

Comparing Vessel Imaging Noncontrast Computed Tomography/Computed Tomographic Angiography Should Be the New Minimum Standard in Acute Disabling Stroke

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The role of vascular imaging in the assessment of acute stroke has been debated for decades since the demonstration of intravenous tissue-type plasminogen activator (tPA) efficacy.¹⁻³ It would seem logical that a disease involving the vasculature of the brain should require evaluation of that vasculature to best plan appropriate treatment. The major limitation to routine vessel imaging had been access to a modality that can provide this information noninvasively, accurately, and efficiently. Currently, there are 4 imaging modalities capable of providing vascular information in acute stroke. Given the high resource intensity and invasive nature of cerebral angiography, there is little place for this modality as a pure diagnostic tool in the acute stroke setting. The 3 noninvasive tests that could be used in acute stroke include computed tomographic (CT) angiography (CTA), magnetic resonance (MR) angiography (MRA), and transcranial Doppler (TCD)/transcranial color-coded sonography (TCCS)+carotid duplex sonography. This review will consider characteristics (Table 1) important for evaluating and comparing the 3 modalities as the diagnostic tool of choice for acute stroke assessment and treatment decision making. In the past, vascular imaging information did not significantly alter the evidence-based acute treatment plan, but this has now changed with new evidence for endovascular treatment renewing the debate on which should the standard imaging approach be if a patient presents acutely (<6 hours from onset) with acute disabling stroke symptoms?

Methodology of the 3 Noninvasive Vascular Imaging Modalities

Each of the 3 modalities have different methods of acquisition but are all capable of imaging both the extracranial and intracranial arterial circulation. CTA is a CT technique that requires an injection of intravenous x-ray contrast in the arm with rapid movement of the CT gantry where x-ray information is gathered by a spiral or helical acquisition in 3-dimensional (3D) that starts usually at the aortic arch level and tracks the bolus through the neck and head for ≈6 s (for a single-phase CTA) to 20 to 25 s (for a multiphase CTA) when

the arteries are maximally filled with contrast agent for excellent signal to noise.

MRA is a group of techniques based on magnetic resonance imaging (MRI) using different MRI techniques. Three-dimensional time of flight MRA does not require gadolinium contrast and is the preferred flow-dependent technique because of fast acquisition time and excellent spatial resolution for imaging of the intracranial arteries. Phase-contrast MRA is a technique that allows for blood flow measurements through encoding of velocity but has less spatial resolution than time of flight. For the extracranial arteries, cervical contrast-enhanced MRA using an intravenous injection of gadolinium contrast is more accurate and superior to noncontrast alternatives.

TCD is an ultrasound technique that flashlights ultrasound energy through 1 of the 4 bone windows through the skull to collect Doppler signals of arterial waveforms. TCCS uses high-resolution systems and sector transducers to enable visualization of the proximal intracranial arteries through intact skull by color coding of blood flow velocity. Angle correction of velocity is only possible with TCCS. Both TCD and TCCS are used in acute stroke for intracranial occlusion detection. Intracranial ultrasonography is complemented by extracranial ultrasound imaging by carotid duplex sonography. Carotid duplex sonography has limitations in extent of visualization, with limited evaluation of the distally internal carotid artery and much of the vertebral artery course.

Time Requirement for Image Acquisition and Interpretation

Each of the 3 noninvasive modalities introduce some measure of time delay to the acute stroke assessment process. This is important when one considers the clinical benefit of minimizing door-to-needle times when intravenous tPA is administered. Recent studies suggest a 3% to 4% absolute reduction in excellent outcomes with intravenous tPA for each hour delay in intravenous tPA initiation from stroke onset.⁴ Endovascular treatment is also time dependent with a 7% to 10% reduction in good outcomes and 2% to 4% increase in mortality per hour

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delay to reperfusion.⁵ CTA can be time efficient when immediately performed after noncontrast CT (NCCT), usually adding only 2 to 5 minutes to CT table time.⁶ CTA information is not required for intravenous tPA decision making, and so it can be performed simultaneously while reconstituting the vial of intravenous tPA, drawing up the tPA bolus in a syringe and preparation of the intravenous tPA infusion pump tubing. tPA bolus administration and infusion can then be performed on the CT table immediately after CTA images have been acquired or even before the CTA in cases where there is a delay to CTA initiation. There should be no delay between tPA bolus administration and initiation of tPA infusion to optimize pharmacokinetics of tPA. MRA is burdened by more significant delays known to the MRI environment, such as metal screening, metal removal, and individual MR sequence acquisition, which can add up to a 20- to 50-minute delay in door-to-needle times compared with CT-based intravenous tPA treatment.^{7,8} TCD has the advantage of being a bedside tool that could be performed before NCCT. However, given limitations in quickly identifying the location of intracranial thrombus and lack of adequately trained transcranial sonographers,⁹ timely evaluation of the vasculature with TCD is not realistic at most centers.

