Policy Statement

Computed tomography perfusion (CTP) imaging may be considered medically necessary to select patients with anterior large-vessel stroke for mechanical embolectomy.

Computed tomography perfusion (CTP) imaging of the brain is considered investigational for all other indications.

Policy Guidelines

Selection criteria for the EXTEND-IA trial included patients with an anterior large-vessel stroke who: were receiving a tissue plasminogen activator; were able to receive endovascular therapy within 6 hours of stroke onset; were functionally independent prior to the stroke; and had evidence of salvageable brain tissue and an ischemic core with a volume of less than 70 mL on computed tomography perfusion imaging.

Coding

There is a CPT category III code specific to this test:

- **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

Description

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.

Related Policies

- Endovascular Procedures for Intracranial Arterial Disease (Atherosclerosis and Aneurysms)

Benefit Application

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Some state or federal mandates (e.g., Federal Employee Program [FEP]) prohibits plans from denying Food and Drug Administration (FDA)-approved technologies as investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.
Regulatory Status

Several postprocessing software packages (e.g., Siemens’ syngo® Perfusion-CT, GE Healthcare’s CTPerfusion 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. Food and Drug Administration product code: JAK.

Rationale

Background

Acute Stroke

The goal of acute stroke thrombolytic treatment is to rescue the ischemic penumbra, an area of the brain that surrounds the infarct core and is hypoperfused 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 sequence is used to exclude intracerebral hemorrhage.

CT angiography and magnetic resonance angiography are used to evaluate intra- and extracranial vasculature to detect the vascular occlusion and potentially guide therapy (e.g., intravenous thrombolysis or mechanical thrombectomy).

The approved therapy, use of an intravenous tissue plasminogen activator, requires only a non–contrast CT scan to exclude the presence of hemorrhage (a contraindication to use of the drug). Current guidelines are to administer tissue plasminogen activator within the first 3 hours after an ischemic event, preceded by a CT scan. Many patients, however, do not present to the emergency department 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 neurologic conditions, such as subarachnoid hemorrhage and head trauma.

The potential utility of perfusion imaging for acute stroke is as follows:

- identification of brain regions with extremely low cerebral blood flow, which represent 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.

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, brain tumors)
- determination of stroke subtype
- determination of stroke extent, including additional vascular territories at risk
- identification of patients at high early risk of 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 minutes) and, because it can be performed with any modern CT equipment, is more widely available in the emergency department setting. 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 and xenon-enhanced CT scanning use a diffusible tracer.) The quantitative perfusion parameters are calculated from density changes for each pixel over time with the commercially available deconvolution-based software, in which cerebral blood flow is equal to regional cerebral blood volume divided by mean transit time. CT angiography and CTP imaging require ionizing radiation and iodinated contrast. It is estimated that typical CTP imaging 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 in patients who survive the initial hemorrhage and can be seen in about two-thirds of patients with aneurysmal subarachnoid hemorrhage. The typical onset of cerebral vasospasm occurs 3 to 5 days after hemorrhage, with maximal narrowing on digital subtraction angiography at 5 to 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 aneurysmal subarachnoid hemorrhage, 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 a 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. Also, 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, CTP imaging 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 used to distinguish recurrent tumor from radiation necrosis.

Literature Review
Evidence reviews assess whether a medical test is clinically useful. A useful test provides information to make a clinical management decision that improves the net health outcome. That is, the balance of benefits and harms is better when the test is used to manage the condition than when another test or no test is used to manage the condition.

The first step in assessing a medical test is to formulate the clinical context and purpose of the test. The test must be technically reliable, clinically valid, and clinically useful for that purpose. Evidence reviews assess the evidence on whether a test is clinically valid and clinically useful. Technical reliability is outside the scope of these reviews, and credible information on technical reliability is available from other sources.
Acute Stroke
Clinical Context and Test Purpose
The purpose of computed tomography perfusion (CTP) imaging in patients with acute stroke is to
guide treatment decisions.

The question addressed in this evidence review is: Does the use of CTP improve the net health
outcome of patients with acute stroke?

The following PICOTS were used to select literature to inform this review.

Patients
The relevant populations of interest are patients with acute stroke who are being evaluated for
thrombolysis or mechanical embolectomy, and patients with acute stroke who are being
evaluated for prognosis.

Interventions
The interventions of interest are CTP imaging.

Comparators
The following practice is currently being used to make decisions about managing acute stroke:
standard stroke management without CTP (e.g., non-contrast computed tomography [NCCT],
computed tomography angiography [CTA]).

Outcomes
The outcomes of interest are function measured with the National Institutes of Health Stroke
Scale (NIHSS) or modified Rankin Scale (mRS) scores following thrombolysis or mechanical
embolectomy.

Timing
The timing for CTP is during the first 12 hours after stroke onset. Functional outcomes are
measured at 90 days after stroke.

Setting
CTP is an add-on to NCCT and CTA and is widely available in hospital emergency departments.

Technical Reliability
Assessment of technical reliability focuses on specific tests and operators and requires review of
unpublished and often proprietary information. Review of specific tests, operators, and
unpublished data are outside the scope of this evidence review and alternative sources exist.
This evidence review focuses on the clinical validity and clinical utility.

Clinically Valid
A test must detect the presence or absence of a condition, the risk of developing a condition in
the future, or treatment response (beneficial or adverse).

