Mechanical thrombectomy is evolving into a significant adjunct in the treatment of acute ischemic stroke.

BY RICHARD E. LATCHAW, MD

Treatment of acute ischemic stroke (“brain attack”) has been the subject of numerous clinical trials. Strategies such as restoring arterial perfusion or stopping the cascade of cellular damage have been proposed. The prevailing strategy has been to dissolve the clot, which is usually an embolus to an intracranial artery rather than in situ thrombosis due to an atherosclerotic stenosis, which is typical of coronary or peripheral vascular arterial disease, to restore adequate blood flow.

Another strategic issue has been whether to administer the thrombolytic agent intravenously or intra-arterially. There were a number of prospective trials utilizing the intravenous approach to test the ability of a tissue plasminogen activator (tPA) to produce recanalization with relatively low risk to the patient, usually within the narrow time window of 3 hours from the onset of symptoms. Given the desire to improve the efficacy of the thrombolytic approach, controlled studies were conducted to determine if the intraarterial infusion of another thrombolytic agent, prourokinase, would dissolve the clot more quickly, within a 6-hour time window from symptom onset and with fewer side effects, such as intracerebral hemorrhage, than with the intravenous approach. Recently, other thrombolytic agents have been used, such as the third-generation tPA (reteplase) and drugs that block IIb/IIIa platelet receptors. Even more recently, an alternative intravenous thrombolytic agent, vampire bat venom (desmoteplase), has been tested successfully with a 9-hour time window from ictus.

Although these trials of drug therapy have been of major importance, demonstrating for the first time that there truly is potential treatment for the acute manifestations of one of the most important diseases in our culture—the third most prevalent cause of death and a significant cause of disability in our society—we have yet to acknowledge that the restoration of cerebral blood flow in the shortest period of time, however that is achieved, is our major goal. Once adequate blood flow to the at-risk tissue is achieved, we can infuse agents to strengthen the endothelium against the unwanted movement of water into the interstitial spaces and compounds to alter the ability of free radicals and calcium to activate the intracellular cascade that will lead to cell death, knowing that these drugs can reach their targets.

How do we achieve rapid recanalization of the cerebral arteries? Thrombolysis is a lengthy procedure, often requiring hours to achieve. In the meantime, cells are dying and the endothelium is becoming more porous, allowing for hemorrhage to occur. One strategy is to begin with thrombolysis, and, if that does not work, move to a mechanical solution. This is because most of the mechanical thrombectomy solutions have not worked well, and most interventionists are...
either unfamiliar with the construction of these devices or are not confident that they can provide vascular recanalization with a high level of efficacy and a low risk of complications. However, if a safe and reliable device were available, one might start with thrombectomy.

Thus, it is important to review the mechanical thrombectomy devices that are available to the stroke interventionist. These devices are classified by their mode of action, and the relative advantages and disadvantages of each are highlighted (Table 1). I have used many of them, and I have strong biases as to their efficacy and have also developed one of the devices.

IMPORTANT PRINCIPLES FOR CEREBROVASCULAR MECHANICAL THROMBECTOMY

Most clots are intracranial. Most ischemic strokes are a result of the occlusion of intracranial arteries, such as the middle cerebral artery or its branches, the basilar artery or its branches, etc. These are usually occluded by emboli of clot or plaque from a cervical site or from the aorta or heart, or due to intracranial vascular occlusive disease. Only in situations in which there is a high-grade stenosis of an extracranial artery will there be a long thrombus in a cervical vessel requiring removal. Thus, the interventionist must be prepared to access the intracranial vessels for treatment.

Intracranial access is crucial. The key to the success of any device is access to the intracranial circulation, which requires that the device be flexible.

The device must be able to remove both hard and soft clot. In my experience, firm-to-rock-hard clot occurs approximately 40% of the time. There is no way at this time for the interventionist to predict the clot’s consistency beforehand. Imaging techniques using CT and MR have not been able to characterize the clot texture with any accuracy. A device that can remove both hard and soft clot will be the “first off the shelf.”

Fragmentation of the thrombus must be avoided. A proximal thrombus allows for collateral circulation to fill the more distal branches. However, clot fragmentation leads to distal embolization and blockage of those collateral channels, which is worse than the original proximal occlusion.

