FEP 6.01.49 Computed Tomography Perfusion Imaging of the Brain

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.

FDA REGULATORY STATUS
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 been cleared for marketing by the U.S. Food and Drug Administration through the 510(k) process 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.

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

Computed tomography perfusion 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.

BENEFIT APPLICATION
Experimental or investigational procedures, treatments, drugs, or devices are not covered (See General Exclusion Section of brochure).
RATIONAL

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 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 a randomized controlled trial. Relevant outcomes are overall survival, test accuracy, symptoms, morbid events, and functional outcomes. CTP is one of the several approaches used in acute stroke to define viable ischemic tissue better and therefore may benefit from mechanical endovascular intervention. Alternative methods of patient selection for mechanical embolectomy have included time from stroke onset, multiphase computed tomography angiography, or Alberta Stroke Program Early CT score. 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 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 non-contrast computed tomography. The evidence is insufficient to determine the effects of the technology on health outcomes.

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

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

SUPPLEMENTAL INFORMATION

Practice Guidelines and Position Statements

American Heart Association and American Stroke Association

The 2012 American Heart Association (AHA) and American Stroke Association (ASA) joint guidelines 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 IIa; level of evidence B). The guidelines stated that 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 2015, AHA and ASA provided a focused update of their 2013 guidelines, which included a review of endovascular treatment of acute ischemic stroke. The 2015 guidelines reviewed the trials on stent retrievers. Regarding CTP, the guidelines concluded that “the benefits of additional imaging beyond CT and CTA [computed tomography angiography] or MRI [magnetic resonance imaging] and MRA [magnetic resonance angiography] such as CT perfusion or diffusion- and perfusion-weighted imaging for selecting patients for endovascular therapy are unknown (Class IIb; Level of Evidence C).”

American Society of Neuroradiology et al

In 2013, the American Society of Neuroradiology, the American College of Radiology (ACR), and the Society of Neuroradiology 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, MRA, DSA [digital subtraction angiography]) is strongly recommended during the initial imaging evaluation. Perfusion imaging may be considered to assess the target tissue “at risk” for reperfusion therapy. However, the accuracy and usefulness of perfusion imaging to identify and differentiate viable tissue have not been well-established.”
- “Determination of tissue viability based on imaging has the potential to individualize thrombolytic therapy and extend the therapeutic time window for some acute stroke patients. Although perfusion imaging has been incorporated into acute stroke imaging algorithms at some institutions, its clinical utility has not been proved.”

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FEP 6.01.49 Computed Tomography Perfusion Imaging of the Brain

- “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 [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.”

In 2017, the American Society of Neuroradiology, the Society for Pediatric Radiology, and ACR 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 1).^{34}

| Table 1. Appropriateness of Head Computed Tomography Perfusion Imaging With Contrast |
|----------------------------------------|--------|
| Recommendation | Rating |
| For asymptomatic individuals with a structural lesion on physical examination (cervical bruit) and/or risk factors | 5 |
| If directly employed in decision making and planning treatment for carotid territory or vertebrobasilar transient ischemic attack on the initial screening survey | 5 |
| For a new focal neurologic defect, fixed or worsening: less than 6 hours | 6 |
| For a new focal neurologic defect, fixed or worsening: longer than 6 hours | 5 |
| For evaluation for cerebral vasospasm after aneurysmal subarachnoid hemorrhage | 5 |

Ratings of 5 and 6 “may be appropriate.”

ACR also noted that CT stroke protocols combining a brain non-contrast CT, CTA, 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.

**Agency for Healthcare Research and Quality**
The Agency for Healthcare Research and Quality published a report on acute stroke in 2005. It addressed multiple issues related to how the CTP imaging and angiography modalities affect the use of thrombolytic therapy for acute ischemic stroke. This report did not identify any studies on the prospective use of CTP imaging and angiography techniques in patient selection for thrombolysis.

**U.S. Preventive Services Task Force Recommendations**
Not applicable.

**Medicare National Coverage**
There is no national coverage determination (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.
REFERENCES


POLICY HISTORY

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>June 2012</td>
<td>New Policy</td>
<td>Policy updated with literature search, references added and reordered, policy statement unchanged</td>
</tr>
<tr>
<td>March 2013</td>
<td>Update Policy</td>
<td>Policy updated with literature search through July 17, 2013; reference 16 added; “of the Brain” added to title and policy statement for clarification.</td>
</tr>
<tr>
<td>December 2014</td>
<td>Update Policy</td>
<td>Policy updated with literature review adding references 18, 25, 27, and 28. The policy statement is unchanged.</td>
</tr>
<tr>
<td>December 2015</td>
<td>Update Policy</td>
<td>Policy updated with TEC Assessment (reference 1). CT perfusion considered medically necessary in patients with anterior large-vessel stroke being evaluated for mechanical embolectomy. CT perfusion in other situations remains not medically necessary.</td>
</tr>
<tr>
<td>December 2016</td>
<td>Update Policy</td>
<td>Policy updated with literature review; references 3, 6, 15, 18, and 30 added; reference 31 updated. The TEC Assessment was not published and has been removed from the reference list. Policy statements</td>
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### FEP 6.01.49  Computed Tomography Perfusion Imaging of the Brain

| December 2017 | Updated Policy | Policy updated with literature review through July 20, 2017; references 4, 18, 20, and 31 added. Policy statements unchanged. |

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