Evaluation for Thrombolysis
Systematic Reviews
Burton et al (2015) reported on a meta-analysis of 13 studies (including 3 randomized controlled
trials [RCTs] and 6 prospective cohort studies) that used CTP imaging and provided intravenous
thrombolytic treatment.¹ The objectives of the studies included comparisons of thrombolytic agents and predictions of clinical outcomes. Relatively few patients received tissue plasminogen
activator (tPA) based on CTP imaging results. One study in the review by Garcia-Bernejo et al
(2012) prospectively compared outcomes between 172 patients treated within 4.5 hours based
on NCCT criteria and 43 patients treated after 4.5 hours based on CTP mismatch criteria.²
Another 49 (54%) patients who presented beyond 4.5 hours were excluded according to CTP
imaging criteria. This exploratory study found similar rates of symptomatic intracranial
hemorrhagic (2.9% in the <4.5-hour group vs 2.3% in the >4.5-hour group) and good long-term outcome (64.5% vs 60.5%, respectively) in both groups, supporting further study in a randomized trial.

**Prospective Cohort Studies**

A study by Bivard et al (2015) examined the effectiveness of CTP imaging by assessing health outcomes in patients who qualified for tPA based on standard clinical and NCCT criteria, who were treated or not treated based on qualitative CTP results. Patients selected for a tPA based on qualitative analysis of CTP imaging (n=366) had higher odds of an excellent outcome (mRS score, 0–1; odds ratio [OR], 1.59, p=0.009) and lower mortality (OR=0.56, p=0.021) than historical controls (n=396) selected for tPA based on clinical and NCCT information. In addition, of patients treated with tPA, those who had a target mismatch by CTP imaging had significantly better outcomes than patients treated with tPA who did not (OR=13.8 for 3-month mRS score, ≤2).

However, 83 (31%) of 269 untreated patients had target mismatch, and 56 (15%) of 366 treated patients had a large ischemic core. This observational study suggested that CTP imaging might identify those patients with acute stroke who are likely and unlikely to respond to thrombolysis. However, questions remain about whether CTP imaging is sufficiently reliable to select individual stroke patients for treatment.

Another area of research is whether CTP imaging can help select ischemic stroke patients for thrombolysis after the standard 3-hour time window. Sztriha et al (2011) studied a cohort of 254 thrombolyzed patients; 174 received tPA at 0 to 3 hours using NCCT, and 80 received tPA at 3 to 6 hours by using CTP imaging criteria. At 3 months, there were no differences between patients thrombolyzed at 0 to 3 hours and those at 3 to 6 hours who had a symptomatic intracerebral hemorrhage (3% vs 4%) or in any intracerebral hemorrhage (7% vs 9%). There were also no differences at 3 months in mortality rates (16% vs 9%) or the mRS score of 0 to 2 (55% vs 54%), all respectively. The authors noted that their results could not be generalized to patients with symptoms in the posterior circulation, an area where CTP imaging is known to underperform.

Obach et al (2011) compared outcomes for 106 patients with acute stroke assessed with multimodal computed tomography (CT), (CT, CTA, and CTP) to a cohort of 262 patients with acute stroke assessed without full multimodal brain imaging during a 5-year period. Clinical and imaging data were collected prospectively, and all imaging studies were assessed by investigators blinded to prognostic data. Good outcome (mRS score, ≤2) at 3 months was higher in the multimodal group than in controls (adjusted OR=2.88) in models adjusted for age, sex, NIHSS score, glucose level, and treatment delay or modality. In a sensitivity analysis, multimodal-assisted thrombolysis yielded superior benefits in those patients treated after 3 hours (adjusted OR=4.48) than in patients treated within 3 hours (adjusted OR=1.31). For patients treated after 3 hours, 63% of patients assessed by multimodal CT had a Rankin Scale score of 2 or less compared with 24% of controls. Mortality (14% vs 15%) and symptomatic hemorrhage (5% vs 7%) rates were similar in the 2 groups, respectively.

**Clinically Useful**

A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, or more effective therapy, or avoid unnecessary therapy, or avoid unnecessary testing.

**Direct Evidence**

Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from RCTs.

No RCTs were identified assessing the use of CTP for stroke patients being evaluated for thrombolysis.
Chain of Evidence

Indirect evidence on clinical utility rests on clinical validity. If the evidence is insufficient to demonstrate test performance, no inferences can be made about clinical utility.

Because the clinical validity of CTP for this population has not been established, a chain of evidence supporting the clinical utility of CTP cannot be constructed.

Subsection Summary: Evaluation for Thrombolysis

Evidence from nonrandomized comparative studies with either concurrent or historical controls 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 those treated within 3 hours. However, randomized trials are needed to provide greater certainty whether a strategy employing CTP imaging lead to improved health outcomes compared with traditional treatment strategies for acute stroke.

