

THE ROLE OF FIRST-PASS, DYNAMIC BRAIN-PERFUSION CT IN THE EVALUATION OF HYPERACUTE STROKE

Mark Pierce, RT (R)(CT)
Baptist Medical Center
Little Rock, AR
Email: Mpierce@baptist-health.org

INTRODUCTION

Advances in chemical and mechanical thrombolysis have renewed interest in finding a more effective therapy for stroke. Consequently, the role of computed tomography (CT) vis-à-vis the acute neuroimaging setting has evolved. Due to its wide availability and high sensitivity for detection of intracranial hemorrhage, noncontrast head CT—typically consisting of 5-mm contiguous axial sections from the skull base to the vertex—was universally regarded as the initial imaging modality of choice for stroke evaluation in the past. However, as treatment emphasis shifts toward more rapid fibrinolytic intervention, the goals of imaging have dramatically expanded.

Previously, the utility of an imaging procedure was predicated on providing anatomic information, but at present the objective of supplying physiologic data that can aid in therapeutic benefit stratification has become paramount. Specifically, emphasis is directed toward differentiation of two types of brain tissue: (1) tissue that has undergone irreversible infarction, which is referred to as the infarct core, and (2) ischemic tissue at direct risk of infarction, which is called the ischemic penumbra.

Noncontrast head CT scanning provides an anatomic picture that indicates the presence or absence of acute cerebral ischemia; this modality also excludes lesions such as hemorrhage or neoplasm that can mimic those of stroke.¹ Unfortunately, if imaging is obtained within the first three hours following symptom onset, tissue abnormalities caused by arterial occlusion are not detectable by conventional CT.

Indeed, approximately 60% of noncontrast head CT

scans that are acquired less than 18 hours after a stroke has occurred are interpreted as normal.² Subtle abnormalities—such as blurring of the demarcation between gray and white matter, sulcal effacement, and the hyperdense artery sign may support the diagnosis of evolving infarct; however, fully developed areas of hypodensity only become evident after 24 to 72 hours.³

Early CT signs of infarction on the baseline examination include hypodensity of the gray matter equivalent to a decrease of 4 to 10 HU as compared with the surrounding tissue. As well, hyperdense artery signs of thromboembolism involving the internal carotid or middle cerebral artery and its branches measuring 60 HU or greater are indicative of early infarct.⁴

A number of imaging techniques supply both anatomic and physiologic data in the clinical setting of hyperacute (ie, less than six hours since symptom onset) stroke. *Diffusion-weighted MR* (DWI) and *perfusion imaging MR* (PI) are two relatively new techniques that have become increasingly available for the evaluation of acute ischemia. Both modalities have a number of advantages when compared with conventional CT, including greater sensitivity for stroke detection and the ability to supply physiologic information in the form of hemodynamic parameters that increase understanding about which cerebral territories are at risk of undergoing infarction.¹ Notwithstanding these advantages, MR imaging remains underused in the hyperacute stroke setting, perhaps due in part to the delay caused by the initial CT scan and because emergency MR is logistically difficult at most institutions.

Although xenon-enhanced CT is a valuable tool for noninvasive measurement of *cerebral blood flow* (CBF), it is not widely used. Only a few institutions have the specialized and expensive equipment required to perform this technique. It is limited by the difficulties patients experience with stable xenon administration, including decreased respiratory rate, headaches, nausea, vomiting, and convulsions. The results of one large study of 1839 patients demonstrated these side effects to occur respectively in 3.6%, 0.4%, 0.2%, and 0.2% of patients.⁵ Also, stable xenon itself can influence cerebral blood flow.

Because almost all patients with suspected acute stroke first undergo conventional CT, and because the treatment window for fibrinolytic therapy demands that imaging be performed more quickly, essential time can be gained by also measuring cerebral blood flow while the patient is in

the CT department. A new technique, *dynamic CT perfusion imaging*, combines a rapid bolus of iodinated contrast medium infused through a peripheral vein with a dynamic (single-level or cine mode) scan. The resulting data are sent via a DICOM network to a workstation for post-processing. Software is used to produce maps of *time to peak* (TTP), *cerebral blood volume* (CBV), and CBF. In some cases, perfusion imaging may be followed by *CT angiography* of the carotid arteries and vessels of the circle of Willis in order to demonstrate stenosis or occlusion of extra- and intracranial arteries.

