Beyond Thrombolytic Therapy: A New Tool for Stroke Treatment

The FDA's recent approval of the Merci Retriever represents a step forward in stroke treatment, but unanswered questions remain.

By Nathan Hall, Associate Editor

While we've seen some significant advances in acute stroke treatment over the past decade, many neurologists still find themselves frustrated by their inability to treat ischemic stroke patients safely and effectively. Effective treatments such as thrombolysis remain elusive, and tend to be slow-acting, leaving neurologist and patient alike with nothing to do but anxiously wait, hoping that the treatment might work. For several years now, it's been a hope for many stroke experts to make use of a device that could remove a clot quickly—a mechanical method that could avoid some of the pitfalls of thrombolysis.

This August, in a move that surprised many experts, the FDA approved the first of such mechanical removal devices, the Merci Retriever from Concentric Medical, Inc. This came after many other devices, such as the angiojet and the ultrasound catheter, have practically disappear from the development pipeline

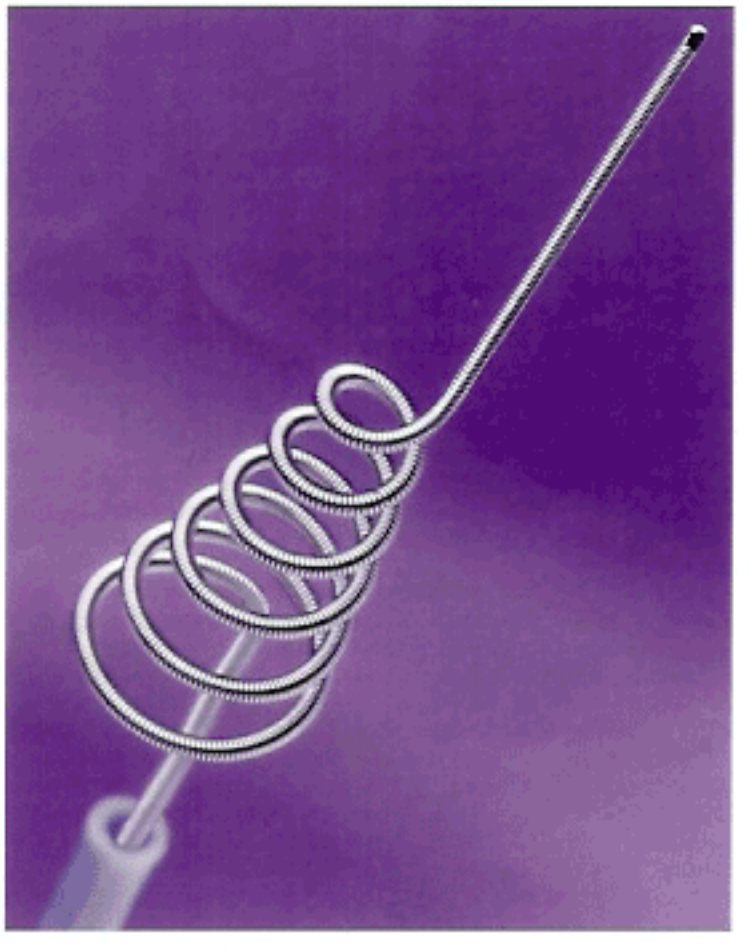
Despite the approval, many stroke specialists remain concerned about using the device in a clinical setting due to the lack of robust clinical data supporting its efficacy in improving the final clinical outcome of patients, as well as the safety and applicability of the device. And while there have been some effusive anecdotes told about its performance, it remains unclear whether the device is better than conventional management. In this month's column, we'll look at what is known about the Merci Retriever and some other mechanical thrombolysis methods in development.

The Turn of the Corkscrew

The FDA has given the Merci Retriever a technical indication for removing clots from stroke patients based on an uncontrolled study with technical feasibility as a primary endpoint. Specifically, the study involved approximately 125 patients at 25 major medical centers throughout the United States. Inclusion criteria were a duration of symptoms of three to eight hours or <3h in rt-PA contraindicated patients (i.e., post surgical, high risk of bleeding, active bleeding, etc.) and a large vessel occlusion on angiogram. In this study, the primary outcome was based upon rate of successful recanalization compared with historical controls reported in the PROACT trial of intra-arterial Prourokinase in acute stroke.

It's important to note that the device, which resembles a corkscrew at the end of a catheter, did not significantly improve clinical outcome, although significant clinical improvement was identified in those patients who were successfully recanalized. Interestingly, the approval does not limit the treatment to a specific time window, and therefore the device could potentially be used far beyond the eight hours window evaluated in the clinical trial.