Evaluation for Mechanical Embolectomy

Randomized Controlled Trials

CTP imaging was used to select patients for mechanical embolectomy in the 2015 EXtending the Time for Thrombolysis in Emergency Neurological Deficits - Intra-Arterial RCT. This trial enrolled patients with ischemic stroke who were receiving IV tPA within 4.5 hours after stroke onset. Eligible patients had an occlusion of the internal carotid artery or M1 or M2 segments of the middle cerebral artery on CTA, were able to receive endovascular therapy within 6 hours of stroke onset and were functionally independent before the stroke. Patients were evaluated before enrollment with CTP imaging and were required to have evidence of salvageable brain tissue and an ischemic core with a volume of less than 70 mL. CTP imaging was analyzed with an operator-independent postprocessing software. Enrollment was planned for 100 patients, but the trial's data safety and monitoring board stopped the study for efficacy after the first 70 enrolled patients. The trial used 2 coprimary end points: reperfusion (measured as the percentage reduction in perfusion-lesion volume between the initial imaging and imaging at 24 hours) and early neurologic improvement (defined as a reduction of ≥8 points on the NIHSS or a score of 0 or 1 at day 3).

About 25% of clinically eligible patients were excluded by perfusion imaging criteria. Endovascular therapy subjects had increased reperfusion at 24 hours, with a median reperfusion of 100% (percentage reduction in perfusion-lesion volume), compared with 37% for the tPA-only group (adjusted OR=4.7; 95% confidence interval [CI], 2.5 to 9.0; p<0.001). Of the endovascular therapy subjects, 28 (80%) of 35 had early neurologic improvement compared with 13 (37%) of 35 of the tPA-only subjects (adjusted OR=6.0; 95% CI, 2.0 to 18.0; p=0.002). Rates of reperfusion of at least 90% at 24 hours without symptomatic intracerebral hemorrhage were higher in endovascular therapy patients (89% vs 34% adjusted OR=27.0; 95% CI, 5.5 to 135.0; p<0.001). Safety outcomes, including death, symptomatic intracerebral hemorrhage, and parenchymal hematoma, did not differ significantly between groups.

It should be noted that other comparable trials of mechanical embolectomy from the same period (e.g., ESCAPE, MR CLEAN, SWIFT PRIME) also used time from stroke onset, multiphase CTA, or Alberta Stroke Program Early CT score to select patients for treatment. Overall, these trials found a significant benefit of mechanical embolectomy with stent retrievers. (See Blue Shield of California Medical Policy: Endovascular Procedures for Intracranial Arterial Disease (Atherosclerosis and Aneurysms), which addresses endovascular procedures for intracranial arterial disease, for discussion of these trials.)

The value of CTP imaging-based patient selection for intra-arterial acute ischemic stroke treatment was assessed by Borst et al (2015) using data from the MR CLEAN trial. In this trial, inclusion was not limited to CTP imaging, so investigators could perform it if it were standard procedure at their institution. Of 500 patients in MR CLEAN, 333 (67%) underwent CTP imaging,
and 175 (52.6%) had adequate images. Of the 175, 102 fulfilled the CTP mismatch criteria. The primary outcome was the mRS score at 90 days, which was assessed for patients with and without CTP mismatch. There was no significant interaction for mismatch and treatment (mechanical embolectomy or usual care) for the mRS score at 90 days, suggesting that CTP imaging cannot reliably identify patients who would not benefit from mechanical embolectomy. In both treatment groups, there was a shift toward better outcomes in patients who had CTP mismatch compared with those who did not, suggesting a benefit for prognosis (see the Evaluation for Prognosis section).

Rai et al (2013) evaluated rates of recanalization and functional outcomes in a cohort of 99 patients selected by CTP for treatment with endovascular stroke therapy and compared results with historical controls from the MERCI [Mechanical Embolus Removal in Cerebral Ischemia], Multi-MERCI, and Penumbra device trials that treated all comers. Patients were included if they had anterior circulation symptoms at presentation with a baseline NIHSS score of 8 or greater and intracerebral vascular occlusion on admission CTA correlating with the neurologic deficit. There was no cutoff time for treatment, and the type of endovascular therapy was thrombolytics in 33 (33.3%), the mechanical device only in 24 (24.2%), and both treatments in 42 (42.4%). Successful recanalization was achieved in 55.6%, with a good outcome in 41.4% of patients. The recanalization rate in this study did not differ significantly from the 46% for MERCI and 68% for Multi-MERCI but was significantly lower than the 82% recanalization rate in the Penumbra trial. In patients successfully recanalized, good outcomes were obtained in 67% in this study compared with 46% in MERCI, 49% in Multi-MERCI, and 29% in Penumbra. The rate of futile recanalization (defined as a poor outcome despite successful recanalization) was 33% in Rai et al (2013) compared with 54% in MERCI, 51% in Multi-MERCI, and 71% for Penumbra.

Cohort Studies
Results of the CRISP (CT Perfusion to Predict Response to Recanalization in Ischemic Stroke Project) study were published by Lansberg et al (2017). CRISP was a multicenter cohort study of 190 acute stroke patients who were assessed by CTP prior to endovascular therapy, although the decision to proceed with endovascular therapy (stent retrievers, manual aspiration, intra-arterial thrombolytic agents, and/or angioplasty with or without stenting, depending on the operator’s preference) was not dependent on the CTP results (automated analysis with RAPID software). Patients up to 18 hours after symptom onset were included. Patients with target mismatch (n=131) had higher odds of a favorable clinical response based on the NIHSS (83% vs 44%, p=0.002; adjusted OR=6.6; 95% CI, 2.1 to 20.9).

Clinically Useful
A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, or more effective therapy, or avoid unnecessary therapy, or avoid unnecessary testing.

Direct Evidence
Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from RCTs.

No RCTs were identified assessing the use of CTP for stroke patients being evaluated for mechanical embolectomy.

