Stroke is the number three cause of mortality in the adult population and affects more than 400,000 people in the United States annually. Ischemic infarcts account for approximately 85% of all strokes. Previously the medical management of infarcts primarily involved diagnosis, stabilization during the acute period, and subsequent rehabilitation. As a result of the development of new therapy options, including thrombolytic agents and brain-protective drugs, stroke is increasingly becoming a treatable condition. These treatment choices have created a significant impetus for the early clinical and radiographic detection of acute infarcts.

Although magnetic resonance (MR) imaging has been shown to be more sensitive than computed tomography (CT) in detecting acute strokes within the first 24 hours, CT remains the emergent imaging test of choice to evaluate acute ischemia. It is fast, noninvasive, and readily available in almost all hospitals. Despite its limitations, CT continues to be used for all major stroke therapy trials. Until other methods of stroke imaging, such as xenon CT and MR diffusion/perfusion, become widely and rapidly available in most institutions, CT remains the primary screening tool for acute ischemia.

**CLINICAL IMPORTANCE OF EARLY STROKE DETECTION BY CT**

Two major drug trials testing the safety and efficacy of early thrombolytic therapy have been completed in the past 4 years. Although both studies demonstrated improved clinical outcomes after the administration of intravenous thrombolytic drugs, the results were dependent on the appropriate screening of potential patients. The National Institute of Neurological Disorders (NINDS) and Stroke rt-PA Stroke Study Group treated 624 acute stroke patients with either intravenous recombinant human tissue plasminogen activator (tPA) or placebo within 3 hours of the onset of Symptoms. Despite an overall increased incidence of symptomatic intracerebral hemorrhage in the therapeutic group, this study demonstrated an improved clinical outcome with thrombolytic therapy without a significant difference in mortality. Patients treated with tPA were 30% more likely to have minimal or no disability at 3 months compared with patients given a placebo.

Further analysis of the NINDS data demonstrated that intracranial hemorrhage was a more common complication in patients with edema or infarct on the initial scan, occurring in 31% of these patients compared with 6% of cases without early CT findings. Despite this complication, this subset of patients was still more likely to have an improved clinical outcome at 3 months. The study therefore concluded that patients with edema or mass effect on the baseline CT were candidates for tPA if it was administered within 3 hours of the onset of symptoms.
A second study was conducted by the European Cooperative Acute Stroke Study (ECASS). This group treated 620 stroke patients with either intravenous thrombolytic agent or placebo within 6 hours after the onset of symptoms. Patients with evidence of major ischemic changes, defined as hypoattenuation lesions involving greater than 33% of the middle cerebral artery (MCA) territory already visible at the time of the first scan, were to be excluded from the protocol. Fifty-two patients with CT findings of extended infarcts were incorrectly admitted into the study because of misinterpretation of the initial film. These patients had no beneficial effect from intravenous tPA and demonstrated a mild increased rate of fatal cerebral hemorrhage compared with the remaining population. The 215 patients with small hypoattenuation lesions experienced an increased chance of good outcome if treated with intravenous thrombolytic therapy. ECASS originally concluded that although intravenous thrombolytic therapy was effective in improving neurologic outcome in a subset of patients with moderate to severe neurologic deficit and no evidence of extended infarct on CT scan, its use was not recommended because of difficulty in identifying this subgroup and the associated unacceptable risk of increased hemorrhagic complications and death.

A subsequent reanalysis of the ECASS data, which correctly reclassified the patients with extended ischemic changes, demonstrated that (1) response to tPA is different for patients with no, small, or large areas of edema visible on initial CT and (2) patients with large ischemic zones already apparent on the initial CT scan most likely will not benefit from thrombolytic therapy. Treatment with tPA significantly increased the cure rate of patients with no or small cytotoxic edema by 8% and 18% but decreased the cure rate to 6% for patients with large cytotoxic edema. If patients with extended infarcts already present on the initial scans are excluded from the treatment population, the probability of clinical improvement with thrombolytic therapy increases.

The results of these two studies underscore the importance of careful clinical and radiologic screening before the administration of thrombolytic drugs. Although tPA has the potential to improve clinical outcomes of patients with acute strokes, the drug must be given to the appropriate population within a relatively small time window. If treatment is delayed or CT scans are not accurately interpreted, the potential benefits of thrombolytic therapy can be negated.

CT FINDINGS IN ACUTE STROKE

When reviewing the CT scan of potential stroke patients, the radiologist should systematically answer several questions that determine the patient's medical management. Can the cause of the neurologic problem be identified on the scan? Are the findings consistent with an acute ischemic infarct, or is there another abnormality? Many neurologic disorders can mimic an acute infarct, including tumors, subdural hematomas, hemorrhages from underlying masses or vascular malformations, and venous occlusive disease. These diagnoses can often be excluded on noncontrast CT scans; however, additional imaging, including contrast-enhanced CT or MR examinations, may be needed to confirm the diagnosis.

