

NEUROSCIENCES UPDATE

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Mayo Clinic Awake Surgery Team's Success Based on Collaboration of Advanced Neuroscience Specialties



Fredric B. Meyer, MD

"Awake brain surgery" refers to the advanced neurosurgical procedure that keeps the patient alert and responsive at various times during aggressive resection of infiltrative tumors such as gliomas and epileptic foci. Having the patient awake helps the surgical team more precisely locate the interface between the tumor and functionally eloquent

cortical and subcortical white matter tracts, thus facilitating aggressive resection with acceptable neurologic morbidity in the hope of improving patient prognosis.

At Mayo Clinic, awake mapping is combined with computer-guided stereotactic surgery because many brain lesions can be best defined with image guidance. "This feature makes the Mayo Clinic approach unique," explains neurosurgeon Fredric B. Meyer, MD. "It's uncommon to combine 2 technologies, awake surgery and computer guidance, for resection of tumors and seizure foci in the brain or deeper structures, but because of our multidisciplinary team focus at Mayo Clinic, this technique has become one of our specialties."

Awake surgery is typically used for resection of gliomas because they usually have an infiltrative zone that may extend into functional regions, both cortical and white matter tracts (Figure 1). "We would not use this approach for a tumor that has sharp demarcations," notes Dr Meyer. The Mayo Clinic team has performed hundreds of awake surgeries, and patients appear to tolerate the procedure well. Despite the functionally vulnerable location of the tumors resected by awake surgery, long-term, lifestyle-altering functional deficits have occurred in less than 15% of patients.

Mayo Clinic neuroscientists developed many of the procedures used during awake surgery. They also helped refine the array of neuroscience specialties required in the operating room to assure the seamless collaboration that produces successful surgical outcomes. In addition to the neurosurgeon and staff, several more neuroscience personnel may be in the operating room conversing with the patient during the resection. By continually monitoring neurologic performance, they help the surgeon identify the margins of the functionally eloquent brain tissues. In patients undergoing resection in the dominant hemisphere, it is typical to map both language and movement.

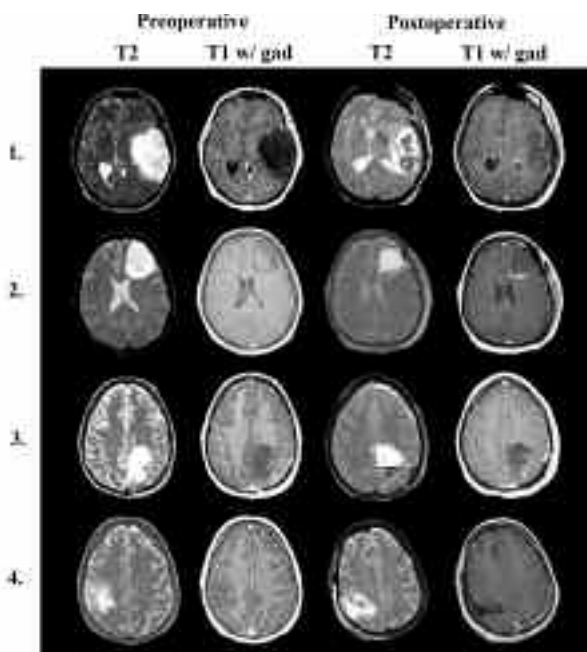


Figure 1. Pre- and postoperative brain scans, with and without gadolinium contrast. These films show 4 different patients with infiltrative gliomas before surgery. Postoperative scans of the same patients show all 4 have good neurologic function after surgery. Some patients may experience weakness after surgery because of edema, which is treated during rehabilitation therapy.

