrombectomy utilizing CT perfusion.

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## Target Audience

- Radiologists
- Related Imaging Professionals

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Estimated time for completion: 1 hour

Date of release: September 1, 2021

Date of Review: October 19, 2023

Expiration date: August 31, 2024

## Disclosures

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*Editor's note: This is the first of a two-part series. The second part will appear in the November-December 2021 issue of Applied Radiology.*

The prevalence of stroke is steadily rising and annual stroke-related deaths (6.55 million) have increased by 43.3% since 1990, according to the global burden of diseases study 2019 data.<sup>1</sup> Ischemic stroke contributed to 62.4% of the reported cases and remains a leading cause of morbidity and the second-most common cause of mortality.<sup>1</sup>

Management of ischemic stroke within the initial 4.5 to 6 hours of presentation may salvage the area of insufficiently perfused brain tissue that is still viable but “at risk” of ischemic injury if not treated. Research has been rapidly evolving with newer approaches to prevention and treatment.<sup>2,3</sup> Despite medicine’s best efforts, preventative therapy may not be enough for some patients. Therefore, a prompt diagnosis with possible emergent treatment of an acute infarct becomes imperative to mitigate permanent neurological deficit and even death.

Cases amenable to endovascular treatment (EVT) require activation of the multidisciplinary stroke service, with rapid patient assessment, imaging, and treatment. The phrase “Time is Brain” forms the essence of acute ischemic stroke management and emphasizes the importance of

early clinical recognition, establishing a diagnosis, and assessment severity based on radiological imaging and treatment. Through extensive studies on the multitude of patients who have suffered acute infarcts, guidelines and timelines have been developed to identify patients who will benefit most by medical therapy, or EVT, and a preventative strategy for future possible stroke.

It has been reported that for every 30-minute delay in treatment after the onset of an acute infarct, the likelihood of a favorable outcome decreases by approximately 11%.<sup>4</sup> Acute ischemic strokes secondary to proximal large-vessel occlusion (LVO) carries a higher risk of morbidity and mortality.<sup>4</sup> The importance of emergent and reliable imaging for the diagnosis of LVO cannot be overstated. We aim to discuss the diagnosis and treatment of acute ischemic stroke in a series of two review articles. In this first article, we review various imaging modalities that are utilized to diagnose acute ischemic stroke. The second part,

appearing in the November/December 2021 issue of *Applied Radiology*, will focus on treatment.

## Noncontrast Computed Tomography

A noncontrast computed tomography (CT) head is the first step in the imaging workup of acute ischemic stroke, as it is widely available and can rapidly rule out a hemorrhagic stroke, which would be treated differently. With minimal risk of radiation, CT is indispensable to providing essential information regarding the size of an infarct, the affected territory, core infarct volume, and collateral supply (Figure 1). It is highly valuable in the setting of patients with implanted cardiac defibrillators or implants, where MRI is contraindicated.

With regard to middle cerebral artery (MCA) territory occlusions/infarcts, the most commonly affected territory, the Alberta stroke program early CT score (ASPECTS) allows for an effective, semi-objective measure of the degree of infarct.<sup>5</sup> ASPECTS is a 10-point scoring system and one point is deducted for each of ten predefined areas (caudate, putamen, internal capsule, insular cortex and six areas in MCA territory). Therefore, the system provides a simple and rapid measure of stroke burden

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**Figure 1.** (A) Noncontrast axial CT head demonstrating a focal hyperdensity in the left MCA due to thromboembolic material, the left “hyperdense MCA sign” (arrow). (B) Noncontrast axial CT head of the same patient at level of the ventricles does not show any hypodensity (as would be seen in an infarct) in the left MCA territory in this older patient with prominent sulci.



that has been validated to prognosticate about the feasibility and likely outcome of reperfusion (Figure 2). ASPECTS 6 or more is the established cut-off criterion as per American Heart Association (AHA) guidelines to consider stroke patients for endovascular intervention.<sup>6</sup>