When the diagnosis of ischemic infarct is suspected, careful review of the film for evidence of major arterial occlusion, early parenchymal edema, or hemorrhage is indicated. These findings help determine if thrombolytic therapy is indicated and may influence how it is administered, either intravenously or intraarterially. Identification of hemorrhage is crucial because its presence precludes thrombolytic therapy.

VASCULAR FINDINGS IN ACUTE INFARCTION

Asymmetric hyperdensity within a major cerebral artery represents one of the earliest CT signs of stroke and is caused by occlusion of the vessel from either an embolus or a thrombus. The density of blood on CT is linearly related to the hemoglobin concentration. Flowing blood has a density of approximately 40 Hounsfield units (HU) with a normal range of 35 to 60 HU. When a thrombus or embolus occurs, serum is extruded from the clot producing an increase in the hemoglobin concentration and a subsequent increase in density. Intraluminal thrombus measures approximately 80 HU with a range of 77 to 89 HU. Atheromatous vessels typically have higher densities because of the presence of wall calcification and usually measure between 114 and 321 HU.

![Hyperdense middle cerebral artery sign](image1.jpg)  
**Figure 1.** Hyperdense middle cerebral artery sign. A, Noncontrast axial CT scan demonstrates a linear focus of hyperdensity in the region of the left middle cerebral artery representing an embolus (arrow). B, Left common carotid angiogram performed twenty hours after the ictus demonstrates complete occlusion of the middle cerebral artery at its origin (arrow). Minimal cortical collaterals are noted on this late arterial phase angiogram.
The hyperdense artery sign has been described primarily in the MCA and basilar artery. Because of their extended courses through the subarachnoid space, these arteries are easily visualized and can be directly compared with other arterial and venous structures. A few cases of calcified emboli to the anterior cerebral artery have been reported; however, noncalcified occlusion of the anterior cerebral distribution is rarely detected. Hyperdense cerebral arteries usually resolve within 1 week secondary to lysis of the clot and recanalization of the vessel.

The hyperdense MCA sign (HMCAS) has been well described in the literature as one of the earliest signs of MCA infarct. It is associated with occlusion of the proximal MCA or its branches and has been identified in 35% to 50% of patients presenting with clinical signs of acute MCA stroke.

Proximal MCA occlusion is one of the most serious cerebrovascular occlusive conditions. Mortality associated with MCA occlusion can range from 5% to 45%, and survivors typically have severe neurologic deficits. If collateral circulation is inadequate, these strokes
can produce malignant brain edema, uncal herniation, and subsequent compression of the midbrain. Rapid detection and early, aggressive treatment of proximal MCA occlusion is indicated to reduce both mortality and morbidity.

Studies have demonstrated that the HMCAS predicts a poorer clinical outcome compared with patients without the sign. 19,31 Occlusion of the proximal M1 segment of the MCA correlates with an infarct of 100 mL or greater in the majority of cases. 36 Tomsick et al noted that the HMCAS is associated with a poor response to intravenous thrombolytic therapy. Clinical follow-up performed 3 months after intravenous tPA demonstrated that patients with a positive HMCAS had larger infarcts and were significantly less likely to be completely neurologically improved compared with the patients without an HMCAS. These results indicate that patients with an HMCAS, if detected before the formation of extensive parenchymal ischemic changes, may benefit from more aggressive initial treatment, such as intra-arterial thrombolysis.

Several conditions may mimic a hyperdense thrombosed vessel, including a high hematocrit or vessel wall calcification. To prevent false-positive results, the radiologist should closely adhere to a narrow definition of HMCAS. The HMCAS is defined as an MCA that is denser than its counterpart and denser than any visualized vessel of similar size that is not attributable to vessel calcifications. 30 Using this definition, the HMCAS is an accurate and moderately sensitive tool in detecting early MCA occlusion. In a blinded analysis performed by six neuroradiologists, Tomsick et al, 37 demonstrated a sensitivity of 78%, specificity of 93%, and accuracy of 91% for the HMCAS.

**PARENCHYMAL CHANGES OF ACUTE INFARCTION**

- **Pathophysiology**

The CT detection of acute infarcts depends on the development of edema within the brain parenchyma, which produces subtle density changes and mass effect. To understand better the CT findings of acute ischemia, a brief review of the histologic changes that occur during a stroke are presented.