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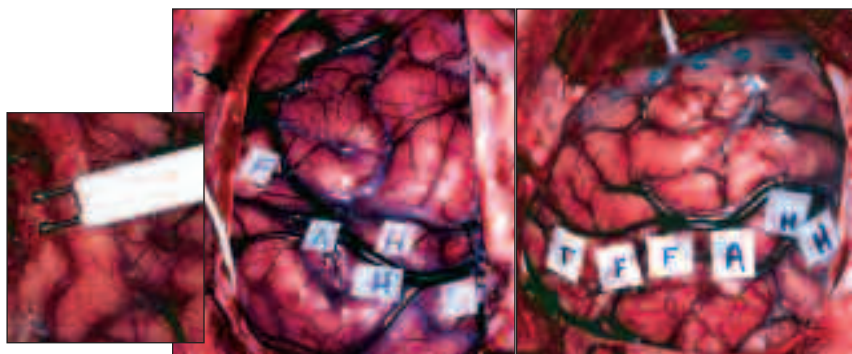


Figure 2. Functional mapping. The surface of the brain is stimulated to identify and map the primary and motor cortex. This allows the surgeon to remove the most tumor and infiltrative tumor zone without damaging functional tissues. The patient is sedated yet awake and able to respond to commands from the intraoperative monitoring team. Based on the patient's responses, the surgical team evaluates function and maps the area of the brain involved in generating the response. A, proximal arm; F, fingers; H, hand.

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The group of specialists may include

- a neurologist to monitor and assess motor and neurologic function during brain stimulation and to alert the surgeon if function begins to be compromised.
- a speech pathologist to perform intraoperative monitoring of language ability when the surgery is proximate to language regions. This complex testing assesses both reading and speech abilities.
- language translator(s) when the patient is multilingual to assess preservation of language competencies.
- a neuroanesthesiologist specially trained to keep the patient comfortable, yet alert enough to respond to tests evaluating neurologic functioning.
- a computer engineer to assure the accuracy of the computer-guided systems.

The Awake Surgery Advantage

Most neurosurgeons can look at an MRI scan and estimate the location of the primary motor or language cortex. To increase precision, functional MRI scans can be obtained before surgery to confirm these locations. But the distinct advantage of the intraoperative monitoring performed by the surgical team at Mayo Clinic is that it helps prevent disruption of connecting white matter tracts between cortical regions. Currently there is no good way to track these anatomic connections with imaging studies. "Therefore, intraoperative monitoring, with assessment of motor, sensory, and language function, minimizes the risk of neurologic injury associated with aggressive resection," Dr Meyer says.

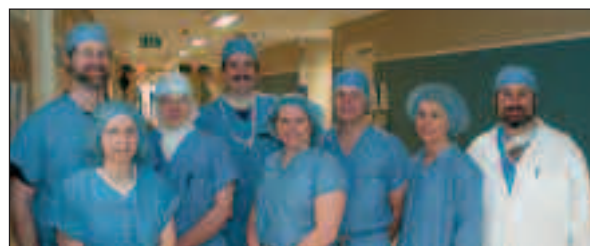
The Procedure

Before the operation, the brain is imaged with MRI techniques. The MRI data are entered into a computer where they produce images of the brain used during the operation to identify the surgical target in 3 dimensions. At the start of the procedure, the patient's head is secured in a pinion to assure stereotactic accuracy. The anesthesiologist in attendance ensures that the patient is sedated but still alert enough to answer questions, read, raise a hand, or otherwise cooperate with the various intraoperative monitoring examinations that assess function while the surgeon stimulates the brain (Figure 2). On the basis of the patient's responses, the awake surgery team evaluates function and maps the area of the brain involved in generating the response. This allows the surgeon to remove the most tumor and infiltrative tumor zone without damaging functional tissues.

During cortical stimulation, electrocorticography is performed to ensure that the stimulation does not induce a seizure, even though the patient is on anticonvulsive medication. Throughout the procedure, the neuroanesthesiologist must be vigilant for signs of patient distress, discomfort, and evidence of cortical irritability.

In awake surgery involving epilepsy foci, the plan may be to purposefully reproduce the patient's seizure in a controlled setting to guide placement of grids for additional mapping. Once again, the goal is to perform an aggressive resection of seizure foci.

