coils SAFER than surgery

Trial shows endovascular coil embolization safer, more effective than surgery in treating brain aneurysms | BY SARAH LONG

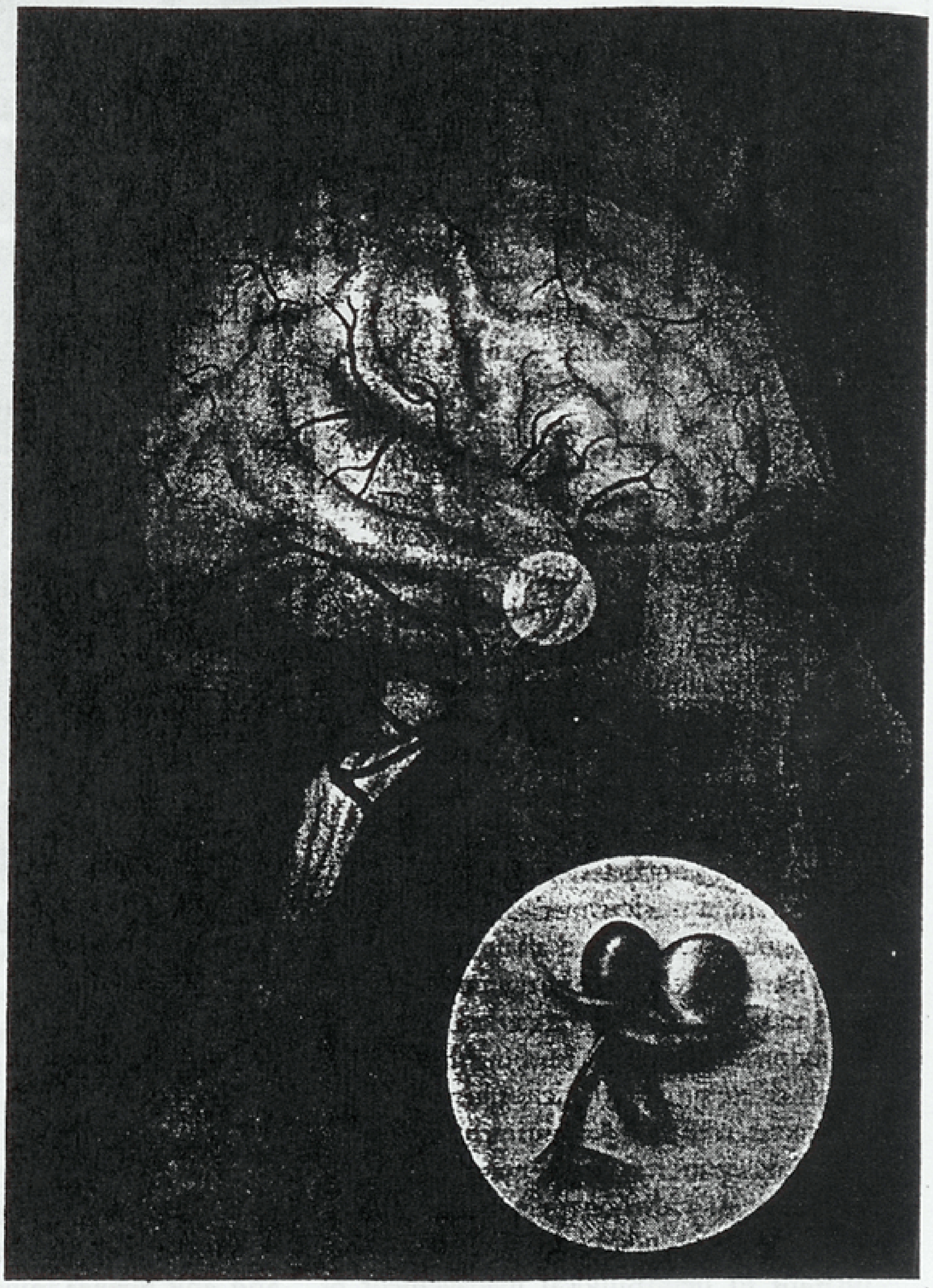


ILLUSTRATION BY NICOLE JONES

Patients who undergo an interventional neuroradiology technique to treat cerebral hemorrhage from a ruptured aneurysm have a lower risk of severe disability or death compared to those who undergo surgery, according to a new study.