ASPECTS was conventionally considered applicable only to the anterior circulation.<sup>7</sup> However, in a recently published study, Caruso, et al, have demonstrated the feasibility and validity of the posterior circulation Alberta stroke program early CT score (Pc-ASPECTS) in 50 patients with posterior circulation strokes. Pc-ASPECT MTT was found to be the most reliable parameter in predicting clinical outcome.<sup>8</sup>

ASPECTS scoring has certain limitations. These include modest

interobserver variability owing to potential subjective bias in interpretation, unequal contribution of the included regions towards clinical outcomes, and difficulty in reproducibility.<sup>9,10</sup> Recent advancements include the use of automated software to evaluate ASPECTS rapidly and potentially eliminate the interobserver variability.<sup>11</sup> When combined with perfusion imaging using an intravascular tracer, a noncontrast CT head may yield information to help detect salvageable brain parenchyma in patients with LVO.<sup>12</sup>

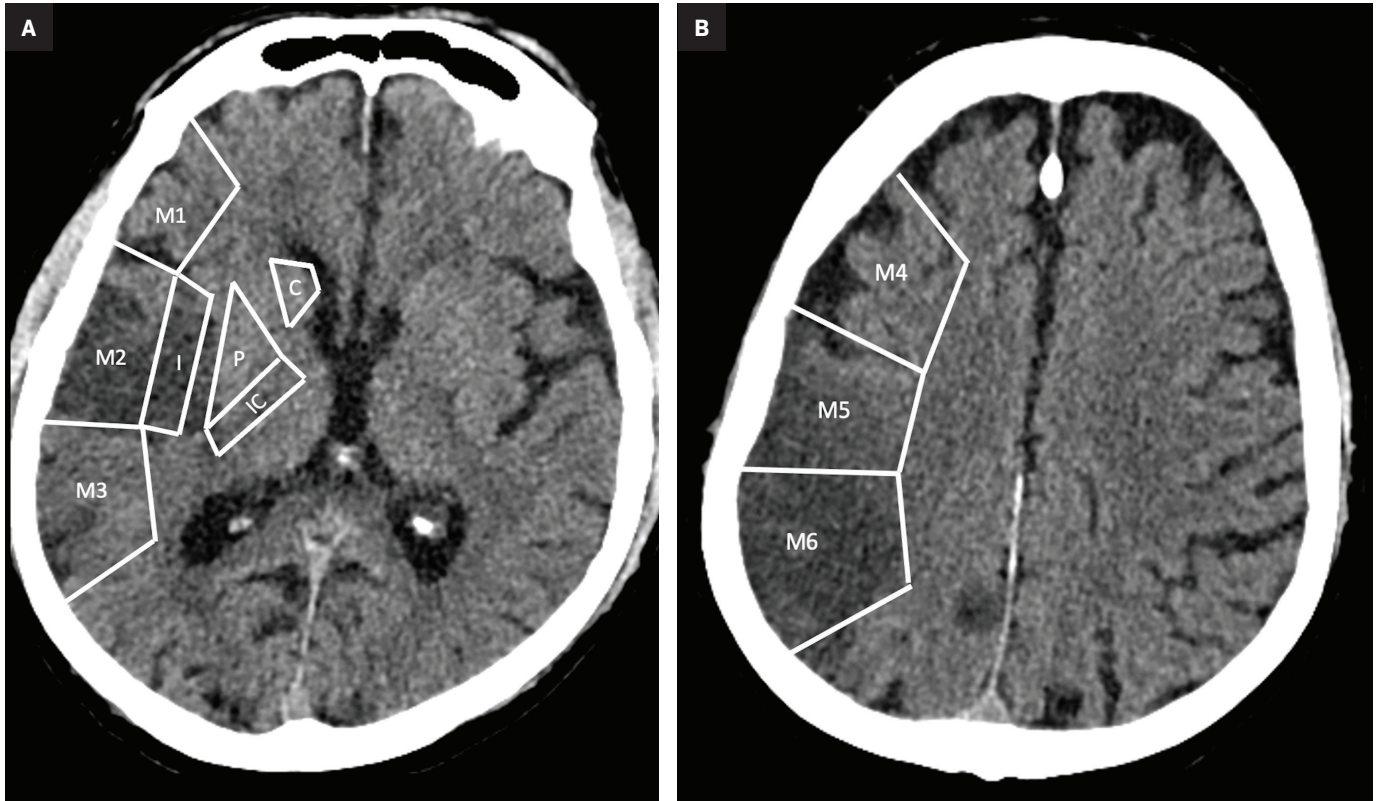
### CT Angiography

Requiring a rapid, well-timed intravenous administration of contrast material, CT angiography (CTA) is an effective method for imaging

cerebrovascular anatomy. CTA is recognized to be a highly sensitive (92-100%) and specific (82-100%) method for detecting LVO.<sup>13</sup> Additionally, the modality allows assessment of the aortic arch anatomy, the branching of large vessels, and the presence of calcifications, atherosclerotic plaques, and/or stenoses — an assessment that is crucial to identifying patients for endovascular intervention (Figure 3). CT angiography also serves an important role in the identification of other conditions that may present with clinical features similar to those of stroke.

The cerebral circulation may have multiple subsidiary vascular channels, called “collateral circulation,” which serve as a backup supply to the brain parenchyma in occlusions of the primary arterial supply.

**Figure 2.** ASPECTS score calculation in a patient who presented with left body hemiparesis suggestive of right MCA infarction. The score is calculated in with consideration of the segmental estimation of the MCA territory. Highest normal score is 10 and 1 point is deducted from the initial score for every region involved evaluated at the cut section of the basal ganglia (A) and at the level above the lateral ventricles (C, caudate; P, putamen; IC, internal capsule; I, insula; M1-6, portions of MCA territory). (B) This patient has an ASPECTS of 6 due to involvement of I, M2, M5, and M6.



Collateral circulation is recognized as an independent predictor of a good outcome in ischemic stroke (Figure 3).<sup>14</sup> Multiphase CTA helps to identify the collateral supply and may prove highly useful regarding treatment decisions (Figure 4).

The ischemic core of the infarct--the irreversibly damaged brain tissue---and surrounding, potentially salvageable brain parenchyma or “penumbra” in the affected vascular territory may be identified by hypodensity or absence of contrast opacification as compared to normally perfused regions of parenchyma. Therefore, CTA can indirectly help estimate perfusion in a vascular territory. A study by Camargo, et al, demonstrated a higher sensitivity with CTA in comparison with

noncontrast CT for detecting ischemic changes and predicting final infarct volume.<sup>15</sup>