Accessibility

All 3 modalities are available in most tertiary level centers. CTA is now possible at most community hospitals given the wide dissemination of multidetector CT systems that acquire multiple slices simultaneously to increase the speed of CT acquisition crucial to high-resolution CTA.¹⁰ CTA has seen a large increase in use during the past decade as a result of multidetector CT technology.¹¹ Older CT systems currently in use in some developing countries may be limited to single-slice or 4-slice acquisition that can affect CTA image quality.

Accessibility is much more limited for MRI in most countries with far fewer numbers of scanners than for CT. Moreover, because CT (whole-body CT in many cases) is the imaging modality of choice for major trauma patients,¹² CT scanners in most hospitals are often near emergency departments and have trained personnel to operate during off-hours unlike MRI scanners. TCD/transcranial color Doppler examinations are operator dependent often requiring a highly specialized ultrasound technician, which is not possible especially in off-hours.

Safety

TCD/transcranial color Doppler and MRA are both safe procedures with minimal risk especially without contrast administration. CTA has perceived safety concerns that include allergic reactions, additional radiation dose, and risk of contrast-induced nephropathy (CIN). Serious x-ray contrast reactions are rare, although occurring in 1 to 2 of 1000 and 1 to 2 of 10000 examinations with high and low osmolarity agents, respectively.^{13,14} Most cases occur immediately post injection and are quickly identified and addressed. In terms of radiation risk, intracranial CTA dose is not markedly different from NCCT unless CTA neck imaging is also performed (aortic arch to vertex is associated with a higher dose of 1–3 mSV because of the increased coverage). The typical radiation dose of a full stroke CT/CT-angio head/neck protocol using current CT systems is ≈ 7 to 9 mSV, which conforms to the 2012 International Commission on Radiological Protection guidelines (Table 2)¹⁵ and compares favorably with routinely performed single CT studies of the chest (7–11.3 mSV) and abdomen (8–11.7 mSV).^{16–18} The estimated lifetime risk of death from cancer attributable to a CT/CTA scan is estimated at 0.02% to 0.04%.¹⁹ CIN is defined as a 25% elevation from baseline of serum creatinine or an absolute increase of 0.5 mg/

Table 1. Comparison of Vascular Imaging Techniques

	CTA	MRA	TCD/TCCD
Time requirement for acquisition and interpretation	3–5 min	With screening/preparing/imaging time: ≈ 30 min	10–30 min
Accessibility	CT technology in most hospitals, available 24 \times 7, mostly near ED	Not available 24 \times 7	Large operator dependence
Safety	Radiation risk low CIN: 3% Allergic: 1/10 000	No risk	No risk
ICH management	Secondary causes (aneurysm and AVM) CTA spot sign		
Occlusion detection	High accuracy proximally	Less accurate distally than CTA	Proximal occlusion only
Collateral assessment	Robust Multiphase CTA captures delay	Limited Dynamic MRA has potential	No value
Great vessel/catheter access	Robust	More artifacts	No value
Validation as selection tool in acute stroke RCTs	5 positive endovascular RCTs
Potential as surrogate measure of treatment effect	Ideal tool for recanalization assessment	Cannot accurately assess distal vasculature	Yes
Emerging techniques	Dynamic CTA Multiphase CTA		

AVM indicates arteriovenous malformation; CIN, contrast-induced nephropathy; CTA, computed tomographic angiography; ED, emergency department; ICH, intracerebral hemorrhage; MRA, magnetic resonance angiography; RCT, randomized controlled trial; TCD, transcranial Doppler; and TCCD, transcranial color Doppler.