Chain of Evidence
Indirect evidence on clinical utility rests on clinical validity. If the evidence is insufficient to demonstrate test performance, no inferences can be made about clinical utility.

A chain of evidence can be constructed based on the clinical validity of CTP for this population.
The available evidence suggests the acute stroke patients who receive CTP and receive mechanical embolectomy benefit and therefore it can be inferred that defining viable ischemic tissue using CTP will lead to management changes facilitating better outcomes.

**Subsection Summary: Evaluation for Mechanical Embolectomy**

CTP imaging is one of the several approaches used in acute stroke to define viable ischemic tissue better and identify patients who might benefit from mechanical endovascular intervention. One RCT showed improved outcomes with mechanical embolectomy when patients were selected based on CTP imaging results, supporting the use of CTP for evaluation for mechanical embolectomy. Other RCTs have used time from stroke onset, multiphase CTA, and Alberta Stroke Program Early CT as selection criteria. CTP may be considered an effective method to determine suitability for mechanical embolectomy.

**Evaluation for Prognosis**

Investigators from the Dutch Acute Stroke Trial (DUST; 2017) evaluated prediction models with NCCT, CTA, or CTP at baseline and day 3 to predict the outcome at 90 days. A total of 224 patients from the DUST trial were selected who had anterior circulation occlusion on CTA with an ischemic deficit on CTP at admission and also had follow-up imaging on day 3. An unfavorable outcome (mRS score of 3-6) at 90 days was identified in 44% of the patients. For models that included baseline variables plus one of the 3 imaging modalities on day 3, the area under the receiver operating characteristics curve was 0.85 for NCCT, 0.86 for CTA, and 0.86 for CTP. All 3 models improved prediction compared with no imaging at day 3, but there was no difference between the models. CTP at day 3 was no better than NCCT in predicting the clinical outcome.

A prognostic model, developed with data from DUST, was reported by van Seeters et al (2015). They analyzed an unselected population of 1374 patients with suspected anterior circulation stroke who underwent multimodal CT. Images were evaluated by an observer blinded to all clinical information except for the side of stroke symptoms. The analysis used 60% of patients for a prediction model and 40% for a validation cohort. Poor outcome (90-day mRS score, 3-6) occurred in 501 (36.5%) patients. Included in the basic prediction model were patient characteristics (age, stroke severity, time from onset to imaging, dependency before stroke symptoms, glucose level, whether the treatment had been given) and NCCT measures. CTA and CTP imaging also were predictive of clinical outcome. However, adding CTA and CTP imaging to the basic prediction model did not improve it. For example, in the validation cohort, the area under the curve was 0.78 (95% CI, 0.73 to 0.82) when using patient characteristics and NCCT. When CTA and CTP imaging were added to the model, the area under the curve was 0.79 (95% CI, 0.75 to 0.83).

Borst et al (2015), discussed above, reported on the relation between CTP imaging–derived parameters and functional outcomes from the MR CLEAN trial. Functional outcome as measured by mRS score at 90 days was associated with the CTP imaging–derived ischemic core volume (OR=0.79 per 10 mL; 95% CI, 0.73 to 0.87 per 10 mL; p<0.001) and percentage ischemic core (OR=0.82 per 10%; 95% CI, 0.66 to 0.99 per 10%; p=0.002), but not the penumbra. This trial population had been selected for treatment using mechanical embolectomy.

**Clinically Useful**

A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, or more effective therapy, or avoid unnecessary therapy, or avoid unnecessary testing.

**Direct Evidence**

Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from RCTs.
No RCTs were identified assessing the use of CTP for stroke patients being evaluated for prognosis.

**Chain of Evidence**
Indirect evidence on clinical utility rests on clinical validity. If the evidence is insufficient to demonstrate test performance, no inferences can be made about clinical utility.

Because the clinical validity of CTP for this population has not been established, a chain of evidence supporting the clinical utility of CTP cannot be constructed.

**Subsection Summary: Evaluation of Prognosis**
Retrospective analyses of data from the MR CLEAN and DUST trials 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 imaging was added to a basic model that used only patient characteristics and NCCT. CTP at day 3 did not outperform NCCT for stroke prognosis.

**Subarachnoid Hemorrhage and Cerebral Vasospasm**

**Clinical Context and Test Purpose**
The purpose of CTP imaging in patients with subarachnoid hemorrhage (SAH) is to evaluate those at high risk for vasospasm or delayed cerebral ischemia and to improve treatment decisions.

The question addressed in this evidence review is: Does the use of CTP improve the net health outcome of patients with aneurysmal SAH?

The following PICOTS were used to select literature to inform this review.

**Patients**
The relevant population of interest is patients with SAH who are being evaluated for vasospasm or delayed cerebral ischemia.

**Interventions**
The intervention of interest is CTP imaging.

**Comparators**
The following practice is currently being used to make decisions about managing SAH: standard management without CTP.

**Outcomes**
The outcomes of interest are function measured with NIHSS or mRS scores.

**Timing**
Functional outcomes (NIHSS, mRS) are measured at 90 days after aneurysmal SAH.

**Setting**
CTP is an add-on to NCCT and is widely available in hospitals.

**Technically Reliable**
Assessment of technical reliability focuses on specific tests and operators and requires review of unpublished and often proprietary information. Review of specific tests, operators, and unpublished data are outside the scope of this evidence review and alternative sources exist. This evidence review focuses on the clinical validity and clinical utility.
Clinically Valid
A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse).