"Mayo Clinic's technique of awake surgery with intraoperative monitoring is necessarily a team approach required by the very structure of the brain itself," Dr Meyer explains. "Much of brain function relates to connections and the integrity of these connections. Without a way to image these connections, awake surgery provides us with a way to monitor the function of all these related connections. Innovative advances such as the merger of stereotactic surgery and cortical and subcortical mapping are critical to achieving excellent clinical outcomes."



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Comprehensive Epilepsy Center Helps Women With Epilepsy Have Safe, Successful Pregnancies and Healthy Babies



Gregory D. Cascino, MD, and Jeffrey W. Britton, MD

Epilepsy in women is very common, with an estimated 180,000 new cases diagnosed each year in the United States. The prevalence in both men and women ranges from 1% to 4%. Irrespective of patient sex, the goals of all epilepsy treatments are the same: to help the individual become seizure free, to avoid adverse drug effects, and to improve the patient's quality of life.

Says Gregory D. Cascino, MD, chair of Mayo Clinic's Division of Epilepsy in the Department of Neurology: "Epilepsy is present in more than 1 million women in the United States, and the vast majority of them—more than 90%—have successful pregnancies if 4 practices are followed before and during pregnancy."

1. Seek and receive high-risk prepregnancy counseling with a physician who specializes in epilepsy to select one—not multiple—antiepileptic drugs for managing seizures.
2. Take supplemental folic acid daily.
3. Refrain from alcohol and tobacco use.
4. Seek and receive high-risk obstetric care.

Dr Cascino and his colleague Jeffrey W. Britton, MD, both emphasize the importance of prepregnancy counseling. The goal is to see that medications taken are the best ones for controlling the patient's seizures without causing adverse effects that could harm the developing fetus or the breast-fed infant. Says Dr Britton: "Because it is not advisable to deprive these women of antiepilepsy medications during pregnancy, the physician needs to be alert for potential interactions between antiepileptic drugs and women's changes during pregnancy."

Concerns About Birth Defects

Many women have poor compliance with medications during pregnancy because of concerns about birth defects. Patient education can change this, Dr Cascino notes. The incidence of birth defects in children born to women with epilepsy is only slightly higher—4% to 6%—than the incidence of birth defects in infants born to women without epilepsy—2% to 3%.

Teratogenesis is not a specific syndrome. Rather, it has multiple factors. Concerns about children born to women with epilepsy include neural tube defects, developmental delay, and major malformations such as oral facial clefts, midline heart defects, polydactyly, clubfoot, and hypospadias. Minor malformations include epicanthal folds, hypertelorism, long philtrum, small nails, and delayed ossification.

All antiepileptic drugs are potential teratogens, although most involve minor anomalies. Neural tube defects are related to older antiepileptic drugs, carbamazepine (0.5%) and valproate (1%-2%). Risks of newer drugs—gabapentin, lamotrigine, levetiracetam, oxcarbazepine, tiagabine, topiramate, and zonisamide—are unknown. What is known is that the risk of teratogenesis is less when monotherapy is used. A 2001 study published in the *New England Journal of Medicine* demonstrated that major anomalies occurred in the infants born to 4.5% of the pregnant women taking 1 drug and 8.6% of the pregnant women taking multiple drugs. Therefore, Mayo Clinic supports monotherapy practices.

One way to reduce the risk of birth defects is to take a multivitamin with folic acid. The optimal daily dose of folic acid is 0.36 to 5 mg. "However, there are still questions about folic acid benefit," Dr Cascino says. "Antiepileptic drugs appear to impair folic acid absorption, which is why it is so important to optimize the antiepileptic drug regimen before pregnancy. Prenatal testing for neural tube defects should be done if the patient is receiving valproate."

Interactions of Hormones and Antiepileptic Drugs

Women with epilepsy using hormonal forms of contraception have 2 major concerns: contraception failure and uncontrolled seizures.

