BlueCross BlueShield of Alabama

Name of Blue Advantage Policy:

Computed Tomography Perfusion Imaging of the Brain

Policy #: 204 | Latest Review Date: October 2020
Category: Radiology | Policy Grade: B

BACKGROUND:

***Blue Advantage** medical policy does not conflict with Local Coverage Determinations (LCDs), Local Medical Review Policies (LMRPs) or National Coverage Determinations (NCDs) or with coverage provisions in Medicare manuals, instructions or operational policy letters. In order to be covered by Blue Advantage the service shall be reasonable and necessary under Title XVIII of the Social Security Act, Section 1862(a)(1)(A). The service is considered reasonable and necessary if it is determined that the service is:*

1. *Safe and effective;*
2. *Not experimental or investigational*;*
3. *Appropriate, including duration and frequency that is considered appropriate for the service, in terms of whether it is:*

   - *Furnished in accordance with accepted standards of medical practice for the diagnosis or treatment of the patient's condition or to improve the function of a malformed body member;*
   - *Furnished in a setting appropriate to the patient's medical needs and condition;*
   - *Ordered and furnished by qualified personnel;*
   - *One that meets, but does not exceed, the patient's medical need; and*
   - *At least as beneficial as an existing and available medically appropriate alternative.*

Routine costs of qualifying clinical trial services with dates of service on or after September 19, 2000 which meet the requirements of the Clinical Trials NCD are considered reasonable and necessary by Medicare. Providers should bill **Original Medicare for covered services that are related to **clinical trials** that meet Medicare requirements (Refer to Medicare National Coverage Determinations Manual, Chapter 1, Section 310 and Medicare Claims Processing Manual Chapter 32, Sections 69.0-69.11).*

POLICY:

<u>Effective for dates of service on or after March 24, 2020:</u>
Blue Advantage will treat **CT-based perfusion imaging** as a **covered benefit** in **select patients with anterior large-vessel stroke for mechanical embolectomy**. (Please see *Blue Advantage* MP# 263- *Endovascular Procedures for Intracranial Arterial Disease (Atherosclerosis and Aneurysm* for criteria related to mechanical embolectomy)

Blue Advantage will treat **CT-based perfusion imaging of the brain** as a **non-covered benefit** and as **investigational for all other indications.**

<u>Effective for dates of service on February 26, 2018 until March 24, 2020, refer to LCD L34555.</u>

<u>Effective for dates of service on and after February 10, 2016 and prior to February 26, 2018:</u>
Blue Advantage will treat **CT-based perfusion imaging** as a **covered benefit** in **select patients with anterior large-vessel stroke for mechanical embolectomy**. (Please see *Blue Advantage* MP# 263- *Endovascular Procedures for Intracranial Arterial Disease (Atherosclerosis and Aneurysm* for criteria related to mechanical embolectomy)

Blue Advantage will treat **CT-based perfusion imaging of the brain** as a **non-covered benefit** and as **investigational for all other indications.**

Blue Advantage does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Advantage administers benefits based on the members' contract and medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.

DESCRIPTION OF PROCEDURE OR SERVICE:

Computed tomography perfusion (CTP) imaging provides an assessment of cerebral blood flow that may help identify ischemic regions of the brain. This technology is proposed to aid treatment decisions in patients being evaluated for acute ischemic stroke, subarachnoid hemorrhage, cerebral vasospasm, brain tumors, and head trauma.

Acute Stroke

The goal of acute stroke thrombolytic treatment is to rescue the ischemic penumbra, an area of brain that surrounds the infarct core and is hypo-perfused but does not die quickly. Multimodal computed tomography (CT) and magnetic resonance imaging (MRI) can be used to assess the cerebral parenchyma, vasculature, and tissue viability in the acute ischemic stroke setting, and are used to detect ischemic tissue, and exclude hemorrhage and other conditions that mimic acute cerebral ischemia.

- Non-contrast CT is used to rule out intracranial hemorrhage, tumor or infection. Diffusion-weighted MRI is used to identify acute infarction, and a gradient-recalled echo (GRE) sequence is used to exclude intracerebral hemorrhage.
- CT angiography (CTA) and MR angiography (MRA) are used to evaluate intra-and extra-cranial vasculature to detect the vascular occlusion and potentially guide therapy (e.g., intravenous thrombolysis or mechanical thrombectomy).

