OBJECTIVE. Perfusion CT is increasingly being used as a diagnostic tool for the evaluation of acute ischemic stroke. It can be performed rapidly and aids in the detection of salvageable tissue (penumbra) from the unsalvageable core infarct. The purpose of this article is to provide an overview of the imaging technique, interpretation pearls, and common pitfalls encountered in perfusion CT of the brain.

CONCLUSION. Perfusion CT has proven to be a valuable tool in the diagnosis of acute ischemic stroke. The knowledge provided by these cases will allow the reader not only to confidently identify the presence of acute ischemic stroke, but also to recognize the common pitfalls and limitations of perfusion CT in this setting.

Perfusion CT is a readily accessible and rapid technique that can aid in the detection of acute ischemic stroke. Moreover, it can help identify patients likely to benefit from early reperfusion. Despite these advantages, interpretation of perfusion CT can be complex and is not without pitfalls. This article will review normal and ischemic perfusion patterns followed by an illustrative case series of common pitfalls and limitations of perfusion CT in the setting of acute ischemic stroke.

Advantages and Potential Disadvantages of Perfusion CT

The advantages of perfusion CT include its widespread availability, speed of image acquisition, relative lower cost compared with MRI, and ease of patient monitoring [1, 2]. Unenhanced CT remains the mainstay of imaging evaluation for the acute stroke patient. Unenhanced CT allows the identification of large areas of clearly infarcted tissue and hemorrhage and can sometimes reveal proximal vessel thrombus. In most medical centers today, unenhanced CT is the main diagnostic test used to triage patients and identify those who are candidates for thrombolysis [3–5]. CT angiography (CTA) and perfusion CT may be performed immediately after unenhanced CT. CTA and perfusion CT allow better identification of infarct, vessel thrombus, and vessel stenosis. CTA shows the vascular anatomy, and perfusion CT shows physiologic processes including cerebral blood volume (CBV) and cerebral blood flow (CBF); the information provided by perfusion CT may allow widening of the reperfusion time window [6–9].

Perfusion CT has been shown to increase diagnostic certainty for stroke detection by expert and nonexpert readers [10]. Among nonexpert readers, review of perfusion CT maps increased correct stroke diagnosis fourfold over that achieved by review of unenhanced CT studies alone [10]. Perfusion CT can also help to identify acute strokes that are too large—that is, cases in which the administration of thrombolytic therapy carries an unacceptably high risk of hemorrhagic conversion.

Perfusion CT has several important drawbacks compared to conventional nonenhanced CT that need to be addressed: additional radiation dose; IV contrast administration; additional cost; and longer total time required for image acquisition, processing, and interpretation. Although CTA and perfusion CT do require additional radiation dose over unenhanced CT, the newest scanners with optimized protocols can image the entire cranium without substantial increases in radiation dose. However, suboptimal protocols have resulted in alarming amounts of radiation exposure—as much as eight times the expected dose. Several instances of excess radiation exposure relating to perfusion CT have recently been uncovered, prompting the U.S. Food and Drug Administration to investigate [10].

Keywords: acetazolamide, ischemia, penumbra, perfusion CT, stroke

DOI:10.2214/AJR.10.7255
Received April 30, 2010; accepted after revision November 16, 2010.
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AJR 2012; 198:52–62
0361–803X/12/1981–52
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The risks of iodinated contrast administration are well known and, overall, are thought to fall within an acceptable level of risk in the workup of the acute stroke patient with regard to risks, benefits, and alternatives. The additional time required to perform CTA and perfusion CT is on the order of mere minutes, an acceptable period of time in the acute stroke setting. Postprocessing time and interpretation time are much more variable however, similar to that of MRI. In our experience, postprocessing and interpretation can be performed in as short a time as a few minutes—that is, in the time it takes for the patient to be moved from the CT scanner to an appropriate clinical care unit. The cost-benefit ratio of perfusion CT needs to be further assessed both from the medical institution perspective and from the public health perspective.

Normal Perfusion

There are several perfusion CT parameters that are commonly discussed: CBF, CBV, mean transit time (MTT), and time to peak enhancement (TTP). CBV is a measure of the total volume of blood within an imaging voxel including blood in the tissues and blood vessels. CBF is measured in units of milliliters of blood per 100 g of brain. CBF is the total volume of blood moving through a voxel in a given unit of time and is commonly measured in units of milliliters of blood per 100 g of brain tissue per minute. After a bolus of contrast material is injected, time is required for each individual molecule of contrast material to circulate. The MTT is the average transit time of all the molecules of contrast medium with the bolus through a given volume of brain measured in seconds. MTT can be approximated according to the central volume principle:

\[
MTT = \frac{CBV}{CBF}.
\]

TTP is defined as the time from the start of the contrast injection to maximal enhancement measured in seconds. These parameters are commonly derived from perfusion CT source data using deconvolution analysis.

