AJNR

Acute Stroke Imaging: What Is Sufficient for Triage to Endovascular Therapies?

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AJNR Am J Neuroradiol 2012, 33 (5) 790-792
doi: https://doi.org/10.3174/ajnr.A3098
http://www.ajnr.org/content/33/5/790

though nationally sensitive work there is off limits to the public, the Mag Lab part of the facility is open and accessible. Los Alamos National Laboratory is located in New Mexico, and the largest nearby town is White Rock; the better known Santa Fe is about 35 miles away. The entire Los Alamos site is a group of about 1800 buildings spanning 35 square miles.

The third and complementary site of this effort resides at the University of Florida in Gainesville, a city of about 130,000 inhabitants located in northern Florida about 100 miles from Disney World. The University is quite large with over 51,000 students and nearly 5000 faculty members. There the Mag Lab facility is located in the McKnight Brain Institute and involves MRI and MR spectroscopy, hence its name: the Advanced MRI and Spectroscopy (AMRIS) facility. The Institute is one of the world's biggest neuroscience research operations with a faculty of over 300. There one finds 7 magnets, including an 11T unit with a 40-cm bore and a whole-body 3T unit. Unfortunately, their Web site seems a bit anachronistic and simple and does not offer a great deal of information.

The Laboratoire National des Champs Magnétiques Intenses in Grenoble is one of the main institutions belonging to the Centre National de la Recherche Scientifique in France and is open to researchers from the 27 states of the European Union and adjacent countries such as Turkey, Israel, and others. Grenoble is located in southeast France, close to the Italian border and at the foot of the Alps, a location that has earned its nickname: the Capital of the Alps. Housed in this laboratory is a 35T magnet with a 34-mm-wide bore The Laboratoire National des Champs Magnétiques Intenses in Toulouse is found in southwest France. Because Toulouse is also known as La Ville Rose, it is not unexpected that its building has pinkish tones. There one finds magnets capable of 45T or 60T during pulses as long as 1 second in duration and of 150T–260T for only microseconds. Both of these facilities form part of the larger EuroMagnet Net II (Research Infrastructures for High Magnetic Field in Europe).[5]

Other facilities that are part of EuroMagnet Net II include the High Field Magnet Laboratory in Nijmegen, the Netherlands.[6] This laboratory is housed in a beautiful modernist building that has a curvy, sensuous façade and contains 32T magnets and is building a new 32 mm magnet which they claim will make 38 T and a hybrid one which will make 45 T. As well as an extensive magnet research and application program in many ways similar to the Mag Lab, some of their work applies magnetic levitation such as is used in magnetic levitation trains and levitation displays (used in those globes that seem to float on air). A provocative idea is that humans, if placed in a strong enough magnetic field, can also levitate. Another EuroMagnet Net II facility is the Dresden High Magnetic Field Laboratory located in Germany.[7] This facility is located in the countryside outside the city of Dresden. It is a part of a large physics campus called the Helmholtz-Zentrum Dresden-Rossendorf. Magnets 70T and above are housed in a no-nonsense, industrial-looking modern building. Laser beams allow spectroscopy at very high field strengths.

The largest similar installation in Asia is the Tsukuba Magnet Laboratories in Japan.[6] This facility was established in 1993, and today it houses 17 high-field strength magnets including resistives, hybrids, pulsed and superconducting magnets. A superconducting unit capable of producing 24T just became operational. The facility was not open to external researchers until 1998. It is under the direction of the National Institute of Materials Science, which has established a collaborative research effort with the University of Washington in Seattle.

I hope that this short editorial complements my previous one about the industry of CT scanning. It is important for us, clinical neuroradiologists, to realize that magnets are used by other researchers whose areas of interest are very different from ours. I wish to thank Dr Robert Quencer, who gave me the idea for this *Perspectives*.

Acknowledgments

I sincerely thank J.S. Blackband, G. Boebinger, and M. Bird from the Mag Lab Tallahassee and Gainesville locations for their corrections, suggestions, and encouragement.

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http://dx.doi.org/10.3174/ajnr.A2802

EDITORIAL

Acute Stroke Imaging: What Is Sufficient for Triage to Endovascular Therapies?

There has been much recent debate regarding the role of advanced imaging in general—and CT perfusion (CTP) in particular—in acute stroke management.[1] Typical questions include the following:

1) CT versus MR imaging: which technique is essential/sufficient/preferred for patient selection for lytic and endovascular stroke therapies?

2) Vascular/collateral imaging: is there a role for CTA or MRA in acute triage to lytic and/or endovascular stroke therapies; are they worth the time required?

3) Core or penumbra: what measures of admission stroke severity (both depth and extent of ischemia) best predict tissue and clinical outcome and the potential risks and benefits of treatment, and how can one best determine these?