Contraception failure may occur in 6% of women with epilepsy who are taking hormonal birth control agents. In addition, women who are using a hormonal form of birth control may have breakthrough bleeding because of interactions with antiepileptic medications. Moreover, hormonal interactions are not limited to oral contraceptives. They also occur in women using

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hormonal implants, patches, injections, and any other birth control method that delays ovulation. Most undesirable hormonal interactions occur with phenytoin, phenobarbital, and carbamazepine. Therefore, if women intend to use hormonal birth control agents, they need to use only 1 antiepileptic drug, namely, valproate, gabapentin, lamotrigine, tiagabine, or levetiracetam.

The second concern about hormone–anti-

epileptic drug interaction is that it will lead to failure of seizure management. Antiepileptic drugs that have reduced efficacy in managing seizures when combined with hormonal agents are phenobarbital, phenytoin, carbamazepine, felbamate, and oxcarbazepine. Topiramate at higher doses may also reduce the efficacy of oral contraceptives.

The Effectiveness of Minimally Invasive Lumbar Discectomy via Tubular Retractors in Selected Patients

Minimally invasive disk surgery is a safe and effective alternative to conventional incisional disk surgery. Developed about 5 years ago, its use is becoming more common as more neurosurgery centers invest in the technology and train surgeons in the procedure and as more patients benefit from it. Approximately 90% of patients experience relief of symptoms as a result of minimally invasive lumbar discectomy and literally walk away from the surgery the same day with only a small bandage covering the small incision made to introduce the specialized instruments.

Typically performed with the patient under general anesthesia, minimally invasive surgery is appealing to many patients because it eliminates a hospital stay and enables them to resume light activity in 2 weeks and full activity in 6 weeks. “We’ve spent a fair amount of time looking for alternatives to the conventional disk surgery, and

this is the first one that has measured up to our standards,” says Mayo Clinic neurologic surgeon William E. Krauss, MD. Adds his colleague, neurologist J. D. Bartleson, Jr, MD: “Mayo Clinic’s integrated practice allows the patient to have a medical evaluation on day 1, see the spine surgeon on day 2, have surgery on day 3, and, after minimally invasive surgery, go home on day 4. This results in very high patient satisfaction.”

History of Minimally Invasive Disk Surgery

Attempts to reduce both the surgical trauma and the recovery period have fallen into 1 of 2 broad groups: intradiskal and open surgical approaches.

Various intradiskal methods have been tried. They include chemonucleolysis, percutaneous manual nucleotomy, automated percutaneous lumbar discectomy, laser discectomy, and intradiskal electrothermal annuloplasty. As outpatient procedures, these are the least invasive approaches and carry the lowest risk. Their limitations range from being based in part on faulty scientific concepts to having unacceptably high recurrence rates, lacking long-term follow-up data, and being vulnerable to misuse. In addition, some of the clinical data supporting their use are compromised by conflict of interest, because some of the data were developed by the makers of the technology.

Variations on open surgical approaches have included endoscopic discectomy and the minimally invasive approach favored by Mayo Clinic neurologic surgeons using tubular retractor technology. These approaches have several advantages:

- They are technically similar to accepted open discectomy surgical techniques.
- Recurrence rates are acceptably low.
- Incisional trauma is reduced.
- The hospital stay is reduced or eliminated.
- The rate of complications is lower than that of standard open surgery.

Its disadvantages are that the procedure is still invasive, although less so than standard

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discectomy, and it requires advanced training and special equipment.

Selection of Patients for Minimally Invasive Discectomy

As attractive as minimally invasive disk surgery attributes are, the procedure is not effective for every patient with a herniated disk. Careful selection is necessary to determine which patients will benefit from physical therapy or conventional surgery. Patients for whom minimally invasive disk surgery is not indicated have local spinal anatomy irregularities or involved pathology that contraindicate the minimally invasive approach. Those best suited for it usually meet 2 criteria: 1) they have not had previous disk surgery and 2) their clinical syndrome is well defined.

If those 2 criteria are met, this approach is generally applicable to patients of all ages, although very elderly patients might require special consideration. Although success rates are good with obese patients, the perfect patient for this procedure is a young athlete, ie, an active patient in pain. Yet many patients in between these 2 extremes fare extremely well with this procedure.

