Name of Policy:  
Computed Tomography Perfusion Imaging

Policy #: 204       Latest Review Date: August 2014
Category:  Radiology       Policy Grade: B

Background/Definitions:
As a general rule, benefits are payable under Blue Cross and Blue Shield of Alabama health plans only in cases of medical necessity and only if services or supplies are not investigational, provided the customer group contracts have such coverage.

The following Association Technology Evaluation Criteria must be met for a service/supply to be considered for coverage:

1. The technology must have final approval from the appropriate government regulatory bodies;
2. The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes;
3. The technology must improve the net health outcome;
4. The technology must be as beneficial as any established alternatives;
5. The improvement must be attainable outside the investigational setting.

Medical Necessity means that health care services (e.g., procedures, treatments, supplies, devices, equipment, facilities or drugs) that a physician, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury or disease or its symptoms, and that are:

1. In accordance with generally accepted standards of medical practice; and
2. Clinically appropriate in terms of type, frequency, extent, site and duration and considered effective for the patient’s illness, injury or disease; and
3. Not primarily for the convenience of the patient, physician or other health care provider; and
4. Not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient’s illness, injury or disease.
**Description of Procedure or Service:**

Perfusion imaging using CT (computed tomography) provides an assessment of cerebral blood flow that may assist in the identification of ischemic regions of the brain. This technology is proposed as a method to aid treatment decisions in patients being evaluated for acute ischemic stroke, subarachnoid hemorrhage and head trauma.

**Stroke**

The goal of acute stroke thrombolytic treatment is to rescue the ischemic penumbra, an area of brain that surrounds the infarct core and is hypoperfused but does not die quickly. Multimodal 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.

- Noncontrast CT is used to rule out intracranial hemorrhage, tumor or infection. MR diffusion-weighted imaging (DWI) demonstrates acute infarction, and a gradient-recalled echo (GRE) sequence excludes intracerebral hemorrhage.
- CT angiography (CTA) and MR angiography MRA) are used to evaluate intra-and extra-cranial vasculature to detect the vascular occlusion and potentially guide therapy (e.g., intravenous thrombolytics, or intra-arterial or mechanical thrombolysis.

The approved therapy, intravenous tissue plasminogen activator (tPA), requires only a non-contrast CT scan to exclude the presence of hemorrhage (a contraindication to the use of the drug). Current guidelines are to administer (tPA) within the first three hours after an ischemic event, preceded by a CT scan. Many patients, however, do not present within the three-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 three hours after an ischemic stroke. Perfusion imaging is also being evaluated in the management of other neurological conditions such as subarachnoid hemorrhage and head trauma.

The potential utility of perfusion imaging of acute stroke is described as the following:

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

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

Similar information can be provided by CT and MRI in terms of infarct core and penumbra. However, multimodal CT has a short protocol time (5-6 min), and because it can be performed with any modern CT equipment, is more widely available in the emergency setting. CT perfusion is performed by capturing images as an iodinated contrast agent bolus passes through the cerebral circulation and accumulates in the cerebral tissues. (Older perfusion methodologies such as single-photon emission CT [SPECT] and xenon-enhanced CT [XeCT] scanning use a diffusible tracer.) The quantitative perfusion parameters are calculated from density changes for each pixel over time with commercially available deconvolution-based software, where cerebral blood flow (CBF) is equal to regional cerebral blood volume (CBV) divided by mean transit time (MTT). CT angiography/CT perfusion requires ionizing radiation and iodinated contrast. It is estimated that a typical perfusion CT deposits a slightly greater radiation dose than a routine unenhanced head CT (approximately 3.3 mSv). CT perfusion covers limited areas of the brain. Commonly used 16- to 64-slice CT scanners can detect an area of 2- to 4-cm of brain tissue. Whole-brain CT perfusion can be performed with greater than 128-detector row CT.