### Mismatch Imaging

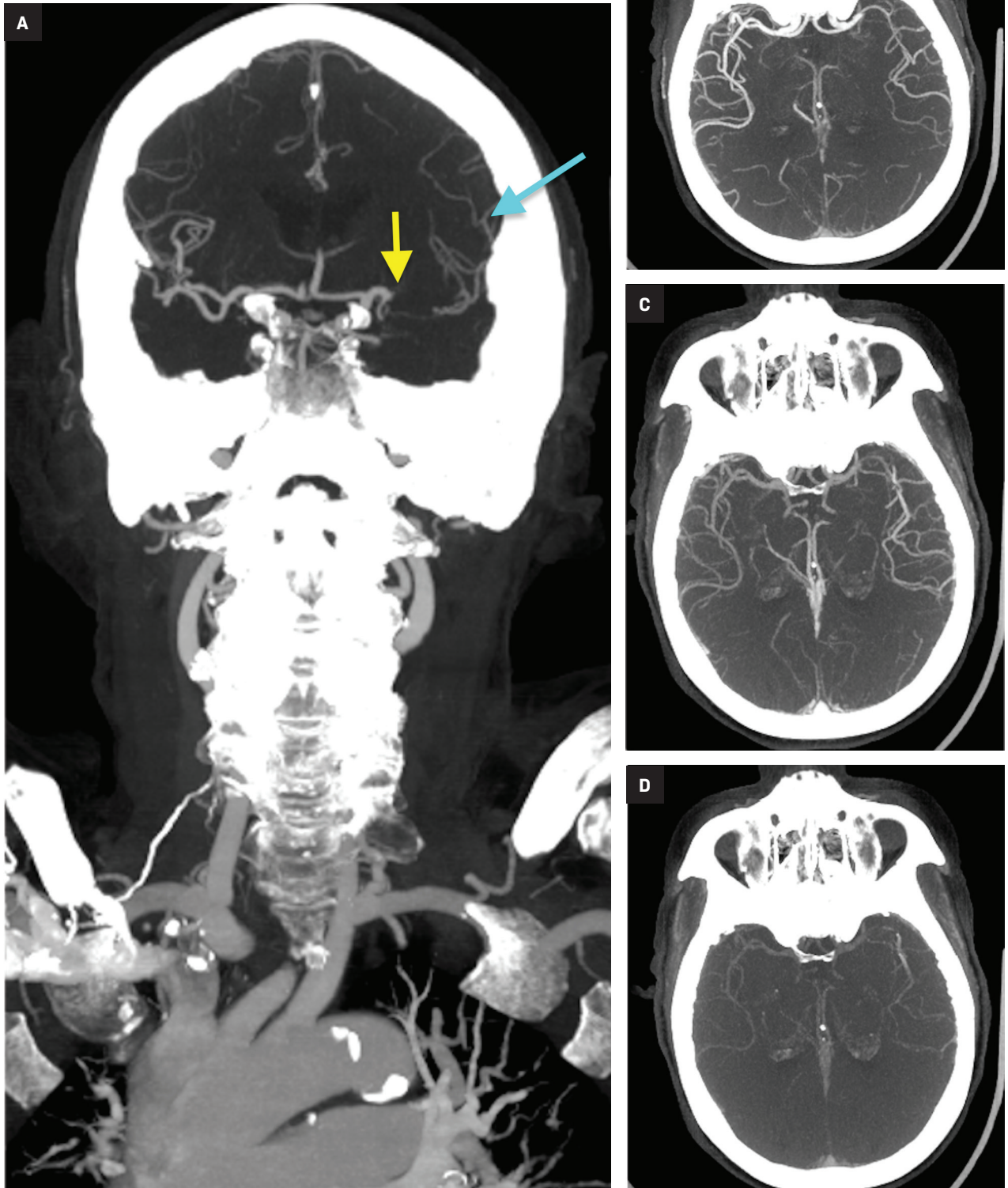
The concept of mismatch imaging relies on differentiating between the infarct core and the surrounding penumbra based on their imaging characteristics. Identifying a large penumbra may help to salvage it with timely intervention, subsequently reducing the final volume of infarct.

The standard treatment for acute ischemic stroke within 6 hours of presentation is mechanical thrombectomy. However, thrombectomy and revascularization may still be beneficial in patients beyond this time window, especially if the

