


## FOCUSED UPDATES

## Optimal Imaging at the Primary Stroke Center

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Primary stroke centers remain the workhorses for stroke care in most systems worldwide. Until recently, the immediate role of the primary stroke center was to deliver thrombolysis as rapidly as possible within 4.5 hours of stroke onset. With evolving evidence, these centers now have the opportunity to use more advanced imaging to fast-track patients with large vessel occlusion to an endovascular-capable center and potentially deliver thrombolysis beyond 4.5 hours. This review will discuss the optimal imaging strategy to achieve a fast, accurate diagnosis and rapidly deliver reperfusion therapies within the resource constraints of a primary stroke center (Table 1).

See related articles, p 1928, p 1941, p 1951, p 1961, p 1969 and p 1978

Computed tomography (CT)-based imaging is almost universal in primary stroke centers as urgent magnetic resonance imaging (MRI) access is not practical and many patients cannot have MRI due to agitation or safety screening difficulties in the acute stroke context. The current practice for imaging of suspected stroke patients at most US primary stroke centers, and in many other countries, is to obtain a noncontrast CT brain and perhaps a CT angiogram, often as a separate imaging session at a later time. Thrombolysis is generally administered on the basis of the noncontrast CT brain. Patients with suspected large vessel occlusion based on hyperdense artery or severe clinical presentation are often transferred to comprehensive stroke centers without having a CT angiogram to prove the occlusion. They are then reimaged on arrival at the comprehensive stroke center, usually with another noncontrast CT brain and CT angiogram. Increasingly, CT perfusion is also performed at

the comprehensive center, particularly when the patient arrives >6 hours after stroke onset.<sup>1</sup>

## HOW CAN WE DO BETTER?

This imaging approach has several pitfalls. Noncontrast CT brain and CT angiography should be the minimum required imaging in suspected stroke patients. Transferring patients without CT angiographic proof of a large vessel occlusion can lead to unnecessary cost and, for long-distance transfers, unnecessary separation of patients from their families and friends if there is no target large vessel occlusion found on arrival at the comprehensive center. When CT angiography is performed, there are often unjustifiable delays between the initial CT and CT angiography at the primary stroke center when this would be better performed in a single sitting. Although this may be done in an attempt to minimize delays to thrombolysis, it delays recognition of large vessel occlusion and activation of the transfer process when it would be more efficient to proceed with both thrombolysis and transfer for endovascular thrombectomy in parallel; thrombolysis can begin in the CT scanner while CT angiography is being performed (Figure 1). The lack of CT perfusion in most primary stroke centers means that patients who are beyond 6 hours after stroke onset, or who will be >6 hours when they arrive at the comprehensive center, and have large ischemic core volumes are unnecessarily transferred when they were never eligible for endovascular thrombectomy in the extended time window. This causes further waste and unnecessary family disruption.

New evidence that thrombolysis benefits patients >4.5 hours after stroke onset if CT perfusion imaging is favorable<sup>2,3</sup> has entered Australian<sup>4</sup> but not yet

**Key Words:** angiography ■ computed tomography angiography ■ perfusion imaging ■ reperfusion ■ stroke

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**Table 1. Aims of Imaging at Primary Stroke Centers**

<b>Fast, accurate diagnosis</b>
requires immediate radiology or neurology interpretation of imaging on-site or via telemedicine±artificial intelligence decision assistance and team notification
<b>Maximize eligibility for intravenous thrombolysis</b>
requires CTP to treat >4.5 h based on current evidence
CTP abnormalities may increase confidence to treat mild stroke
<b>Maximize eligibility for endovascular thrombectomy</b>
requires CTP to treat >6 h based on current evidence
patients with noncontrast CT ASPECTS 0–5 may have relatively small CTP core and benefit from reperfusion
<b>Minimize futile transfers to reduce cost and social dislocation</b>
only transfer patients who at least meet eligibility criteria pretransport
<b>Streamline the path to reperfusion</b>
minimize the need for repeat imaging
ensure images accessible to receiving center
facilitate referral and decision-making at the comprehensive center