An Illustrative Case

An example helps illustrate this point. A 42-year-old female marathon runner was confined to the couch 10 days before she presented to the emergency department. For several months, she had experienced progressive right hip, posterior thigh, and calf pain. The pain was described as intermittently “shooting and aching.” There were some paresthesias and numbness, especially in the sole of the foot. She had no bowel or bladder symptoms. Minimally invasive lumbar discectomy was successful in resolving her pain (Figure 1).

Mayo Clinic neuroscience physicians are ideally suited to evaluate candidates for minimally invasive disk surgery because of the comprehensive, multispecialty depth within the department and their considerable experience with the procedure. In the patient described, the multidisciplinary team’s evaluation determined that motor function was intact. She had a negative straight leg raise, but lumbar extension reproduced

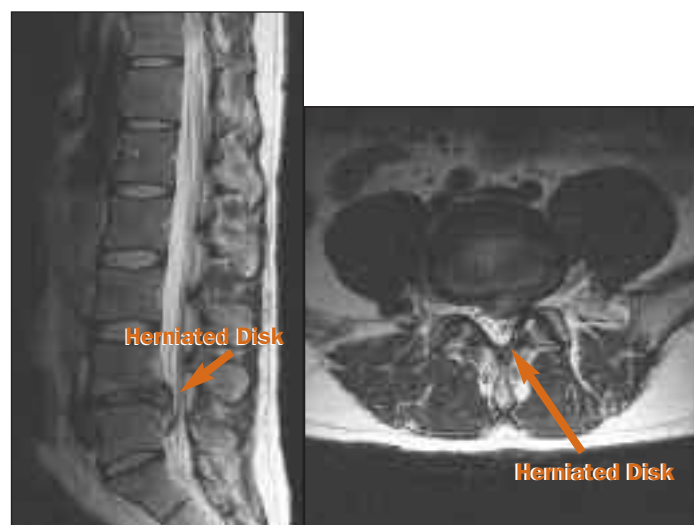


Figure 1. Preoperative MRI scans of a 42-year-old female marathon runner. She had progressive right hip, posterior thigh, and calf pain described as intermittently “shooting and aching.” Left lower leg pain with L5 radicular symptoms were refractory to chiropractic manipulation, analgesics, and nonsteroidal anti-inflammatory drugs. Minimally invasive lumbar discectomy was successful in resolving pain.

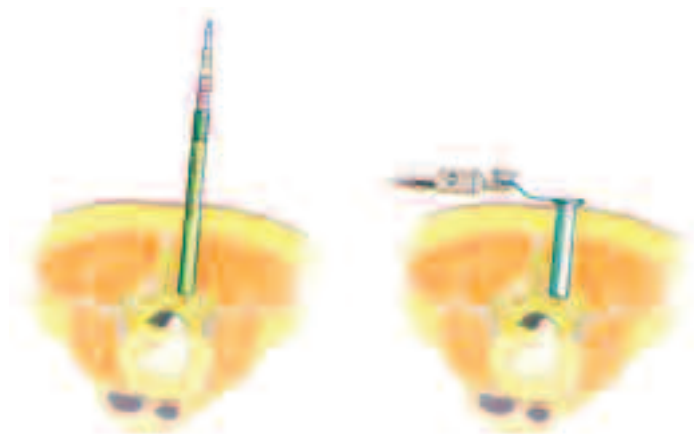


Figure 2. Apparatus and technique. Left, Contact is made with the injured area, which is enlarged with serial dilators. Right, A tubular retractor holds the wound open. An operating microscope is then used to drill a hole in the bone, 2 cm in diameter, through which the disk fragment is removed.

the left lower leg pain. She had diminished sensation to pinprick along L5.

Because conservative medical treatment failed, surgical options were considered. She was deemed well suited to minimally invasive surgery. A standard parasagittal incision was made; dilators were used to split the paraspinal musculature. A tubular retractor was placed on the left L4 hemilamina. A left L4 inferior hemilaminectomy and L4-5 medial facetectomy were performed, as was excision of synovial cyst. An L4-5 foraminotomy

was performed. Closure consisted of a single-layer suture, adhesive skin closures, and a small bandage.