Candidates for CT perfusion are those patients presenting with obvious hemispheric symptoms such as hemiparesis, aphasia, or hemianopia within 0 to 6 hours of symptom onset as well as those patients who are at risk for stroke from vasospasm.

The purpose of this article is twofold: first, to more broadly enhance the technologist's knowledge of the dynamics of stroke—both anatomically and physiologically; second, to provide an overview of the emerging technology involved with brain perfusion CT.

EPIDEMIOLOGY OF STROKE

According to data from the National Institute of Neurological Disorders and Stroke (NINDS), stroke—also known as cerebrovascular accident (CVA) or brain attack—is the third leading cause of mortality worldwide, ranking only behind diseases of the heart and all forms of cancer. It is a principal source of serious, long-term disability. Stroke occurs more commonly among men than women; however, greater than 50% of total stroke fatalities occur in women.

For the year 2000, NINDS data, which categorized stroke fatalities by incidence among populations of 100,000, indicated death rates of 58.6% for white males and 87.1% for black males. A similar disparity exists among the female population, with statistics demonstrating fatality rates of 57.8% for white females and 78.1% for black females. Asians and Hispanics also have a higher incidence of stroke than do whites; this disparity is related in part to greater prevalence of hypertension among these nonwhite populations.

Risk for stroke is increased for people with diabetes, heart disease (especially atrial fibrillation), hypertension, previous CVA, or transient ischemic attack (TIA). Risk increases tenfold for an individual who has a history of one or more TIAs.⁶

Of the approximately 2000 people per million affected each year by stroke, one third will recover completely from their attack, one third will die over the following year, and the remaining third will be permanently disabled. Although stroke occurs in all age groups, risk increases markedly with age. Ninety percent of all stroke cases occur in people 55 or older.

ANATOMY OF THE BRAIN

The clinical manifestations of stroke are dependent on both region and extent of the brain affected. There are three primary components of the brain: the *cerebrum*, the *cerebellum*, and the *brainstem*. Each component possesses distinct functions. Of the three regions, the cerebrum is the largest and most developmentally advanced, maintaining responsibility for higher intellectual function, speech, emotion, integration of sensory stimuli of all types, initiation of the final common pathways for movement, and fine motor skills.

The cerebellum, the second largest area, maintains balance and provides further control of movement and coordination. The brainstem serves as the link between cerebral structures and the spinal cord. Its responsibilities include a variety of autonomic functions, including respiration control, heart rate and blood pressure, wakefulness, arousal, and attention.

The entire cerebrum is arranged into two strata. The 20-mm-thick outermost layer, called the *cerebral cortex* (or *gray matter*), controls cognition and personality as well as the coordination of complicated movements. The underlying *white matter* is a network of fibers that enables regions of the brain to communicate with each other.

The cerebrum is divided in the midline by the great longitudinal fissure, which extends the length of the cerebrum and partitions it into right and left hemispheres. It is interrupted anteriorly by the *corpus callosum*, a broad transverse commissure of white matter that connects the two hemispheres together. The hemispheres are comprised of pairs of frontal, parietal, temporal, and occipital lobes, with each presenting an outer stratum of gray matter called the cortical substance. This substance is thrown into a number of infoldings called fissures (or *sulci*) that separate the surface into a series of irregular eminences named convolutions (or *gyri*).

The left hemisphere commands the majority of functions on the right side of the body, whereas the right hemisphere controls most functions on the left. Accordingly, injury to the left cerebral hemisphere produces sensory and motor deficits on the right side, and vice versa. One hemisphere has a slightly more developed, or dominant, area in which written and spoken language is organized. However, greater than 95% of right-handed people and even the majority of left-handed people have dominance for speech and language in the left hemisphere; therefore, left hemisphere stroke is more likely to produce aphasia and other language-related deficits.

A stroke involving the cerebellum results in lack of coordination, shaking, or other muscular difficulties. In this instance, swelling may cause brainstem compression or hydrocephalus; these consequences underscore the need for early diagnosis. Strokes in the brainstem are generally attributed to *basilar artery occlusion*, although in many cases the clinical syndrome may also fit the criteria for a lacunar stroke (see next section).