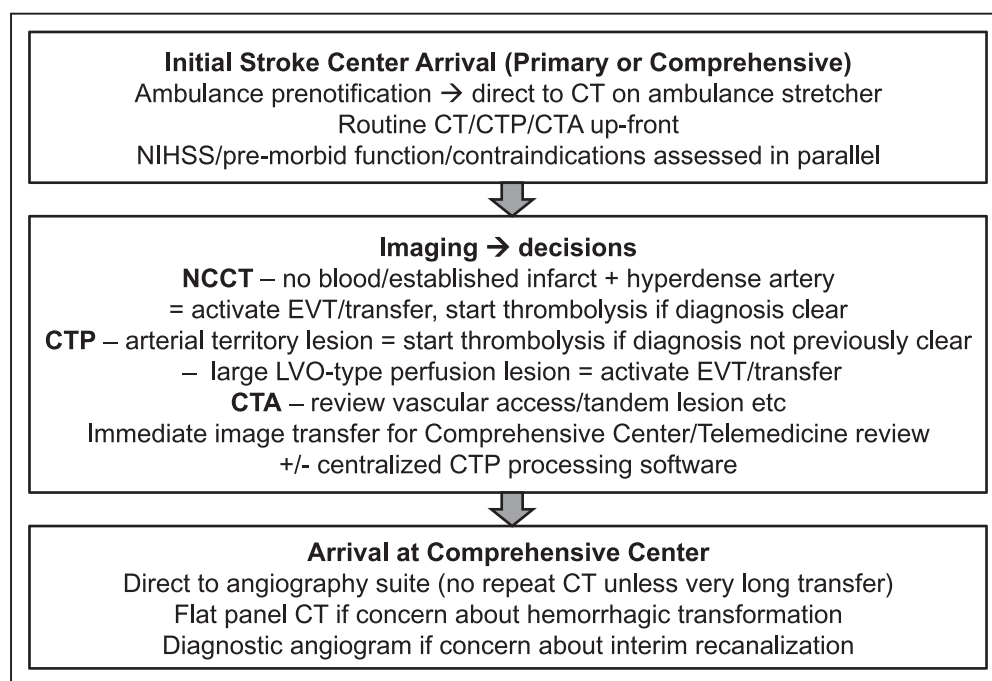
ASPECTS indicates Alberta Stroke Program Early CT Score; CT, computed tomography; and CTP, computed tomographic perfusion.

American Heart Association guidelines and is currently off-label. Nonetheless, these data add further impetus to perform CT perfusion at the primary stroke center as wake-up stroke, and other late-presenting patients could receive reperfusion treatment on-site, regardless of whether subsequent transfer for endovascular thrombectomy is warranted.

The benefits of CT perfusion extend beyond guiding late-window thrombolysis and thrombectomy. Accurate

diagnosis of stroke versus mimics can be challenging, even at the most expert centers, as illustrated by the 17% mimic rate in the NOR-TEST trial (Norwegian Tenecteplase Stroke Trial).<sup>5</sup> This is even more relevant at less experienced or telemedicine-based centers. Although the risk of thrombolysis in mimics is relatively low,<sup>6</sup> there are other adverse consequences of delayed accurate diagnosis, for example, in functional patients who require a different management approach, and can be difficult to undiagnose once they have been labeled as having had a stroke. The presence of a perfusion abnormality concordant with the clinical deficit provides diagnostic confidence and prevents missed diagnosis of a treatable stroke. Conversely, the absence of a concordant perfusion lesion raises the possibility of a mimic and flags the need for further diagnostic consideration. In some cases, there are specific abnormalities in mimics such as hyperperfusion after a seizure that can be diagnostic.<sup>7</sup>

The requirement to reimaging patients at the comprehensive stroke center wastes further valuable time. If the endovascular team is activated before reimaging at the comprehensive center, then frequent stand-downs cause fatigue and add cost. If the endovascular team is not activated until after repeat imaging, then that causes unacceptable delay in commencing the procedure. Observational studies have repeatedly shown worse outcomes in patients transferred for thrombectomy versus those who present directly to an endovascular-capable center, and delays in treatment are the main contributor.<sup>8,9</sup> Prehospital triage and bypass to a comprehensive