The approved thrombolytic therapy, an intravenous tissue plasminogen activator (tPA), requires only a non-contrast CT scan to exclude the presence of hemorrhage (a contraindication to the use of the drug). Current guidelines are to administer (tPA) within the first three hours after an ischemic event, preceded by a CT scan. Many patients, however, do not present to the emergency room within the three-hour window, and thrombolysis carries a risk of intracranial hemorrhage. Thus, more sophisticated imaging may be needed to inform the proper use of intra-arterial thrombolysis or mechanical thrombectomy in patients who present more than three hours after an ischemic stroke. Perfusion imaging is also being evaluated in the management of other neurological conditions, such as subarachnoid hemorrhage and head trauma.

The potential utility of perfusion imaging of acute stroke is as follows:
- Identification of brain regions with extremely low cerebral blood flow, which represents the core;
- Identification of patients with at-risk brain regions (acutely ischemic but viable penumbra) that may be salvageable with successful intra-arterial thrombolysis beyond the standard three-hour window;
- Triage of patients with at-risk brain regions to other available therapies, such as induced hypertension or mechanical clot retrieval;
- Decisions regarding intensive monitoring of patients with large abnormally perfused brain regions;
- Biologically-based management of patients who awaken with a stroke for which the precise time of onset is unknown.

Additional potential uses of CT perfusion (CTP) in acute stroke may include the following:
- detection and differential diagnosis (e.g., excluding stroke mimics such as transient ischemic attack, complex migraine, seizure, conversion disorders, hypoglycemia, or brain tumors);
- determination of stroke subtype;
- determination of stroke extent including additional vascular territories at risk;
- identification of patients at high early risk for stroke following transient ischemic attack;
- determining the need for blood pressure management;
- establishing prognosis

Similar information can be provided by CT and MRI regarding infarct core and penumbra. However, multimodal CT has a short protocol time (5-6 min), and because it can be performed with any modern CT equipment, is more widely available in the emergency department setting. CT perfusion (CTP) is performed by capturing images as an iodinated contrast agent bolus passes through the cerebral circulation and accumulates in the cerebral tissues. (Older perfusion methodologies such as single-photon emission CT [SPECT] and xenon-enhanced CT [XeCT] scanning use a diffusible tracer.) The quantitative perfusion parameters are calculated from density changes for each pixel over time with commercially available deconvolution-based software, in which cerebral blood flow (CBF) is equal to regional cerebral blood volume (CBV) divided by mean transit time (MTT). CT angiography and CTP imaging require ionizing radiation and iodinated contrast. It is estimated that a typical CT perfusion deposits a slightly greater radiation dose than a routine unenhanced head CT (~ 3.3 mSv).

Subarachnoid Hemorrhage and Cerebral Vasospasm

Cerebral vasospasm is a major cause of morbidity and mortality following aneurysmal subarachnoid hemorrhage (ASAH) in patients who survive the initial hemorrhage and can be seen in about two-thirds of patients with ASAH. The typical onset of cerebral vasospasm occurs at three to five days after hemorrhage, with maximal narrowing on digital subtraction angiography at 5-14 days. Currently, the diagnosis of vasospasm and the management decisions rely on clinical examination, transcranial Doppler sonography, and digital subtraction angiography. Although symptomatic vasospasm affects 20% to 30% of patients with ASAH, not all patients with angiographic vasospasm manifest clinical symptoms and the symptoms can be nonspecific. Also, patients do not always have both clinical and imaging findings of vasospasm. Due to these limitations, more accurate and reliable methods to detect cerebral vasospasm are being investigated.

Brain Tumors

The current standard for tumor grading is histopathologic assessment of tissue. Limitations of histologic assessment include sampling error due to regional heterogeneity and interobserver variation. These limitations can result in inaccurate classification and grading of gliomas. Because malignant brain tumors are characterized by neovascularity and increased angiogenic activity, perfusion imaging has been proposed as a method to assess tumor grade and prognosis. In addition, perfusion imaging can be repeated and may help to assess the evolution of tumors and the treatment response. Traditionally, perfusion imaging of brain tumors has been performed with MRI, which can estimate tumor blood volume, blood flow, and permeability. More recently, CT perfusion has been investigated for glioma grading. Potential advantages, compared with magnetic resonance perfusion, include the wider availability, faster scanning times, and lower cost. CTP imaging may also be useful in distinguishing recurrent tumor from radiation necrosis.