**Table 1. Pathological stages of cerebral infarction**

<table>
<thead>
<tr>
<th>Time</th>
<th>Gross pathology</th>
<th>Microscopical pathology</th>
</tr>
</thead>
<tbody>
<tr>
<td>From 8-18 Hr</td>
<td>The damaged zone become pale, and the demarcation between the white and gray matter is indistinct. Edematous swelling is apparent and accompanied by cortical congestion. At this stage the the infarcted area is soft in consistency.</td>
<td>Ischemic neuronal death, with capillary endothelial swelling accompanied by exudation of edematous fluid and extravasation of RBCs even in anemic infarction</td>
</tr>
<tr>
<td>2- 10 days</td>
<td>The edema and the swelling persist but to a decreasing degree and the infarcted zone becomes friable and its boundary becomes better defined.</td>
<td>Stage of phagosytic activity and parenchymatous liquefaction:</td>
</tr>
<tr>
<td></td>
<td>Liquefaction begins and after 3 weeks cavitations becomes more evident. From then on the necrotic tissues is replaced by yellowish tissue which causes depression of the cerebral cortex.</td>
<td>Exudation of neutrophil leukocytes begins for a brief time and causes inflammatory reaction and is replaced on the second day by macrophages laden with Sudanophilic breakdown products originating from disintegration of myelin sheaths. Macrophage activity becomes most marked from the 5th to the 30th day i.e. during the phase of parenchymatous liquefaction</td>
</tr>
<tr>
<td>After 10 days</td>
<td>A cystic cavity is organized, the cavity has ragged outlines and is intersected by vascular connective tissues strands and is covered on its outer surface by a thin meningeal membrane.</td>
<td>Stage of cicatrization:</td>
</tr>
<tr>
<td>After several months</td>
<td></td>
<td>The residual cystic cavity becomes surrounded by glial proliferation which is first protoplasmic and then fibrillary (astrogliosis) with frequent vascular connective tissues strand that run across the cavity</td>
</tr>
</tbody>
</table>

Severe ischemia can cause a 7 to 8 HU change at 1 hour that should be visible on CT. With marginal cerebral blood flows between 15 and 20 mL/100 g, ischemic edema takes longer to develop and may not be detected on early CT scans.

Normal cerebral blood flow ranges from 50 to 60 mL/100 g tissue/min. During an ischemic infarct, blood supply to a portion of the brain is significantly reduced. As cerebral blood flow decreases, injury occurs in the brain progressing from electrical dysfunction to reversible cellular damage and eventually to cell death. At approximately 20 mL/100 g, electrical activity in the brain ceases, and water homeostasis begins to be disrupted. 13,16 At critical flow rates of 10 to 15 mL/100 g, there is disruption of ion homeostasis within the cells producing rapid increases of extracellular potassium and intracellular sodium.

This disruption causes water to shift into the intracellular compartment producing astrocytic swelling (cytotoxic edema).
The development of cytotoxic edema aggravates ischemia by causing progressive compression of the microcirculation, which further decreases blood flow. As the ischemic changes worsen, capillary walls become permeable allowing leakage of intracellular proteins and subsequent accumulation of extracellular water (vasogenic edema). Worsening edema produces additional mass effect causing a decrease in cerebral perfusion pressure and collateral flow. Cytotoxic edema may be detectable within 1 hour of the onset of stroke; however, vasogenic edema usually does not develop until 6 hours or more after ictus.

**Table 2. Comparison between the cytotoxic and vasogenic edema of recent infarction**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Cytotoxic (intracellular)</th>
<th>Vasogenic (extracellular)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time</td>
<td>Within 1 hour of the onset of stroke</td>
<td>Does not develop until 6 hours or more after ictus.</td>
</tr>
<tr>
<td>Pathophysiology</td>
<td>At critical flow rates of 10 to 15 mL/100 g, there is disruption of ion homeostasis within the cells producing rapid increases of extracellular potassium and intracellular sodium. This disruption causes water to shift into the intracellular compartment producing astrocytic swelling (cytotoxic edema).</td>
<td>The development of cytotoxic edema aggravates ischemia by causing progressive compression of the microcirculation, which further decreases blood flow. As the ischemic changes worsen, capillary walls become permeable allowing leakage of intracellular proteins and subsequent accumulation of extracellular water (vasogenic edema).</td>
</tr>
<tr>
<td>Composition</td>
<td>Increased intracellular water and sodium</td>
<td>Plasma filtrate including plasma proteins</td>
</tr>
<tr>
<td>Location of edema</td>
<td>Gray and white matter</td>
<td>Chiefly white matter</td>
</tr>
<tr>
<td>Pathology</td>
<td>Cellular swelling, usually of astrocytes in the grey matter.</td>
<td>Grossly, the gyri are flattened and the sulci narrowed; the white matter is moist and swollen. Microscopically, there is micro-vacuolization of the white matter, poor staining, and &quot;halo's&quot; around nuclei.</td>
</tr>
<tr>
<td>Capillary permeability to large molecules</td>
<td>Normal</td>
<td>Increased</td>
</tr>
<tr>
<td>Neuroimaging</td>
<td>Normal</td>
<td>(1) obscuration of the lentiform nucleus, (2) loss of the insular ribbon, (3) diffuse low density with loss of the gray-white interface, and (4) sulcal effacement, (5) mass effect</td>
</tr>
</tbody>
</table>
Ischemic changes that occur above 15 mL/100 g can be reversible. At flow rates below 10 to 15 mL/100 g, tissue damage is usually irrevocable after 1 hour of hypoperfusion. Other factors also play a role in the reversibility of ischemic changes. During low levels of perfusion, small amounts of glucose may be available to brain tissue for glycolysis, but oxidation cannot occur. The subsequent development of lactic acidosis adversely affects the viability of brain tissue.