**Figure 1. Integrated imaging workflow for accelerated treatment.**

CT indicates computed tomography; CTA, computed tomography angiography; CTP, computed tomographic perfusion; EVT, endovascular thrombectomy; LVO, large vessel occlusion; NCCT, noncontrast computed tomography; and NIHSS, National Institutes of Health Stroke Scale.

center is an attractive approach to avoid unnecessary interhospital transfers in metropolitan regions where a comprehensive center may be only a few minutes further away than the nearest primary center.<sup>10</sup> However, in many regions, interhospital travel time to a distant comprehensive center is not a modifiable factor. Therefore, streamlining the process of care from primary to comprehensive center must be a key priority to maximize patient outcomes. Imaging is a key facilitator (and unnecessary repeat imaging a key barrier) to streamlining care.

## OPTIMAL IMAGING AT THE PRIMARY CENTER CAN REDUCE SUBSEQUENT REIMAGING

For most metropolitan transfers for endovascular thrombectomy, there is no indication to repeat imaging, and patients should go directly to the angiography suite, provided adequate imaging was performed at the primary center and that imaging is electronically transferred to the comprehensive center. However, this is often not the case in practice. Even for long-distance transfers, if the patient arrives at the comprehensive center within 6 hours of stroke onset and initially had proof of large vessel occlusion, it is important to critically consider whether repeat imaging findings would change the decision to treat. Significant clinical deterioration could indicate hemorrhagic transformation, although that is rare in the first few hours, even when intravenous (IV) thrombolysis has been administered.<sup>11</sup> Most angiography equipment can now acquire a flat-panel CT adequate to exclude hemorrhage, and this is probably the most efficient way to exclude bleeding if that is a concern. Significant clinical improvement could indicate resolution of the target occlusion. However, this remains uncommon (<10% overall with IV alteplase,<sup>12</sup> likely higher after tenecteplase<sup>11</sup> or longer transfers<sup>13</sup>), and collateral blood flow improvement with persistent occlusion is more likely. Rather than delaying to repeat a noncontrast CT and CT angiography, a diagnostic angiogram can efficiently establish whether a target for thrombectomy remains. Performing this awake and then converting to general anesthesia only if required may be a prudent strategy, particularly in these patients with clinical improvement.

If we accept that hemorrhage can be excluded by flat-panel CT on the angiography table and angiography can efficiently determine the presence of a treatment target, then the only reason not to proceed directly to the angiography suite on arrival at the comprehensive center (provided adequate imaging has been performed at the primary center) would be concern that the noncontrast CT appearance may have progressed to an extent that rendered treatment futile. The rate of deterioration in noncontrast CT ischemic changes is dependent on the quality of collateral blood flow. Good collateral flow makes

serious deterioration in the noncontrast CT appearance unlikely over the subsequent few hours. In one study, only 9% of CT scans deteriorated below Alberta Stroke Program Early CT Score (ASPECTS) 6 over  $\approx$ 3 hours when collateral flow was moderate-good.<sup>14</sup> This compared with 53% deterioration if collaterals were poor.

These data on collateral-dependent rates of noncontrast CT deterioration support going directly to the angiography suite on arrival at the comprehensive center unless initial collaterals were poor. However, selectively reimaging patients with poor initial collaterals may also not be in the best interests of the patient, given this is the group in whom added delay to reimage is most likely to lead to infarct progression. Whether ASPECTS <6 should exclude patients from thrombectomy within 6 hours of onset is argued. HERMES collaboration (Highly Effective Reperfusion Evaluated in Multiple Endovascular Stroke Trials) analyses have suggested potential benefit of thrombectomy despite ASPECTS as low as 3<sup>15</sup> and ischemic core volumes as high as 150 mL.<sup>16</sup> The caveat is that several of the trials pooled in HERMES excluded patients with large ischemic core so the numbers of patients in that category are relatively limited. Another potentially useful parameter derived from CT perfusion is the hypoperfusion intensity ratio, calculated as time to maximum (Tmax) >10 s volume/Tmax >6 s volume.<sup>17</sup> Hypoperfusion intensity ratio >0.5 has been associated with more rapid infarct growth during transfer and worse patient outcomes. This may provide a crystal ball–like insight into the likely extent of noncontrast CT changes on arrival at the comprehensive center. Further research into the precise time window beyond which imaging should be repeated in an individual patient undergoing prolonged transfer is required. However, the majority of transfers fall within 1 to 2 hours when reimaging appears unnecessary.