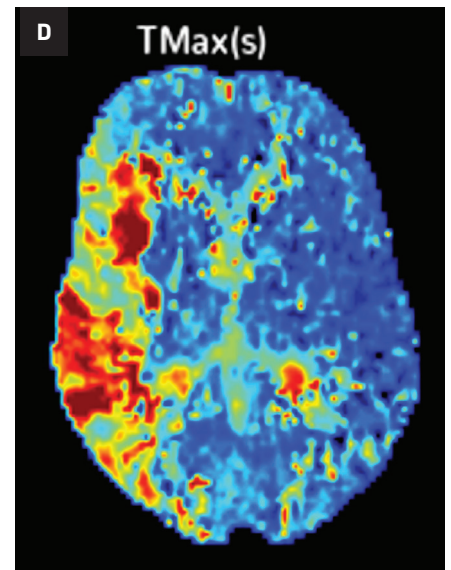
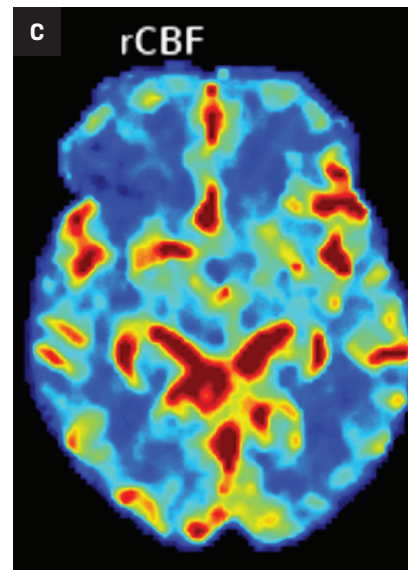
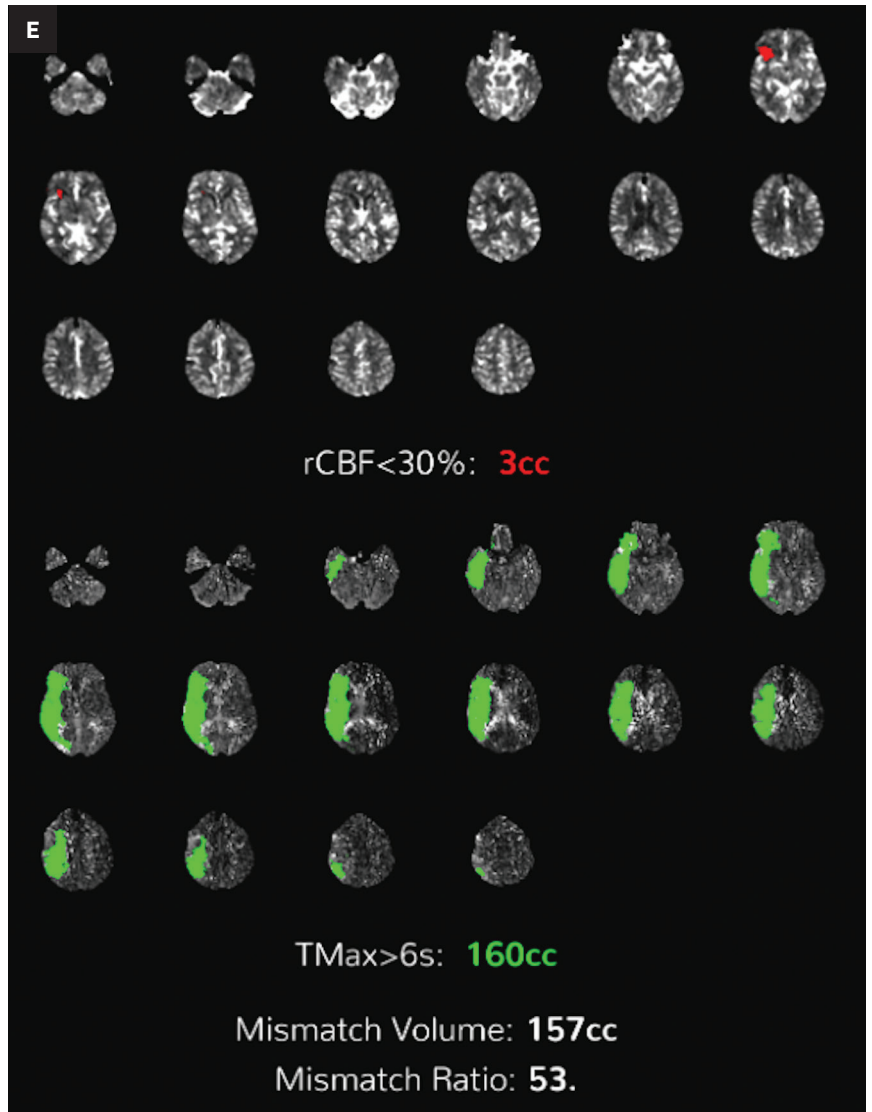
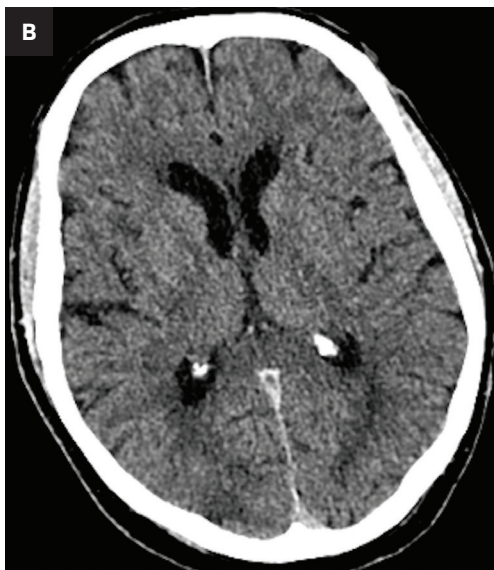
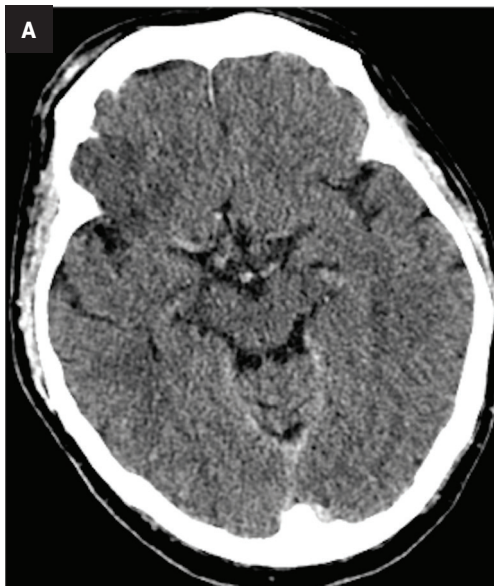
ischemic penumbra is large.<sup>16</sup> Both CT and MRI can be used to assess this mismatch.<sup>16</sup>