4) Perfusion imaging: when is it indicated, does it have added value for acute stroke assessment, and, if so, how should

it be technically performed (acquisition and postprocessing) and optimally interpreted (which map, what threshold)?

The response to these queries depends critically on the sensitivity, specificity, and reproducibility of the various imaging techniques, which not only vary in a nonlinear manner with time post-ictus but also reflect a "snapshot" in time of a rapidly changing hemodynamic and physiologic process. We define "core" as critically ischemic brain tissue likely to be irreversibly infarcted despite early robust reperfusion and "penumbra" as severely ischemic but still viable tissue, likely to infarct in the absence of early robust reperfusion.

In brief, the answers are the following:

1) An **unenhanced head CT** excluding hemorrhage is necessary and sufficient screening for standard IV thrombolytic therapy.

2) A **CTA** to detect proximal large-vessel occlusion

a) Is quick and highly accurate (more than MRA) for identifying candidates for endovascular stroke treatment; and

b) Can be obtained without slowing IV thrombolysis.

3) **"Core is critical"** for determining endovascular treatment eligibility.

a) Patients with admission core volume >70–100 mL are highly likely to have poor clinical outcome despite early robust reperfusion (and more likely to bleed following recanalization).

b) The most accurate practical way to determine core, with strong level 1 evidence, is with **DWI**.

c) Despite the superiority of DWI for sensitive core detection—especially at early (<3 hours) times postonset—many neurointerventionalists consider an unenhanced CT good enough for endovascular triage (yet-to-be validated).

4) **If MR imaging is unavailable,** appropriately thresholded CT cerebral blood flow (CBF) maps can distinguish small (<70–100 mL) from large (>70–100 mL) admission cores

a) With high specificity for poor outcome, and

b) With greater accuracy than other CTP maps, including cerebral blood volume (CBV).

c) However, thresholds vary by postprocessing platform.

5) Advanced imaging, most notably **CT or MR perfusion**, can facilitate accurate diagnosis, patient selection, outcome prediction, and other management decisions, but

a) Most patients with proximal large-vessel occlusion and small core have mismatch (so mismatch does not add much to the endovascular triage decision).

b) Penumbral imaging has not been validated for extending the time window for IV thrombolysis; and, most important

c) The time needed for perfusion scanning must never slow the administration of definitive reperfusion therapies.

For triage to IV-tPA, opponents of advanced imaging argue—convincingly, on the basis of level 1 evidence—that 1) IV lysis is FDA-approved ≤3 hours post-ictus on the basis of prospective randomized trials proving clinical benefit; 2) IV lysis is safe and effective, albeit with a high "number needed to treat," ≤4.5 hours post-ictus; 3) "Time-Brain"; delays in IV lysis result in the death, on average, of almost 2 million neurons/minute[2]; and 4) an unenhanced head CT showing no hemorrhage is sufficient for deciding tPA eligibility.[1]

Once the decision to administer thrombolysis has been made, a rapid head and neck CTA can be obtained immediately during the 10 minutes required to mix the IV-tPA, without slowing treatment. The CTA identifies vascular occlusions that are targets for endovascular approaches (including FDA-approved clot retrieval ≤8 hours post-ictus) and can characterize both collateral flow and parenchymal "first pass" perfusion (from the CTA source images [SI]).[3] This approach presupposes that despite FDA approval for a variety of clot-retrieval devices, endovascular therapy is indeed indicated. Some evidence-based purists counter that "until and unless the Interventional Management of Stroke 3 trial is completed . . . management of proximal occlusions remains speculative and thus patients should be offered the trial or be informed of the unproven nature of the proffered 'rescue' treatment."[1]

What other imaging is required to weigh the risks versus benefits of treatment? Expert recommendations[4] suggest that the admission core lesion volume >70–100 mL, together with admission NIHSS score, is one of the most important independent predictors of poor outcome[5] and hence a necessary exclusion for endovascular treatment.[5,6] This makes sense; why risk a large hemorrhage by attempting "futile" recanalization of already dead tissue?