In the International Subarachnoid Aneurysm Trial (ISAT), the less invasive technique of endovascular coil embolization produced significantly better outcomes in terms of survival free of disability than brain surgery. In fact, the trial ended ahead of schedule because early results were so compelling that the researchers felt it was no longer ethical to randomize patients to brain surgery.

Kieran Murphy, MD, the primary investigator for the study at Johns Hopkins Medical Institutions, Baltimore, said ISAT provided insight for him similar to that which one of his patients experienced while working in public administration during the 1960s. As he walked down the corridor in the State Department, the patient told Dr. Murphy, he occasionally would realize that what he and his colleagues were doing truly was significant.

"They were aware at the time that they were doing something that would make history," Dr. Murphy said. "I honestly think this paper makes history in the same way in that it indicates a new moment in neurosurgery where an endovascular technique for treating an intracranial problem has shown to be actually better than what was considered to be the gold standard."

The study, published in the Oct. 26, 2002 issue of *The Lancet*, signals the beginning of a wave of technological change to treat the complex and "wicked" lesions that have life-altering effects on patients, Dr. Murphy said. Also, the study emphasizes that patients with ruptured aneurysms should be offered the option of both endovascular treatment and traditional surgical clipping.

Trial overview

About 6 percent of the U.S. population have unruptured aneurysms, and between 25,000 and 30,000 people a year rupture their aneurysms. When that happens, about 15 percent will die immediately, and 50 percent will be dead at 30 days, according to Dr. Murphy. Many of those who survive will have permanent neurological defects such as strokes and seizure disorders.

"They are very different people than they were before the event and they are unable to look after themselves," Dr. Murphy said.

A brain aneurysm develops when a weakened area of a blood vessel fills with blood and bulges or balloons out, usually at the base of the brain, explained Charles M. Strother, MD, president-elect of the American Society for Neuroradiology.

These types of aneurysms are most common in people between the ages of 35 and 60. Unfortunately, most patients do not realize that they have an aneurysm until it ruptures.

"They're often discovered when they rupture and this causes injury to the brain in a variety of ways," Dr. Strother said. "Blood may simply be in the space between the brain, causing an increase in the pressure in the skull vault. It may bleed into the substance of the brain, often leading to severe brain damage and death at the time of rupture."

The main goal, initially, is to stabilize the patient and then try to prevent the aneurysm from rebleeding. If nothing is done, there

is a high incidence of rebleeding in the days immediately following the initial bleeding.

About 75 percent of patients with aneurysms in the United States are treated by neurosurgical clipping and 25 percent are treated by coiling. In Europe, the distribution is reversed—about 75 percent of patients are coiled and 25 percent are clipped, according to Dr. Murphy.

ISAT is the first randomized trial since the 1960s to evaluate treatment of patients with subarachnoid hemorrhage. It took place in 44 countries and at one U.S. site, with 2,100 patients enrolled. Two of the patients were from the United States. Run by the Medical Research Council, the English equivalent of the National Institutes of Health, the study's principal investigators were Andrew Molyneux, MD, and Richard Kerr, MD, of the Department of Neuroradiology at the Radcliffe Infirmary, Oxford, England.

The patients chosen for the trial had aneurysms that the researchers thought could be treated successfully either way: by coiling or clipping. Of the 2,100 patients who were randomized, those who were coiled had a 23 percent better outcome than those who were clipped, according to the study results.