In acute cerebral ischemia, cell edema occurs first, followed by angioedema. Diffusion weighted imaging (DWI) is the most sensitive noninvasive method for detecting cytotoxic edema associated with ischemic injury.<sup>16</sup> A fluid-attenuated inversion-recovery (FLAIR) sequence can detect vasogenic edema caused by cerebral ischemia and hypoxia in tissue that is not completely beyond viability. The amount of FLAIR hyperintensity beyond areas of reduced diffusivity is called the DWI-FLAIR mismatch, and it is used to quantify the extent of penumbra. DWI-FLAIR mismatch plays an important role in treatment decisions for patients

**Figure 3.** (A) CT angiogram coronal reformation in a patient who presented with a “wake-up” left MCA stroke demonstrating the site of occlusion at the left M1 segment (yellow arrow) and retrograde filling of the cortical MCA branches through collateral vessels (blue arrow). Multiphase CT angiograms (axial views, MIP images) performed (B) in the arterial phase, (C) first delay scan after 4 seconds, and (D) second delay scan after 8 seconds demonstrate the left M1 occlusion and collateral supply through anterior temporal branch as delayed filling of the left MCA branches.



**Figure 4.** (A, B) A patient with ASPECTS score 9 (one point deducted for right MCA territory hypodensity) on initial noncontrast CT imaging underwent CT perfusion mismatch imaging (C, D) which demonstrated a small ischemic core in the right frontal lobe (rCBF less than 30%) with a large penumbra (TTP >6 seconds) which was salvageable. (E) A significant mismatch volume of 157 cc was observed in this patient, who subsequently underwent thrombectomy.