On October 8, 2009, the U.S. Food and Drug Administration (FDA) issued an Initial Communication about excess radiation during perfusion CT imaging to aid in the diagnosis and treatment of stroke from one facility. Together with state and local health authorities, the FDA has identified at least 250 patients who were exposed to excess radiation during CT perfusion scans. The FDA has received reports of possible excess exposures at facilities in other states, involving more than one manufacturer of CT scanners. In response, the FDA has provided recommendations for facilities and practitioners and is continuing to work with manufacturers, professional organizations, and state and local public health authorities to investigate the scope and causes of these excess exposures and their potential public health impact. A November 2010 update of this issue is available at www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm185898.htm.

**Subarachnoid Hemorrhage and Cerebral Vasospasm**

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

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

**Policy:**
Computed tomography perfusion imaging does not meet Blue Cross and Blue Shield of Alabama’s medical criteria for coverage for all indications including the diagnosis and management of acute cerebral ischemia (stroke) and is considered investigational.

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

**Key Points:**
**Acute Cerebral Ischemia**
At the time this policy was created, the literature focused on technical capabilities and feasibility. A number of retrospective studies indicated that blood flow values obtained using a diffusible gas indicator are accurate and that the flow rates correlate with physiologic changes such as the onset of neurologic deficits. The limited availability of medical-grade Xe gas was another issue with this approach to computed tomography (CT) perfusion imaging. Because of more widespread availability, studies were also being done using non-diffusible tracers, i.e., contrast agents. As of 2008, studies were identified that reported on the use of CT perfusion imaging to identify infarcted tissue versus viable tissue (penumbra). However, many studies evaluating use of thrombolytic therapy in acute stroke beyond three hours of symptom onset were based on magnetic resonance (MR) imaging with perfusion-diffusion mismatching. As Lev commented in an editorial, although many investigators have advocated CT perfusion imaging as a reliable method for detecting both infarct core and penumbra, almost all the major clinical trials aimed at
extending the time window for thrombolysis used advanced MR rather than CT imaging for triage. Prospective controlled studies had not been reported that demonstrated that use of perfusion imaging (CT or MR) improved outcomes in patients with acute stroke.

In 2009, the American Heart Association (AHA) Council on Cardiovascular Radiology and Intervention, Stroke Council, and the Interdisciplinary Council on Peripheral Vascular Disease published a scientific statement that included a review of the evidence on CT perfusion. The scientific review determined that:

- Creation of accurate, quantitative CT perfusion has been validated in comparison with xenon-CT, PET [positron emission tomography], and MR perfusion. CT perfusion appears to have greater spatial resolution than MR perfusion, and MR perfusion 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 CT perfusion than with MR perfusion.
- Studies are evaluating various thresholds to predict the upper and lower limits of final infarct size, and outcome prediction studies suggest that CT perfusion 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 National Institutes of Health Stroke Score (NIHSS). Because of the superior quantitative capability compared to MR perfusion imaging, application of specific CT perfusion thresholds to predict tissue survival or infarction appears promising; however, it is essential that these thresholds be validated in larger patient cohorts for which reperfusion status is known.
- There is increasing but as yet indirect evidence that 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.

A systematic review from 2011 examined definitions and thresholds for MR and CT perfusion imaging. Twenty papers on CT perfusion met the inclusion criteria for analysis of definitions, and ten papers on CT perfusion (median sample size of 22) provided thresholds. The quality of the studies was generally poor. There were multiple definitions for tissue states. For example, there were eight different definitions of at-risk tissue, resulting in many-fold differences in the extent of tissue defined as tissue at risk. There was also considerable variability in quantitative thresholds. The review concluded that CT perfusion thresholds in stroke are derived from small numbers of patients, variable perfusion analysis methods and definitions of tissue states. As indicated in the 2009 AHA statement, thresholds should be validated in larger patient cohorts for which reperfusion status is known. Assessment of functional outcomes is also needed to evaluate if CT perfusion improves clinical outcomes.