Table 2. Mean Effective Radiation Dose With Our Protocol for Multimodal Imaging, Including Multiphase CTA When Compared With a Conventional Protocol for Multimodal Imaging

Type of Examination	Mean Estimated Effective Dose in an Established Center, mSv	Mean Estimated Effective Dose at Our Center, mSv	Radiation Dose to the Eye, mGy*
Unenhanced CT head	2.7 ± 0.3	2.0 ± 0.5	N/A
Routine CT angiogram head and neck	5.4 ± 2.2	5.0 ± 0.5	15
2 additional phases of multiphase CTA	N/A	1 ± 0.5	45
Smart preparation	0.1 ± 0.1	0.1 ± 0.1	N/A
Total dose	8.2	8.1	
CT perfusion	4.9 ± 0.0	3.5 ± 0.5	200
Postcontrast CT head	2.6 ± 0.2	N/A	N/A

CTA indicates computed tomographic angiography; and N/A, not available.

*Measured using a RadCal AccuProbe meter equipped with a 20×5-3 ion chamber and a human head phantom. The above radiation doses conform to the 2012 International Commission on Radiological Protection guidelines.¹⁵

dL within 48 to 72 hours of contrast administration.²⁰ CTA has the potential risk of CIN especially in patients with preexisting renal insufficiency, diabetes mellitus, congestive heart failure, anemia,²¹ and with specific contrast agents.²² The concept of CIN has recently been called into question by a case–control study, which demonstrated higher rates of creatinine elevation in patients who did not receive CTA (control subjects), suggesting that what we are really observing is a hospital-induced nephropathy caused by homeostatic balance changes that may occur in hospitalized patients independent of contrast administration.^{23,24} Considering the rapid rate of neuronal loss in acute disabling stroke (1.9 million neurons per minute²⁵) and major questions about the true effect or even existence of CIN, there is now sufficient understanding in this field to accept the mantra neurons over nephrons when balancing the benefits versus safety of performing an acute disabling stroke CTA. CTA should be performed immediately after NCCT while still on the CT table and not be delayed awaiting blood testing for creatinine level. The one circumstance where caution is still needed is in nonhemodialysis patients with known severe renal insufficiency (estimated glomerular filtration rate, <25), where CTA should be avoided in most instances.

Intracerebral Hemorrhage

A growing body of evidence suggests that there may be considerable utility in performing noninvasive vascular imaging during the acute to early phase of intracerebral hemorrhage (ICH). Because NCCT remains the parenchymal imaging tool of choice in acute stroke to rule out ICH in all patients presenting with acute disabling stroke symptoms, CTA can be performed immediately in patients with ICH as well. CTA has significant advantages compared with MRA and TCD/transcranial color Doppler for identifying the cause of ICH. CTA is sensitive and specific for detecting vascular causes of secondary ICH, such as aneurysms, arteriovenous malformations, dural arteriovenous fistulae, and other rare vascular lesions. CT venography can also diagnose dural sinus thrombosis with hemorrhagic infarction. Overall, 13% to 15% of patients with ICH have detectable vascular lesions on CTA.^{26,27} More recently, the visualization of the source of bleeding or leak point within an ICH has become possible with CTA. This acute contrast extravasation within the hematoma has been described as the CTA spot sign.²⁸ CTA spot sign has a

prevalence of 20% to 30% within the first few hours of ictus. Enhancement is thought to represent extraluminal extravasation with a varied appearance that can be single or multiple. CTA spot sign is the key independent predictor of hematoma expansion in large prospective validation studies.^{29,30} Ongoing randomized clinical trials of different hemostatic treatments, such as recombinant factor VIIa, are selecting patients with ICH by CTA when the CTA spot sign is present to attempt to arrest hematoma expansion and improve clinical outcome.^{31,32}

Occlusion Detection and Thrombus Length

Detection of the site of arterial occlusion has major implications for acute stroke management especially in the new era of endovascular treatment. All 3 modalities have been evaluated for occlusion detection. CTA has a higher sensitivity, positive predictive value, and inter-rater reliability compared with MRA for identification of an occlusion.³³ CTA is considered the gold standard when evaluating TCD for occlusion detection. TCD is only able to detect skull base/proximal occlusions and has limited accuracy³⁴ when compared with CTA as the gold standard³⁵ but can be complementary to CTA in the acute setting given the dynamic nature of stroke where changes in occlusion status can occur quickly.^{36,37}