Systematic Reviews
A systematic review and meta-analysis by Cremers et al (2014) included 11 studies (total N=570 patients) on the use of CTP to identify delayed cerebral ischemia. CTP imaging measures at admission did not differ between patients who did and did not develop delayed cerebral ischemia. Some measures of CTP (cerebral blood flow [CBF] and mean transit time, but not cerebral blood volume [CBV]) differed between groups during the 4 to 14 days after SAH, suggesting a possible role in diagnoses of delayed cerebral ischemia.

A meta-analysis by Greenberg et al (2010) assessed the diagnostic accuracy of CTA and CTP for cerebral vasospasm identified 3 studies (total N=64 patients) that met the inclusion criteria and contained the appropriate data for statistical analysis. In these studies, “vasospasm” was defined on CTP as a perfusion deficit demonstrating prolonged mean transit time and decreased CBF. However, there were no standardized thresholds for mean transit time or CBF to determine vasospasm, contributing to the heterogeneity among these studies. For this meta-analysis, “angiographic vasospasm” was defined as evidence of arterial narrowing compared with the parent vessel or with a baseline examination; symptomatic and asymptomatic patients were included. Compared with digital subtraction angiography, CTP pooled estimates had 74% sensitivity and 93% specificity. Given the small pooled sample size and the heterogeneity of the CTP imaging data, these results should be considered preliminary.

Cohort Studies
One study included in the Cremers meta-analysis is the prospective study by Sanelli et al (2011) of 97 patients that evaluated the accuracy of CTP imaging to diagnose delayed cerebral ischemia following aneurysmal SAH. CTP imaging was performed between days 6 and 8 in asymptomatic patients and on the day of clinical deterioration in symptomatic patients. Perfusion maps were qualitatively evaluated by 2 neuroradiologists, both blinded to clinical and imaging data, and compared with the reference standard. Based on a multistage hierarchical reference standard that incorporated both imaging and clinical criteria, 40 (41%) patients were diagnosed with delayed cerebral ischemia. Overall diagnostic accuracy for CTP, determined from receiver operating characteristic curves, was 93% for CBF, 88% of mean transit time, and 72% of CBV. The study also sought to determine a quantitative threshold for delayed cerebral ischemia with CTP imaging, although it was noted that absolute thresholds might not be generalizable due to differences in scanner equipment and postprocessing methods. Clinical outcomes of the delayed cerebral ischemia group included 19 (48%) patients with no permanent neurologic deficit, 16 (40%) with the permanent neurologic deficit, and 5 (13%) who died during hospitalization.

Sanelli et al (2011) also retrospectively studied the development of vasospasm in 75 patients with the aneurysmal SAH who had a CTP imaging assessment (likely overlap in subjects with the study described above). Based on a multistage reference standard, 28 (37%) patients were classified using vasospasm. CTP imaging values (CBF, mean transit time) on days 0 to 3 were significantly lower in the vasospasm group. Optimal thresholds were then determined for CBF (50% sensitivity, 91% specificity), mean transit time (61% sensitivity, 70% specificity), and CBV (36% sensitivity, 89% specificity). Clinical outcomes of the vasospasm group included 15 (54%) patients with no permanent neurologic deficit, 11 (39%) with the permanent neurologic deficit, and 2 (7%) who died during hospitalization.

Clinically Useful
A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, or more effective therapy, or avoid unnecessary therapy, or avoid unnecessary testing.
Direct Evidence
Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from RCTs.

No RCTs were identified assessing the use of CTP for patients with SAH being evaluated for vasospasm or delayed cerebral ischemia.

Chain of Evidence
Indirect evidence on clinical utility rests on clinical validity. If the evidence is insufficient to demonstrate test performance, no inferences can be made about clinical utility.

Because the clinical validity of CTP for this population has not been established, a chain of evidence supporting the clinical utility of CTP cannot be constructed.

Section Summary: Subarachnoid Hemorrhage and Cerebral Vasospasm
One prospective study has shown a qualitative measure of CBF to have 93% accuracy for the detection of delayed cerebral ischemia, with lower accuracy for CBV. No studies identified provided evidence of a change in management leading to improved function following CTP imaging. Further study is needed to evaluate whether CTP in patients with aneurysmal SAH leads to the early identification of patients at high risk for vasospasm or delayed cerebral ischemia, alters treatment decisions, and improves health outcomes.

Brain Tumors
Clinical Context and Test Purpose
The purpose of CTP imaging in patients with brain tumors is grading gliomas. Potential uses are to guide biopsy and to monitor low-grade gliomas.

The question addressed in this evidence review is: Does the use of CTP improve the net health outcome of patients with brain tumors?

The following PICOTs were used to select literature to inform this review.

Patients
The relevant population of interest is patients with gliomas.

Interventions
The intervention of interest is CTP imaging.

Comparators
The following practice is currently being used to make decisions about managing brain tumors: standard management without CTP.

Outcomes
The outcome of interest is glioma grade.

Timing
Outcomes are measured at the time of CTP imaging.

Setting
CTP is an add-on to NCCT and is widely available in hospitals.

Technically Reliable
Assessment of technical reliability focuses on specific tests and operators and requires review of unpublished and often proprietary information. Review of specific tests, operators, and
unpublished data are outside the scope of this evidence review and alternative sources exist. This evidence review focuses on the clinical validity and clinical utility.