**Figure 5.** Post-thrombectomy Spectral CT imaging in the same patient as Figure 4. (A) A hyperdense signal is observed in the area corresponding to the involved territory (arrow). (B) Mono energetic scan at 50 KeV demonstrates the hyperdensity (arrow) which resolves on (C) a high energetic (140 KeV) scan (arrow) suggesting that the hyperdensity is due to the injected contrast medium during the thrombectomy.



who present within 6 to 24 hours of onset and for those with “wake-up strokes,” where the timing of onset is unknown.<sup>16</sup>

Perfusion-based quantitative assessments can also provide valuable information, including such data as cerebral blood flow (CBF), defined as the flow rate of blood within a region of brain. Cerebral blood flow drops in cases of compromised arterial supply.<sup>17</sup> The time to perfuse a territory with compromised arterial supply is higher than that of normally perfused tissue. This phenomenon can be quantified by the time-to-peak (TTP), a measurement of time required for a given region of brain to reach maximal attenuation.<sup>17</sup>

In viable but ischemic tissue, cerebral blood volume (CBV), the total amount of blood within a given region of the brain, may be normal or slightly increased as a result of autoregulatory vasodilation. However, in irreversibly injured tissue, CBV is low owing to loss of autoregulation.<sup>17</sup> Mean transit time (MTT) is the length of time a certain volume of blood spends in the capillary phase. Mean transit time can be calculated by dividing the cerebral blood volume by cerebral blood flow.

Both MTT and TTP can be used to determine whether a significant amount of salvageable tissue remains after an ischemic event. The TTP threshold of 6 seconds is commonly used to define hypoperfused territory, which includes salvageable penumbra and ischemic core. The core is commonly defined as a decrease in CBF <30% of the contralateral territory (Figure 5).<sup>17</sup>

One study that compared the predictive clinical outcomes from CT ASPECTS and CT perfusion-based quantitative assessment of the core volume in 508 patients with acute, emergent, large-vessel occlusion did not demonstrate any statistical difference between the two methods.<sup>7</sup>

## Dual-layer Spectral CT

An advanced imaging technique, dual-layer spectral CT (DLSCT) is increasingly being utilized by leading stroke centers worldwide. The technique is based on an advanced detector system that can capture the photons of low and high energy simultaneously without requiring a change in the X-ray tube parameters.<sup>18</sup>

It has been well established that parenchymal hyperdensity may be observed on post-thrombectomy noncontrast CT scans as result of iodinated contrast injection during the procedure. Therefore, differentiating this hyperdensity from hemorrhage is highly pertinent (Figure 6). The dual-layer detection system in DLSCT can differentiate between hemorrhage and extravasation of iodinated K-edge, which proves highly useful in acute stroke management, especially after mechanical thrombectomy.<sup>18-20</sup>

Such information is crucial in deciding whether to use anticoagulants and antiplatelet agents after mechanical thrombectomy and in stroke patients receiving iodinated contrast prior to transfer to a thrombectomy-capable center. A recently published study by Riederer, et al, demonstrated 100% sensitivity and specificity for DLSCT in the detection of blood.<sup>19</sup>

## New Technologies for Analysis

New telemedicine platforms permit more efficient workups to be performed even before patients present in the hospital.<sup>21</sup> With advances in personal mobile device hardware, radiological imaging can be viewed remotely in almost any situation.<sup>21</sup>

Artificial intelligence (AI) and machine learning (ML) software tools are increasingly being used for stroke diagnosis. For instance, Viz

LVO (Viz.ai, San Francisco California) uses an algorithm to detect LVOs on CT angiography. The software is able to alert stroke specialists within minutes of image completion, a crucial component when “Time is Brain.”<sup>21</sup>

In summary, rapid, effective, and reliable medical imaging plays a crucial role in the diagnosis and treatment of acute ischemic stroke. Applied on a case-by-case basis, imaging modalities such as MRI and CT provide for effective approaches to acute stroke management.

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