Radiology Rounds

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Interventional Treatments for Ischemic Stroke

- **Ischemic stroke is the third leading cause of death in the United States and >25% of stroke survivors over age 60 are permanently disabled**
- **Intravenous recombinant tissue plasminogen activator (tPA) is the first line of treatment for ischemic stroke but must be administered within 3 hours of stroke onset and is relatively ineffective for proximal occlusions**
- **Intra-arterial thrombolysis is more effective for proximal occlusions and can be used up to 6 hours after stroke onset and later in some cases**
- **Mechanical disruption (thromborhexis) and/or clot removal (thrombectomy) can be performed using a number of devices and is beneficial for about 50% of patients with proximal occlusions**

Each year, more than 700,000 Americans have strokes. In about one-third of these cases, the cause is an occlusion in the internal carotid artery, middle cerebral or anterior cerebral arteries, vertebral artery, or basilar artery. Without recanalization, the outcome from these occlusions is devastating; this population accounts for all deaths due to ischemic stroke, 80% of those who go to rehabilitation centers, and 90% of the societal costs of strokes.

The first line of treatment for ischemic stroke is intravenous (IV) infusion of recombinant tissue plasminogen activator (tPA), which must be given within 3 hours of stroke onset because the risk of treatment-associated hemorrhage increases over time. This treatment has the advantage that it can be given with relatively little preparation time and can be performed in most community hospitals. Unfortunately, few patients are treated with IV tPA because many do not arrive for treatment soon enough, while others have contraindications to the administration of tPA, such as anticoagulant therapy, evidence of active bleeding, high blood pressure, or history of head trauma, stoke or myocardial infarction within past 3 months. In addition, IV tPA is relatively ineffective for proximal occlusions. Thus, the people who would benefit most from prompt recanalization are also the people least likely to respond to IV tPA.

Interventional endovascular therapies offer alternate avenues for the treatment of proximal occlusions. Endovascular treatments can be used in many patients who do not qualify for treatment with IV tPA. There are two endovascular strategies: intra-arterial (IA) thrombolysis and mechanical disruption (thromborhexis) and/or removal of the thrombus (thrombectomy). The inclusion criteria for selecting patients for intra-arterial treatments are shown in Table 1. The absolute exclusion criteria are hemorrhage, well-established acute infarct on CT involving more than one-third of the affected vascular territory, a CNS lesion with a high likelihood of hemorrhage (e.g. tumor or abscess), and bacterial endocarditis. Patients who are at risk of bleeding, for example, because of recent trauma or surgery, can be treated with mechanical devices. There are no established time limits for the safe administration of endovascular therapy, although these treatments are usually administered within 6 hours of stroke onset (when thrombolytics are used) or within 8 hours of stroke onset (when mechanical devices are used without adjunctive thrombolytics).

Table 1. Inclusion Criteria for Endovascular Treatment of Acute Ischemic Stroke
Significant neurological deficit, attributable to large vessel occlusion (basilar, vertebral, internal carotid, or middle cerebral artery)
Non-contrast CT without hemorrhage or well-established infarct
Stroke symptom onset known to be within past 6 hours
Mechanical clot removal with Concentric Retriever device may be considered up to 8 hours after stoke onset
Occlusions in the posterior circulation (vertebral/basilar occlusion) may be considered for treatment at a later time than other occlusions

Endovascular therapies can be more effective than IV tPA for proximal occlusions. However, it takes longer to initiate IA therapy, compared to IV tPA, because of the logistics of performing an angiogram and advancing micro-catheters to reach the site of the occlusion.