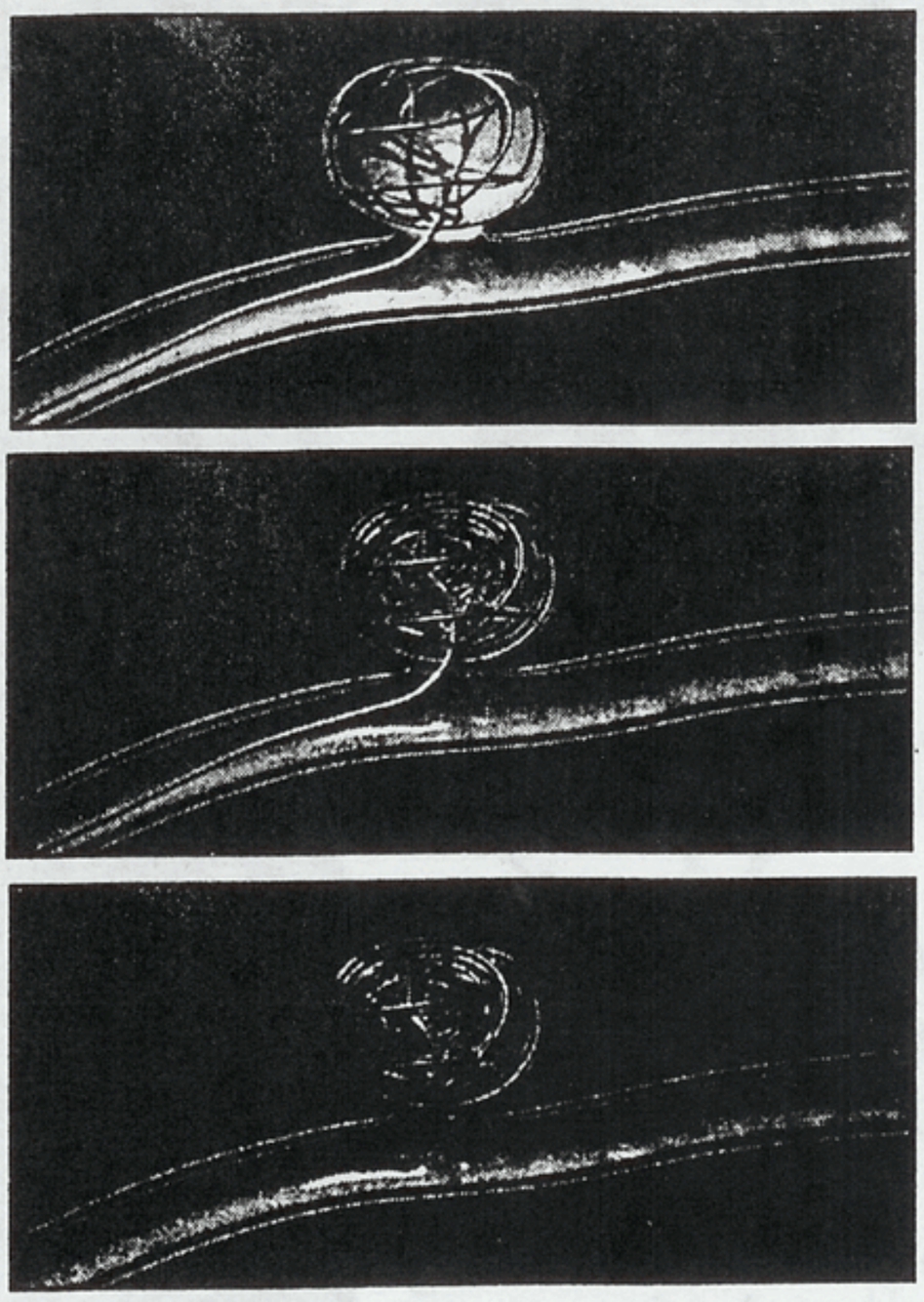
"This is very, very important," Dr. Murphy said. "It is unusual in medicine to be able to change the outcomes and care with that kind of percentage change. The risk of death and significant disability at one year was 22.6 percent lower in those coiled than those treated by conventional open surgery. This is a very significant step forward in neurosurgical management of these patients."

A limited number of physicians in this country perform endovascular coil embolization, and only about 300 of the approximately 3,000 U.S. medical centers can do these procedures.

"One of the things that's important here is to make sure that patients with these aneurysms get referred to the right kind of center … where they will be managed by an interdisciplinary team that makes available all the appropriate options for the achievement of the best possible outcome for them," Dr. Murphy said.

The procedures

The traditional surgical technique for treating ruptured aneurysms involves making an incision in the scalp, removing a piece of the bone of the skull plate, gently lifting the brain, and placing a surgical clip across the aneurysm, isolating it from the circulation.



Successive drawings of a side wall aneurysm with coils inside the aneurysm dome. *(photo/courtesy Boston Scientific)*

"This is done to stop blood flowing into the aneurysm, and that prevents rebleeding and any further injury to the brain," Dr. Strother said.

After the clipping, the bone plate is put back in place, the wound is closed and the patient undergoes recovery from the injury received at the time of the aneurysm rupture.