## IMAGING COLLATERALS AT THE PRIMARY STROKE CENTER

Based on the arguments above, if collateral quality were routinely imaged at the primary stroke center, this would prevent transfer of patients who are already destined not to receive treatment and remove the need for reimaging on arrival for at least the majority of patients. The options to do this are CT perfusion and multiphase CT angiography. Grading collaterals using standard single-phase CT angiography is suboptimal as, by its nature, collateral flow arrives at a delay after peak arterial phase. Standard single-phase CT angiography is timed to peak arterial phase and so collateral flow is underestimated,<sup>18</sup> potentially leading to exclusion of patients incorrectly assessed as having poor collaterals. Incidentally, the study quoted above regarding noncontrast CT ASPECTS deterioration used standard CT angiography to grade

collaterals, and hence the 53% positive predictive value of poor collaterals for major noncontrast CT deterioration during transfer<sup>14</sup> may have been improved using a more accurate measurement technique.

CT perfusion can quantify blood flow and delayed collateral arrival throughout the entire brain, generally with a single contrast injection on current CT scanners, using multiple acquisitions over  $\approx 60$  seconds.<sup>19</sup> Multiphase CT angiography involves 2 additional intracranial phases after the initial CT angiogram at  $\approx 8$  and 16 seconds delay.<sup>20</sup> Advantages and disadvantages of CT perfusion versus multiphase CT angiography are listed in the Table 2. The main criticisms of CT perfusion are the expertise required to create maps and sensitivity to motion. However, with multiple automated software packages now commercially available to process CT perfusion data without user intervention (including motion correction), these issues are mitigated, albeit at some financial cost. There are still some older CT scanners in operation that cannot achieve whole-brain CT perfusion in a single acquisition, and 2 slabs (with separate contrast injections) may be required. Capacity for CT perfusion stroke imaging should be considered alongside trauma and cardiac CT capability when tendering for new CT scanners at primary stroke centers.

The acquisition of CT perfusion is actually easier than CT angiography for radiographers as no timing of the contrast bolus is required. Therefore, once radiographers are trained to acquire CT angiography, there should be no additional barrier to them acquiring CT perfusion. In the case of severe patient motion causing degraded CT perfusion map quality, the worst case is that the user interprets the CT perfusion as a high temporal resolution multiphase CT angiography. Multiphase CT angiography still has some dependence on

the timing of the contrast bolus and may be less reliable when cardiac output is poor. Perhaps more importantly, the randomized trials that established benefit of thrombectomy beyond 6 hours and thrombolysis beyond 4.5 hours used CT perfusion or MRI, not multiphase CT angiography, and hence guidelines do not recommend the use of multiphase CT angiography to select patients for these therapies.<sup>1</sup> The ongoing MR-CLEAN LATE randomized trial (Endovascular Treatment of Acute Ischemic Stroke in the Netherlands for Late Arrivals; <https://doi.org/10.1186/ISRCTN19922220>) is currently testing whether CT angiographic collaterals can suffice for thrombectomy selection in patients  $>6$  hours after stroke onset.