The device must be easy to use, rapid, efficacious, and safe. The device must be so easy to use that any practitioner with reasonable catheter skills can use it. The insertion and manipulation of the device and subsequent removal of thrombus must be rapid, taking only minutes. The device must be efficacious: it will be used frequently if the interventionist has faith that it will work. And, it must be safe, with essentially no chance of vessel perforation or dissection.

ANALYSIS OF DEVICES BY CATEGORY

Suction Devices

Obtaining adequate suction usually requires a large catheter, even when a catheter with an occluding balloon on the end is used. Thus, this old technique is primarily used when there is a large clot burden within an extracranial vessel or a straight intracranial vessel, such as the basilar artery. Getting a large catheter into the intracranial anterior circulation is usually impossible and risks dissection. In addition, aspirating hard clot is usually not possible.

One device now in clinical trials is the Penumbra (Penumbra, Inc., San Leandro, CA), which appears in its patent application to consist of a small-caliber catheter with a protruding “cap” that is placed against the proximal end of an intracranial thrombus. Suction is then applied to the catheter, and the clot is removed. The efficacy of such a technique remains to be seen. This author has found that a major principle for the removal of a firm-to-hard thrombus is engaging the distal aspect of the clot so that the device does not become disengaged during withdrawal.

Balloon “Angioplasty”

There are a variety of catheters with balloons that are flexible enough to access the intracranial circulation. The goal is not really angioplasty of the artery, but the crushing of the clot. The problem with this approach, of course, is that the fragments will then embolize to distal branches, which may cause more harm than good.

Snares

Snares come in a variety of configurations, all meant to grab an object, usually a piece of catheter or a metallic coil. The Alligator (Chestnut Medical Technologies, Inc., Menlo Park, CA) has three pincers that close together when the device is retracted, and others are shaped like the leaves of a tulip or a lariat. All of these devices can access the
intracranial circulation, and all can make a hole in a soft to mildly firm clot, increasing the surface area to potentiate the action of a thrombolytic agent. However, in doing so, fragmentation may occur. None are very efficacious at engaging a hard clot—they either do not engage or slip off.

Snare-Like Device
The Merci Retriever is a bit different than the usual snare because it is a corkscrew that engages the clot initially at its distal end and then progressively toward the proximal end of the clot as the device is withdrawn (Figure 1).20-23 Although a microcatheter can pass through a soft to medium-firm clot, it is important to realize that the catheter does not pass through a firm thrombus but next to the clot (between it and the intima) and that one can almost always manipulate a microcatheter and microguidewire past the clot. Like a regular corkscrew, the diameter of its proximal end is greater than its distal, which is a point. Imagine engaging a wine cork in this manner. The clot must be sufficiently soft for the Merci to become engaged and to stay engaged during removal. Newer versions have fibers to keep the coils from pulling apart during withdrawal and to aid in this engagement. However, a major reason for its less-than-desired efficacy is the inability to engage and remove firm-to-hard clot.

Enveloping Coil
The NexGen Thrombectomy Device is essentially a series of coils that are placed around the thrombus to envelop it and then pulled tightly with a pull-wire or pull-string (Figure 2). After the microcatheter has been passed beyond the occluding thrombus, just like it is for thrombolysis or for use of the Merci Retriever, coils are placed around the distal aspect of the clot. More coils are progressively placed around the middle and proximal aspects of the thrombus as the catheter is pulled back. The formation of a “knot” of coils along the distal aspect of the clot is key, so that the coils will not simply slip down the side between the clot surface and the intima. This envelope keeps the thrombus from fragmenting during withdrawal.24

I am a member of the team that has developed this device. We have tested it in a porcine model, demonstrating its ability to remove both soft and hard clot. Rock-hard thrombi were embolized into a variety of arteries in the neck and extremities and then extracted, achieving complete angiographic patency (TIMI 3) of the previously occluded artery 88% of the time. The coils are so soft that dissection is not an issue. Any diameter and any number of coils can be constructed so that the device can be used to remove a long length of clot burden from a cervical artery, a leg, or a dialysis graft. Clinical trials should begin in the near future.

Propeller-Like Devices
There are a number of such catheters, used mainly in large-diameter, straight vessels, such as those in the leg.25 They all have a spinning blade that emulsifies the clot. Unfortunately, all are sufficiently rigid that intracranial access, other than for possibly the relatively straight vertebrobasilar system, is not possible. However, they can be used in the cervical carotid artery to decrease clot burden above a high-grade stenosis.