Endovascular treatment was introduced in 1992 and approved by the U.S. Food and Drug Administration in 1995 for treating high risk or inoperable aneurysms. Although less than 25 percent of patients in the United States are admitted to hospitals where endovascular coiling is an option for them, the treatment has gained wide acceptance worldwide and has been used in more than 125,000 patients.

In the procedure, a catheter is inserted into the femoral leg artery, navigated through the vascular system through fluoroscopic guidance, and into the brain aneurysm. Tiny, "slinky like" platinum coils then are threaded through the catheter and deployed into the aneurysm to fill it and obstruct blood flow.

Demetrius Klee Lopes, MD, a neurosurgeon at Rush Presbyterian Medical Center, Chicago, likens the process to a road system. Entering the artery in the leg to gain access to the arterial system is like getting to the expressway via the fastest route. The femoral artery's proximity to the skin makes it easy to access.

"Once you get to the expressway, you'll have access to where the aneurysm is located," Dr. Lopes said. "You have a tunnel that will allow you to go in and out of the area, deliver the coils and get your procedure done."

Constant fluoroscopic imaging allows the surgeons to see immediate results of their therapy. The procedure also offers flexibility in patient preparation; some patients remain awake for the procedure while others are sedated. Once the surgeons are satisfied with the position of the coil, it is detached and the procedure is completed.

"The coil can be retrieved at any time," Dr. Lopes said. "You can pull it out and choose another size. You are not committed to the treatment until you detach the coil."

At the end of the procedure, the catheter is removed and the patient is left with a small incision in his groin where the arterial puncture was made.

The study's endovascular patients, who were followed for one year after the procedure, were treated using coils developed by Target Therapeutics, Fremont, Calif., now a division of Boston Scientific, Natick, Mass; Micrus Corp., Mountain View, Calif.; and Cook Inc., Bloomington, Ind.

"This study suggests that improved outcomes for all of these patients can be gained should they be referred to hospitals where both endovascular coiling and traditional surgical techniques are available," Dr. Strother said. "I think this trial will effect that change and, as a result, we'll see a change in the way rup-

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tured aneurysms are treated in the United States."

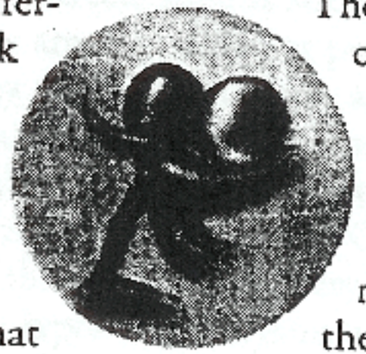
More research needed

Although members of the interventional radiology and neurosurgery community widely agree that ISAT is a historical study, some have raised concerns about the data.

Robert E. Harbaugh, MD, FACS, director of cerebrovascular surgery at Dartmouth-Hitchcock Medical Center, Lebanon, N.H., and president of the Cerebrovascular Section of American Association of Neurosurgery, said the study needs further analysis.

"There's unlikely to be a huge difference based on geography but it should be noted that this was primarily a European study," Dr. Harbaugh said. "I think there were only a couple of patients from the United States that were entered. And if there's a difference in the experience of the vascular neurosurgeons at the neurovascular centers, that may make a difference."

For example, how many aneurysms per practitioner were clipped versus how many aneurysms per practitioner were coiled? If those two numbers are greatly different, there's a concern that the risk reduction with coiling may not represent any difference in the procedure per se but in the experience of the practitioner, Dr. Harbaugh said.



Also, Dr. Harbaugh worried that patients who undergo surgical clipping may think they are getting second-rate care. Although 2,100 patients were randomized because their cases were appropriate for either therapy, most patients who were considered for treatment in the ISAT study actually went to surgery.

"There will always be the need to clip some aneurysms; there will always be the need to coil some aneurysms," Dr. Murphy agreed. "If we focus on the group that can be treated either way, again, there just has to be a balanced discussion about what the right thing might be for that particular person. The person's age and other factors will come into the picture."

Finally, long-term follow-up research is needed, Dr. Harbaugh said.

"I think it's encouraging that the rebleed rate after one year in both the surgical and the endovascular treatment groups is very low, but to really know which treatment option is safer for patients, over the course of a lifetime, you need to follow the patients much longer than one year," he said. ■

Sarah Long is an assistant editor at ADVANCE. *She can be reached at* slong @merion.com