KEY POINTS:

The most recent literature update was performed through July 21, 2020.

Summary of Evidence
Acute Stroke
For individuals who have acute stroke who are being evaluated for thrombolysis who receive CTP imaging, the evidence includes a systematic review with meta-analysis, an RCT and cohort studies. Relevant outcomes are overall survival, test accuracy, symptoms, morbid events, and functional outcomes. One potential area of benefit is greater individualization of therapy for acute stroke by better defining at risk ischemic areas that may benefit from thrombolysis. Evidence from nonrandomized comparative studies has suggested that outcomes after thrombolysis are better in patients who have target mismatch on perfusion imaging than in patients without target mismatch and that patients with target mismatch treated after a three-hour time window have outcomes similar to patients treated within three hours. However, the therapeutic changes that would be associated with identifying specific target mismatch pattern on CTP are not well-defined. Additionally, although available evidence from the RCT suggests some modest benefit for acute stroke patients who receive CTP or MRI and receive alteplase up to nine hours post-stroke, the overall net health outcome is unclear because there was no significant benefit on the secondary outcome of functional improvement and a trend toward increased risk of symptomatic intracranial hemorrhage and there were important limitations in relevance and potential limitations in statistical power. Therefore, randomized controlled trials are needed to determine with greater certainty whether a strategy employing CTP imaging improves health outcomes compared with traditional strategies for the treatment of acute stroke. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have acute anterior large-vessel stroke who are being evaluated for mechanical embolectomy who receive CTP imaging, the evidence includes a randomized controlled trial and cohort studies. Relevant outcomes are overall survival, test accuracy, symptoms, morbid events, and functional outcomes. CTP is one of the several approaches used in acute stroke to define viable ischemic tissue better and therefore may benefit from mechanical endovascular intervention. Alternative methods of patient selection for mechanical embolectomy have included time from stroke onset, multiphase computed tomography angiography, or Alberta Stroke Program Early CT score. Three randomized controlled trials showed improved outcomes with mechanical embolectomy when patients were selected based on CTP results within 6 hours, at 6 to 16 hours, and at 6 to 24 hours. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have acute stroke who are being evaluated for prognosis who receive CTP imaging, the evidence includes retrospective analyses of large randomized trials. Relevant outcomes are OS, test accuracy, symptoms, morbid events, and functional outcomes. Retrospective analysis of data from the MR CLEAN and DUST trials have found that the ischemic core detected on CTP imaging was predictive of functional outcomes. However, a prognostic model developed with analysis of data from the DUST trial study was not improved when CTP imaging was added as a predictor variable to a basic model that used only patient characteristics and NCCT. The evidence is insufficient to determine the effects of the technology on health outcomes.

Subarachnoid Hemorrhage and Cerebral Vasospasm

For individuals who have suspected subarachnoid hemorrhage and cerebral vasospasm who receive CTP imaging, the evidence includes a prospective study. Relevant outcomes are overall survival, test accuracy, symptoms, morbid events, and functional outcomes. CTP imaging is being evaluated for the diagnosis of vasospasm and delayed cerebral ischemia following aneurysmal subarachnoid hemorrhage. One prospective study showed a qualitative measure of cerebral blood flow to have 93% accuracy for the detection of delayed cerebral ischemia, with lower accuracy for cerebral blood volume. Prospective trials are needed to determine whether CTP imaging in patients with aneurysmal subarachnoid hemorrhage leads to the early identification of patients at high risk for vasospasm or delayed cerebral ischemia, alters treatment decisions, and improves health outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.