### CT Perfusion Improves Diagnostic Accuracy and Confidence

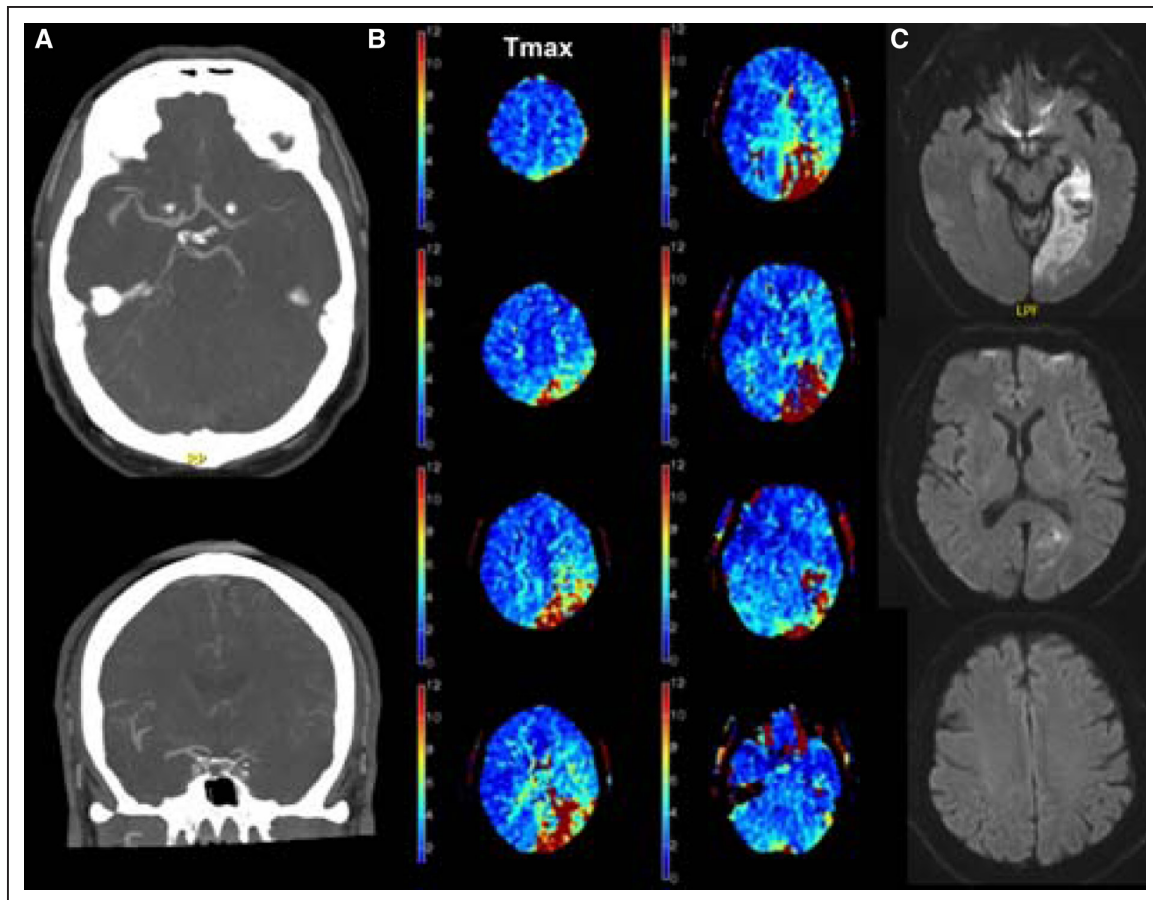
The interpretation of CT perfusion is straightforward for diagnostic purposes,<sup>21</sup> and the availability of automated software means that even inexperienced clinicians will not miss large vessel occlusion. The pattern of delayed blood flow arrival assessed using time to peak,  $T_{max}$ , or delay time indicates the site of vessel occlusion and confirms the diagnosis of stroke when a lesion corresponding to an arterial territory is identified (Figure 2). The presence of a CT perfusion lesion may increase confidence to treat mild stroke patients.<sup>22</sup> Approximately 50% of lacunar stroke patients are also identifiable using CT perfusion if a high-quality acquisition is obtained.<sup>23</sup> It is important to remember that small, reperfused strokes and a proportion of lacunar strokes may not be detected. However, the risk of missing a treatable stroke is minimized when using CT perfusion.<sup>21</sup>

**Table 2. Comparison of CTP and Multiphase CTA**

	Multiphase CTA	CTP
Additional diagnostic accuracy for ischemic stroke/mimics vs CT+standard CTA	✓✓ Greater conspicuity of distal occlusions vs standard CTA	✓✓✓ More sensitive to small occlusions and hyperperfusion (mimics) vs mCTA provided whole brain coverage
Additional prognostic accuracy	✓ Accurate collateral assessment	✓✓ Core volume and location, collateral quantification, HIR
Guideline recommended for late-window reperfusion therapy selection	No	Yes
Acquisition simplicity	✓✓ Timed bolus	✓✓ No bolus timing required
Interpretation simplicity	✓	✓✓
Requirement for processing software	None	Yes
Robust to patient motion	✓✓	✓ Can still use as high temporal resolution mCTA
Robust to bolus timing	✓ Can be mistimed if cardiac output is poor	✓✓
Additional radiation	✓	✓✓
Additional contrast	No	Perhaps*
Hardware requirements	Standard	Standard

HIR= $T_{max} > 10$  s volume/ $T_{max} > 6$  s volume. CT indicates computed tomography; CTA, computed tomography angiography; CTP, computed tomographic perfusion; HIR, hypoperfusion intensity ratio; mCTA, multiphase CTA; and  $T_{max}$ , time to maximum.