With the advent of endovascular treatment, there has been increasing attention given to understanding recanalization rates with treatments, such as intravenous thrombolysis, to determine when endovascular treatment is necessary. This question on the need for additional endovascular treatment gains significant importance when patients arrive in primary stroke centers and have to be referred to endovascular capable tertiary hospitals. Important factors that influence systemic thrombolysis recanalization efficacy include thrombus extent and residual flow through the thrombus. Thrombus extent is measurable without requiring vascular imaging by the detection of the hyperdense artery sign most commonly seen in the M1 segment of the middle cerebral artery (MCA). Thrombus length was measured as length of arterial hyperdensities in admission nonenhanced CT images with a slice width of 1.25 to 2.5 mm.³⁸ No recanalization was noted in any intravenous tPA patient with a thrombus length >8 mm.³⁹ Thrombus detection on NCCT is not as reliable as CTA. In a series of horizontal segment MCA occlusions identified by CTA, only 43% had evidence of a hyperdense MCA sign on NCCT.⁴⁰ CTA

Table 3. Efficient Workflow and Utility of Acute Ischemic Stroke NCCT/mCTA Protocol/Image Processing Methods

Workflow Sequence	Image Processing Methods	Clinical Utility
NCCT performed ↓	NCCT head standard 5-mm slice thickness	Early ischemic change detection with ASPECTS Subacute infarcts/severe leukoaraiosis Subtle hemorrhage
IV tPA decision ↓	NCCT head thin section 0.5-mm slice thickness	Hyperdense artery signs and length detection—tPA response
Multiphase CTA performed while IV tPA mixed and prepared if eligible ↓	Neck CTA with mCTA head 0.5-mm source images	Quick determination of proximal occlusion Residual flow at intracranial occlusion site/ Nonocclusive thrombi Extracranial thrombus (donut sign)
IV tPA bolus given and infusion started in CT scanner ↓		
Call endoteam ↓		
Patient removed from CT suite or CTP imaging performed ↓	mCTA 1st phase head axial thick MIPs Peak arterial to equilibrium acquisition	Arterial occlusion site Fast collateral filling (excellent collaterals) Circle of Willis variation
	mCTA 2nd phase head axial thick MIPs Peak venous acquisition	Arterial occlusion site with slow cardiac output/mistimed bolus Slow flow versus occlusion (distal ICA occlusion versus near occlusion) Clot length Delayed collateral filling (good collaterals)
	mCTA 3rd phase head axial thick MIPs Late venous acquisition	Clot length Impaired washout (fair collaterals) Region of impaired washout—territory at risk No collateral filling by 3rd phase (no or poor collaterals/large core)
	NCCT head only standard 5-mm slice thickness	Reevaluate ASPECTS in light of collateral information especially if ultraearly scan/significant motion artifact/old infarcts
Discussion with endo team on suitability for EVT ↓	CTA neck 0.5mm source images	Evaluate access Cervical ICA stenosis severity Circle of Willis variation
	CTA neck with mCTA coronal/sagittal neck/head axial thin MIPs	Arch anatomy/atheroma Great vessel thrombi Neck tortuosity Variations of anatomy (fetal PCA etc)
	mCTA head coronal thick MIPs	Terminal ICA occlusion type M1 versus M2 occlusion
	mCTA head sagittal thick MIPs	Distal M2 and beyond occlusions; ACA occlusions Distal vasculopathy
Plan endovascular procedure		

ACA indicates anterior cerebral artery; ASPECTS, Alberta stroke program early CT score; CT, computed tomography; CTP, computed tomographic perfusion; EVT, endovascular treatment; ICA, internal carotid artery; IC, intravenous; mCTA, multiphase computed tomographic angiography; MIP, maximum intensity projection; PCA, posterior cerebral artery; and tPA, tissue-type plasminogen activator.

also has the added advantage of being able to evaluate not only occlusion site but also thrombus burden/length and residual flow together. These imaging parameters on CTA can help physicians estimate the likelihood of early recanalization with tPA. Patients with residual flow within the clot were 5× more likely to reperfuse than those without it. Patients with residual flow and a shorter clot length (≤15 mm) were most likely to reperfuse (70.6%). Patients with proximal M1 clots without

residual flow reperfused only 8% of the time and carotid-T/L occlusions rarely reperfused (1.7%).⁴¹

Leptomeningeal Filling/Collateral Assessment

There is a large body of evidence to suggest that leptomeningeal collaterals play an important role in maintaining blood flow to brain regions distal to an arterial occlusion.⁴² Imaging assessment of leptomeningeal collaterals in humans does not