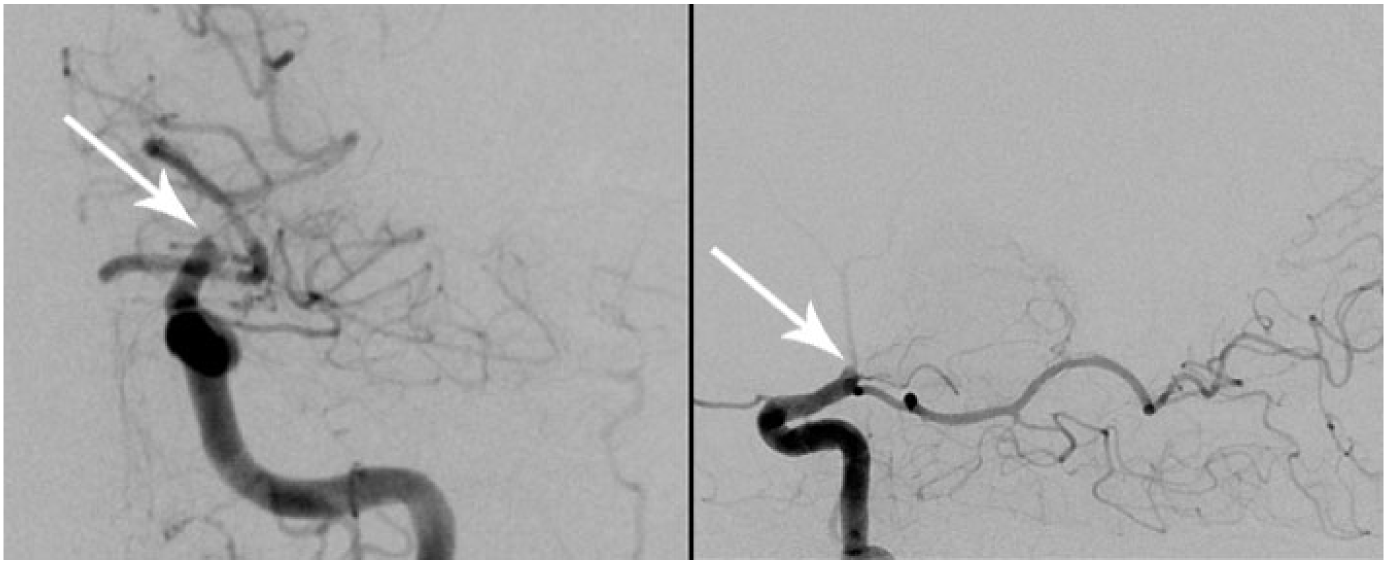

Figure 1. Angiogram of 79 year old man, performed 4 hours and 50 minutes after symptom onset, showing complete occlusion of the left interior carotid artery distal to the origin of the posterior communicating artery (arrows). IV tPA had been started started 2 hours after symptom onset and the patient sent to MGH via Medflight. His symptoms were assessed as 19 on the NIH Stroke Scale.

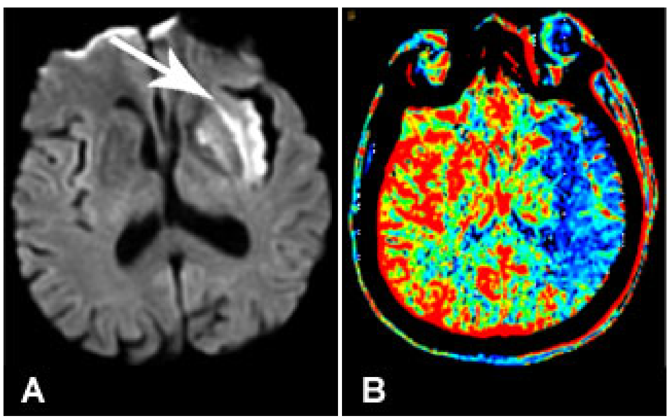

Figure 2. Diffusion weighted MRI (A) of the same patient as in figure 1 shows abnormality restricted to a smaller volume than that seen in perfusion weighted MRI (B). This perfusion/ diffusion mismatch suggested that the patient would benefit from interventional treatment to remove the clot.

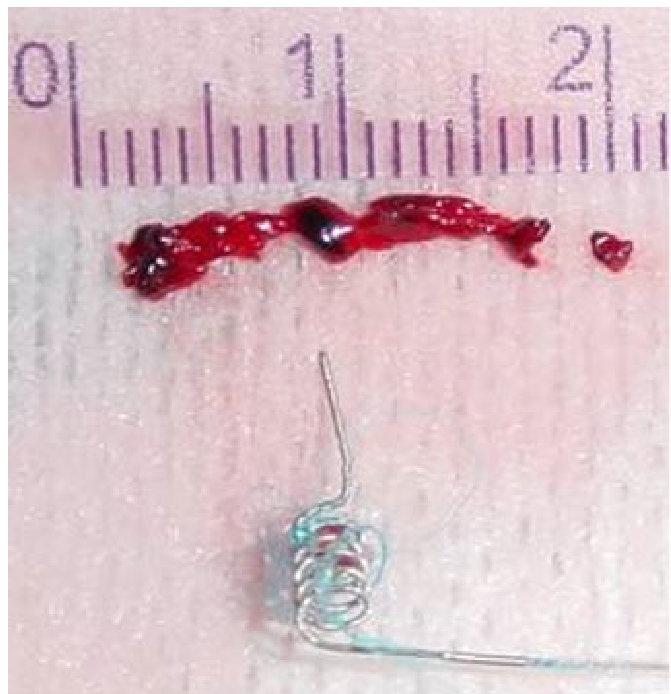

Figure 3. Blood clot removed after thrombectomy with the MERCI device.