Arterial and venous regions of interest (ROIs) and pre- and postenhancement cutoff values are selected from the perfusion CT source images to generate representative arterial input and venous outflow time-attenuation curves. These time-attenuation curves are then used to calculate the perfusion CT parameters. The A2 segment of the anterior cerebral artery is commonly used to obtain the arterial input function (AIF) ROI because it travels perpendicular to the axial plane. This segment is present on several axial slices and is typically easy for either a technologist or a radiologist to locate. Similarly, the superior sagittal sinus can be used to obtain the venous output function (VOF) ROI.

Interpretation of perfusion CT maps is most commonly done through visual inspection, an effective method for identifying areas of core infarct and penumbra. This method has the advantage of speed and simplicity; however, qualitative methods are highly dependent on user interpretation. Some centers advocate calculating quantitative perfusion parameters. These parameters have been shown to be effective in showing core infarct and penumbra and in predicting therapeutic outcome; however, protocols and guidelines for quantitative thresholds vary and clearly defined thresholds for guiding therapy have not yet been standardized.

In cases of normal perfusion (Fig. 1), there is bilateral symmetric perfusion of all perfusion CT parameters. The CBF and CBV are higher in gray matter than in white matter secondary to normal physiologic differences between these tissues [11].

Acute Infarction

The diagnosis of acute ischemic stroke is made on perfusion CT by identifying areas of decreased CBF and CBV, and increased MTT and TTP. Matched perfusion abnormalities on CBV and MTT maps correspond to areas of nonsalvageable brain tissue and neuronal death, also known as “core infarct” [12] (Figs. 2 and 3).

Mismatched areas of abnormal perfusion—namely, areas of prolonged MTT and diminished CBF where CBV is relatively preserved—correspond to areas of salvageable tissue. In such an area, also called “ischemic penumbra,” decreases in CBV may be only mild. Because of compensatory cerebrovascular mechanisms, many patients are able to preserve CBV within an area at risk for ischemic injury shortly after the initial insult. Patients with areas of CBV- MTT mismatch that are large or that involve eloquent areas of brain may be good candidates for reperfusion therapy. CBF may also be decreased to a lesser degree within ischemic penumbra [2].

Assessment of Cerebrovascular Reserve

Cerebrovascular stenoocclusive disease is most commonly related to intracranial atherosclerotic disease and can result in diminished distal arterial perfusion pressure. There are, however, mechanisms for compensation including autoregulatory vasodilation and collateral circulation. During stress, areas affected by cerebrovascular stenoocclusive disease are at risk for ischemia because cerebrovascular reserve, in the form of collateral vessels and autoregulatory response, is limited. Acetazolamide, a carbonic anhydrase inhibitor, causes short-term vasodilatation of the cerebral arterioles and when used in conjunction with perfusion CT helps estimate cerebrovascular reserve.

Comparison of baseline perfusion CT maps with those obtained after acetazolamide administration shows decreases in CBF and prolongation of MTT (Fig. 4) in areas of hemodynamic impairment [13, 14]. These changes occur because vessels already maximally dilated because of autoregulatory reflex vasodilation do not have the same response to acetazolamide. One investigator has shown that regions showing prominent changes in MTT after acetazolamide should be considered at-risk territories [14].

Pitfalls in Perfusion CT

Arterial and Venous Outflow Function

The ability to obtain appropriate AIFs and VOFs is crucial for obtaining valid perfusion maps. Arterial and venous ROIs and pre- and postenhancement cutoff values are selected from the perfusion CT source images to generate representative AIF and VOF time-attenuation curves. These time-attenuation curves are then used to calculate the perfusion CT parameters. The A2 segment of the anterior cerebral artery is commonly used to obtain the AIF ROI because it travels perpendicular to the axial plane and is easy to locate on multiple images. Similarly, the superior sagittal sinus is frequently used to obtain the VOF ROI (Fig. 5).

Technical problems may arise in cases of intracranial and extracranial stenosis and occlusion that result in decreased intracranial blood flow. Decreased blood flow may impair accurate calculation of perfusion CT maps (Fig. 6). Improper placement of ROIs can affect both visual and quantitative assessments of perfusion CT metrics [15]. For example, poor placement of either the AIF ROI or the VOF ROI can result in the appearance of global hypoperfusion (Fig. 5).

