

Corporate Medical Policy

CT Perfusion Imaging of the Brain

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Description of Procedure or Service

Perfusion imaging using CT (computed tomography) provides an assessment of cerebral blood flow that may 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 hypoperfused but does not die quickly. Multimodal 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.

- Noncontrast CT is used to rule out intracranial hemorrhage, tumor or infection. MR diffusion-weighted imaging (DWI) demonstrates acute infarction, and a gradient-recalled echo (GRE) sequence excludes 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 thrombolytics, or intra-arterial or mechanical thrombolysis).

The approved therapy, 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 3 hours after an ischemic event, preceded by a CT scan. Many patients, however, do not present within the 3-hour window, and thrombolysis carries a risk of intracranial hemorrhage. Thus, more sophisticated imaging may be needed to select the proper use of intra-arterial thrombolysis or mechanical thrombectomy in patients who present more than 3 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 described as the following:

- 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 3-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.

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Additional potential uses of perfusion CT 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 in terms of infarct core and penumbra. However, multimodal CT has a short protocol time (5-6 min), and since it can be performed with any modern CT equipment is more widely available in the emergency setting. CT perfusion 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, where cerebral blood flow (CBF) is equal to regional cerebral blood volume (CBV) divided by mean transit time (MTT). CT angiography/CT perfusion requires ionizing radiation and iodinated contrast. It is estimated that a typical perfusion CT deposits a slightly greater radiation dose than a routine unenhanced head CT (approximately 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 3 to 5 days after hemorrhage, with maximal narrowing on digital subtraction angiography at 5-14 days. Currently, the diagnosis of vasospasm and 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. In addition, 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. Since 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 MR perfusion, include the wider availability, faster scanning times, and lower cost. CT perfusion may also be useful in distinguishing recurrent tumor from radiation necrosis.

******Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.***

Policy

BCBSNC will provide coverage for CT Perfusion Imaging when it is determined to be medically necessary because the medical criteria and guidelines shown below are met.

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Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When CT Perfusion Imaging is covered

Computed tomography perfusion imaging may be considered medically necessary to select patients with anterior large-vessel stroke for mechanical embolectomy within 24 hours of symptom onset.

When CT Perfusion Imaging is not covered

CT perfusion imaging of the brain is considered investigational for all other indications.

Policy Guidelines

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 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 3-hour time window have outcomes similar to patients treated within 3 hours. However, the therapeutic changes that would be associated with identifying specific target mismatch pattern on CTP are not well-defined. 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 randomized controlled trials 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 identify patients who might 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. One randomized controlled trial showed improved outcomes with mechanical embolectomy when patients were selected based on CTP results. 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 overall survival, 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, analysis of data from the DUST study found no improvement in a prediction model when CTP

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imaging was added to a basic model that used only patient characteristics and non-contrast computed tomography. The evidence is insufficient to determine the effects of the technology on health outcomes.

Subarachnoid Hemorrhage

For individuals who have subarachnoid hemorrhage and cerebral vasospasm who receive CTP imaging, the evidence includes systematic reviews with meta-analysis and a cohort 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 a 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.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable codes: 0042T

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

BCBSA Medical Policy Reference Manual [Electronic Version]. 6.01.49, 7/10/08

Khandelwal N. (2008). CT perfusion in acute stroke. *Indian J Radiol Imaging*, 18;4, 281-6. Retrieved 1/22/ 09 from <http://medind.nic.in/ibn/t08/i4/ibnt08i4p281.pdf>

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Latchaw RE, Alberts MJ, Lev MH et al.; on behalf of the American Heart Association Council on Cardiovascular Radiology and Intervention, Stroke Council, and the interdisciplinary Council on Peripheral Vascular Disease. Recommendations for imaging of acute ischemic stroke: a scientific statement from the American Heart Association. Stroke 2009; 40(11):3646-78

BCBSA Medical Policy Reference Manual [Electronic Version]. 6.01.49, 5/13/2010

BCBSA Medical Policy Reference Manual [Electronic Version]. 6.01.49, 5/12/2011

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BCBSA Medical Policy Reference Manual [Electronic Version]. 6.01.49, 9/13/2012

Medical Director review 11/2012

Specialty Matched Consultant Advisory Panel 7/2013

BCBSA Medical Policy Reference Manual [Electronic Version]. 6.01.49, 8/8/2013

Specialty Matched Consultant Advisory Panel 7/2014

BCBSA Medical Policy Reference Manual [Electronic Version]. 6.01.49, 8/14/2014

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BCBSA Medical Policy Reference Manual [Electronic Version]. 6.01.49, 10/15/2015

BCBSA Medical Policy Reference Manual [Electronic Version]. 6.01.49, 10/13/2016

BCBSA Medical Policy Reference Manual [Electronic Version]. 6.01.49, 9/14/2017

Nogueira RG, Jadhav AP, Haussen DC. Thrombectomy 6 to 24 Hours After Stroke with a Mismatch Between Deficit and Infarct. N Engl J Med 2018; 378:11–21. DOI: 10.1056/NEJMoal706442

BCBSA Medical Policy Reference Manual [Electronic Version]. 6.01.49, 9/13/2018

Policy Implementation/Update Information

2/16/09	New policy issued. CT perfusion imaging is considered investigational. Notification given 2/16/09. Effective date 5/18/09. (adn)
6/22/10	Policy Number(s) removed (amw)
9/28/10	Description section extensively revised. Rationale added to Policy Guidelines section. References updated. Specialty Matched Consultant Advisory Panel review 8/25/2010. No change to policy statement. Draft policy approved as written. (adn)
7/19/11	Routine annual review. No changes. Specialty Matched Consultant Advisory Panel review. Approved as written. (adn)
7/10/12	Descriptions added for subarachnoid hemorrhage/cerebral vasospasm and brain tumors. Policy guidelines updated. Specialty Matched Consultant Advisory Panel review 6/20/12. No change to policy statement. (sk)
11/13/12	Reference added. Description section updated. No change to policy statement. (sk)
7/30/13	Specialty Matched Consultant Advisory Panel review 7/17/13. No change to policy statement. (sk)
10/29/13	Reference added. “of the brain” added to title and policy statement. No change to policy intent. Medical director review. (sk)

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- 8/12/14 Specialty Matched Consultant Advisory Panel review 7/29/14. No change to policy statement. (sk)
- 7/28/15 Specialty Matched Consultant Advisory Panel review 6/24/2015. Reference added. No change to policy statement. (lpr)
- 11/24/15 Reference added. No change to policy statement. (lpr)
- 7/26/16 Specialty Matched Consultant Advisory Panel review 6/29/2016. No change to policy statement. (an)
- 6/30/17 FDA information deleted from Description section. Policy Guidelines updated. Reference added. Specialty Matched Consultant Advisory Panel review 5/31/2017. No change to policy statement. (an)
- 6/29/18 Reference added. Specialty Matched Consultant Advisory Panel review 5/23/2018. No change to policy statement. (an)
- 7/1/19 Policy statement changed to read: Computed tomography perfusion imaging may be considered medically necessary to select patients with anterior large-vessel stroke for mechanical embolectomy within 24 hours of symptom onset. References added. Specialty Matched Consultant Advisory Panel review 5/15/2019. (an)

Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.