Diagnostic Imaging

When a patient arrives with stroke-like symptoms, the first step is to establish the correct diagnosis. Imaging plays a vital part in this process (see Radiology Rounds, October 2004). Non-contrast CT can detect hemorrhage or other possible causes of symptoms. CT angiography can detect the site of an occlusion, stenoses, or other vascular abnormalities. If the patient is to be treated with IV tPA, no further imaging is necessary, in the belief that "time is brain" and that any delay in treatment will result in more brain damage. If the occlusion is proximal and the patient is seen within three hours of symptoms onset, IV tPA may be used as a bridge treatment until endovascular treatment is initiated.

Recent data suggest that advanced imaging techniques can differentiate between the region of the brain that is irreversibly damaged (infarct core) and the region with reduced perfusion that is likely to recover if circulation is restored (ischemic penumbra). These imaging techniques are not used for patients who are selected for treatment based on time of stroke onset and location of occlusion. However, they have been used to select patients for treatment in cases that would otherwise be excluded from treatment, for example, because the time of stroke onset is unknown.

Where ischemia is profound, cell death occurs within minutes, forming the stroke core. Diffusion weighted MR imaging (DWI) is the most sensitive method to visualize the stroke core because the edema that develops in response to severe ischemia alters the diffusion of water. In the ischemic penumbra, collateral

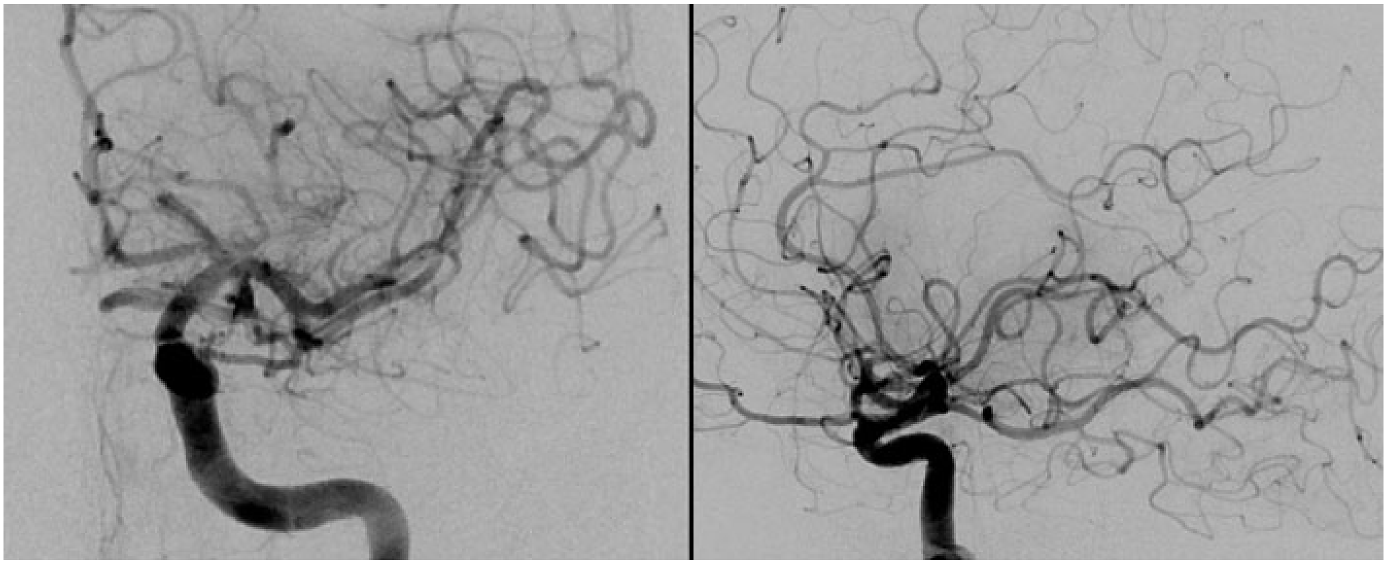

Figure 4. Angiogram performed after thrombectomy shows complete internal carotid artery recanalization and a mild residual blood clot in the distal M3 segment of the middle cerebral artery.