Table 4. Acute Intracerebral Hemorrhage NCCT/mCTA Protocol

Image Processing Methods	Clinical Utility
NCCT head only 5-mm slice thickness	Intracranial hemorrhage location and volume
NCCT head only 0.5-mm slice thickness	Venous hyperdense signs (cord sign)
mCTA head only 0.5-mm source images	Vascular abnormality detection
mCTA 1st phase axial thick MIPs	Cerebral aneurysm detection (no venous contamination)
Peak arterial to equilibrium acquisition	Early spot sign (greater hematoma expansion)
mCTA 2nd phase axial thick MIPs	Late spot sign (smaller hematoma expansion)
Late venous acquisition	Filling of AVM
mCTA 3rd phase axial thick MIPs	Contrast extravasation (ongoing leak)
Very late venous acquisition	Dural fistula detection
	<u>Venous occlusions</u>

AVM indicates arteriovenous malformation; mCTA, multiphase computed tomographic angiography; MIP, maximum intensity projection; and NCCT, noncontrast computed tomography.

visualize these vessels directly but instead relies on an indirect assessment of the extent and rate of backfilling of pial arteries receiving blood flow through these small interarterial connections.^{43–46} Angiographic grade of collateral flow strongly influences the rate of hemorrhagic transformation after therapeutic recanalization for acute ischemic stroke. Significant ICH risk (25.0%) has been seen in patients with poor pial collaterals especially when recanalization is achieved.^{47,48} There is a paucity of literature evaluating MRA and TCD to assess collaterals directly given the limitations of both techniques to evaluate the distal vasculature. Collaterals have been evaluated with MR perfusion source images, but this is not commercially available as yet.⁴⁹ Many CTA-based collateral scoring systems have been published, which correlate collateral extent with clinical outcome. Good collateral status as assessed by CTA was significantly associated with small initial infarct volume, reduced infarct expansion, and more favorable functional outcomes.^{50–55} Patients with no collaterals had much larger infarcts on diffusion-weighted MRI than those with better collaterals.⁵⁶ Patients with poor collaterals continue to have major infarct growth even in the presence of reperfusion.⁵⁷ One challenge with the advent of fast spiral CT imaging is that image acquisition of brain is sometimes too fast on a single-phase CTA before collaterals have a chance to fill in. This misclassifies patients as having no collaterals when in fact collaterals are simply delayed. Such patients may still be good candidates for reperfusion treatment. CTA also has the added advantage of providing leptomeningeal backfilling information to estimate collaterals for both anterior cerebral artery–MCA and posterior cerebral artery–MCA collaterals, which is not possible with selective carotid injections performed with conventional angiography. Posterior cerebral artery–MCA collaterals are generally more robust with greater size, extent, and faster filling.⁵⁸ In the Interventional Management of Stroke (IMS-3) trial, baseline CTA collaterals were a robust determinant of final clinical outcome with maximal benefit with endovascular treatment seen in patients with intermediate collaterals.⁵⁹ The Endovascular Treatment for Small Core and Anterior Circulation Proximal Occlusion With Emphasis on Minimizing CT to Recanalization Times (ESCAPE) trial was the first acute stroke trial to use CTA-based collateral assessment for selected patients. The ESCAPE trial excluded patients with poor or no collaterals.⁶⁰ Noninvasive

collateral assessment with CTA should now have a role in the endovascular treatment decision-making process.

Catheter Access

Neurointerventional practice is now based on achieving recanalization using multiple devices and techniques tailored to the needs of a specific situation. All necessary information for procedural planning can be easily obtained by CTA and then reviewed by the interventionalist before initiating the procedure. Neurointerventionists require not only information on the site of occlusion but also the anatomy of the arch of aorta and proximal extracranial neck vessels. CTA provides high-resolution images of the arch of aorta and neck vessels that provide information on great vessel thrombi,⁶¹ aortic atherosclerosis,⁶² anatomic variants (ie, bovine or type 1–3 arch⁶³), vessel angles, and tortuosity,⁶⁴ which each can affect the planning and duration of the endovascular procedure.^{65,66} Access to the carotid circulation may require specialized access catheters to handle the curves and angles at bifurcation points. TCD/transcranial color Doppler and MRA are both impractical given the added time required to perform each test and the limited visualization of the great vessel anatomy each provides.