- Sensitivity of CT in Evaluating Acute Ischemia: How Early Can Stroke Be Detected?

How quickly an acute infarct can be visualized is governed primarily by the severity of hypoperfusion; however, the duration, size, and location of ischemia also play important roles. When cerebral blood flow drops below the critical value of 10 to 15 mL/100 g, ischemic changes are usually irreversible, and edema develops fast, permitting early detections.

As edema progresses, water content within the parenchyma increases. This increase causes a subsequent decrease in the brain's specific gravity, which is linearly proportional to CT attenuations. In other words, as edema increases, brain density proportionately decreases. A 1% change in water content changes the CT attenuation by 2.6 HU. Typically a change of 4 HU or greater is needed to detect the change visually. In cases of severe ischemia caused by proximal MCA occlusion, cytotoxic edema can produce a 3% increase in water within 1 hour of the onset of symptoms. This can increase to 6% at 2 to 4 hours. Therefore, severe ischemia can cause a 7 to 8 HU change at 1 hour that should be visible on CT. With marginal cerebral blood flows between 15 and 20 mL/100 g, ischemic edema takes longer to develop and may not be detected on early CT scans.

In the future, more advanced imaging techniques, such as MR perfusion and xenon CT, may play an important role in determining the cerebral blood flow of ischemic areas to help determine tissue viability. Until then, noncontrast CT can provide important information. If hypoperfusion is less severe and collaterals to an ischemic area are adequate, edema may not develop, and early CT scans are negative. Conversely the presence of more extensive edema on an early CT scan indicates severe hypoperfusion and may predict a less favorable outcome after thrombolytic therapy.

The sensitivity of early CT scans in detecting acute strokes also depends on the duration, location, and size of the infarct. As the time of ischemia increases, CT abnormalities become more obvious; however, the absolute presence or absence of edema primarily relies on the severity of hypoperfusion and adequacy of collateral circulation. Larger infarcts are visible earlier than smaller infarcts because of the increased volume of tissue involved (i.e., MCA infarcts are detected sooner than small cortical or lacunar infarcts).

Several researchers have studied the sensitivity and accuracy of detecting infarcts on CT. Bryan et al performed MR imaging and CT...
when analysis is restricted to the assessment of MCA infarcts, the overall sensitivity of CT significantly increases. Moulin et al. (21) reviewed 100 patients with MCA stroke. Ninety-four percent of all CT scans performed within 14 hours after the onset of symptoms were abnormal; 88% of CT scans obtained within 6 hours of ictus were abnormal. These results compare favorably with data of von Kummer et al. A review of 44 patients demonstrated that CT performed within 6 hours of the onset of symptoms has an accuracy of 95% and a mean sensitivity of 82% of detecting MCA infarcts. CT scans performed within the first 2 hours of symptoms, however, were much less sensitive in detecting early ischemia. Truwit et al. (40) and Tomura et al. (38) described subtle findings of MCA stroke that can increase the sensitivity of CT to greater than 90% in detecting major MCA occlusions.

The presence of parenchymal changes on early CT scans also correlates with the degree of intracranial occlusive disease. Horowitz et al. (14) studied 50 patients with ischemic strokes that produced at least hemiparesis. CT scans were performed within 4 hours of ictus and were correlated with angiography or carotid ultrasound. Acute CT abnormalities, including hypodensities and mass effect, were seen in 56% of patients. When there was major vascular occlusion, however, either occlusion of the MCA trunk or two or more MCA branches, the CT scan was positive in 86% of cases.

**CT Findings**

Several articles describing early CT findings of acute infarcts have been published in recent years. These findings have primarily focused on MCA ischemia and have significantly improved the overall sensitivity of CT in detecting early MCA infarcts. The major CT findings of acute MCA stroke include (1) obscuration of the lentiform nucleus, (2) loss of the insular ribbon, (3) diffuse low density with loss of the gray-white interface, (4) sulcal effacement, (5) gray matter enhancement and (6) hemorrhagic infarction.