Five relevant cohort studies have been identified that were published after the AHA review. One of these studies attempted to define the technical CT parameters that best detect perfusion mismatches. In 2011, Bivard et al reported a prospective clinical validation study of perfusion CT for acute (<6 hr) ischemic stroke in 314 consecutive patients. If eligible, patients were treated with intravenous thrombolysis. All patients underwent baseline multimodal CT examination and follow-up MRI at 24 hours, with MRI used as the gold standard for tissue
perfusion. The most accurate CT perfusion threshold at defining infarct core was determined to be cerebral blood flow less than 40% of contralateral with a relative delay time less than 2 sec (area under the curve [AUC] of 0.86). Using this threshold, the correlation between extent of CT perfusion mismatch tissue (the volume of “at-risk” tissue) salvaged from infarction and clinical improvement was $R^2=0.59$ at 24 h (NIHSS) and $R^2=0.42$ at 90 days (Rankin scale).

Obach et al compared outcomes of 106 patients with acute stroke who were assessed with multimodal CT (CT/CT angiography[CTA]/CT perfusion) versus a cohort of 262 patients with acute stroke who were assessed without full multimodal brain imaging during a five-year period. Clinical and imaging data were collected prospectively, and all imaging studies were assessed by investigators blinded to prognostic data. The two groups were comparable at baseline, with the exception of a greater percentage of patients with a time-to-treatment of greater than three hours (28% vs. 16%) and a greater percentage treated with endovascular therapy (26% vs. 11%, all respectively) in the multimodal CT group. Good outcome (modified Rankin scale score $\leq$2) at three months was increased in the multimodal group compared with controls (adjusted odds ratio [OR] of 2.88) in models adjusted for age, gender, NIHSS, glucose, and treatment delay or modality. Fifty-six percent of patients assessed by multimodal CT had a Rankin score equal to or less than two in comparison with 41% of controls ($p=0.008$). In a sensitivity analysis, multimodal-assisted thrombolysis yielded superior benefits in those patients treated after three hours (adjusted OR, 4.48) than for patients treated within three hours (adjusted OR, 1.31). For patients treated after three hours, 63% of patients assessed by multimodal CT had a Rankin score equal to or less than two in comparison with 24% of controls. Mortality (14% and 15%) and symptomatic hemorrhage (5% and 7%, all respectively) were similar in the two groups.

Sztriha et al evaluated whether CT perfusion imaging mismatch could help to select ischemic stroke patients for thrombolysis between three and six hours. A cohort of 254 thrombolysed patients were studied; 174 (69%) were thrombolysed at zero to three hours using non-contrast CT, and 80 (31%) were thrombolysed at three to six hours by using CT perfusion mismatch criteria, defined as a cerebral blood volume ASPECTS [Alberta Stroke Program Early CT Score] of at least seven and an ASPECTS mismatch of at least two. Baseline characteristics were comparable in the two groups. Efficacy endpoints included disability at three months, as assessed by the Rankin score. Safety endpoints included overall mortality, any intracerebral hemorrhage, and symptomatic intracerebral hemorrhage. At three months, there were no differences between patients thrombolysed at zero to three hours or at three to six hours in symptomatic intracerebral hemorrhage (3% vs. 4%), or in any intracerebral hemorrhage (7% vs. 9%). There were also no differences at three months in mortality (16% vs. 9%) or the modified Rankin scale score zero to two (55% vs. 54%, all respectively). The NIHSS score was the only independent determinant of a favorable functional outcome at three months (Rankin score of zero to two; odds ratio [OR]: of 0.89) in patients treated using CT perfusion mismatch criteria beyond three hours. This study is limited by the lack of a control group of patients without CT perfusion. The authors also note that results of this study cannot be generalized to patients with symptoms in the posterior circulation, an area where CT perfusion is known to underperform.

Rai et al evaluated rates of recanalization and functional outcomes in a cohort of 99 patients selected by CT perfusion 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 eight or greater and intracerebral vascular occlusion on admission CT angiography correlating with the neurologic deficit. There was no cut-off time for treatment. The type of endovascular therapy involved intra-arterial thrombolytics in 33.3% of patients, mechanical device in 24.2%, and both thrombolytics and mechanical thrombectomy in 42.4%. Successful recanalization was achieved in 55.6%, with a good outcome in 41.4% of patients. The recanalization rate in this study was not significantly different 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 who were successfully recanalized, good outcomes were obtained in 67% of patients in this study in comparison 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% compared with 54% in MERCI, 51% in Multi-MERCI, and 71% for Penumbra. A small cerebral blood volume abnormality and large mean transit time-cerebral blood volume mismatch were strong predictors of a good outcome. This study is limited by the comparison of a retrospective cohort with results from prospective device trials and by the reliance on recanalization rates as the primary outcome rather than clinical measures.

