



Louisiana

Computed Tomography Perfusion Imaging of the Brain

Policy # 00495

Original Effective Date: 03/16/2016

Current Effective Date: 03/21/2018

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Note: Endovascular Procedures for Intracranial Arterial Disease (Atherosclerosis and Aneurysms) is addressed separately in medical policy 00198.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider computed tomography perfusion (CTP) imaging to select patients with anterior large-vessel stroke for mechanical embolectomy to be **eligible for coverage**.

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers CTP imaging of the brain for all other indications to be **investigational**.*

Background/Overview

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 computed tomography (NCCT) 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 (tPA), 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 tPA within the first 3 hours after an ischemic event, preceded by a CT scan.

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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 (SAH) 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 (CBF), 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 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 CBF is equal to regional cerebral blood volume (CBV) 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 SAH in patients who survive the initial hemorrhage and can be seen in about two-thirds of patients with aneurysmal SAH. The

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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 SAH, 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.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

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. FDA through the 510(k) process for use with a CT system to perform perfusion imaging. The software is being distributed with new CT scanners. FDA product code: JAK.

Centers for Medicare and Medicaid Services (CMS)

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.

Rationale/Source

Assessment of a diagnostic technology typically focuses on 3 categories of evidence: (1) its technical reliability (test-retest reliability or interrater reliability); (2) clinical validity (sensitivity, specificity, and positive and negative predictive value) in relevant populations of patients; and (3) clinical utility demonstrating that the diagnostic information can be used to improve patient outcomes.

ACUTE STROKE

Clinical Context and Test Purpose

The purpose of CTP imaging in patients with acute stroke is to guide treatment decisions.

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

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

Patients

The relevant population of interest is patients with stroke who are being evaluated for thrombolysis or mechanical embolectomy.

Interventions

The interventions of interest are CTP imaging.

Comparators

The comparator of interest is standard stroke management without CTP (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

In 2009, the American Heart Association published a scientific statement that included a review of the evidence on CTP imaging. The scientific review determined that:

- Creation of accurate, quantitative CTP imaging has been validated in comparison with xenon CT, positron emission tomography, and magnetic resonance perfusion imaging (MRPI). CTP imaging appears to have greater spatial resolution than MRPI, and MRPI may be more sensitive to contamination by large vascular structure, leading to the possibility that visual assessment of core/penumbra mismatch is more reliable with CTP imaging than with MRPI.
- Even relatively imprecise measures of core/penumbra mismatch may be used to select patients for treatment beyond a strict 3-hour time window for intravenous thrombolysis. Multimodal CT may also determine suitability for other therapies, such as mechanical clot retrieval and intra-arterial thrombolysis, and increase patient access to new treatments.
- CTP imaging has the potential to serve as a surrogate marker of stroke severity (final size of infarction), possibly exceeding current predictors of outcome such as the NIHSS. Because of the superior quantitative capability compared with MRPI, application of specific CTP imaging thresholds

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to predict tissue survival or infarction appears promising; however, these thresholds must be validated in larger patient cohorts for which reperfusion status is known.

One area of active research is defining the technical parameters of CT that best detect perfusion mismatches. For example, in 2011, Bivard et al reported on a prospective clinical validation study of CTP imaging for acute (<6 hours) ischemic stroke in 314 consecutive patients. Using a threshold of CBF less than 40% of contralateral blood flow with a relative delay time less than 2 seconds, the correlation between the extent of CTP mismatch tissue (volume of "at-risk" tissue) salvaged from infarction and clinical improvement was a coefficient (R^2) of 0.59 ($p=0.04$) at 24 hours (NIHSS score) and an R^2 of 0.42 ($p=0.02$) at 90 days (Rankin Scale score). In 2016, this group of investigators reported a validation study in the threshold settings for whole-brain 320-detector CTP imaging and compared its performance with limited-coverage CTP imaging. Automated analysis software is also being evaluated.

Clinical Validity and Clinical Utility

Evaluation for Thrombolysis

A 2015 study by Bivard et al 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 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. Sztrihai et al (2011) studied a cohort of 254 thrombolysed 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 thrombolysed 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.

In 2011, Obach et al compared outcomes for 106 patients with acute stroke assessed with multimodal 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

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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% and 15%) and symptomatic hemorrhage (5% vs 7%) rates were similar in the 2 groups, respectively.