**Clinically Valid**
A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse).

Xyda et al (2011) reported on a prospective study of the feasibility and efficacy of volume perfusion computed tomography (VPCT) for the preoperative assessment of suspected cerebral gliomas in 46 consecutive patients.21 (Whereas typical CTP imaging covers a relatively narrow range of brain tissue, the VPCT system with multispiral acquisition covers the entire tumor.) Two blinded readers independently evaluated VPCT by drawing volumes of interest around the tumor according to maximum intensity projection volumes. The volumes of interest were mapped onto the CBV, CBF, and permeability perfusion datasets, which correspond to histopathologic microvascular density. VPCT was followed by stereotactic biopsy or surgery to evaluate the histopathology of the tumor and classified into low grade (I-II) and high grade (III-IV). The diagnostic power of the perfusion parameters was assessed using receiver operating characteristic curve analysis. Permeability demonstrated the highest diagnostic accuracy (97% sensitivity, 100% specificity), positive predictive value (100%), and negative predictive value (94%) to identify or exclude high-grade tumors.

A review by Jain (2011) indicated that most of the literature on the utility of perfusion imaging for glioma grading is based on various magnetic resonance perfusion techniques.22 A study by Ellika et al (2007) compared CTP imaging with conventional MRI in 19 patients.23 With a cutoff point of greater than 1.92 normalized CBV, there was a sensitivity of 85.7% and a specificity of 100% to differentiate high-grade gliomas. There were no significant differences in normalized CBV between grade III and IV tumors. A subsequent study by Jain et al (2008) correlated CTP imaging findings with histopathologic grade in 32 patients with astroglial tumors.24 Eight additional patients with oligodendrogliomas were excluded from analysis because of the known higher blood volume compared with astroglial tumors. Of the 32 patients included in the study, 8 had low-grade gliomas, and 24 had high-grade gliomas. In this select set of patients, CTP imaging showed significant differences in the grade III and IV tumors.

**Clinically Useful**
A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, or more effective therapy, or avoid unnecessary therapy, or avoid unnecessary testing.

**Direct Evidence**
Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from RCTs.

No RCTs were identified assessing the use of CTP for patients with brain tumors undergoing grading of gliomas.

**Chain of Evidence**
Indirect evidence on clinical utility rests on clinical validity. If the evidence is insufficient to demonstrate test performance, no inferences can be made about clinical utility.

Because the clinical validity of CTP for this population has not been established, a chain of evidence supporting the clinical utility of CTP cannot be constructed.
Section Summary: Brain Tumors
For indications such as brain tumors, data on CTP imaging are limited. One study assessed the diagnostic accuracy of CTP imaging to differentiate between high-grade and low-grade gliomas. Prospective studies in an appropriate patient population 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 analysis to evaluate the diagnostic accuracy of VPCT. This is the first report using VPCT to differentiate gliomas; therefore, replication of these findings in an independent sample is needed. Consistency in the thresholds used is also needed. Studies are also needed to show an improvement in health outcomes following the use of CTP imaging. No recent reports on the use of CTP imaging for the evaluation of brain tumors were identified.

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 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.

**Supplemental Information**

**Clinical Input from Physician Specialty Societies and Academic Medical Centers**

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

In response to requests from Blue Cross Blue Shield Association, input was received from 4 physician specialty societies (8 reviewers) and 3 academic medical centers while this policy was under review in 2012. Most input supported some uses of computed tomography perfusion (CTP) imaging; however, there was little consensus on specific indications that would be considered medically necessary. For use in late stroke, most reviewers agreed that CTP imaging could identify patients with late stroke who may benefit from thrombolysis, but there was no consensus whether the benefits of using this strategy to select patients with late stroke for thrombolysis outweighed the risks. Some additional indications recommended by reviewers included differential diagnosis, eg, excluding stroke mimics, determination of stroke subtype, determination of stroke extent, identification of patients at high early risk for debilitating stroke following transient ischemic attack, determining the need for blood pressure management, guiding disposition decisions such as the need for intensive care unit placement, and establishing prognosis. Evaluation of chronic cerebral ischemia and head trauma were also noted as potential indications. There was near consensus that CTP imaging is investigational for head trauma and for the staging and management of brain tumors.

**Practice Guidelines and Position Statements**

**American Heart Association and American Stroke Association**

The American Heart Association (AHA) and American Stroke Association (ASA; 2012) joint guidelines on the management of aneurysmal subarachnoid hemorrhage recommended that perfusion imaging with computed tomography or magnetic resonance can be useful to identify regions of potential brain ischemia (class Ila; level of evidence B). The guidelines stated there are emerging data that perfusion imaging, demonstrating regions of hypoperfusion, may be more accurate for identifying delayed cerebral ischemia than anatomic imaging of arterial
narrowing or changes in blood flow velocity by transcranial Doppler. The guidelines concluded that computed tomography perfusion (CTP) imaging is a promising technology, although repeat measurements are limited by the risks of dye load and radiation exposure.

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

In 2018, AHA and ASA revised their joint 2015 statement on the use of CTP for the early management of adults with ischemic stroke. Table 1 summarizes the new recommendations were made.