Slice Selection

Most symptomatic cerebral ischemic events involve the middle cerebral artery (MCA) territory; therefore, many current perfusion CT pro-
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Seizure Mimicking Stroke

In the setting of seizures, perfusion CT maps may show hyperperfusion in theictal regions suggesting ischemia in the contralateral hemisphere (Fig. 11). Clinically, this finding may lead to a diagnostic dilemma because both postictal paralysis and status epilepticus can mimic acute stroke. Seizures may also be the initial presentation of an acute stroke, further complicating perfusion CT interpretation. Although perfusion CT in the setting of seizures has not been studied in detail [21], seizure activity should be considered a potential pitfall in perfusion CT.

Vasospasm

Vasospasm is another condition in which perfusion CT findings may mimic areas of penumbra in the setting of acute stroke. Severe vasospasm has been correlated with transient prolongation of MTT and with diminished CBF [22]. Prolongation of MTT in the setting of subarachnoid hemorrhage was associated with vasospasm and early mortality in animal models [23]. Additionally, perfusion CT has been used in humans to assess the therapeutic effect of both intraarterial vasodilators [24] and intravascular stent placement [25], with improved CBF and MTT after treatment. Perfusion abnormalities in the setting of vasospasm should be considered at-risk territories similar to what is seen in the ischemic penumbra.

Summary

Perfusion CT is increasingly being used in the setting of acute cerebral ischemia because it can be performed rapidly and is readily accessible. Common pitfalls include chronic infarct, vascular stenosis, chronic white matter changes, seizures, and vasospasm—all of which can be mistaken for acute ischemia. Vascular stenosis can mimic and overestimate areas of ischemic penumbra; therefore, perfusion CT should always be performed and interpreted in conjunction with CTA. Care must also be taken to avoid technical pitfalls in slice selection and post-processing selection of ROIs. Perfusion CT pitfalls can be avoided as the interpreter becomes familiar with their appearance and knowledgeable of the potential technical and physiologic causes.

References

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Fig. 1—Healthy 53-year-old man. 
A–D, Unenhanced CT scan (A) and perfusion CT maps showing cerebral blood flow (B), cerebral blood volume (C), and mean transit time (D) reveal normal symmetric brain perfusion. All color maps are coded red for higher values and blue for lower values.
Fig. 2—88-year-old woman who presented with acute-onset right facial droop and aphasia. 
A, Unenhanced CT scan shows no abnormal areas of perfusion to suggest acute infarction. 
B–D, Perfusion CT maps showing cerebral blood flow (B), cerebral blood volume (CBV) (C), and mean transit time (MTT) (D) depict large area of matched deficit on CBV and MTT maps (arrows) indicative of core infarct in left middle cerebral artery territory. All color maps are coded red for higher values and blue for lower values.

Fig. 3—51-year-old man who presented with right facial droop and acute aphasia. 
A, Unenhanced CT scan shows no evidence of acute infarction. 
B, Perfusion CT map showing cerebral blood flow reveals region of decreased perfusion within left middle cerebral artery (MCA) territory (arrows). All color maps are coded red for higher values and blue for lower values. 
C, Perfusion CT map showing cerebral blood volume shows relative symmetric maintenance of blood volume. Entire left MCA territory shown here represents area of ischemic penumbra. 
D, Perfusion CT map showing mean transit time reveals prolongation within same region (arrows) corresponding to region shown in B.
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Fig. 4 — 54-year-old woman who presented with 1-month history of dizziness and recent right-sided weakness.

A, Unenhanced CT scan shows no evidence for acute ischemia.

B, Axial maximum-intensity-projection image from CT angiography shows severe stenosis (arrow) of M1 segment of left middle cerebral artery (MCA). Note adjacent prominent collateral vessels.

C–H, Perfusion CT maps show cerebral blood flow (CBF) before (C) and after (D) administration of acetazolamide, cerebral blood volume (CBV) before (E) and after (F) administration of acetazolamide, and mean transit time (MTT) before (G) and after (H) administration of acetazolamide. Technique and scaling of images are identical before and after acetazolamide administration. There is minimal increase in CBF and moderate global increase in CBV after acetazolamide administration. However, there is increased asymmetric perfusion between poststenotic territory (left) and nonstenotic territory (right). This asymmetry is best shown by MTT prolongation after acetazolamide administration in portions of left MCA territory relative to baseline perfusion CT scan. All color maps are coded red for higher values and blue for lower values.
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Fig. 5—68-year-old man with right upper extremity weakness. (Reprinted with permission from [26]: Lui YW, Tang ER, Allmendinger AM, Spektor V. Evaluation of CT perfusion in the setting of cerebral ischemia: patterns and pitfalls. American Journal of Neuroradiology, volume 31, issue 9, pages 1552–1563, 2010 © by the American Society of Neuroradiology)

A, Cerebral blood volume (CBV) map shows findings that mimic appearance of global hypoperfusion because of inappropriate venous region-of-interest (ROI) selection. All color maps are coded red for higher values and blue for lower values.