In 2015, Burton et al reported on a meta-analysis of 13 studies (including 3 RCTs and 6 prospective cohort studies) that used CTP imaging and provided intravenous thrombolytic treatment. The objectives of the studies included comparisons of thrombolytic agents and predictions of clinical outcomes. Relatively few patients received tPA based on CTP imaging results. One study (2012) in the review 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. 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.

Section 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

CTP imaging was used to select patients for mechanical embolectomy in the 2015 EXTEND-IA randomized controlled trial (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).

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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% 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 medical policy 00198, 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 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 will 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 results compared 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 compare 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 compared with 54% in MERCI, 51% in Multi-MERCI, and 71% for Penumbra.

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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).

Section Summary: Evaluation for Mechanical Embolectomy

CTP imaging is one of the several approaches used in acute stroke to define viable ischemic tissue better that may 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

In 2015, Borst et al (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.

A prognostic model, developed with data from the Dutch Acute Stroke Trial (DUST), was reported by van Seeters et al in 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 basic prediction model, the area under the curve was 0.79 (95% CI, 0.75 to 0.83).

In 2017, DUST investigators 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

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models that included baseline variables plus one of the 3 imaging modalities at 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.

Section 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 aneurysmal 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 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 comparator of interest is 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.

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Technical Reliability

The technical reliability of CTP for delayed cerebral ischemia is expected to be the same as for acute stroke.

Clinical Validity and Clinical Utility

A 2010 meta-analysis on 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.

A 2014 systematic review and meta-analysis by Cremers et al 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 (CBF and mean transit time, but not CBV) differed between groups during the 4 to 14 days after SAH, suggesting a possible role in diagnoses of delayed cerebral ischemia.

One study included in the Cremers meta-analysis is the 2011 prospective study 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 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

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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.

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 patients with brain tumors is for grading of gliomas. Potential uses are to guide biopsy and to monitor low-grade gliomas.

The question addressed in this evidence review is: Does 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 comparator of interest is 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.

Technical Reliability

There is limited data on the technical reliability of CTP for brain tumors.

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Computed Tomography Perfusion Imaging of the Brain

Policy # 00495

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Clinical Validity and Clinical Utility

In 2011, Xyda et al 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. (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 (VOIs) around the tumor according to maximum intensity projection volumes. The VOIs 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 2011 review by Jain indicated that most of the literature on the utility of perfusion imaging for glioma grading is based on various magnetic resonance perfusion techniques. One study (2007) compared CTP imaging with conventional MRI in 19 patients. 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. 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.

Section Summary: Brain Tumors

For indications such 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 use of CTP imaging. No recent reports on the use of CTP imaging for the evaluation of brain tumors were identified.

SUMMARY OF EVIDENCE

For individuals who have acute stroke who are being evaluated for thrombolysis who receive CTP imaging, the evidence includes nonrandomized comparative 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

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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, RCTs 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 RCT. 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 CTA, or Alberta Stroke Program Early CT score. One RCT 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 a retrospective analysis of data from large prospective 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 NCCT. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have suspected SAH 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 SAH. One prospective study showed a qualitative measure of CBF to have 93% accuracy for the detection of delayed cerebral ischemia, with lower accuracy for CBV. Prospective trials are needed to determine whether CTP imaging 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. The evidence is insufficient to determine the effects of the technology on health outcomes.

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

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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 VPCT. This is the first report using VPCT 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.

