

REVIEW

Imaging in Ischemic Stroke State of the Art

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ABSTRACT

Exciting advances in anatomical imaging have greatly improved our capacity to detect pathologic process in nervous system, localize these processes in the nervous system precisely, and predict the type of disease. The rapid evolution of techniques of anatomical imaging has occurred in parallel with developments in physiologic imaging.

Cerebrovascular disease and stroke

Stroke is the third most common cause of death in developed countries. The age adjusted annual death rate from stroke is 116 per 100,000 population in the USA, some 200 per 100,000 in the UK, some 12% of all deaths; it is higher in black African population than in Caucasian. Stroke is uncommon below the age of 40 years and is more common in males. The death rate following a stroke is around 25%. Hypertension is the most important treatable risk factors. Stroke is decreasing in the 40-60 age range as hypertension is treated; however, in the elderly, it remains a major cause of morbidity and mortality.¹

Stroke is a complex, heterogeneous disease with several major subtypes. The sudden onset of focal sensory loss, weakness, or speech disorder raises the possibility of cerebral ischemia or infarction. The three most common causes of cerebral infarction are atherothrombotic occlusion, embolism, and hypoperfusion.² Rapid and accurate assessment is crucial for treatment, since recombinant tissue plasminogen activator provides effective treatment for acute ischemic infarction in the absence of cerebral hemorrhage if given within three hours after onset.³

Through a careful medical history and a complete physical examination, the most likely vascular territories and related causes of a particular stroke can be identified. Primary

symptoms, and vascular territories of ischemic stroke are summarized in **Table 1**.²

Table 1. Primary Symptoms, and Vascular Territories of Ischemic Stroke

Primary Symptoms	Vascular Territories
Aphasia + right side weakness	Middle Cerebral Artery (Dominant)
Neglect + left side weakness	Middle Cerebral Artery (Non-dominant)
Weakness on one side (no other findings)	Lacunar syndrome †
Weakness + sensory loss on one side (no other findings)	Lacunar syndrome †
Sensory loss on one side (no other findings)	Lacunar syndrome †
Weakness of leg more than arm, incontinence, personality change	Anterior Cerebral Artery
Isolated homonymous visual field deficit	Posterior Cerebral Artery
Bilateral weakness + cranial nerve deficits + ataxia	Basilar artery

† Refers to strokes with defined symptom complexes that do not include aphasia, change in consciousness, or other cortical symptoms; they appear to be caused by occlusion of small subcortical or brain stem arterioles, although they may also result from micro-emboli.

Various Imaging Techniques

Passage of x-radiation through tissue attenuates the radiation, and the intensity of the exiting radiation can be measured with sensitive film or detectors. X-ray computed (CT) permits the examination of tissue by the same principle

as conventional x-ray imaging, except that radiation passes successively through tissue from multiple different directions, detectors measure the degree of attenuation of the exiting radiation relative to the incident radiation, and computers integrate the information and construct the images in cross section. Administration of contrast material increases x-ray attenuation owing to the high atomic number and electron density of the iodinated compounds used. CT has the advantages of widespread availability, short study time, sensitivity for detection of calcifications and acute hemorrhages, and excellent visualization of the anatomy of bone, such as skull base and vertebrae. The use of intravenous contrast medium with CT allows examination of the integrity of the blood brain barrier, which consists of tight junctions between endothelial cells of blood vessels and astrocytes.⁴

Placement of tissue in a strong magnetic field causes certain naturally occurring isotopes (atoms) within the tissue to line up within the field, orienting the net tissue magnetization in the longitudinal direction. Many isotopes are affected, but current MRI uses signals derived from ¹H, the most plentiful endogenous isotope. When in a magnetic fields, these atoms do not orient precisely with the axis of the field, but wobble a few degrees off center. Application of different gradient magnetic fields to the tissue under study permits reconstruction of the signal from individual volume units in space. Use of the intravascular contrast material gadolinium-diethylenetriamine pentaacetic acid (gadolinium-DTPA) with MRI alters the magnetic susceptibility of adjacent tissue, thereby providing information about the integrity of the blood-brain barrier.⁴