Endovascular Treatment Trials Required CTA for Selection

The most compelling argument for vascular imaging, in particular CTA, is the recently completed endovascular treatment randomized trials in acute stroke. Each successful randomized controlled trial required the identification of a large vessel (M1 MCA or internal carotid artery) occlusion predominantly by CTA, and each consistently showed a robust clinical benefit of mechanical thrombectomy with predominantly stent retrieval devices compared with noninterventional approaches.^{67–71} Revisions to acute stroke guidelines are now published in several countries, which now confirm the level 1 evidence for endovascular treatment within a 6-hour onset to groin puncture time window.^{72–74} Noninvasive vascular imaging with modalities, such as CTA, are also mentioned in these guidelines to identify suitable candidates for endovascular treatment by the detection of a proximal intracranial occlusion.⁷⁵

Emerging Vascular Imaging Technologies

Many recent technological advances are revolutionizing how we can evaluate the cerebral vasculature. Methods to provide temporal resolution during the CTA acquisition allows for capture of critical information over time. The current standard of single-phase CTA is a snapshot in time that can miss crucial pathophysiology, such as slow flow versus thrombus,⁷⁶ delayed collateral backfilling,⁷⁷ or delayed contrast leakage (ICH)^{78,79} that is best appreciated with imaging several seconds after peak arterial phase acquisition. Dynamic CTA or 4D CTA is a technique that derives time-resolved images of pial arterial filling from perfusion CT images. It requires postprocessing and whole-brain perfusion CT.^{58,80} Multiphase CTA is an alternative technique that generates time-resolved cerebral angiograms of brain vasculature from the skull base to the vertex in 3 phases after contrast injection. It identifies crucial pathophysiology, such as slow flow, delayed collateral filling, and delayed contrast leakage (ICH), similar to 4D CTA. Aortic arch to vertex CTA is performed with a multidetector CT scanner during the first phase of acquisition timed to capture the peak arterial phase in a healthy brain for 7 s. The remaining 2 phases are from the skull base to the vertex in the equilibrium/peak venous and late venous phases by the movement of the CT gantry over the cranium \approx 8 s apart. Multiphase CTA has advantages, including the speed of acquisition and interpretation, minimal additional radiation, no additional contrast material, whole-brain coverage, and no postprocessing.⁸¹ Advances in vascular MRI include improvements in visualization of vessel wall abnormalities, which may have a role in acute stroke investigation. Microparticles of iron oxide can detect inflammatory molecules (molecular MRI),⁸² bright blood and black blood high-resolution MRI can evaluate vulnerable carotid^{83,84} and intracranial plaque,⁸⁵ and thin-section multicontrast vessel wall MRI can examine different intracranial vascular pathologies.⁸⁶ Compressed sensing allows for dynamic (time resolved) contrast-enhanced MRA imaging that could include collateral filling.⁸⁷ Ultrafast Doppler imaging is a novel technique to quantify blood flow and anatomically mapping of blood vessels, but it is still in the development stage.⁸⁸ Advances in transcranial color sonography include vascular enhancement technology and 3D-TCCS, which increase clarity and reliability of vessel imaging.⁸⁹

Suggested Time-Efficient but Clinically Comprehensive NCCT/Multiphase CTA Protocol

In Tables 3 and 4, we provide a suggested workflow process and protocol for an acute stroke NCCT and multiphase CTA for both ischemic stroke and ICH. This workflow encourages a time-efficient use of CTA with careful interpretation of NCCT and CTA-specific imaging process methods at each step. This protocol limits radiation exposure and contrast dose and is rapidly obtained (3–5 minute total time on the CT table) to provide the stroke clinician and radiologist all the necessary clinically relevant components of the vasculature, such as occlusion site(s), thrombus extent, and collateral backfilling, for efficient treatment decision making and procedural planning.

Conclusions

The time has come for the standard inclusion of vascular imaging in all initial acute stroke assessments. CTA has many advantages compared with other modalities and should become the standard for assessment of patients with acute disabling stroke worldwide. The recent endovascular trials all required the detection of a proximal large-artery occlusion by CTA. To minimize delay, it should be done immediately after the NCCT while the patient is still on the CT table without information about kidney function. Time-resolved CTA in the form of dynamic CTA or multiphase CTA is poised to provide additional information on delayed collateral backfilling and thrombus extent, which further influences acute stroke decision making. Future phase 2 clinical trials of reperfusion treatment could also benefit from proof-of-concept surrogate outcome assessment of recanalization by baseline and follow-up CTA before large phase 3 trials are initiated.

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Stroke

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