In 2013, Sheth et al reported a retrospective study of the effect of multi-modal CT on outcomes from endovascular therapy in 556 patients from ten stroke centers. Patients were included if they presented within eight hours of symptom onset and were then divided into groups based on the imaging modality employed prior to treatment. Non-contrast CT was used in 51% of patients, CT perfusion in 34%, and MRI in 14% of patients. Patients were selected for endovascular therapy based on specific imaging criteria. Non-contrast CT patients had significantly lower median times to groin puncture (61 min.) compared with CT perfusion (114 min.) or MRI (124 min.). There were no differences in clinical outcomes, hemorrhage rates, or final infarct volumes among the groups. This study is limited by the retrospective analysis and differences between groups at baseline. Patients selected for endovascular treatment by non-contrast CT alone had a higher baseline NIHSS score and were more likely to have been transferred from an outside facility. In addition, there was limited information regarding the patients who did not proceed to endovascular therapy.

A large number of case series have been published that have retrospectively assessed how CT perfusion at admission might facilitate clinical decision making and predict outcomes in patients with suspected acute ischemic stroke. Prospective trials are needed to evaluate the impact of this technology on health outcomes.

Four recent cohort studies describe how CT perfusion can be used in clinical care to select patients for endovascular therapy. However, these trials lack concurrent control groups and, therefore do not provide relevant evidence on the comparative efficacy of this approach compared to alternative strategies. A fifth stratified cohort study found shorter time to treatment and no difference in clinical outcomes in patients who underwent CT perfusion compared with non-contrast CT or MRI. Randomized trials are needed to establish with greater certainty the value of CT perfusion to assist decision making for thrombolytic or mechanical therapy in acute stroke.
Subarachnoid Hemorrhage and Cerebral Vasospasm
A 2010 meta-analysis on the diagnostic accuracy of CTA and CT perfusion for cerebral vasospasm identified three studies (64 patients) that met the inclusion criteria and contained the appropriate data for statistical analysis. In these studies, “vasospasm” was defined on CT perfusion as a perfusion deficit demonstrating prolonged mean transit time and decreased cerebral blood flow. However, there were no standardized thresholds of mean transit time and cerebral blood flow 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, with both symptomatic and asymptomatic patients included. In comparison with digital subtraction angiography, CT perfusion pooled estimates had 74% sensitivity and 93% specificity. Given the small sample size and the heterogeneity in the CT perfusion data, these results are considered preliminary. A 2014 meta-analysis by Cremers et al included 11 studies (570 patients) on the use of CT perfusion to identify delayed cerebral ischemia. CT perfusion measures at admission did not differ between patients who did and did not develop delayed cerebral ischemia. Some measures of CT perfusion (cerebral blood flow and mean transit time, but not cerebral blood volume) were found to differ between the two groups during the period of four to 14 days after subarachnoid hemorrhage, suggesting a possible role in diagnoses of delayed cerebral ischemia.

In 2011, Sanelli et al reported a prospective study with 97 patients that evaluated the accuracy of CT perfusion to diagnose delayed cerebral ischemia following aneurysmal subarachnoid hemorrhage. CT perfusion was performed between days six and eight in asymptomatic patients and on the day of clinical deterioration in symptomatic patients. Perfusion maps were qualitatively evaluated by two neuroradiologists who were blinded to clinical and imaging data and compared to the reference standard. Based on a multistage hierarchical reference standard that incorporated both imaging and clinical criteria, 40 patients (41%) were diagnosed with delayed cerebral ischemia. Overall diagnostic accuracy for CT perfusion, determined from receiver operating characteristic (ROC) curves, was 93% for cerebral blood flow, 88% for mean transit time, and 72% for cerebral blood volume. The study also sought to determine a quantitative threshold for delayed cerebral ischemia with CT perfusion, although it was noted that absolute thresholds may not be generalizable due to differences in scanner equipment and post-processing methods. Clinical outcomes of the delayed cerebral ischemia group included 19 patients (48%) with no permanent neurologic deficit, 16 (40%) with permanent neurologic deficit, and five (13%) who died during hospitalization.