\*Some centers use 40 mL CTP+60 mL CTA, whereas stand-alone CTA uses 100 mL.



**Figure 2. Example of diagnostic benefits of multimodal computed tomography (CT) including CT perfusion and CT angiography performed at a primary stroke center.**

The patient had a left middle cerebral artery occlusion (A) that appeared suitable for endovascular thrombectomy. However, the lack of significant middle cerebral artery (MCA) perfusion delay and the presence of a posterior cerebral artery (PCA) territory perfusion lesion (B) alerted the clinician at the comprehensive center to this being an acute left PCA ischemic stroke with chronic left MCA occlusion, supported by the follow-up magnetic resonance imaging, which showed infarction confined to the left PCA territory (C).

### Estimating Tissue Viability With CT Perfusion

The interpretation of CT perfusion to identify candidates for late-window thrombolysis and endovascular thrombectomy requires greater sophistication but is greatly assisted by automated software. The principle used in the perfusion mismatch–based trials<sup>2,3,24</sup> was to identify patients with a region of critically delayed flow that was substantially greater than the area already estimated to be irreversibly injured. This mismatch indicates likely salvageable brain if rapid reperfusion can be achieved, regardless of the time from stroke onset. The critically delayed region was defined as Tmax >6-second delay<sup>25</sup> and the irreversibly injured ischemic core as cerebral blood flow (CBF) <30% of that in normal brain tissue.<sup>26</sup> The DEFUSE 3 trial (The Endovascular Therapy Following Imaging Evaluation for Ischemic Stroke) of endovascular thrombectomy<sup>24</sup> and the EXTEND trial (Extending the time for Thrombolysis in Emergency Neurological Deficits) of IV alteplase<sup>3</sup> both required an ischemic core volume <70 mL. If there was also a Tmax >6 s lesion

>15 mL larger than the core with a volume ratio >1.8, then the patient met criteria for the DEFUSE 3 trial and >10 mL and a ratio >1.2 was required in the EXTEND trial. In practice, most patients with large vessel occlusion and a core volume <70 mL also meet the mismatch volume and ratio criteria, but for more distal occlusions eligible for thrombolysis, the combination of criteria is more important. All of these thresholds and volumes are probabilistic. With ultrafast reperfusion, it may be possible to at least partially salvage some brain regions with <30% relative cerebral blood flow.<sup>27</sup> However, this is generally not a relevant consideration for patients at primary stroke centers, and in the trials, these thresholds were reliable predictors of tissue fate when an accurate measure such as diffusion MRI  $\geq 24$  hours after treatment was used as reference standard.<sup>28,29</sup> Some studies have used follow-up noncontrast CT, which is insensitive or early MRI in the period when temporary reversal of ischemic changes can occur,<sup>30</sup> leading to a false impression of tissue salvage. There is also a fundamental oversimplification in the dichotomous definition of infarcted versus salvaged

brain when there is likely to be a gradient of injury;<sup>30a</sup> even 10 minutes of ischemia caused neuronal loss in rodents, despite complete normalization of diffusion restriction.<sup>31</sup>

In many cases, the CT perfusion ischemic core has congruent changes visible on noncontrast CT, although these can be subtle and, therefore, subject to inter-rater variability. In the first couple of hours after stroke onset, changes may be invisible on noncontrast CT,<sup>32</sup> and it is important to remember that so-called late-window patients often actually have unknown onset and could be within that early period when noncontrast CT does not reflect the extent of ischemic injury. CT perfusion may be particularly useful in institutions that assess the ASPECTS score when making treatment decisions. The ASPECTS 0 to 5 range that would be excluded from therapy at some institutions includes patients with a wide range of ischemic core volumes. In one study, 60% of ASPECTS 0 to 5 patients had core volumes <50 mL, and these patients have a much improved outcome compared with the larger core patients.<sup>33</sup>