- **Obscuration of the Lentiform Nucleus.**

  In 1988, Tomura et al. (38) described obscuration of the lentiform nucleus as an early sign of MCA infarct. This finding is caused by cellular edema arising within the basal ganglia and closely correlates with a proximal MCA occlusion. Twenty-five patients who had clinical evidence of MCA infarcts underwent CT scanning within 6 hours of the onset of symptoms. The scans were then retrospectively reviewed for obscuration of the lentiform nuclei as well as decreased density within the brain parenchyma and sulcal effacement. Twenty three of the patients (92%) demonstrated an obscured outline or partial disappearance of the lentiform nucleus. This sign was visualized earlier than other CT findings and in a few cases was present within 1 hour after the onset of the stroke. Parenchymal hypodensities and sulcal effacement occurred later and were present on significantly fewer initial scans.

  The lenticular nuclei receive their blood supply from the lenticulostriate arteries which arise from the MI trunk of the MCA. Collateral circulation to this area is poor compared with the cortex. Occlusion of the proximal MCA disrupts the primary blood supply to these structures. (7) As a result of the insufficient collaterals as well as the relatively high metabolic rate of the lenticular nuclei, (5) proximal MCA occlusion can quickly cause critically low cerebral blood flow, which produces early ischemic changes on CT.

  Firlick et al. (5) performed CT, xenon CT, and angiography on 20 patients with acute MCA infarcts. Early CT changes in the basal ganglia were associated with significantly lower cerebral blood flows in the MCA territory compared with patients with normal CT scans. An early basal ganglia hypodensity correlated with a mean cerebral blood flow in the affected MCA territory of less than 10 mL/100 g. Patients with more distally located occlusions, beyond the origins of the lenticulostriate arteries, preserve blood supply to the basal ganglia and do not develop this early sign.

  Bozzao et al. (3) evaluated 36 patients with acute MCA infarcts with CT and angiography and correlated changes on early CT scans with the angiographic findings. CT scans were performed within 4 hours, and angiograms were obtained within 6 hours from the onset of symptoms. Bozzao et al. (4) noted that all patients with early CT findings of MCA infarcts demonstrated an arterial occlusion on angiography. Involvement of the lenticular nuclei corresponded closely with a proximal MCA occlusion.

- **Loss of the Insular Ribbon. (LIR)**

  Another early sign of acute MCA infarction is loss of the insular ribbon (LIR) which is described as loss of definition of the gray-white interface in the lateral margins of the insula. This area is supplied by the insular segment of the MCA and its claustral branches and is the region most distal from anterior and posterior cerebral collateral circulation. As a result, collateral flow to the insular region is decreased compared with other portions of the cerebral cortex.
Truwit et al.\(^4\) performed both retrospective and prospective evaluations of CT scans in patients with clinical evidence of acute MCA distribution infarcts to evaluate the sensitivity and accuracy of the LIR sign. In a retrospective analysis of 11 cases, LIR was seen in all patients (100%). In a prospective study, the LIR sign was identified in 12 of 16 patients (75%). Obscuration of the lenticular nucleus occurred less frequently and was identified in 73% and 63% of patients. They concluded that LIR is more frequently observed in acute MCA infarcts than other early CT findings.

In two patients, the LIR was localized to the posterior segment of the insula and was associated with a more limited infarct. This situation may be due to more distal occlusion of posterior MCA branches within the operculum.

The presence of obscuration of the lenticular nucleus or LIR without other signs of extensive infarct does not preclude the use of thrombolytic agents. These patients may receive significant benefit from intravenous or intraarterial thrombolysis; because of the presence of early CT changes, however, they may be more likely to have areas of irreversible damage compared with patients with negative CT scans.

- **Diffuse Parenchymal Hypodensity and Sulcal effacement.**

As ischemic changes progress, both cytotoxic and vasogenic edema increase producing areas of hypoattenuation throughout the affected circulation. In larger infarcts, mass effect also increases producing effacement of sulci and compression of ventricles.

Detection of anterior and posterior cerebral artery infarcts as well as posterior fossa lesions relies predominantly on the presence of parenchymal hypodensity and sulcal effacement. As a result of the lack of other subtle CT findings, such as obscuration of the lenticular nucleus and LIR, these infarcts may not be detected as early as large MCA strokes.

In cases of MCA infarcts, extensive parenchymal hypodensity on early CT scans is associated with a high mortality rate as well as a poor clinical outcome in survivors. When greater than 50% of the vascular territory was involved, the mortality rate increased up to 85% because of malignant brain edema.\(^4\) Early craniectomy decreases the mortality rate for patients with severe edema; however, clinical outcome remains poor.

**Figure 6.** A 52-year-old woman who presented with sudden onset of left arm weakness. A and B, CT scan performed three hours after the onset of symptoms demonstrates focal loss of the insular ribbon posteriorly (arrows). A more superior image performed through the lateral ventricles demonstrates an area of low attenuation in the right posterior frontal cortex with loss of the gray-white interface (arrows) consistent with ischemic change in the right MCA distribution.