Minimally Invasive Diskectomy Surgical Technique

A specialized apparatus is used to perform minimally invasive diskectomy. At Mayo Clinic, it consists of an operating microscope, flexible arm assembly, progressively larger-diameter dilators, and tubular retractors (Figure 2). A 1.5-cm midline incision is made to accommodate a guidewire directed by fluoroscopic images to

the injured disk. Dilators are inserted to perform a lateral-motion step referred to as “twisting and sweeping.” With the aid of the assembly arm, sequential dilation is performed to enlarge the contact. Tubular retractors are then inserted to hold the wound open. An operating microscope is used to drill away a 2-cm-diameter opening in the bone through which the disk fragment is removed. Neurosurgeons have performed more than 100 such procedures at Mayo Clinic in Rochester

Mayo Clinic Investigates New Approach to Surgical Revascularization of Carotid Artery Occlusions



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Between 10% and 15% of patients who present with a stroke or a transient ischemic attack (TIA) also have carotid artery occlusion. Carotid artery occlusion contributes to an estimated 61,000 first-ever strokes and 19,000 TIAs per year. Some of these patients may benefit from a new form of carotid occlusion bypass surgery that restores blood supply to revascularize the brain. The approach involves taking an extracranial artery from the scalp and surgically attaching it to a healthy portion of the intracranial carotid artery so it can provide blood flow to the brain.

The idea of surgically revascularizing the brain to treat occluded carotid arteries was first developed in the 1960s, but the current approach is new. When the early version of the technique was studied 20 years ago, a 1985 *New England Journal of Medicine* report determined the procedure was not effective. “However, we suspected that we were missing a group of patients who were not identified in that study who would in fact benefit from this operation,” says Mayo Clinic neurosurgeon John L. D. Atkinson, MD. “It’s a new era, and because of advances, we have the resources and technology to help develop new surgical options for treating carotid artery occlusion and identifying the patient population for whom it’s best suited.”

Adds his colleague neurologist Jimmy R. Fulgham, MD: “There are several developments that improve outcomes. One is that the technique