### Decision-Making in Patients With Large Ischemic Core

Treatment of low ASPECTS and large ischemic core patients requires careful consideration of multiple factors. The restriction of ischemic core volume to <70 mL was useful to standardize trial enrollment,<sup>24,34</sup> but a more nuanced approach can be applied in clinical practice. A large CT perfusion core should flag cases that require more thought about the benefits of reperfusion. First, the degree of confidence in the estimated core volume should be considered. Patients in whom there is a sharp border to the core (ie, little difference between CBF <20% and CBF <30% volumes) and congruence between the low cerebral blood volume (CBV) and low CBF regions are, in this author's experience, unlikely to have an overestimation of the irreversibly injured brain. White matter regions may be overestimated when reperfusion is ultrafast,<sup>29</sup> and so consideration of the expected time to reperfusion is relevant. Brain eloquence is a complicated concept to implement at the bedside, but there is no question that motor cortex and corticospinal tract integrity are a key determinant of modified Rankin Scale and relevant to patients. Individual patient factors such as comorbidity, attitudes to disability, and likely tolerance of prolonged rehabilitation are also relevant factors to weigh when interpreting imaging.

### PRACTICAL IMPLEMENTATION OF ADVANCED IMAGING IN PRIMARY STROKE CENTERS

The Victorian Stroke Telemedicine system in Australia is an example of a model in which routine CT, CT

perfusion, and CT angiography are obtained up-front at the primary stroke center in all suspected stroke patients, combined with telemedicine consultation with a stroke physician. This network of 17 thrombolysis-capable rural stroke centers feeding to 2 comprehensive stroke centers, in combination with other metropolitan primary and comprehensive centers, means that 99% of the ≈6 million Victorian population are within 1-hour road transport from a primary stroke center across an area the size of the United Kingdom. Many of these rural hospitals would be classified as stroke-ready rather than true primary stroke centers under the Joint Commission framework and are run by family physicians with a junior doctor (intern) manning the emergency department. The routine use of CT perfusion in this context ensures that no large vessel occlusions are missed and greatly assists the telemedicine stroke physician in making an accurate diagnosis of stroke versus mimics. It also ensures that only patients likely to be eligible for endovascular thrombectomy after a transfer that may take 2 to 5 hours and cost over US \$50 000 are brought to the comprehensive centers. If the transport time means the patient will arrive at the endovascular center >6 hours after stroke onset, then, in general, only patients meeting the DEFUSE 3 eligibility criteria with ischemic core volume of <70 mL<sup>24</sup> are transferred, unless other treatments such as hemicraniectomy are being considered. To simplify image access and avoid the requirement for multiple perfusion software installations, the Victorian system uses a central imaging server to which all participating centers automatically send the raw data of all stroke protocol CTs for processing and visualization. This minimizes human error and requirement for local expertise. It also removes one of the major barriers to implementation of CT perfusion in smaller hospitals, which is the cost of perfusion processing software. There are increasingly sophisticated options for automated processing and artificial intelligence detection of abnormalities. Commercial software exists that can notify clinicians as soon as imaging indicative of large vessel occlusion or hemorrhage is detected. These advances are likely to reduce misdiagnosis and reduce the time delay to comprehensive center referral.

In Victoria, patients who arrive at the comprehensive center within 6 hours of onset are not reimaged and proceed directly to the angiography suite. Patients arriving beyond 6 hours in whom >2 hours have elapsed since initial imaging are generally reimaged. However, having initial imaging for these long transfers that showed favorable collateral flow means that the endovascular team can be called in, based on the initial imaging, to minimize the delay incurred on arrival. The probability of having to stand down the team without proceeding to thrombectomy is relatively low. The metropolitan primary stroke

centers also all perform routine CT perfusion and angiography, eliminating the need for any repeat imaging on arrival at the comprehensive center for these patients in whom transfer time is <1 hour.