Positrons are the antimatter equivalent of electrons. The collision of an electron and a positron annihilates both particles, converting their masses to energy in the form of two photons (gamma rays) that leave the brain at an angle of 180° to each other and can be detected. The radioligands most frequently used to emit positrons are [¹⁸F] fluorodeoxyglucose for measuring cerebral metabolic of glucose⁵ and [¹⁸O] water for determining cerebral blood flow.⁶ PET and SPECT use this highly versatile method of studying cerebral function. SPECT uses principles similar to those of PET but the radioligands decay to emit only a single photon.⁴

Preferred Imaging Procedures in the Ischemic Strokes

Head CT scans are excellent for detecting large hemorrhages, tumors, and other structural lesions that can produce symptoms mimicking acute stroke symptoms. The differences in X-ray attenuation (density) between bone, brain, and cerebrospinal fluid (CSF) makes it possible to distinguish

normal and infarcted tissue, tumors, extravasated blood or edema.^{1,7} Currently, CT is the brain-imaging method of choice for the assessment of acute ischemic injury to determine whether hemorrhage is present, because it is highly sensitive to hemorrhage, rapid, widely available, relatively low cost, and noninvasive (**Fig. 1**).⁸ Hyperdensity of major cerebral vessels is an important sign that can be detected by CT within minutes of vessel thrombosis and hours before parenchymal changes occur.⁹ The finding of a hyperdense vessel can be used in the appropriate clinical setting to consider a patient for aggressive endovascular lytic therapy.

MRI, particularly diffusion-weighted and perfusion-weighted MRI is more sensitive than CT, particularly for early pathologic changes of ischemic infarction because it is superior in detecting brain edema.^{10,11} lacunar infarctions, and strokes involve the brain stem region.¹² MRI is superior to CT in detecting small lacunar lesions, particularly those located deep within cerebral hemispheres and in brain stem and cerebellum (**Fig. 2**). Another advantage of MRI is that the cerebral vessels can be imaged using a magnetic resonance angiography protocol, allowing non-invasive imaging of both the extracranial and intracranial large cerebral vessels.¹³ New MRI technologies, such as magnetic resonance diffusion, perfusion, and spectroscopy, may provide information on the metabolic status of, and blood flow to, ischemic brain regions.¹⁴

Carotid ultrasound, and carotid duplex can image atherosclerotic lesions at the bifurcation of the carotid arteries. Continuous-wave Doppler employs two separate transducers, one to send and one to receive the Doppler signal. Since the transmitted Doppler signal is continuous, continuous-wave Doppler is not limited by aliasing and is particularly useful for detecting a wide range of frequencies. Pulsed Doppler allows sampling at discrete locations in vessels and has improved depth resolutions. Duplex ultrasound combines high resolution gray scale imaging of carotid vessels with physiologic blood flow information provided by Doppler techniques (usually pulsed Doppler).¹⁵ Compared with angiography, the overall accuracy of either carotid duplex or magnetic resonance angiography can image atherosclerotic lesions at the bifurcation of the carotid arteries.^{16,17} Transverse carotid images of the bifurcation help establish the optimal orientation for longitudinal scans in which Doppler spectral analysis will be performed (**Fig. 3**).¹⁵