Normal function of the brain's control centers depends

upon a sufficient supply of oxygen and nutrients through a dense network of vessels. Blood is supplied to the brain by two major sets of vessels: the *right and left common carotid arteries* and the *right and left vertebral arteries*. The common carotid arteries have two divisions. The *external carotid arteries* supply the face and scalp with blood, whereas the *internal carotid arteries* provide blood to the anterior three fifths of the cerebrum, except for parts of the temporal and occipital lobes. The *vertebro-basilar arteries* supply the posterior two fifths of the cerebrum, part of the cerebellum, and the brainstem.

Any decrease in blood flow in an internal carotid artery results in impairment of frontal lobe function. This impairment may result in numbness, weakness, or paralysis on the side of the body opposite to the obstructed artery. Occlusion of one of the vertebral arteries can cause many serious consequences that range from blindness to paralysis.

In the base of the brain, the carotid and vertebral arteries form a circle of communicating arteries known as the *circle of Willis*. Other arteries—the *anterior cerebral artery (ACA)*, *middle cerebral artery (MCA)*, and *posterior cerebral artery (PCA)*—arise from this circle and course to differing regions of the brain.

The ACA extends in a cephalic and anterior direction from the internal carotid artery. It supplies the frontal lobes as well as parts of the brain that control logical thought, personality, and voluntary movement, especially the legs. Stroke involving the anterior cerebral artery typically results in opposite leg weakness. If both anterior cerebral territories are affected, profound mental symptoms may ensue.

The MCA is the largest branch of the internal carotid and is the artery most often occluded in stroke. It supplies a portion of the frontal lobe and the lateral surface of the temporal and parietal lobes, including the primary motor and sensory areas of the face, throat, hand, arm, and areas of speech in the dominant hemisphere.

In most individuals, the PCA arises from the basilar artery; however, it may originate from the ipsilateral internal carotid artery. It supplies the temporal and occipital lobes of the left and right cerebral hemispheres. When infarction occurs in the territory of the posterior cerebral artery, it is usually secondary to embolism from lower segments of the vertebral basilar system or heart. Although clinical symptoms associated with occlusion of the posterior cerebral artery depend on the location of the occlusion, the most common finding is occipital lobe infarction leading to an opposite visual field defect.

CLASSIFICATION OF STROKE

Stroke is classified into two main categories: (1) *ischemic stroke*, caused by a blockage in an artery, and (2) *hemorrhagic stroke*, caused by a tear in the artery's wall that produces bleeding in the brain. A third less prevalent type is *hypotensive stroke*, which occurs as a result of blood pressure that is too low.

Ischemic strokes are by far the most common, accounting for 80% of all strokes. Ischemia is defined as a deficiency of oxygen in vital tissues. Two main types of ischemic stroke exist: (1) *thrombotic*, due to a blood clot at a fatty deposit within one of the brain's arteries; and (2) *embolic*, resulting from a traveling thrombus that has formed elsewhere in the body but eventually lodges in a smaller artery because it is too large to pass through small vessels. In addition to the two main types, a less acute form of ischemic stroke known as *lacunar stroke* exists. This type of stroke occurs when one of the small arteries supplying the deep cerebral white matter of the brain is blocked. For these deep parts of the brain, no other blood vessels exist that can help supply blood to the area. Therefore, a blockage results in regional tissue death.

PERFORMING CT BRAIN PERFUSION

The most common technique associated with CT perfusion scanning is based on the first pass of a contrast bolus through the brain tissue. With this technique, a 40-cc bolus of nonionic intravenous contrast is injected at 4 to 5 cc/sec through an 18- to 20-gauge antecubital catheter. A helical CT scanner is used to produce a dynamic set of images at a single location. A 5-second scan delay is used, and either 5- or 10-mm slice thickness may be used. Ten-millimeter slices produce perfusion maps with relatively greater signal-to-noise ratio. However, 5-mm slices are preferred because they reduce partial volume artifact within the plane of the section, thus providing more accurate perfusion parameter values.¹ Typical scan durations are in the range of 40 to 45 seconds.

The slices are produced by repeatedly scanning the same region at the same table position, a technique some manufacturers refer to as the *cine mode*. However, with multislice scanners, more than one Z position may be scanned simultaneously, depending on the detector selection. In this case, the perfusion software provides a means of selecting the various slice levels to be examined.