## QUALITY OF MULTIMODAL CT STROKE IMAGING

Simply performing the various imaging sequences is not sufficient. Quality of the imaging can be highly variable and requires attention to scan parameters. A high-quality noncontrast CT in which gray-white differentiation is maximized requires careful optimization of the acquisition parameters. Sufficient radiation and judicious use of iterative reconstruction are important, as well as the reconstruction kernel and slice thickness (usually 5 mm for parenchymal detail). The images then need to be appropriately windowed for viewing. A window width 35 to 40, contrast level 35 to 40 setting is recommended to scrutinize gray-white differentiation after standard window images have been reviewed. Thin (1 mm) slice reconstructions substantially increase detection of hyperdense arteries<sup>35</sup> with no extra radiation or delay and should be routinely reconstructed. These may also assist in differentiation of subacute versus chronic infarction and sulcus from gliosis.

CT perfusion acquisitions should cover the entire brain ( $\geq 8$  cm z axis coverage), the entire passage of the contrast bolus ( $\geq 60$ -second scan duration), and use sufficient radiation to give good contrast to noise. When processing maps for the purposes of estimating ischemic core, validated thresholds should be used. However, the primary role of CT perfusion is for accurate diagnosis. In some cases, CT perfusion may help compensate for reduced clinical experience with stroke at primary stroke centers or to supplement the more challenging telemedicine-based examination of patients.

CT angiography is essential for all acutely presenting patients to identify candidates for endovascular thrombectomy, and primary stroke centers must be able to perform this efficiently 24/7.<sup>36</sup> The urgent interpretation of CT angiography can be provided on-site, via teleradiology or stroke telemedicine, in some cases with automated software assistance to flag abnormalities. Images should be transferred as thin slices to the comprehensive center. This allows flexibility in creating multiplanar reconstructions and maximum intensity projections that are useful for endovascular planning.

The acquisition workflow of CT followed by CT perfusion followed by CT angiography needs to be streamlined to avoid unnecessary delays and then image transfer optimized,<sup>37</sup> particularly at primary centers when telemedicine services or endovascular teams at comprehensive centers will need to review images to advise on treatment.

## FUTURE DEVELOPMENTS

Technology continues to evolve both in acquisition and processing of stroke imaging. Some of the latest CT scanners may be able to achieve a combined arch to vertex CT angiogram and perfusion study in a single acquisition using a single (reduced dose) contrast bolus, which would achieve substantial time savings. Improved detectors and low kilovolt acquisitions are also reducing the radiation dose. Artificial intelligence-based algorithms are likely to further improve the prognostication of tissue fate. Our treatments are also likely to extend beyond reperfusion-based approaches. Current trials are investigating a new wave of treatments aiming to preserve penumbra or reduce reperfusion injury, and these are likely to require a degree of targeting to patients likely to benefit from these approaches. For example, the CHARM trial (Phase 3 Study to Evaluate the Efficacy and Safety of Intravenous BIIB093 [Glibenclamide] for Severe Cerebral Edema Following Large Hemispheric Infarction) of glyburide aiming to reduce cerebral edema includes patients with 80 to 300 mL ischemic core (<https://www.clinicaltrials.gov>; unique identifier: NCT02864953).

## CONCLUSIONS

In conclusion, the key principles of optimal imaging at the primary stroke center are to get all the necessary imaging up-front, in a single sitting, maximize eligibility for intravenous thrombolysis, and transfer out only those who need more advanced treatment. Acquiring CT perfusion at primary centers would improve diagnostic confidence and identify patients with poor collaterals who do not qualify for late-window therapy and are likely to have major deterioration in noncontrast CT appearance by the time of arrival at the comprehensive center. This should remove the need to reimagine most patients on arrival at the comprehensive center unless there has been an extended transfer. The Australian experience has demonstrated the feasibility of multimodal CT stroke imaging, even in small remote hospitals staffed by family physicians. Streamlined transfer of images for review at the comprehensive center allows appropriate activation of the endovascular team and facilitates transfer of the patient directly to angiography on arrival. This combination of approaches has the potential to dramatically reduce onset-to-reperfusion time, which is the key to improving patient outcomes.

## ARTICLE INFORMATION

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## Disclosures

None.

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