Intracranial atherosclerosis is responsible for up to 10% of strokes and transient ischemic attacks (TIAs). When extracranial internal carotid disease is excluded as the mechanism of these strokes and TIAs, it may be important for

clinicians to identify intracranial arterial stenosis, particularly when warfarin is considered a therapeutic option. Initial direct noninvasive test included continuous-wave and pulsed Doppler imaging, which quantified stenosis according to peak frequency shifts, detected in a vessel. In these instances, Transcranial Doppler (TCD) is often used as a screening test to identify patients requiring invasive cerebral arteriography. TCD, another noninvasive technique, provides information about flow direction and velocities in the major intracranial vessels.¹⁸ The use of the monitoring probe even allows continuous and instantaneous information on changes in cerebral hemodynamics. Currently, TCD is of established value in assessing patterns and extent of collateral circulation in patients with known regions of severe stenosis or occlusion. Significant stenosis causes increased velocities maximal at the site of obstruction (**Fig. 4**). Marked acceleration is seen at stenosis exceeding 80%. Reversed and markedly accelerated flow in the ipsilateral cerebral artery suggests the presence of collateral flow across the communicating artery from contralateral circulation (**Fig. 5**).¹⁹

Cerebral angiography remains the gold standard for diagnosing large vessel vascular disease and intracranial vasculitides. It is indicated particularly in young patients with stroke, in cases of suspected vasculitis or vascular dissection (**Fig. 6**).²⁰ However, recent studies have shown that magnetic resonance angiography (MRA) and CT angiograms are at least as sensitive as angiography for diagnosing dissections.^{21, 22} On the other hand, there are few prospective data that TCD and MRA in combination can effectively replace angiography at this time for identification of intracranial atherosclerosis. The recently launched Stroke Outcomes and Neuroimaging of Intracranial Atherosclerosis (SONIA) study will provide some answers to these concerns.¹⁹

Impact on implementing guidelines

Early diagnostic testing should be selected to establish the anatomical regions and structures involved and the cause of infarction, since early intervention and subsequent secondary prevention should vary accordingly.²³ Because ischemic stroke results from an occluded blood vessel, reversing or bypassing the occlusion should decrease the adverse effects of the stroke.²⁴ If the diagnosis of ischemic stroke without hemorrhage can be made and all inclusion and exclusion criteria are met (**Table 2**), treatment with intravenous thrombolytic therapy may be indicated.²³ The FDA approved this treatment on the basis of the results of the National Institute of Neurological Disorders and Stroke (NINDS) rt-PA study³ in which 624 ischemic stroke patients were treated with

t-PA 0.9 mg/kg BW (10% given as an intravenous loading dose and the remainder administered intravenously over 1 hour, with a maximum dose of 90 mg) within 3 hours of stroke onset. The value of this activator administered more than three hours after the onset of symptoms is not known.

Table 2. Major Treatment Guidelines for Using Recombinant Tissue Plasminogen Activator (t-PA) in Stroke Patients

Inclusion criteria

- Ischemic stroke in any circulation.
- Ability to establish the time of onset unambiguously.
- Ability to begin t-PA therapy within 3 hours of symptom onset.
- Head CT scan without any evidence of hemorrhage or other complicating disease
- Age 18 years or older.

Exclusion criteria

- Stroke or serious head trauma within the past 3 months.
- Any past history of any type of brain hemorrhage (subarachnoid or intracerebral) or suspicion of a subarachnoid hemorrhage.
- CT scan showing evidence of hemorrhage, arteriovenous malformation, tumor or aneurysm.
- Systolic Blood Pressure > 185 mmHg or Diastolic > 110 mmHg (on 3 occasions, 10 minutes apart).
- Seizure preceding or during current stroke.
- Active internal bleeding.
- Coagulopathy with abnormal prothrombin or partial thromboplastin time, or platelet count < 100,000 per microliter.
- Rapidly improving or minor symptoms.
- Coma or stupor.
- Major surgery or invasive procedures within the past 2 weeks.
- Gastrointestinal or genitourinary hemorrhage within the past 3 weeks.
- Noncompressible arterial puncture or biopsy within the past week
- Glucose < 50 mg/ dl or > 400 mg/ dl.
- Evidence of active pericarditis, endocarditis, septic emboli, recent pregnancy, lactation, or inflammatory bowel disease,
- Active alcohol or drug abuse.

