The Case:
A 70-year-old woman presents within 4 hours of acute onset of loss of consciousness and right-sided weakness. NIHSS score is 17. Plain, non-contrast, head CT scan (NCCT) shows no ICH or early signs of ischemia. She meets all eligibility criteria for intravenous thrombolysis (IV tPA).

The Questions:
(1) Should vascular imaging (CTA, MRA, or TCD) be performed prior to consideration of tPA?
(2) Should brain perfusion imaging studies be performed prior to consideration of tPA?
(3) Are the results of these studies likely to change management decisions?

The Controversy:
Should advanced brain imaging studies be performed in patients with suspected stroke presenting within 4.5 hours of symptom onset.

Advanced Brain Imaging Studies Should Be Performed in Patients With Suspected Stroke Presenting Within 4.5 Hours of Symptom Onset

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This case, on superficial glance, is a classic example of a patient who should receive intravenous tissue-type plasminogen activator (IV tPA). Indeed, for the “lumpers,” who worship at the altar of evidence-based medicine, this would be the only appropriate course of action. On the other hand, the “splitters” believe that stroke treatment should be individually tailored and guided by tissue pathophysiology. Since the 1980s, the more devout splitters have been searching for what they believe to be the “Holy Grail” of stroke, the ischemic penumbra. They argue that unless we use the now widely available modern imaging techniques in the routine assessment of patients with acute stroke, we will never gain a sophisticated understanding of acute stroke pathophysiology nor will we learn how to influence its natural history with current and new treatment approaches.

The case example illustrates the chasm in philosophy. The patient fulfills the guidelines for IV tPA treatment. According to the lumpers, no more information is needed, go ahead and treat. How easy! Let us follow a splitter’s approach to this case and see how modern brain imaging helps assist clinical decision-making (and may ultimately advance scientific knowledge). What are the modern brain imaging techniques? “Multimodal CT” includes vascular and tissue imaging (CT angiography and CT perfusion) as does MRI (MR angiography, diffusion-weighted imaging, and perfusion-weighted imaging). Stroke MRI has some diagnostic advantages but is definitely slower, less accessible, and at least 10% of patients are not MR-compatible. Both modalities have their place. Transcranial Doppler does not have a tissue imaging equivalent; thus, I consider this to be an inferior approach. So, what would a splitter like to know about this patient?

What is the diagnosis? This seems relatively straightforward, although there is no positive finding on noncontrast CT to support the clinical diagnosis. Does “the acute loss of consciousness” simply reflect aphasia? Could the patient have had a seizure with a postictal clinical deficit that would entirely explain her presentation? Vascular imaging, in isolation, would probably give a positive diagnosis in this patient, but the addition of tissue imaging (CT perfusion or diffusion- and perfusion-weighted MRI) provides added diagnostic confidence to the splitter that they are not dealing with a stroke mimic.

What is the topography and mechanism of the stroke? No information is provided by noncontrast CT. We are expecting to see a large artery occlusion (probably internal carotid artery or M1-middle cerebral artery) on vascular imaging. However, it is also not uncommon to see a relatively severe clinical deficit due to distal emboli in the middle cerebral artery that are difficult to directly visualize on vascular imaging. Perfusion imaging is more sensitive in this situation.
Another scenario is a small vessel occlusion (e.g., thalamic) mimicking a proximal large artery occlusion. Diffusion-weighted imaging probably wins here, but in our center, we have been impressed with the sensitivity of perfusion CT to detect single perforator perfusion lesions.

How much brain is dead? No information provided by noncontrast CT. Why is it important to know? Well, it may not change our decision to treat, but there is considerable evidence that infarct core volume on baseline imaging is one of the most powerful predictors of outcome, even with successful reperfusion. What is most accurate at measuring dead brain? Diffusion-weighted imaging probably, but there is accumulating evidence to indicate CT perfusion infarct core measurements are also accurate.

How much brain is there to salvage (“the Holy Grail”)? Clearly, this is correlated with extent of infarct core, and perfusion imaging is required to determine. Why is it important? Patients with small penumbral volumes, for example, may do as well without tPA as they do with it.

What method should we use to salvage brain and how long do we have to do so? Vascular imaging provides crucial information here. The probability of recanalizing a terminal internal carotid artery (or even proximal M1 middle cerebral artery) occlusion with IV tPA is so low that many splitters now would consider endovascular (or bridging) approaches to be first-line treatment. However, again, perfusion imaging adds to the splitter’s pathophysiological assessment by determining whether there is much brain left to salvage. Indeed, aggressively reperfusing large regions of dead brain is unlikely to favorably impact the patient’s outcome. Perfusion imaging may also quantify collateral flow so that we can gain an insight into “penumbral life expectancy.” Poor collateral flow may also predict lack of response to IV tPA.

If we can salvage ischemic brain, will it make any difference to the patient’s outcome? This is the most difficult question and one that we will never answer if we persist in performing only noncontrast CT. The answer will vary dramatically depending on modern brain imaging data. The current patient is at 4 hours and has a National Institutes of Health Stroke Scale score of 17. Notably, this is much more severe than the median of 9 in European Cooperative Acute Stroke Study (ECASS) III, so clinically you might hazard a guess that her chances of benefit from IV tPA would be less. However, modern brain imaging should be able to tell us that in her individual case, the odds might be as good as 1 in 2 of an excellent outcome with IV tPA (e.g., distal M1 or M2 occlusion, small core, big penumbra, good collaterals) or might be very close to zero (e.g., T-internal carotid artery occlusion, large core).

We are not quite at the stage of an individualized acute treatment approach based on modern brain imaging, but we have the tools now to refine this approach and implement it. Surely, this is a worthwhile scientific goal, and surely our patients and their families deserve this information.

**Disclosures**

M.W.P. receives a Fellowship from the Australia Research Council, Project ID FT0991128.

**References**


**Key Words:** acute Rx acute stroke imaging thrombolysis
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Stroke. 2011;42:2666-2667; originally published online August 4, 2011;
doi: 10.1161/STROKEAHA.111.621771
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2011 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/42/9/2666

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