circulation provides enough oxygen to support the brain tissue for some time after stroke onset. This region can be detected with perfusion weighted MR imaging (PWI), which measures the passage of contrast agent through the brain parenchyma over time. If the region of reduced perfusion (ischemic penumbra) is greater than the stroke core, this provides physiological evidence that there is brain tissue that can be salvaged with successful recanalization. CT perfusion imaging (CTP) techniques have also been developed to show the differences in the degree of perfusion deficit and identify potentially salvageable ischemic regions. Patients are likely to benefit from endovascular treatment if the stroke core does not exceed one-third of the territory of the occluded vessel and the ischemic penumbra is at least 20% larger than the stroke core.

Intra-arterial Thrombolysis

IA thrombolysis, mechanical disruption, and/or removal of the thrombus can be performed independently or in conjunction. The IA thrombolysis procedure is initiated by placing a guide catheter into the occluded vessel, under angiographic guidance, and then extending a wire-guided micro-catheter so that it passes through the clot. Once the micro-catheter is beyond the clot, the thrombolytic agent is infused while the micro-catheter is withdrawn through the thrombus. This manipulation is repeated several times and serves to mechanically break up the clot as well as break it down enzymatically. By infusing a thrombolytic agent directly where it is needed, a higher local concentration is achieved than that used for IV tPA although the total dose is less. For this reason, the treatment window for safe administration of IA tPA is considered to be 6 hours. Dissolution of the clot takes 90 minutes on average, with freshly formed thrombi taking less time than more organized clots.

In some cases recanalization fails because the vessel is occluded by emboli composed of cholesterol, calcium, or other debris from atherosclerotic lesions that are resistant to enzymatic degradation. At times, reperfusion does not occur even though the clot is dissolved, which may be attributed to edema of the surrounding tissue.

Figure 5. Non-contrast CT performed after therapy shows stroke-related abnormality corresponding to that seen earlier in diffusion weighted MR image (Figure 2). At this time the patient was assessed as 5 on the NIH Stroke Scale.

Mechanical Thrombolysis / Thrombectomy

In addition to the wire-guided micro-catheter described above, there are several other mechanical devices to break up or remove the clot. If one device fails, others may be tried in succession to obtain the best outcome.

In addition, if an underlying atherosclerotic lesion is found after clot lysis or removal, angioplasty or stenting may be used to improve perfusion.

The disadvantages of mechanical techniques include the difficulty of navigating into, and manipulating the devices in, the cerebral circulation, the risk of excessive trauma to the vasculature, and fragmented thrombus forming distal emboli. Nonetheless, the advantages appear to outweigh the disadvantages. For example, in the mechanical embolus removal in cerebral ischemia (MERCI) trial (Concentric Retriever device), recanalization was achieved in 47% of patients with occlusions in the internal carotid artery or middle cerebral artery, who were ineligible for IV tPA treatment and within 8 hours of stroke onset. After adjunctive therapy, the rate of recanalization increased to 60%. Of these, about half had good functional outcomes measured at 90 days post-treatment. In the more recent Multi-MERCI trial, treatment with the retriever alone resulted in successful recanalization in 55% treatable vessels, and in 68% after adjunctive therapy. Favorable outcome at 90 days was seen in 36% of the patients (49% in recanalized vs. 9.6% non-recanalized patients; $p < 0.001$).

MGH Comprehensive Stroke Center

The MGH is a Comprehensive Stroke Center, with the full range of services recommended by the Brain Attack Coalition in order to improve outcomes of patients with strokes. The Center provides integrated services of health care personnel, including those with expertise in neurosurgery, vascular neurology, and interventional neuroradiology; advanced neuroimaging capabilities, a dedicated neurointerventional suite, a neuro intensive care unit, and a stroke registry.

Further Information

For further questions, please contact Joshua A. Hirsch, M.D., 617-726-1767, or R. Gilberto Gonzalez, M.D., Ph.D., 617-726-8628, Division of Neuroradiology, Massachusetts General Hospital.

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