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>SOE</th>
<th>LOB</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Administration of IV alteplase should not be delayed based on “multimodal CT aden MRI, including perfusion imaging” because trial analysis “has failed to demonstrate clinical efficacy in patients with various pretreatment imaging biomarkers compared with those without those markers”</td>
<td>III</td>
<td>Strong harm</td>
<td>B-NR (nonrandomized)</td>
</tr>
<tr>
<td>In selected patients with acute ischemic stroke and large vessel occlusion, CTP is recommended for clinical decision making regarding mechanical thrombectomy, “but only when imaging and other eligibility criteria from RCTs showing benefit are being strictly applied in selecting patients for mechanical thrombectomy”</td>
<td>I</td>
<td>Strong benefit</td>
<td>A (high quality evidence from multiple RCTs)</td>
</tr>
<tr>
<td>In selected patients with acute ischemic stroke (&gt;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</td>
<td>IIa</td>
<td>Moderate benefit</td>
<td>B-R (nonrandomized)</td>
</tr>
</tbody>
</table>

CT: computed tomography; CTP: computed tomography perfusion; IV: intravenous; LOC: level of benefit; LOE: level of evidence; MRI: magnetic resonance imaging; RCT: randomized controlled trial; SOE: strength of evidence.

American Society of Neuroradiology et al
The American Society of Neuroradiology, the American College of Radiology (ACR), and the Society of NeuroInterventional Surgery (2013) issued a joint statement on imaging recommendations for acute stroke and transient ischemic attack. The following statements were made on perfusion imaging:

- “In acute stroke patients who are candidates for endovascular therapy, vascular imaging (CTA [computed tomography angiography], MRA [magnetic resonance angiography], 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...
Computed Tomography Perfusion Imaging of the Brain

[ 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 [middle cerebral artery] branches; 2) excluding stroke mimics; 3) better assessment of the ischemic core and collateral flow; and 4) prediction of hemorrhagic transformation and malignant edema."

The American Society of Neuroradiology, the Society for Pediatric Radiology, and ACR (2017) revised their joint practice parameters on the performance of CTP 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 therapy effectiveness, in patients with a contraindication to magnetic resonance imaging, in the setting of acute traumatic brain injury, and intracranial tumors. There was “little data” to support a role of brain CTP imaging in pediatric stroke.

American College of Radiology
ACR Appropriateness Criteria, updated in 2016, have provided the following ratings for head CTP imaging with contrast (see Table 2).30

Table 2. Appropriateness of Head Computed Tomography Perfusion Imaging with Contrast

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>For asymptomatic individuals with a structural lesion on physical examination (cervical bruit) and/or risk factors</td>
<td>5</td>
</tr>
<tr>
<td>If directly employed in decision making and planning treatment for carotid territory or vertebrobasilar transient ischemic attack on the initial screening survey</td>
<td>5</td>
</tr>
<tr>
<td>For a new focal neurologic defect, fixed or worsening; less than 6 hours</td>
<td>6</td>
</tr>
<tr>
<td>For a new focal neurologic defect, fixed or worsening; longer than 6 hours</td>
<td>5</td>
</tr>
<tr>
<td>For evaluation for cerebral vasospasm after aneurysmal subarachnoid hemorrhage</td>
<td>5</td>
</tr>
</tbody>
</table>

Ratings of 5 and 6 “may be appropriate.”

ACR also noted that computed tomography stroke protocols combining a brain noncontrast computed tomography, computed tomography angiography, and CTP might 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. Preventive Services Task Force Recommendations
Not applicable.

Medicare National Coverage
There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

Ongoing and Unpublished Clinical Trials
Some currently unpublished trials that might influence this review are listed in Table 3.

Table 3. Summary of Key Trials

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ongoing</td>
<td>NCT02360670</td>
<td>Penumbra and Recanalisation Acute Computed Tomography in Ischaemic Stroke Evaluation</td>
<td>400</td>
</tr>
<tr>
<td></td>
<td>NCT01387113</td>
<td>Expanding the Time Window for IV Thrombolysis with Rt-PA in Acute Ischemic Stroke Patients Using Computed Tomography Perfusion Imaging: The PERFusion Use in Stroke Evaluation (PERFUSE) Study</td>
<td>100</td>
</tr>
<tr>
<td>Unpublished</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**References**


**Documentation for Clinical Review**

Please provide the following documentation (if/when requested):
- History and physical and/or consultation notes
- Reason for CT perfusion imaging

**Post Service**
- CT Imaging report

**Coding**

This Policy relates only to the services or supplies described herein. Benefits may vary according to product design; therefore, contract language should be reviewed before applying the terms of the Policy. Inclusion or exclusion of codes does not constitute or imply member coverage or provider reimbursement.

**MN/IE**

The following services may be considered medically necessary in certain instances and investigational in others. Services may be considered medically necessary when policy criteria are met. Services may be considered investigational when the policy criteria are not met or when the code describes application of a product in the position statement that is investigational.