References

1. Blue Cross and Blue Shield Association, Medical Policy Reference Manual, "Computed Tomography Perfusion Imaging of the Brain", 6.01.49, 10:2017.
2. Latchaw RE, Alberts MJ, Lev MH, et al. Recommendations for imaging of acute ischemic stroke: a scientific statement from the American Heart Association. *Stroke*. Nov 2009;40(11):3646-3678. PMID 19797189
3. Bivard A, Spratt N, Levi C, et al. Perfusion computer tomography: imaging and clinical validation in acute ischaemic stroke. *Brain*. Nov 2011;134(Pt 11):3408-3416. PMID 22075524
4. Lin L, Bivard A, Krishnamurthy V, et al. Whole-brain CT perfusion to quantify acute ischemic penumbra and core. *Radiology*. Jun 2016;279(3):876-887. PMID 26785041
5. Haussen DC, Dehkharghani S, Rangaraju S, et al. Automated CT Perfusion Ischemic Core Volume and Noncontrast CT ASPECTS (Alberta Stroke Program Early CT Score): Correlation and Clinical Outcome Prediction in Large Vessel Stroke. *Stroke*. Sep 2016;47(9):2318-2322. PMID 27507858
6. Bivard A, Levi C, Krishnamurthy V, et al. Perfusion computed tomography to assist decision making for stroke thrombolysis. *Brain*. Jul 2015;138(Pt 7):1919-1931. PMID 25808369
7. Schaefer PW, Souza L, Kamalian S, et al. Limited reliability of computed tomographic perfusion acute infarct volume measurements compared with diffusion-weighted imaging in anterior circulation stroke. *Stroke*. Feb 2015;46(2):419-424. PMID 25550366
8. Liebeskind DS, Parsons MW, Wintermark M, et al. Computed tomography perfusion in acute ischemic stroke: is it ready for prime time? *Stroke*. Aug 2015;46(8):2364-2367. PMID 26159791
9. Sztrihai LK, Manawadu D, Jarosz J, et al. Safety and clinical outcome of thrombolysis in ischaemic stroke using a perfusion CT mismatch between 3 and 6 hours. *PLoS One*. 2011;6(10):e25796. PMID 22016775
10. Obach V, Oleaga L, Urrea X, et al. Multimodal CT-assisted thrombolysis in patients with acute stroke: a cohort study. *Stroke*. Apr 2011;42(4):1129-1131. PMID 21330631
11. Burton KR, Dhanoa D, Aviv RI, et al. Perfusion CT for selecting patients with acute ischemic stroke for intravenous thrombolytic therapy. *Radiology*. Jan 2015;274(1):103-114. PMID 25243539
12. Garcia-Bermejo P, Calleja AI, Perez-Fernandez S, et al. Perfusion computed tomography-guided intravenous thrombolysis for acute ischemic stroke beyond 4.5 hours: a case-control study. *Cerebrovasc Dis*. 2012;34(1):31-37. PMID 22759450
13. Campbell BC, Mitchell PJ, Kleinig TJ, et al. Endovascular therapy for ischemic stroke with perfusion-imaging selection. *N Engl J Med*. Mar 12 2015;372(11):1009-1018. PMID 25671797
14. Berkhemer OA, Fransen PS, Beumer D, et al. A randomized trial of intraarterial treatment for acute ischemic stroke. *N Engl J Med*. Jan 1 2015;372(1):11-20. PMID 25517348
15. Goyal M, Demchuk AM, Menon BK, et al. Randomized assessment of rapid endovascular treatment of ischemic stroke. *N Engl J Med*. Mar 12 2015;372(11):1019-1030. PMID 25671798
16. Saver JL, Goyal M, Bonafe A, et al. Solitaire with the Intention for Thrombectomy as Primary Endovascular Treatment for Acute Ischemic Stroke (SWIFT PRIME) trial: protocol for a randomized, controlled, multicenter study comparing the Solitaire revascularization device with IV tPA with IV tPA alone in acute ischemic stroke. *Int J Stroke*. Apr 2015;10(3):439-448. PMID 25777831
17. Borst J, Berkhemer OA, Roos YB, et al. Value of computed tomographic perfusion-based patient selection for intra-arterial acute ischemic stroke treatment. *Stroke*. Dec 2015;46(12):3375-3382. PMID 26542698