**Figure 7.** A 67-year-old man who presented with a 5-hour history of left leg weakness. A and B, CT scan shows subtle low attenuation and loss of sulcation in the right parasagittal frontal lobe extending to the convexity (arrowheads) consistent with an anterior cerebral artery distribution infarct. C, MR diffusion scan demonstrates abnormal high signal in the right frontal parasagittal region confirming the
The presence of extensive ischemic change typically excludes the use of thrombolytic therapy. The likelihood of clinical improvement is low, whereas the rate of complication, including hemorrhage, is significantly increased. In the future, faster mechanical methods of removing clot within the MCA may offer benefit to these patients; however, in most cases, irreversible damage has been done.

### TABLE 3. EARLY CT SCAN FEATURES OF HYPERACUTE ISCHEMIC STROKE

<table>
<thead>
<tr>
<th>RADIOLOGICAL FEATURE</th>
<th>DESCRIPTION</th>
</tr>
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<tbody>
<tr>
<td><strong>Hyperdense thrombosed vessel</strong></td>
<td>When a thrombus or embolus occurs, serum is extruded from the clot producing an increase in the hemoglobin concentration and a subsequent increase in density. The hyperdense MCA sign (HMCAS) has been well described in the literature as one of the earliest signs of MCA infarct. It is associated with occlusion of the proximal MCA or its branches and has been identified in 35% to 50% of patients presenting with clinical signs of acute MCA stroke. It is defined as an MCA that is denser than its counterpart and denser than any visualized vessel of similar size that is not attributable to vessel calcifications.</td>
</tr>
<tr>
<td><strong>Diffuse Parenchymal Hypodensity and Sulcal effacement.</strong></td>
<td>A 1% change in water content changes the CT attenuation by 2.6 HU. Typically a change of 4 HU or greater is needed to detect the change visually. In cases of severe ischemia caused by proximal MCA occlusion, cytotoxic edema can produce a 3% increase in water within 1 hour of the onset of symptoms. This can increase to 6% at 2 to 4 hours. Therefore, severe ischemia can cause a 7 to 8 HU change at 1 hour that should be visible on CT. If hypoperfusion is less severe and collaterals to an ischemic area are adequate, edema may not develop, and early CT scans are negative. Conversely, the presence of more extensive edema on an early CT scan indicates severe hypoperfusion and may predict a less favorable outcome after thrombolytic therapy.</td>
</tr>
<tr>
<td><strong>Loss of the Insular Ribbon. (LIR)</strong></td>
<td>Loss of definition of the gray-white interface in the lateral margins of the insula.</td>
</tr>
<tr>
<td><strong>Obscuration of the Lentiform Nucleus.</strong></td>
<td>Obscuration of the lenticular nucleus is an early sign of MCA infarct. This finding is caused by cellular edema arising within the basal ganglia and closely correlates with a proximal MCA occlusion.</td>
</tr>
</tbody>
</table>

- **Gray matter enhancement (GME)**

One early pattern seen with MRI is areas of increased signal intensity (long T2) involving cortical and deep gray matter structures. This may be demonstrating the selective vulnerability of these structures to ischemia and hypoxia. A CT correlate of this MRI finding may be the inconsistently visualized regions of gray matter enhancement (GME). To date, nearly all cases of GME visualized by CT have shown a corresponding area of increased signal (long T2) by MRI. This long T2 abnormality, corresponding to the region, of GME may persist for years although a frank area of infarction may not be demonstrable by CT.

- **Hemorrhagic infarction**

This type of infarction is regarded as distinct from anemic infarction although microscopical haemorrhage is frequent in the later. It has frankly hemorrhagic features which consist of petechial zones that are frequently confluent and are situated in the cortex. These hemorrhagic areas may involve the entire infarction but tend most often to involve the boundary zones supplied by meningeal arterial anastomosis or, in case of middle cerebral infarct, in the basal ganglia. Hemorrhagic infarction is secondary cortical reirregation which takes place in the capillary blood vessels that have been damaged by the initial hypoxia. Reirregation takes place when lysis (natural or by therapeutic thrombolysis) or secondary mobilization of the thrombus takes place.
Figure 8. Haemorrhagic infarctions. They have frankly hemorrhagic features which consist of petechial zones that are frequently confluent and are situated in the cortex.

Figure 9. A, Plain CT scan showing middle cerebral artery hemorrhagic infarction, notice petechial zones situated in the basal ganglia. B, MRI T2 image showing a left sided hemorrhagic infarction, notice cortical hypointense petechial zones composed mainly of deoxyhemoglobin

- Fogging effect

Fogging is the temporary loss of visibility of an infarct on CT which occurs in the subacute phase at about 2 weeks after stroke. It occurs in up to 40% of medium to large infarcts on CT. Cerebral infarcts therefore may be overlooked or grossly underestimated if the scan is performed during the second and third week after stroke.  