Brain Tumors

For individuals who have brain tumors who receive CTP imaging, the evidence includes studies on diagnostic accuracy. Relevant outcomes are test accuracy, symptoms, morbid events, and functional outcomes. For indications such as brain tumors and head trauma, the data on CTP imaging are limited. One study assessed the diagnostic accuracy of CTP imaging to differentiate high-grade from low-grade gliomas. Prospective studies in an appropriate population of patients are needed to evaluate the sensitivity and specificity of CTP glioma grading, with histopathologic assessment of tumors as the independent reference standard. One prospective study performed receiver operating characteristic curve analysis to evaluate the diagnostic accuracy of volume perfusion computed tomography. This is the first report using volume perfusion computed tomography to differentiate gliomas; therefore, replication of these findings in an independent sample of patients is needed as well as clarification of the clinical utility of this information. Studies showing the consistency in the thresholds used are needed as are studies showing improvement in health outcomes with CTP imaging. No recent reports on the use of CTP imaging for the evaluation of brain tumors have been identified. The evidence is insufficient to determine the effects of the technology on health outcomes.

Practice Guidelines and Position Statements

American Heart Association and American Stroke Association

The 2012 American Heart Association (AHA) and American Stroke Association (ASA) joint guidelines for the management of aneurysmal subarachnoid hemorrhage recommend that perfusion imaging with CT or MR can be useful to identify regions of potential brain ischemia (Class IIa; Level of Evidence B). The guidelines state that there are emerging data that perfusion imaging, demonstrating regions of hypoperfusion, may be more accurate for identification of delayed cerebral ischemia than anatomic imaging of arterial narrowing or changes in blood flow velocity by transcranial Doppler. The guidelines concluded that CTP imaging is a promising technology, although repeat measurements are limited by the risks of dye load and radiation exposure.

The AHA and ASA 2013 guidelines on the early management of adults with ischemic stroke recommend that CTP and magnetic resonance perfusion, and diffusion imaging, including measures of infarct core and penumbra, may be considered for selecting patient for acute reperfusion therapy beyond IV fibrinolytic time windows. The guidelines state that these techniques provide additional information that may improve diagnosis, mechanism, and severity of ischemic stroke and permit more informed clinical decision making (Class IIb, Level of Evidence B).

The AHA and ASA (2019) revised their joint 2018 statement on the use of CTP for the early management of adults with ischemic stroke. Table 1 summarizes the new recommendations that were made.

Table 1. New Guidelines Recommendations on Use of Computed Tomography Perfusion

Recommendation	SOR	LOB	LOE
In patients eligible for IV alteplase, because benefit of therapy is time dependent, treatment should be initiated as quickly as possible and not delayed for additional multimodal neuroimaging, such as CT and MRI perfusion imaging.	I	Strong benefit	B-NR (nonrandomized)
When selecting patients with AIS within 6 to 24 hours of last known normal who have large vessel occlusion in the anterior circulation, obtaining CTP or DW-MRI, with or without MRI perfusion, is recommended to aid in patient selection for mechanical thrombectomy, but only when patients meet other eligibility criteria from one of the RCTs that showed benefit from mechanical thrombectomy in this extended time window.	I	Strong benefit	A (high-quality evidence from multiple RCTs)
In selected patients with acute ischemic stroke (> 16-24 hours of last normal) and large vessel occlusion, DAWN criteria (which may include imaging findings from CTP) may be used for clinical decision making regarding mechanical thrombectomy	IIa	Moderate benefit	B-R (nonrandomized)

CT: computed tomography; CTP: computed tomography perfusion; DW-MRI: diffusion-weighted magnetic resonance imaging; IV: intravenous; LO B: level of benefit; LOE: level of evidence; MRI: magnetic resonance imaging; RCT; randomized controlled trial; SOR

American Society of Neuroradiology et al

In 2013, the American Society of Neuroradiology, the American College of Radiology, and the Society of Neuro-Interventional Surgery issued a joint statement on imaging recommendations for acute stroke and transient ischemic attack patients. The following statements were made regarding perfusion imaging:

- "In acute stroke patients who are candidates for endovascular therapy, vascular imaging (CTA, MRA, DSA) [digital subtraction angiography]) is strongly recommended during the initial imaging evaluation. Perfusion imaging may be considered to assess the target tissue "at risk" for reperfusion therapy. However, the accuracy and usefulness of perfusion imaging to identify and differentiate viable tissue have not been well-established."
- "Determination of tissue viability based on imaging has the potential to individualize thrombolytic therapy and extend the therapeutic time window for some acute stroke

patients. Although perfusion imaging has been incorporated into acute stroke imaging algorithms at some institutions, its clinical utility has not been proved."