Local intraarterial thrombolysis performed with a microcatheter that is placed into, beyond, and proximal to an arterial occlusion is in use worldwide. In the past, the agent most commonly studied was urokinase; intraarterial t-PA and prourokinase have mainly been used in recent investigational studies. Approximately 40 percent of the patients who undergo this treatment have complete arterial recanalization, and approximately 35 percent have partial recanalization. These rates of recanalization are higher than those that have been reported for patients who undergo intravenous thrombolytic therapy.²³

For patients who have a nondisabling stroke (or TIAs) resulting from high-grade extracranial carotid artery disease,

carotid endarterectomy (CEA) is recommended, assuming the patient is a good surgical candidate. CEA in these patients decreases the occurrence of ipsilateral stroke or death from 26% to 9% at 2 years. The efficacy of CEA in patients with moderate stenosis (50-69%) is less than in patients with high-grade disease. The benefits of CEA require a low rate of perioperative complications. Complication rates of no more than 5% to 6% are desirable. Studies have evaluated the safety and efficacy of carotid artery angioplasty and stenting in these patients.²⁴

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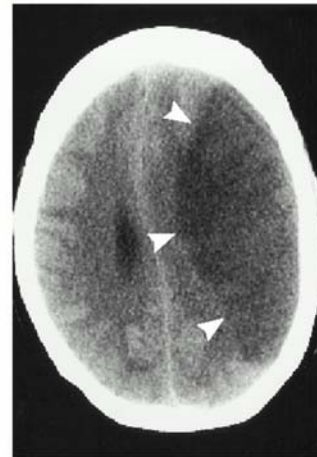


Figure 1. A CT Scan shows a large, subacute, nonhemorrhagic infarction in the territory of the left middle cerebral artery (arrowheads). Reprint request was permitted by Dr. Gilman at the Department of Neurology, University of Michigan, Ann Arbor, MI 48109-0316. E-mail: sgilman@umich.edu

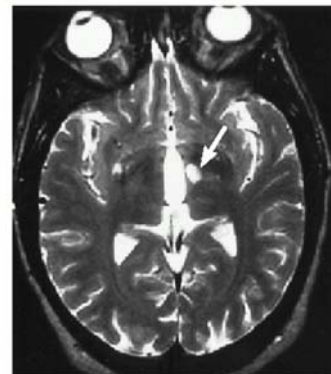


Figure 2. An axial T₂-weighted MRI shows a 1-cm lacunar infarction (arrow) in the region of the left internal capsule. Reprint request was permitted by Dr. Gilman at the Department of Neurology, University of Michigan, Ann Arbor, MI 48109-0316. E-mail: sgilman@umich.edu

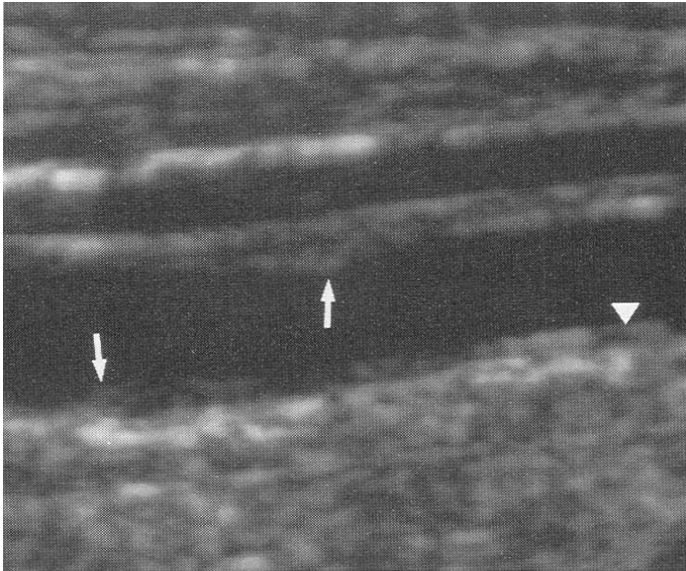


Figure 3. Early focal atherosclerotic changes (arrows) are seen at the carotid bifurcation. The normal vessel wall configuration is seen proximally (arrowhead) on this longitudinal scan. Permission is granted by The Radiology Society of North America (RSNA). E-mail: mstrassner@rsna.org