Increase of x-ray attenuation on day 10 is known as the fogging effect and appears to be a favorable prognostic factor. Fogging is generally considered to be due to macrophage invasion and proliferation of capillaries within the infarct area, but probably also represents partial restoration of some viable tissue.
During the first week, there is a transient inflammatory reaction, especially around blood vessels and in the meninges, due to release of arachidonic and other fatty acids. As the core of the infarcted area disintegrates, endothelial cells from the periphery proliferate and capillaries grow into the dead tissue. Neovascularization (which accounts for contrast enhancement) peaks at 2 weeks.

Mononuclear cells from the blood stream enter the infarct through damaged vessels. They ingest the products of degradation of neurons and myelin and are transformed into lipid-laden macrophages. Macrophage reaction appears early and peaks at 3-4 weeks. Astrocytes from the surrounding undamaged brain proliferate and form a glial scar around the infarct (astrogliosis). This is completed in approximately 2 months. After that, the infarct remains unchanged. With maturation of new capillaries and glial scar formation, the blood brain barrier is once again sealed. Neurons do not regenerate. So, some brain tissue is lost forever.

With progression of time the infarction gets more hypodense and the mass effect gradually decreases with time due to gradual reduction of brain edema because the blood brain barrier is once again sealed. Negative mass effect is the end result. It is tempting to consider that these CT changes in old infarctions represent edema. The question then arises: Is this vasogenic edema or cytotoxic edema? Because the blood-brain barrier is sealed in old infarctions, vasogenic edema is unlikely. The cells are not dead or dying, so that cytotoxic edema is also unlikely.

**Figure 10.** A, Initial CT scan examination showed multiple small hypodense lesions in the right parieto-temporo-occipital lobes, left occipital and left frontal lobe representing acute infarcts. B, Repeated CT examination 10 days later in the same patient as (A) showed that the lesions are no longer apparent (fogging effect)

**Figure 11.** A, subacute infarction, B, old infarction with extensive gliosis and cavitations
Perhaps the edema results from the increased number of astrocytic cells that spread apart the normal myelinated axons of the white matter. The presence of significant amount of normal appearing astrocytes (hyperplasia), with marked cytoplasmic hypertrophy and low nuclear to cytoplasm ratio result in total increase in the water content of the brain. These cells may merely have different physical and chemical properties than the normal tightly packed bundles of axons that traverse through the brain. Astrogliosis is commonly associated with widened fluid filled extracellular spaces (microcavitations and macrocavitations) which definitely increase tissues water content resulting in the characteristic CT scan/MRI picture. \(^{48,49,50}\)

Figure 12. (A) Old infarction with extensive gliosis, microcavitations, the infarction is hypodense with negative mass effect (B)

Figure 13. With progression of time (from A to C) the infarction gets more hypodense, more well defined and the mass effect gradually decreases with time due to gradual reduction of brain edema because the blood brain barrier is once again sealed. The initial hypodensity in acute infarction is due to edema (A) while the the ultimate hypodensity in old infarction (C) is due to astrogliosis with widened fluid filled extracellular spaces (microcavitations and macrocavitations). During the evolution of the infarction the edema and the swelling decreases and the infarction boundary becomes better defined, and the infarcted area becomes more hypodense.
**Figure 14.** Astrocytes have extensive vascular foots, Astrogliosis (astrocytic hyperplasia) commonly results in the formation of a mesh with enlargement of extracellular spaces and extensive fluid-filled microcavitations. This, coupled with marked cytoplasmic hypertrophy of astrocytes-that results in low nuclear to cytoplasm ratio- are responsible for the CT scan picture of old infarction.

**Figure 15.** Reactive astrocytosis. Notice the mesh between the astrocytes

**Table 4. Comparison between CT hypodensity of recent and old infarctions**

<table>
<thead>
<tr>
<th>Aetiology of CT hypodensity</th>
<th>Recent infarction</th>
<th>Old infarction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vasogenic edema (cytotoxic edema does not contribute to CT hypodensity)</td>
<td>Astrogliosis with widened fluid filled extracellular spaces (microcavitations and macrocavitations)</td>
<td></td>
</tr>
</tbody>
</table>

**THROMBOLYSIS: WHO AND WHEN TO TREAT**

Both the radiologist and the clinician play important roles in determining who is a candidate for thrombolytic therapy and how it is administered. The clinician must carefully assess the patient for the extent of ischemic symptoms; time of onset; and presence of other complicating factors that may preclude thrombolysis, such as recent major surgery or other contraindications for anticoagulation. The radiologist then must carefully review the imaging studies for the presence of hemorrhage or extensive ischemic change that would prevent treatment.
Figure 16. A 62-year-old woman who presented with a 4-hour history of right hemiparesis and aphasia. A and B, Noncontrast CT scan demonstrates a large area of low attenuation in the left middle cerebral artery distribution with obscuration of the lentiform nuclei, loss of the gray-white interface, and effacement of sulci. Due to the presence of a well-defined infarct this patient was not considered a candidate for thrombolytic therapy. C, CT scan performed 4 days later demonstrates a large left MCA infarct with mass effect and moderate midline shift to the right. A craniectomy has been performed to relieve intracranial pressure.