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18. Rai AT, Raghuram K, Domico J, et al. Pre-intervention triage incorporating perfusion imaging improves outcomes in patients undergoing endovascular stroke therapy: a comparison with the device trials. *J Neurointerv Surg.* Mar 2013;5(2):121-127. PMID 22345110
19. Lansberg MG, Christensen S, Kemp S, et al. Computed tomographic perfusion to Predict Response to Recanalization in ischemic stroke. *Ann Neurol.* Jun 2017;81(6):849-856. PMID 28486789
20. van Seeters T, Biessels GJ, Kappelle LJ, et al. The prognostic value of CT angiography and CT perfusion in acute ischemic stroke. *Cerebrovasc Dis.* 2015;40(5-6):258-269. PMID 26484857
21. Dankbaar JW, Horsch AD, van den Hoven AF, et al. Prediction of clinical outcome after acute ischemic stroke: the value of repeated noncontrast computed tomography, computed tomographic angiography, and computed tomographic perfusion. *Stroke.* Sep 2017;48(9):2593-2596. PMID 28716981
22. Greenberg ED, Gold R, Reichman M, et al. Diagnostic accuracy of CT angiography and CT perfusion for cerebral vasospasm: a meta-analysis. *AJNR Am J Neuroradiol.* Nov 2010;31(10):1853-1860. PMID 20884748
23. Cremers CH, van der Schaaf IC, Wensink E, et al. CT perfusion and delayed cerebral ischemia in aneurysmal subarachnoid hemorrhage: a systematic review and meta-analysis. *J Cereb Blood Flow Metab.* Feb 2014;34(2):200-207. PMID 24281744
24. Sanelli PC, Ugorec I, Johnson CE, et al. Using quantitative CT perfusion for evaluation of delayed cerebral ischemia following aneurysmal subarachnoid hemorrhage. *AJNR Am J Neuroradiol.* Dec 2011;32(11):2047-2053. PMID 21960495
25. Sanelli PC, Jou A, Gold R, et al. Using CT perfusion during the early baseline period in aneurysmal subarachnoid hemorrhage to assess for development of vasospasm. *Neuroradiology.* Jun 2011;53(6):425-434. PMID 20694461
26. Xyda A, Haberland U, Klotz E, et al. Brain volume perfusion CT performed with 128-detector row CT system in patients with cerebral gliomas: a feasibility study. *Eur Radiol.* Sep 2011;21(9):1811-1819. PMID 21573969
27. Jain R. Perfusion CT imaging of brain tumors: an overview. *AJNR Am J Neuroradiol.* Oct 2011;32(9):1570-1577. PMID 21051510
28. Ellika SK, Jain R, Patel SC, et al. Role of perfusion CT in glioma grading and comparison with conventional MR imaging features. *AJNR Am J Neuroradiol.* Nov-Dec 2007;28(10):1981-1987. PMID 17893216
29. Jain R, Ellika SK, Scarpace L, et al. Quantitative estimation of permeability surface-area product in astroglial brain tumors using perfusion CT and correlation with histopathologic grade. *AJNR Am J Neuroradiol.* Apr 2008;29(4):694-700. PMID 18202239
30. Connolly ES, Jr., Rabinstein AA, Carhuapoma JR, et al. Guidelines for the management of aneurysmal subarachnoid hemorrhage: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke.* Jun 2012;43(6):1711-1737. PMID 22556195
31. Jauch EC, Saver JL, Adams HP, Jr., et al. Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke.* Mar 2013;44(3):870-947. PMID 23370205
32. Powers WJ, Derdeyn CP, Biller J, et al. 2015 American Heart Association/American Stroke Association focused update of the 2013 guidelines for the early management of patients with acute ischemic stroke regarding endovascular treatment: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke.* Oct 2015;46(10):3020-3035. PMID 26123479
33. Wintermark M, Sanelli PC, Albers GW, et al. Imaging recommendations for acute stroke and transient ischemic attack patients: A joint statement by the American Society of Neuroradiology, the American College of Radiology, and the Society of NeuroInterventional Surgery. *AJNR Am J Neuroradiol.* Nov-Dec 2013;34(11):E117-127. PMID 23907247
34. American College of Radiology, American Society of Neuroradiology, Society for Pediatric Radiology. ACR-ASNR-SPR practice parameter for the performance of computed tomography (CT) perfusion in neuroradiologic imaging. 2017 (revised); <http://www.acr.org/-/media/D541B09581DB46A0A89AC6543646B156.pdf>. Accessed August 30, 2017.
35. American College of Radiology (ACR). ACR Appropriateness Criteria®: Cerebrovascular Disease. 2016; <https://acsearch.acr.org/docs/69478/Narrative/>. Accessed August 30, 2017.
36. Sharma M, Clark H, Armour T, et al. *Acute stroke: evaluation and treatment (Evidence Report/Technology Assessment No. 127)*. Rockville, MD: Agency for Healthcare Research and Quality; 2005.

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01/01/2017 Coding update: Removing ICD-9 Diagnosis Codes
 03/02/2017 Medical Policy Committee review
 03/15/2017 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
 03/01/2018 Medical Policy Committee review
 03/21/2018 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
 Next Scheduled Review Date: 03/2019

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