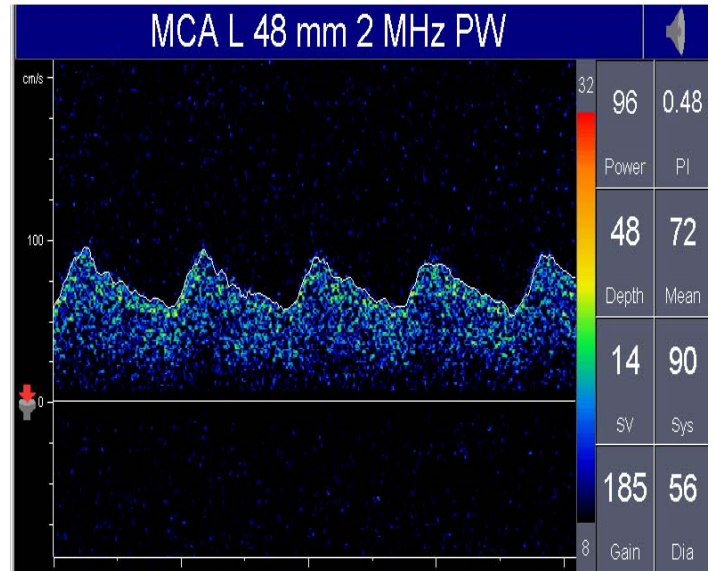


Figure 5. Low velocity and pulsatility in the Middle Cerebral Artery (MCA) at 48 mm ipsilateral to an occluded Internal Carotid Artery (ICA). Reprint request was permitted by Dr. Ramani at the National Neuroscience Institute, Singapore. E-mail: Ramani_NV@nni.com.sg

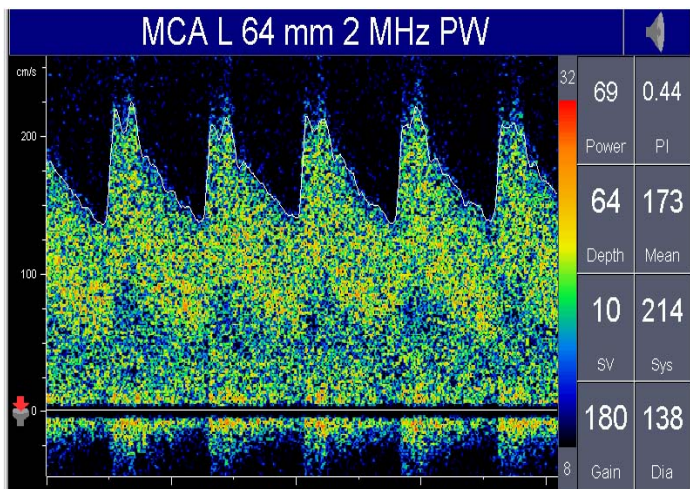


Figure 4. Stenosis of the left Middle Cerebral Artery (MCA) at 64 mm, with $V = 225$ cm/s. Reprint request was permitted by Dr. Ramani at the National Neuroscience Institute, Singapore. E-mail: Ramani_NV@nni.com.sg



Figure 6. Cerebral arteriogram in a patient with dysphasia and right hemiplegia shows the embolic occlusion in the trunk of the left middle cerebral artery (arrow). Reprint request was permitted by Dr. Brott at the Department of Neurology, Mayo Clinic, 4500 San Pablo Road, Jacksonville, FL. 32224. E-mail: brott.thomas@mayo.edu