Patients may be considered for three different treatment options: intravenous, intra-arterial, or combined intravenous and intra-arterial thrombolysis. The type of thrombolytic therapy is determined by the duration and severity of symptoms. If a patient presents within 3 hours of ictus and has no contraindications to thrombolysis, he or she is a candidate for intravenous tPA therapy. Intravenous therapy is not considered if the duration of ischemia is longer than 3 hours or the time of onset is unknown.

As mentioned earlier in this article, patients with major vessel occlusion, such as internal carotid, proximal MCA, or basilar artery thrombosis, have a poorer response to intravenous therapy compared with those with smaller branch occlusions and should be considered for intra-arterial therapy, if available. Clinical and radiographic features of this group include a dense vessel sign, either MCA or basilar; clinical evidence of ischemia in these vascular distributions; and a National Institutes of Health Stroke Scale Score greater or equal to 10.

Intra-arterial thrombolysis can also be administered after longer duration of ischemia than intravenous therapy. MCA occlusions can be treated up to 6 hours after onset of symptoms. After 6 hours, the risk of hemorrhage is believed to outweigh the potential benefits. Basilar artery occlusions typically have dire clinical outcomes and therefore may be treated up to 24 or 48 hours after ictus.

CONCLUSION

Despite the development of advanced imaging techniques, such as xenon CT, MR diffusion/perfusion, and MR angiography, CT scanning continues to play a major role in the assessment of acute strokes. Although CT is less sensitive than MR imaging in detecting acute ischemia, it is useful in screening patients for potential thrombolytic therapy. When reviewing CT scans of potential thrombolysis patients, several key points should be considered. The presence of hemorrhage is a contraindication for thrombolytic agents. Stroke patients with negative CT scans or small areas of edema are candidates for treatment; however, the presence of early MCA ischemic changes indicates more severe hypoperfusion, which may predict a poorer clinical outcome. Evidence of extensive MCA infarct on the initial CT scan usually precludes treatment with thrombolysis because of the increased risk of hemorrhage and decreased clinical benefit. The presence of a hyperdense MCA sign is associated with a poorer outcome after intravenous therapy; therefore, more aggressive therapy, such as intra-arterial thrombolysis, should be considered if technically feasible.

### TABLE 5. CT SCAN FEATURES ASSOCIATED WITH A POORER OUTCOME AFTER THROMBOLYTIC FEATURES

<table>
<thead>
<tr>
<th>Radiological feature</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brain edema, diffuse low density on the initial CT scan</td>
<td>The absolute presence or absence of edema primarily relies on the severity of hypoperfusion and adequacy of collateral circulation. The presence of more extensive edema on an early CT scan indicates severe hypoperfusion and may predict a less favorable outcome after thrombolytic therapy. The rate of complication, including hemorrhage, is significantly increased in this subgroup of patients.</td>
</tr>
<tr>
<td>Hyperdense MCA sign</td>
<td>It is associated with occlusion of the proximal MCA or its branches and it is present in 30% to 50% of patients presenting with clinical signs of acute MCA stroke.</td>
</tr>
<tr>
<td>Sites of occlusion</td>
<td>Internal carotid, proximal MCA, or basilar artery thrombosis, have a poorer response to intravenous therapy compared with those with smaller branch occlusions and should be considered for intra-arterial therapy, if available.</td>
</tr>
</tbody>
</table>


Figure 17. Topography of the cerebral main vascular territories

Figure 18. Topography of the cerebral main vascular territories
References


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**Addendum**

- A new version of this software is uploaded in my web site every month (it remains month and is changed with the monthly update of the neurology bulletin at: [http://neurology.yassermetwally.com](http://neurology.yassermetwally.com))

- To download the current version follow the link "[http://neurology.yassermetwally.com/topic.zip](http://neurology.yassermetwally.com/topic.zip)"

- You can also download the current version from within the publication or go to my web site at: "[http://yassermetwally.com](http://yassermetwally.com)" to download it.

- At the end of each year, all the publications are compiled on a single CD-ROM, please author to know more details.

- Screen resolution is better set at 1024*768 pixel screen area for optimum display

- For an archive of the previously reported cases go to [www.yassermetwally.net](http://www.yassermetwally.net), then under pages in the right panel, scroll down and click on the text entry "topic of the month"

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