In order to produce reliable results, the scan acquisition must fully capture the precontrast, first-pass enhancement as well as the recirculation phases of enhancement. As the bolus diffuses through the tissue, its shape becomes spread out and delayed as compared with the shape and timing of the bolus demonstrated in the imaged artery. The bolus is collected by the venous system and recirculates.

The first-pass technique assumes no recirculation; therefore, the effect of the recirculation must be compensated for by mathematical means. There are several mathematical techniques that can be used to approximate the measurements for first pass of the bolus. The perfusion results are represented by maps demonstrating *regional cerebral blood volume (rCBV)*, *mean transit time (MTT)*, and *regional cerebral blood flow (rCBF)*.

In order to improve the signal-to-noise ratio of the contrast enhancement, the CT perfusion series acquisition should precede the CTA series acquisition. This pro-

to col eliminates residual contrast that would appear in the pre-enhancement phase of the perfusion series and maximizes the differential between unenhanced and enhanced tissue.

Although the level for scanning may be selected at the time of examination based on the unenhanced CT findings, a transverse slice through the level of the basal ganglia contains territories supplied by the anterior, middle, and posterior cerebral arteries, thus offering the opportunity to interrogate each of the major vascular regions. The typical 10- to 20-mm anatomic coverage provided with CT perfusion remains the major limiting factor with this technique. If indicated, a second bolus of contrast may be infused so that the patient can be scanned at a different location, typically in a more cephalad direction above the lateral ventricles. However, as larger multidetector array scanners become more prevalent, increased anatomic coverage may obviate this issue.

Before attempting to produce perfusion maps at the workstation, the technologist should review slices to exclude the presence of a compromised *blood-brain barrier* (eg, hemorrhage) or motion artifact. If either of these conditions exists, the resulting CT brain perfusion measurements should not be relied upon. The computations performed by the software assume an intact blood-brain barrier and no motion; therefore, the accuracy of measurements not fulfilling these criteria will be compromised.

In order to produce the perfusion maps at the workstation, the technologist should obtain an arterial and a venous region of interest. The optimal locations are large vessels that follow courses perpendicular to the transverse plane. Eastwood and coworkers reported excellent results selecting either the unaffected anterior cerebral artery or unaffected middle cerebral artery as the *reference artery* and the superior sagittal sinus as the reference vein.¹ In general, the software algorithm requires the earliest artery transit time and the maximum venous total intensity. These parameters can be accurately defined by observing the data from the software's displayed perfusion graphs.

The earliest artery is defined as the location within an artery that has the lowest transit time as displayed on the perfusion graph. The maximum or most dense vein is defined as the location within the vein with the maximum total density as displayed on the graph.

In another study conducted by Eastwood and coworkers,⁸ CBV values ranging between 0 to 10 mL/100 g per minute were considered consistent with severe ischemia. Changes in the CBF were deemed severe if flow was 30% or less compared to that of the unaffected side. A TTP lag of more than 6 seconds as compared with the unaffected side was also considered severe.

For patients who have MCA occlusion, less-than-severe perfusion abnormalities are considered to be indicators of better leptomeningeal collateral blood flow, which aids in survival of ischemic tissue until reperfusion can be achieved.⁹

CONCLUSION

Dynamic perfusion CT imaging with iodinated contrast is a rapid and effective means of determining cerebral perfusion. Combined with unenhanced CT and CT angiography, it provides a means for prompt assessment of vascular anatomy and regional hemodynamics. This technique provides a valuable alternative when *magnetic resonance imaging* is unavailable or contraindicated, and may ultimately direct the best therapy for acute stroke. *The author wishes to gratefully acknowledge the invaluable assistance of Doctor Edward Angtuaco, staff Radiologist at Baptist Medical Center, Little Rock, Arkansas, who gave freely of his time and expertise in order that this article be more precise.*

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SUGGESTED READING

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THE ROLE OF FIRST-PASS, DYNAMIC BRAIN-PERFUSION CT IN THE EVALUATION OF HYPERACUTE STROKE POST TEST

Expires: May 15, 2011 Approved for 1 Category A CE Credit.