Sanelli et al also reported a retrospective study of the development of vasospasm in 75 patients with aneurysmal subarachnoid hemorrhage who had an earlier CT perfusion assessment (likely overlap in subjects with the study described above). Based on a multistage reference standard, 28 patients (37%) were classified as vasospasm. CT perfusion values (cerebral blood flow and mean transit time) on days zero to three were found to be significantly lower in the vasospasm group. Optimal thresholds were then determined for cerebral blood flow (50% sensitivity and 91% specificity), mean transit time (61% sensitivity and 70% specificity) and cerebral blood volume (36% sensitivity and 89% specificity). Clinical outcomes of the vasospasm group included 15 patients (54%) with no permanent neurologic deficit, 11 (39%) with permanent neurologic deficit, and two (7%) who died during hospitalization.
CT perfusion is being evaluated for the diagnosis of vasospasm and delayed cerebral ischemia following aneurysmal subarachnoid hemorrhage. A prospective trial 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 evaluate whether CT perfusion in patients with aneurysmal subarachnoid hemorrhage leads to the early identification of patients at high risk for vasospasm/delayed cerebral ischemia, alters treatment decisions, and improves health outcomes.

**Brain Tumors**

A 2011 review by Jain indicates that most of the literature on the utility of perfusion imaging for glioma grading is based on various MR perfusion techniques. One study compared CT perfusion with conventional MRI in 19 patients. With a cut-off point of greater than 1.92 normalized cerebral blood volume (nCBV), there was sensitivity of 85.7% and specificity of 100% to differentiate high-grade gliomas. There were no significant differences in nCBV between Grade III or IV tumors. A subsequent study by Jain and colleagues correlated CT perfusion 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, eight had low-grade gliomas and 24 had high-grade gliomas. In this selected set of patients, CT perfusion showed significant differences in the Grade III and grade IV tumors. Prospective studies in an appropriate population of patients are needed to evaluate the sensitivity and specificity of CT perfusion glioma grading, with histopathologic assessment of tumors as the independent reference standard.

In 2011, Xyda et al reported a prospective study of the feasibility and efficacy of volume perfusion CT (VPCT) for the preoperative assessment of cerebral gliomas in 46 consecutive patients with suspected cerebral gliomas. (Whereas typical perfusion CT covers a relatively narrow range of brain tissue, the VPCT system with multi-spiral 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 cerebral blood volume, flow, 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 and II) and high-grade (III and IV). The diagnostic power of the perfusion parameters were analyzed by receiver operating characteristic (ROC) 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. Potential uses of VPCT are to guide biopsy and to monitor low-grade gliomas. This is the first report using VPCT to differentiate gliomas; therefore, replication of these findings in an independent sample of patients is needed.

**Summary**

Perfusion imaging using computed tomography (CT) provides an assessment of cerebral blood flow that may assist in the identification of ischemic regions of the brain. This technology is proposed as a method to aid treatment decisions in patients being evaluated for acute ischemic stroke, subarachnoid hemorrhage, cerebral vasospasm, brain tumors, and head trauma. One of
the potential areas of benefit is greater individualization of therapy for acute stroke by better defining ischemic areas at risk that may benefit from thrombolysis and/or endovascular intervention. However, the current evidence is insufficient to determine whether outcomes are improved with use of this technique. Randomized clinical trials are needed in which a strategy employing CT perfusion in the treatment of acute stroke is compared with traditional strategies. For other indications such as subarachnoid hemorrhage and brain tumors, the data on CT perfusion are limited. Because the impact of CT perfusion imaging on clinical outcomes is not known, this technique is considered investigational.