<table>
<thead>
<tr>
<th>Type</th>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CPT®</strong></td>
<td>0042T</td>
<td>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</td>
</tr>
<tr>
<td><strong>HCPCS</strong></td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>B02000Z</td>
<td>Computerized Tomography (CT Scan) of Brain using High Osmolar Contrast, Unenhanced and Enhanced</td>
<td></td>
</tr>
<tr>
<td>B0200ZZ</td>
<td>Computerized Tomography (CT Scan) of Brain using High Osmolar Contrast</td>
<td></td>
</tr>
<tr>
<td>B02010Z</td>
<td>Computerized Tomography (CT Scan) of Brain using Low Osmolar Contrast, Unenhanced and Enhanced</td>
<td></td>
</tr>
<tr>
<td>B0201ZZ</td>
<td>Computerized Tomography (CT Scan) of Brain using Low Osmolar Contrast</td>
<td></td>
</tr>
<tr>
<td>B020Y0Z</td>
<td>Computerized Tomography (CT Scan) of Brain using Other Contrast, Unenhanced and Enhanced</td>
<td></td>
</tr>
<tr>
<td>B020YZZ</td>
<td>Computerized Tomography (CT Scan) of Brain using Other Contrast</td>
<td></td>
</tr>
<tr>
<td>B02700Z</td>
<td>Computerized Tomography (CT Scan) of Cisterna using High Osmolar Contrast, Unenhanced and Enhanced</td>
<td></td>
</tr>
<tr>
<td>B0270ZZ</td>
<td>Computerized Tomography (CT Scan) of Cisterna using High Osmolar Contrast</td>
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<tr>
<td>B02710Z</td>
<td>Computerized Tomography (CT Scan) of Cisterna using Low Osmolar Contrast, Unenhanced and Enhanced</td>
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<td>B0271ZZ</td>
<td>Computerized Tomography (CT Scan) of Cisterna using Low Osmolar Contrast</td>
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<tr>
<td>B027Y0Z</td>
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<td>Computerized Tomography (CT Scan) of Cisterna using Other Contrast</td>
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<tr>
<td>B02800Z</td>
<td>Computerized Tomography (CT Scan) of Cerebral Ventricle(s) using High Osmolar Contrast, Unenhanced and Enhanced</td>
<td></td>
</tr>
<tr>
<td>Type</td>
<td>Code</td>
<td>Description</td>
</tr>
<tr>
<td>------</td>
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<td>------------------------------------------------------------------------------</td>
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<tr>
<td></td>
<td>B0280ZZ</td>
<td>Computerized Tomography (CT scan) of Cerebral Ventricle(s) using High Osmolar Contrast</td>
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<tr>
<td></td>
<td>B02810Z</td>
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<td>Computerized Tomography (CT scan) of Cerebral Ventricle(s) using Low Osmolar Contrast</td>
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<td></td>
<td>B028Y0Z</td>
<td>Computerized Tomography (CT scan) of Cerebral Ventricle(s) using Other Contrast, Unenhanced and Enhanced</td>
</tr>
<tr>
<td></td>
<td>B028YZZ</td>
<td>Computerized Tomography (CT scan) of Cerebral Ventricle(s) using Other Contrast</td>
</tr>
</tbody>
</table>

**Policy History**

This section provides a chronological history of the activities, updates and changes that have occurred with this Medical Policy.

<table>
<thead>
<tr>
<th>Effective Date</th>
<th>Action</th>
<th>Reason</th>
</tr>
</thead>
<tbody>
<tr>
<td>06/28/2007</td>
<td>BCBSA Medical Policy adoption</td>
<td>Medical Policy Committee</td>
</tr>
<tr>
<td>10/01/2010</td>
<td>Policy Revision with title change from CT (Computed Tomography) Cerebral Perfusion Imaging</td>
<td>Medical Policy Committee</td>
</tr>
<tr>
<td>08/23/2013</td>
<td>Title change from Computed Tomography Perfusion Imaging and policy revision without position change. Policy placed on No Further Routine Literature Review and Update status.</td>
<td>Medical Policy Committee</td>
</tr>
<tr>
<td>10/31/2014</td>
<td>Policy revision with no position change</td>
<td>Medical Policy Committee</td>
</tr>
<tr>
<td>12/04/2015</td>
<td>Policy title change from Computed Tomography (CT) Perfusion Imaging of the Brain</td>
<td>Medical Policy Committee</td>
</tr>
<tr>
<td>12/01/2016</td>
<td>Policy revision without position change</td>
<td>Medical Policy Committee</td>
</tr>
<tr>
<td>11/01/2017</td>
<td>Policy revision without position change</td>
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</tr>
<tr>
<td>11/01/2018</td>
<td>Policy revision without position change</td>
<td>Medical Policy Committee</td>
</tr>
</tbody>
</table>

**Definitions of Decision Determinations**

**Medically Necessary:** A treatment, procedure, or drug is medically necessary only when it has been established as safe and effective for the particular symptoms or diagnosis, is not investigational or experimental, is not being provided primarily for the convenience of the patient or the provider, and is provided at the most appropriate level to treat the condition.

**Investigational/Experimental:** A treatment, procedure, or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

**Split Evaluation:** Blue Shield of California/Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a split evaluation, where a treatment, procedure, or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.
Prior Authorization Requirements (as applicable to your plan)

Within five days before the actual date of service, the provider must confirm with Blue Shield that the member's health plan coverage is still in effect. Blue Shield reserves the right to revoke an authorization prior to services being rendered based on cancellation of the member's eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should be directed to the Prior Authorization Department. Please call (800) 541-6652 or visit the provider portal at www.blueshieldca.com/provider.

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. Blue Shield of California may consider published peer-reviewed scientific literature, national guidelines, and local standards of practice in developing its medical policy. Federal and state law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over medical policy and must be considered first in determining covered services. Member contracts may differ in their benefits. Blue Shield reserves the right to review and update policies as appropriate.