Rheolytic Devices
The AngioJet (Possis Medical, Inc., Minneapolis, MN) is the best known and most frequently used device in this category. The rapid forward movement of fluid below a hole produces the Venturi effect, sucking a clot into the hole like a vacuum and emulsifying it. It is commonly used in the extremities but may be used in the extracranial carotid artery.26 It is sufficiently large and stiff so that its only intracranial use has been for declotting dural sinus occlusions and occasionally in a straight artery, such as the basilar.28 Hard clot is also a problem. A smaller version was being developed for intracranial arterial use a few years ago, but that development has stopped.

Laser-Based Devices
The EPAR (EndoVasix Corporation, Belmont, CA) is based on the conversion of laser light energy into acoustical energy that bombards the clot to fragment and, ideally, emulsify it.14 The tip is sufficiently stiff so that intracranial arterial access is an issue, as is the fragmentation and distal

Figure 3. The EKOS infusion catheter (EKOS Corporation, Bothell, WA) flutters when the associated ultrasound unit is activated. This fluttering action cracks the thrombus, increasing the surface area for a thrombolytic agent that is infused through the same catheter.
<table>
<thead>
<tr>
<th>Category</th>
<th>Device</th>
<th>Company</th>
<th>Action</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suction</td>
<td>Catheter (± balloon)</td>
<td>Various</td>
<td>Suction</td>
<td>Simple</td>
<td>Access; cannot aspirate hard clot</td>
</tr>
<tr>
<td>Penumbra</td>
<td>Penumbra, Inc.</td>
<td>Cap + suction</td>
<td>Access to small vessels</td>
<td>Removal of hard clot</td>
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<td>Balloon “Angioplasty”</td>
<td>Stealth</td>
<td>Boston Scientific Corporation</td>
<td>Crush thrombus</td>
<td>Access</td>
<td>Fragmentation, distal embolization</td>
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<tr>
<td>Hyperglide</td>
<td>ev3 Inc.</td>
<td>Crush thrombus</td>
<td>Access</td>
<td>Fragmentation, distal embolization</td>
<td></td>
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<tr>
<td>Coronary Balloon</td>
<td>Various</td>
<td>Crush thrombus</td>
<td>Access</td>
<td>Fragmentation, distal embolization</td>
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<td>Snare</td>
<td>In Time</td>
<td>Boston Scientific Corporation</td>
<td>Grab—elliptical mesh</td>
<td>Simple, access</td>
<td>Removal of hard clot, clot fragmentation</td>
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<td>Ensnare</td>
<td>Angiotech</td>
<td>Grab—tulip</td>
<td>Simple, access</td>
<td>Removal of hard clot, clot fragmentation</td>
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<td>Gooseneck</td>
<td>ev3 Inc.</td>
<td>Grab—lariat</td>
<td>Simple, access</td>
<td>Removal of hard clot, clot fragmentation</td>
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<td>Alligator</td>
<td>Chestnut Medical Technologies, Inc.</td>
<td>Grab—pincers</td>
<td>Simple, access</td>
<td>Removal of hard clot, clot fragmentation</td>
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<td>Attracter-18</td>
<td>Boston Scientific Corporation</td>
<td>Grab—fiber mesh</td>
<td>Simple, access</td>
<td>Removal of hard clot, clot fragmentation</td>
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<td>Neuronet</td>
<td>Abbott Vascular</td>
<td>Grab—basket</td>
<td>Simple, access</td>
<td>Removal of hard clot, clot fragmentation</td>
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<td>Concentric Retriever</td>
<td>Concentric Medical, Inc.</td>
<td>Grab—corkscrew</td>
<td>Simple, access</td>
<td>Removal of hard clot, clot fragmentation</td>
<td></td>
</tr>
<tr>
<td>Snare-Like</td>
<td>Merci Retriever</td>
<td>Concentric Medical, Inc.</td>
<td>Engage—corkscrew</td>
<td>Access</td>
<td>Removal of hard clot, clot fragmentation, finite clot size, break</td>
</tr>
<tr>
<td>Enveloping Coil</td>
<td>NexGen Thrombectomy Device</td>
<td>NexGen Medical Systems</td>
<td>Coils distal, middle proximal = envelope</td>
<td>Access, remove hard clot, no fragmentation, remove long clot</td>
<td>None known</td>
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<tr>
<td>Propeller</td>
<td>X-Sizer</td>
<td>ev3 Inc.</td>
<td>Emulsify</td>
<td>Rapid</td>
<td>No intracranial arterial access, hard clot a problem</td>
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<tr>
<td>Clot Buster</td>
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<td>Emulsify</td>
<td>Rapid</td>
<td>No intracranial arterial access, hard clot a problem</td>
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<tr>
<td>Hydrolyser</td>
<td>Cordis Endovascular</td>
<td>Emulsify</td>
<td>Rapid</td>
<td>No intracranial arterial access, hard clot a problem</td>
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<tr>
<td>Rheolytic</td>
<td>Angiojet</td>
<td>Possis Medical, Inc.</td>
<td>Venturi “vacuum”</td>
<td>Rapid</td>
<td>No intracranial arterial access, hard clot a problem</td>
</tr>
<tr>
<td>Laser</td>
<td>EPAR</td>
<td>EndoVasix</td>
<td>Laser→ acoustic energy→ emulsify</td>
<td>Rapid</td>
<td>Difficult intracranial arterial access, clot fragmentation</td>
</tr>
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<td>Ultrasound</td>
<td>TCD-Aided Thrombolysis</td>
<td>Various</td>
<td>Crack clot for lytic agent</td>
<td>Easy</td>
<td>Efficacy, especially with hard clot</td>
</tr>
<tr>
<td>MicroLysus</td>
<td>EKOS Corporation</td>
<td>US-induced flutter of infusion cath</td>
<td>Aids lytic infusion</td>
<td>Efficacy, clot fragmentation</td>
<td></td>
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</table>
embolization of clot. The development and testing of this device has recently been stopped.