- "It is important to note that perfusion imaging has many applications beyond characterization of the penumbra and triage of patients to acute revascularization therapy. These applications include, but are not limited to, the following: 1) improving the sensitivity and accuracy of stroke diagnosis (in some cases, a lesion on PCT [perfusion CT] leads to more careful scrutiny and identification of a vascular occlusion that was not evident prospectively, particularly in the M2 and more distal MCA branches); 2) excluding stroke mimics; 3) better assessment of the ischemic core and collateral flow; and 4) prediction of hemorrhagic transformation and malignant edema."

In 2017, ACR, ASNR, and the Society for Pediatric Radiology revised their joint practice parameter on the performance of computed tomography perfusion in neuroradiologic imaging. The primary indications for CTP imaging of the brain were described as acute neurologic change suspicious for stroke, suspected vasospasm following subarachnoid hemorrhage, and cerebral hemorrhage with secondary local ischemia. Secondary indications included follow-up of acute cerebral ischemia or infarction, to assist in planning and evaluating the effectiveness of therapy, in patients with a contraindication to MRI, in the setting of acute traumatic brain injury, and intracranial tumors. There were "little data" to support a role of brain CTP imaging in pediatric stroke.

American College of Radiology
American College of Radiology (ACR) Appropriateness Criteria, updated in 2016, provide the following ratings for head CTP imaging with contrast:

- Rating of 5 (may be appropriate) for asymptomatic individuals with structural lesion on physical examination (cervical bruit) and/or risk factors.
- Rating of 5 (may be appropriate) if directly employed in decision making and planning treatment for carotid territory or vertebrobasilar transient ischemic attack on the initial screening survey.
- Rating of 6 (may be appropriate) for a new focal neurologic defect, fixed or worsening; less than 6 hours.
- Rating of 5 (may be appropriate) for a new focal neurologic defect, fixed or worsening; longer than 6 hours.
- Rating of 5 (may be appropriate) for evaluation for cerebral vasospasm after aneurysmal subarachnoid hemorrhage.
- The ACR also notes that CT stroke protocols combining a brain non-contrast CT, CTA, and CTP may produce a relative radiation level of 1 to 10 mSv, and repeated use of this protocol in an individual patient might result in high radiation exposure to the scalp and eyes.

U.S. Preventative Services Task Force Recommendations
Not applicable.

KEY WORDS:

Computed tomography (CT), computed tomography perfusion (CTP), perfusion CT (PCT), acute stroke, ischemic stroke, hemorrhagic stroke, anterior large vessel stroke, volume perfusion computed tomography(VPCT).

APPROVED BY GOVERNING BODIES:

Several postprocessing software packages (e.g., Siemens' syngo® Perfusion-CT, GE Healthcare's CT Perfusion 4, Philips Medical System's Brain Perfusion Option) have been cleared for marketing by the U.S. Food and Drug Administration for use with a CT system to perform perfusion imaging. The software is being distributed with new CT scanners.

BENEFIT APPLICATION:

Coverage is subject to member's specific benefits. Group specific policy will supersede this policy when applicable.

CURRENT CODING:

CPT Codes:

0042T	Cerebral perfusion analysis using computed tomography with contrast administration, including post-processing of parametric maps with determination of cerebral blood flow, cerebral blood volume, and mean transit time

PREVIOUS CODING:

CPT Codes:

76497	Unlisted computed tomography procedure (e.g., diagnostic, interventional)

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POLICY HISTORY:

Adopted for Blue Advantage, March 2005
Available for comment May 1-June 14, 2005
Medical Policy Group, September 2006
Medical Policy Group, December 2007
Medical Policy Group, December 2008
Medical Policy Group, May 2010
Medical Policy Group, September 2012
Medical Policy Group, March 2014
Medical Policy Group, August 2014
Medical Policy Group, September 2015
Medical Policy Group, February 2016
Available for comment February 10 through March 25, 2016
Medical Policy Group, November 2016
Medical Policy Group, October 2017
Medical Policy Group, February 2018
Medical Policy Group, September 2020: Reinstated policy effective March 24, 2020. Follow L34555 for dates of service February 26, 2018 until March 24, 2020. L34555 (Non-Covered Category III CPT Codes) retired effective March 23, 2020.
Medical Policy Group, October 2020