- 1. Which of the following terms best describes the type of brain tissue that could potentially benefit from fibrinolytic therapy?**
 - a. Necrotic core
 - b. Ischemic core
 - c. Infarct core
 - d. Ischemic penumbra
- 2. Approximately what percentage of noncontrast head CT scans obtained less than 18 hours following stroke are interpreted as normal?**
 - a. 20
 - b. 50
 - c. 60
 - d. 80
- 3. Which of the following magnetic resonance techniques is most effective at imaging acute stroke?**
 - a. FLAIR
 - b. T1
 - c. T2
 - d. DWI
- 4. Which of the following is NOT a side effect associated with the administration of stable xenon?**
 - a. Convulsions
 - b. Hemorrhage
 - c. Decreased respiratory rate
 - d. Nausea and vomiting
- 5. Which of the following demographic groups is most likely to suffer a stroke?**
 - a. White male
 - b. White female
 - c. Black male
 - d. Black female
- 6. Which of the following is NOT a true statement concerning stroke epidemiology?**
 - a. It is a principal source of serious, long-term disability.
 - b. Stroke is more common in women than among men.
 - c. Greater than 50% of stroke fatalities occur in women.
 - d. Stroke is the third leading cause of mortality in the United States.
- 7. Which of the following risk factors increases the likelihood of stroke tenfold?**
 - a. Heredity
 - b. History of transient ischemic attack
 - c. Hypertension
 - d. Thrombocytopenia
- 8. Which of the following bodily functions is not controlled by the brainstem?**
 - a. Vision
 - b. Respiration
 - c. Blood pressure
 - d. Wakefulness
- 9. Which of the following structures contains the centers for cognition and personality?**
 - a. Septum pellucidum
 - b. Thalamus
 - c. White matter
 - d. Gray matter
- 10. The broad transverse commissure of white matter that connects the two hemispheres of the brain together is called the**
 - a. falx cerebri.
 - b. septum pellucidum.
 - c. corpus callosum.
 - d. great longitudinal fissure.
- 11. Left hemisphere stroke is more likely to produce which kind of symptoms?**
 - a. Aphasia and other language-related deficits
 - b. Lack of coordination
 - c. Loss of fine motor skills
 - d. Memory loss
- 12. Which artery is most often occluded in stroke?**
 - a. Posterior communicating artery
 - b. Middle cerebral
 - c. Anterior cerebral
 - d. Anterior communicating artery
- 13. The posterior cerebral artery most often arises from which vessel?**
 - a. Basilar artery
 - b. Carotid artery
 - c. Vertebral artery
 - d. Middle cerebral artery
- 14. How much nonionic intravenous contrast is typically administered with CT brain perfusion imaging?**
 - a. 40 cc
 - b. 75 cc
 - c. 100 cc
 - d. 200 cc
- 15. Which of the following would be considered an appropriate injection protocol for CT brain perfusion?**
 - a. 2-3 cc/sec, 20-second delay
 - b. 4-5 cc/sec, 20-second delay
 - c. 2-3 cc/sec, 5-second delay
 - d. 4-5 cc/sec, 5-second delay
- 16. If CT brain perfusion is performed in conjunction with CTA acquisition, the perfusion study should be performed first to**
 - a. reduce the risk of motion.
 - b. prevent contrast toxicity.
 - c. eliminate residual contrast appearing in the pre-enhancement phase of the perfusion series.
 - d. detect the presence or absence of AVM.

- 17. A transverse slice through the level of which of the following structures provides the opportunity to examine the major vascular territories of the brain?**
- a. Basal ganglia
 - b. Corpus callosum
 - c. Thalamus
 - d. Hypothalamus
- 18. Which of the following conditions adversely affects the reliability of CT perfusion measurements?**
- a. Arterial plaque
 - b. Hemorrhage
 - c. Neoplasm
 - d. Thrombus
- 19. In producing the perfusion maps at the workstation, the optimal choices for the placement of the region of interest are**
- a. small, branching vessels.
 - b. large vessels that follow courses perpendicular to the transverse plane.
 - c. any artery or vein that exhibits contrast enhancement.
 - d. the soft tissues adjacent to large vessels, such as the area around the jugular vein.
- 20. In the case of suspected MCA territory stroke, which of the listed arteries would be considered an optimal choice for the arterial input function used in perfusion software?**
- a. Unaffected MCA
 - b. PICA
 - c. Posterior communicating artery
 - d. Basilar artery



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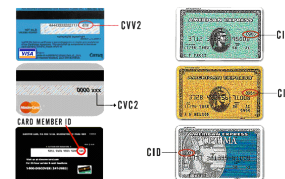
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