**Practice Guidelines and Position Statements**

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

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

American College of Radiology (ACR) Appropriateness Criteria® from 2011 provides the following ratings for CT head perfusion with contrast:

- Rating of 2 (usually not appropriate) for asymptomatic individuals with structural lesion on physical examination (cervical bruit) and/or risk factors.
- Rating of 6 (may be appropriate) if directly employed in decision making and planning treatment for carotid territory or vertebrobasilar transient ischemic attack; initial screening survey.
- Rating of 6 (may be appropriate) for a new focal neurologic defect, fixed or worsening; less than three hours, if CT is used for planning treatment such as thrombectomy.
- Rating of 6 (may be appropriate) for a new focal neurologic defect, fixed or worsening; three to 24 hours, if CT is used for planning treatment such as thrombectomy within eight hours of symptom onset.
- Rating of 5 (may be appropriate) for a new focal neurologic defect, fixed or worsening; longer than 24 hours, if used for decision making or planning treatment such as angioplasty and stenting.
- The ACR also notes that CT stroke protocols combining a brain non-contrast CT, CT angiography, and CT perfusion may produce a relative radiation level of 1 to 10 mSv, and repeated use of this protocol in an individual patient may result in high radiation exposure to the scalp and eyes.
In 2013, the American Society of Neuroradiology, the American College of Radiology, and the Society of Neuro-Interventional Surgery issued a joint statement on imaging recommendations for acute stroke and transient ischemic attack patients. The following statements were made regarding perfusion imaging:

- In acute stroke patients who are candidates for endovascular therapy, vascular imaging (CTA, MRA, DSA) is strongly recommended during the initial imaging evaluation. Perfusion imaging may be considered to assess the target tissue “at risk” for reperfusion therapy. However, the accuracy and usefulness of perfusion imaging to identify and differentiate viable tissue have not been well-established.

- Determination of tissue viability based on imaging has the potential to individualize thrombolytic therapy and extend the therapeutic time window for some acute stroke patients. Although perfusion imaging has been incorporated into acute stroke imaging algorithms at some institutions, its clinical utility has not been proved.

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

The Agency for Healthcare Research and Quality (AHRQ) published a report on acute stroke in 2005. This report addressed multiple issues regarding CT perfusion and also angiography in terms of how these modalities affect the use of thrombolytic therapy for acute ischemic stroke. This report indicated that studies with prospective use of CT perfusion and angiography techniques in patient selection for thrombolysis were not identified.

**U.S. Preventive Services Task Force Recommendations**
Perfusion CT imaging is not a preventive service.

**Key Words:**
Computed tomography (CT), computed tomography perfusion imaging, perfusion CT (PCT), acute stroke, ischemic stroke, hemorrhagic stroke

**Approved by Governing Bodies:**
Several post-processing software packages (e.g., Siemens’ Syngo Perfusion-CT, GE Healthcare’s CT Perfusion 4, Philips Medical System’s Brain Perfusion Option) have received 510(k) marketing clearance from the FDA for use with a CT system to perform perfusion imaging. The software is being distributed with new CT scanners.
**Benefit Application:**
Coverage is subject to member’s specific benefits. Group specific policy will supersede this policy when applicable.

ITS: Home Policy provisions apply
FEP contracts: FEP does not consider investigational if FDA approved and will be reviewed for medical necessity.

**Current Coding:**
CPT Codes:

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

**Previous Coding:**
CPT Codes:

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

**References:**


Policy History:
Medical Policy Group, September 2004 (3)
Medical Policy Administration Committee, October 2004
Available for comment October 15-November 29, 2004
Medical Policy Group, September 2006 (1)
Medical Policy Group, December 2007 (1)
Medical Policy Group, December 2008 (2)
Medical Policy Group, May 2010 (1): Policy updated, no coverage changes

This medical policy is not an authorization, certification, explanation of benefits, or a contract. Eligibility and benefits are determined on a case-by-case basis according to the terms of the member’s plan in effect as of the date services are rendered. All medical policies are based on (i) research of current medical literature and (ii) review of common medical practices in the treatment and diagnosis of disease as of the date hereof. Physicians and other providers are solely responsible for all aspects of medical care and treatment, including the type, quality, and levels of care and treatment.

This policy is intended to be used for adjudication of claims (including pre-admission certification, pre-determinations, and pre-procedure review) in Blue Cross and Blue Shield’s administration of plan contracts.