Ultrasound-Aided Thrombolysis

Transcranial Doppler analysis of flow during thrombolytic procedures is a relatively common practice. Improvement in the efficacy of the infusion is thought to stem from the “cracking” of the thrombus by the ultrasonic waves, increasing the surface area upon which the lytic agent can work. The relative efficacy of this procedure has been debated.29 The EKOS device is an FDA-approved catheter that rapidly vibrates from an ultrasonic input (Figure 3). After being imbedded in a clot, it makes cracks in the thrombus to increase the surface area, potentiating the activity of the thrombolytic agent.29 It will not be effective for a hard clot that it cannot penetrate, and fragmentation of softer clot may be an issue.

Mechanical Thrombectomy

May Change Stroke Therapy

Vascular recanalization should be rapid and efficacious. A mechanical thrombectomy device that is easy to use and consistently opens vessels should become the first line of treatment. That would mean that a lower dose—or no dose—of a thrombolytic agent needs to be infused. Such drugs are associated with a significant risk of hemorrhage, and the use of a mechanical device would potentially decrease that risk. However, reperfusion injury may still be an issue after recanalization. Hopefully, new drugs to stabilize the endothelium will become available. Such agents could more easily reach the target vessels once recanalization has been achieved. The Desmoteplase in Acute Ischemic Stroke (DIAS) trial7 has demonstrated the ability to select the patient population most amenable to recanalization, no matter the time from stroke onset, using imaging strategies such as MR perfusion and diffusion sequences, or the CT equivalents. Thus, patients can be selected who have salvageable tissue being kept alive by collateral flow, while also having a relatively small volume of infarcted tissue that might bleed with recanalization. Such patients can be detected beyond the classical 3- or 6-hour time windows, thus offering the potential of treatment to many more people. Using a thrombectomy-first approach on such patients will further increase the therapeutic window and potentially decrease complications.

CONCLUSION

Using a combination of high-tech imaging and mechanical thrombectomy, acute stroke therapy is destined to become much more common and efficacious, an outcome that we all have desired for a very long time.

Richard E. Latchaw, MD, is Professor of Radiology and Chief of Neuroradiology at the University of California at Davis in Sacramento, California. He has disclosed that he is the unpaid Vice-President and Medical Director of NexGen Medical Systems, Inc. Dr. Latchaw may be reached at (916) 734-5720; richard.latchaw@ucdmc.ucdavis.edu.