How best to measure core? Here, opinion diverges on the basis of local practice and available resources. The most accurate, but least practical, is carbon 11 flumazenil PET.[7] Unenhanced CT is rapid, convenient, and affordable but insensitive for the detection of early (<3–6 hours) ischemia. Many consider CT good enough for endovascular triage—at least for later times post-ictus—by using a "one-third MCA territory hypoattenuation" or "Alberta Stroke Program Early CT score ≤7" (corresponding to a >70–100-mL core) as the cutoffs for poor outcome. CTA-SI is more sensitive than unenhanced CT for ischemia detection at <3–6 hours, although the source images obtained by using fast current-generation multidetector row scanners tend to be flow- rather than volume-weighted and hence less well-correlated with DWI core.[8] CTA-SI also allows collateral vessel assessment; a "malignant" (near-zero) collateral pattern has recently been shown to be both highly specific for poor outcome and strongly correlated with a large DWI core.[9]

DWI, based on Level 1 evidence, is unequivocally the most accurate practical imaging test for core, as early as 30 minutes post-ictus. However, what if MR imaging is unavailable? Which CT parameters can accurately estimate core? As already noted, the "jury is still out" on the use of standard unenhanced CT for endovascular triage; it's sensitivity at very early time post-ictus (<3hr) may be insufficient. Moreover, the paradigm that admission CT-CBV maps optimally correlate with DWI has recently been challenged; ongoing studies by multiple groups suggest that appropriately thresholded CT-CBF maps, obtained by using updated current-generation acquisition and postprocessing protocols, provide the most accurate estimate of core.[10,11] Ideally, CTP acquisitions should be sufficiently long (>60–90 seconds) to avoid truncation of the contrast time-attenuation curves and postprocessed by using delay-insensitive software.

An important caveat is that the quantitative thresholds used for CTP map interpretation vary widely, not only among

software of different vendors but also among different software versions from the same vendor, limiting their generalizability. This problem is one of standardization; effort is currently underway within the stroke community to address this.[12] It is equally noteworthy, however, that for the purpose of selecting patients for endovascular stroke therapy, the correlation between CTP and DWI ischemic lesion volumes need not be perfect: CTP should only be able to accurately distinguish large (>70–100 mL) from small (<70–100 mL) admission ischemic lesion volumes. Preliminary data suggest that this is indeed the case.[13]

On the basis of these considerations, our neuroradiology section, in a consensus symposium led by Gil Gonzalez, developed the following acute stroke imaging algorithm delineating the imaging evaluation that we consider to be essential and sufficient for determining stroke treatment eligibility in our practice:[6]

1) Unenhanced head CT to exclude hemorrhage

2) Head and neck CTA, performed immediately following head CT (while the IV-tPA is being mixed, so as not to slow thrombolysis administration)

a) Axial, coronal, and sagittal thick-slab maximum intensity projections (3-cm section thickness at 0.5-cm overlapping intervals) reviewed in real-time at the scanner console

b) If MR imaging is contraindicated and endovascular therapy will not immediately to be performed, CT perfusion imaging should be considered.

3) DWI

a) If large-vessel occlusion is present and infarct core is <70–100 mL, proceed immediately to endovascular treatment.

b) If the patient is not an endovascular candidate, MR perfusion imaging should be considered.

With regard to perfusion imaging, which is not required for either IV lysis or endovascular treatment selection, valid indications include the following: 1) excluding stroke mimics; 2) identifying high-risk patients following TIA; 3) specifying stroke subtype and hemodynamics; 4) clarifying/confirming the presence/site of vessel occlusion; 5) assessment of vasospasm; 6) determining the need for blood pressure management; 7) guiding disposition decisions, such as transfer to an intensive care unit; and 8) establishing prognosis, especially of large "malignant" perfusion patterns at early time points, for which the risks of treatment may outweigh the benefits (ie, too bad to treat). For these reasons, perfusion imaging is routine in our institutional acute stroke imaging algorithm, provided that definitive standard of care IV or endovascular reperfusion therapy will not be delayed.

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http://dx.doi.org/10.3174/ajnr.A3098

EDITORIAL

Acute Stroke Imaging: CT with CT Angiography and CT Perfusion before Management Decisions

With less than stellar success of immediate intra-arterial therapy for acute stroke, Cloft[1] mentions the need for "penumbra imaging" or advanced imaging to aid in management decisions. CT and MR approaches to such imaging are still not used by many interventionalists. There is more than just a side interest for acute stroke imaging protocols to be performed before such urgent management decisions. The goal of acute stroke therapy is the treatment of patients with ischemic brain to minimize infarct progression while not intervening when infarction is already complete.

For decades, imaging was performed to exclude other causes of stroke, parenchymal hematoma, mass, subdural hematoma, and seizure foci. Present day management decisions need imaging protocols with the following features: 1) demonstration of the intracranial arteries, extent of ischemia, and extent of completed infarction; 2) ability to be carried out promptly, conveniently, consistently, and accurately; and 3) immediate availability, facilitating management decisions for treatment (whether intra-arterial or intra-venous treatment).

Simple reliance on a NCCT and NIHSS threshold to inform clinicians of the presence and possible proximal location of a thrombus is not dependable for distinguishing ischemia from completed infarction. Although a higher NIHSS score may be seen with more proximal occlusions, a recent study of