B, Example of appropriate placement of arterial input function and venous outflow function ROIs is shown: in anterior cerebral artery (ACA) and superior sagittal sinus, respectively.

C, CBV map corresponding to B shows normal perfusion.

Fig. 6—55-year-old woman who presented with left hemiparesis. Unenhanced CT (not shown) was normal.

A, Perfusion CT source image shows poor contrast opacification in right anterior cerebral artery (ACA). A2 segment of ACA is commonly used for placement of arterial input function region of interest (ROI). In this case, this ROI was inadequate and resulted in nondiagnostic functional perfusion CT maps.

B, Mean transit time map is shown as example.

Fig. 7—65-year-old man with right-sided weakness and aphasia.

A, Unenhanced CT scan shows no evidence for acute stroke.

(Fig. 7 continues on next page)
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Fig. 7 (continued)—65-year-old man with right-sided weakness and aphasia. B–D, Perfusion CT performed at admission shows symmetric and normal-appearing perfusion on cerebral blood flow (B), cerebral blood volume (C), and mean transit time (D) maps. All color maps are coded red for higher values and blue for lower values. E, Diffusion-weighted image obtained 12 hours after A–D shows multiple left periventricular infarcts outside volume imaged during perfusion CT.

Fig. 8—83-year-old man with change in mental status. A, Unenhanced CT scan shows left peritral microvascular ischemic changes (arrows). (Fig. 8 continues on next page)
Fig. 8 (continued) — 83-year-old man with change in mental status. 

B–D, Left periatrial microvascular ischemic changes shown in A correspond to perfusion abnormalities (arrows, B and C) on cerebral blood flow (B) and cerebral blood volume (C) maps and, to lesser extent, on mean transit time (MTT) map (D). This patient also had right internal carotid artery stenosis leading to prolongation of MTT. All color maps are coded for higher values and blue for lower values.

Fig. 9 — 58-year-old woman with left-sided weakness.

A, Unenhanced CT scan shows normal findings. 

B–D, Maps show subtle, asymmetric diminished cerebral blood flow (B) and cerebral blood volume (C) and prolongation of mean transit time (D) in posterior limb of right internal capsule. These findings were not prospectively identified. All color maps are coded red for higher values and blue for lower values.

E, Diffusion-weighted image obtained same day as A–D confirms small acute infarct in posterior limb of internal capsule. (Reprinted with permission from [26]: Lui YW, Tang ER, Allmendinger AM, Spakor V. Evaluation of CT perfusion in the setting of cerebral ischemia: patterns and pitfalls. American Journal of Neuroradiology, volume 31, issue 9, pages 1552–1563, 2010 © by the American Society of Neuroradiology)
Fig. 10—83-year-old man with change in mental status (same patient as Fig. 8). Unenhanced CT (not shown) was normal.

A, There is decreased cerebral blood flow in right middle cerebral artery and anterior cerebral artery territories (arrows). All color maps are coded red for higher values and blue for lower values.

B, Cerebral blood volume appears relatively normal.

C, Mean transit time is prolonged in right middle cerebral artery and anterior cerebral artery territories (arrows).

D, CT angiogram reveals long segment of severe right internal carotid artery stenosis (arrow).
Fig. 11—55-year-old man who presented with acute altered mental status, right facial droop, and right upper extremity weakness. These symptoms were preceded by witnessed generalized tonic-clonic seizure. Initial unenhanced CT (not shown) was normal. (Reprinted with permission from [26]: Lui YW, Tang ER, Allmendinger AM, Spektor V. Evaluation of CT perfusion in the setting of cerebral ischemia: patterns and pitfalls. American Journal of Neuroradiology, volume 31, issue 9, pages 1552–1563, 2010 © by the American Society of Neuroradiology)

A, Diffusion-weighted image shows normal findings. B, Cerebral blood volume map shows hypoperfusion in left hemisphere, mimicking core infarct. EEG and PET studies performed later showed right hemispheric seizure focus, which supports belief that postictal hyperperfusion is related to seizure rather than relative hypoperfusion related to left hemispheric infarct. Patient’s condition improved and his symptoms eventually resolved.

FOR YOUR INFORMATION

This article is part of a self-assessment module (SAM). Please also refer to “Imaging of Stroke: Part 2, Pathophysiology at the Molecular and Cellular Levels and Corresponding Imaging Changes,” which can be found on page 63.

Each SAM is composed of two journal articles along with questions, solutions, and references, which can be found online. You can access the two articles at www.ajronline.org, and the questions and solutions that comprise the Self-Assessment Module via http://www.arrs.org/Publications/AJR/index.aspx.

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