The main theoretical advantage of the Merci Retriever is its use for large-vessel strokes, according to interventional neurologist Wade Smith, MD, PhD, Director of Stroke Service at the Department of Neurology at the University of California, San Francisco and the national principle investigator for the Merci study. Large-vessel strokes have



The Merci Retriever

a high mortality rate, frequently have poor outcomes, and are often resistant to thrombolytic therapy due to the size of the clot.

One of the major potential uses of the Retriever, Dr. Smith says, is that it may be used to treat patients who are otherwise ineligible for thrombolytic therapy because they missed the time window or have other disqualifying conditions. He relates the story of one patient ineligible for thrombolytics who was successfully treated with the Retriever in only seven minutes after it was first inserted through the patient's groin. "We've had some exciting outcomes," he says. "We've had some fast ones and we've had some slow ones. The hope is that, as people get better with the techniques, this will translate into better results."

Although there hasn't been a definitive study showing that the Retriever yields better results than thrombolytics, Dr. Smith believes it probably still offers some benefit. "It probably does improve the outcome quite well, when you look at who had it versus those who didn't those who did clearly have a better outcome," he says. He also notes that the researchers often administered thrombolytics when applicable during the Retriever cases if the clot moved further down the vessel or in case another clot was present.

While controversy continues over the clinical efficacy of this treatment, future studies may help clarify the question. The NIH is funding a randomized trial, called the MR RESCUE Trial, comparing the Retriever with current medical therapy. The trial uses MRI diffusion and perfusion weighted imaging in an attempt to determine whether neuroimaging can help identify patients who are most likely to respond to retriever therapy. This study is planned to enroll 120 patients randomized to the Retriever or conventional medical therapy. In addition, Dr. Smith believes that future studies might look at combining the Retriever with various types of thrombolytics to determine the optimal treatment method.

Bumps in the Rollout

Interest in the Retriever is likely to be very high. However, Dr. Smith says the company is planning a gradual roll-out of the Retriever. At first, it will likely only be sold to the investigational sites. Over time, he believes it will allow interventional neuroradiologists to "hang out their shingle" and advertise that their facility offers this new, approved treatment and enhance their treatment options. "Now that there's an approved device, it allows people to improve their programs," he says, noting that although other thrombolytic interventional methods (except tPA) are used off-label they cannot be used in advertising. Such might not be the case with this device.

However, he notes there will be two big bumps in the road. First, he says, there are only a small number of sites in the United States capable of using this therapy in an acute stroke patient. Second, there are only a few hundred interventional neuro-radiologists potentially available to use this nationwide.

Even though it may be a while before the Retriever is commonly used in emergency rooms, Dr. Smith says this approval has implications beyond current clinical uses. If financially and medically successful, the Retriever could inspire other companies to create more devices. "This will be what's on the shelf soon," he says. "It will usher in a new era, and hopefully lead to new innovations."

Still Some Reservations

Although Dr. Smith and the other investigators express excitement about the Retriever earning FDA approval, many experts in the stroke treatment community are concerned about the potential overuse of the device. "A number of my colleagues have voiced strong concern about the possible inappropriate use of this device, particularly since the precise indications for its effective use have not been completely defined," says David Tong, MD, PhD, Associate Professor of Neurology, Stanford University Medical Center. "Nevertheless, if properly evaluated and used, there is certainly great potential for this therapeutic approach."

One major concern, Dr. Tong says, is the lack of a specific time window for use in the FDA approval. Because the time window for treatment isn't defined, this could lead to the device being used in situations many hours after irreversible tissue injury has occurred. "Certainly, neurologists could and should play a pivotal role in defining the best use of this new technology," Dr. Tong says.

Open Doors for Headway

Despite these misgivings, the Merci Retriever still offers an exciting new era for stroke therapy. What's more, it also opens up the possibility for a slew of new devices and treatments with new mechanisms of action, which could improve our treatment of stroke. It may even lead to a revival as some of the older mechanical thrombolytic devices get re-evaluated and restudied to determine if they can be useful for physicians and profitable for the manufacturers.

Neurologists may want to look at taking part in these trials, if only to have the option for patients who missed the tPA window or otherwise are ineligible for the drug. If the experimental devices can offer patients hope for treating acute stroke patients when the conventional methods, they may be worth considering in a difficult case. **PN**