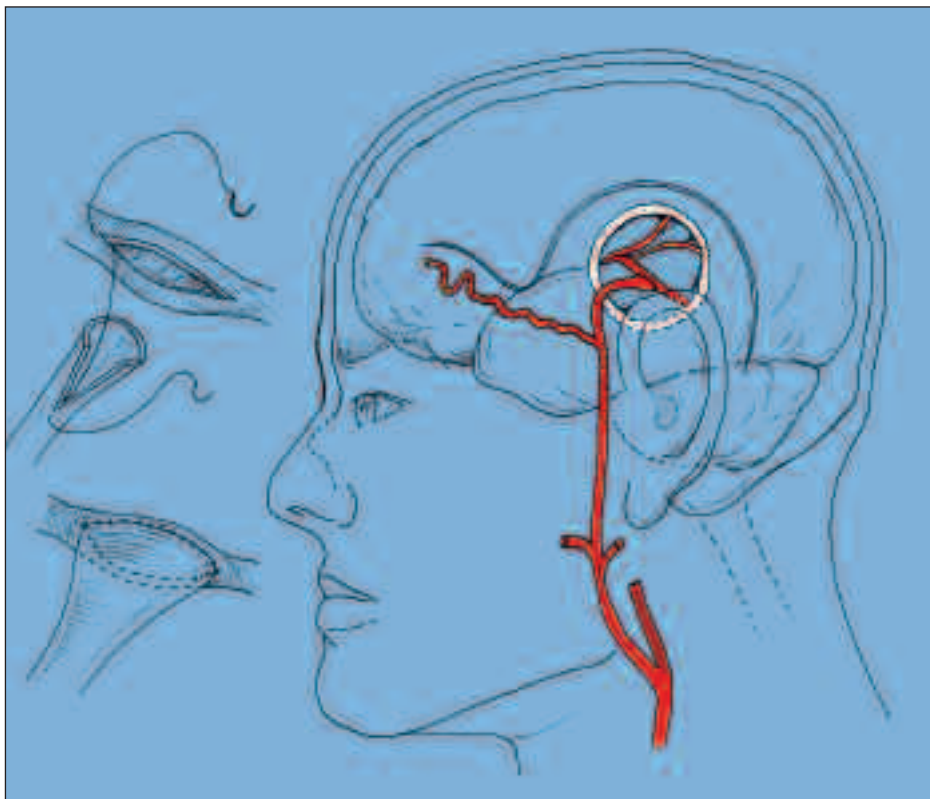
Jimmy R. Fulgham, MD

now under study is new, and another is that patients are evaluated and selected by advanced neuroimaging technologies that were not previously available.” Chief among the helpful new technology is the use of positron emission tomography (PET) with oxygen extraction. Obtaining

the oxygen extraction fraction measured by PET helps identify the subset of symptomatic stroke patients most likely to benefit from revascularization surgery.

The New Study: COSS

The National Institutes of Health (NIH) has mounted a large-scale multicenter study to systematically reexamine the possibility of successfully revascularizing blood flow in cases of carotid artery occlusion. Called the Carotid Occlusion Surgery Study, or COSS, the study involves 25 “centers of excellence” in the United States. The Department of Neurology and the Department of Neurologic Surgery at Mayo Clinic are one of these centers. Patient recruitment is now under way. The COSS design calls for a total of 930 patients. During the 3 years of the study, half the patients will be randomly assigned to the new surgical revascularization approach, and half will



In carotid occlusion bypass surgery, the neurosurgeon moves the extracranial superficial temporal artery from the scalp to bypass a blockage formed by an occluded internal carotid artery. The extracranial artery is surgically attached (inset) to the intracranial artery on the surface of the brain. This revascularizes the brain.

not have the revascularization surgery. Instead, they will receive the current best medical therapy such as physician-directed use of blood-thinning agents.

Because Mayo Clinic has such a large, advanced neurosurgical practice and its specialists collaborate across disciplines, Mayo is well suited to participate in the study. Notes Dr Atkinson: "We have a lot of experience in cerebral artery bypass, and we do bypasses frequently for other reasons and on a large scale, so it makes sense for us to make the best use of our extensive experience by participating in this trial."

The COSS hypothesis is this: Surgically moving the superficial temporal artery and attaching it to the middle cerebral artery—in conjunction with the best medical therapy—can successfully bypass the diseased or blocked artery. This revascularization approach can reduce by 40% subsequent ipsilateral ischemic stroke, either fatal or nonfatal, over the ensuing 2 years after surgery.

If data support this hypothesis, the procedure could positively affect a large number of people.

An estimated 730,000 Americans have a stroke each year and 80% of the strokes are ischemic.

Imaging Advances

A key difference between the 2005 attempts to revascularize the brain and 1985 efforts is the availability of new imaging technology. In particular, PET with oxygen extraction is useful in determining whether the brain is at risk of stroke. The advantage of a PET scan is that it can image oxygen levels in the brain to give an accurate assessment of the brain in jeopardy and at risk of stroke. If the PET scan reveals increased oxygen extraction, about 33% of these patients develop stroke. Says Dr Atkinson: "The Mayo Clinic team has both the experience and the technology to determine whether revascularization under these new and improved circumstances is possible."

Eligible Patients for COSS

To recruit COSS participants, Mayo Clinic physicians are currently screening patients who have symptomatic unilateral carotid occlusion, as determined by various vascular imaging techniques. Symptoms of this condition include transient loss of vision in 1 eye; numbness or weakness of the arm, leg, or face; and slurred speech. Vascular imaging techniques that can confirm the diagnosis include Doppler ultrasonography, magnetic resonance angiography, CT angiography, or intra-arterial catheter arteriography. The symptoms must be observed by a clinician no more than 120 days before performance of PET. On meeting entrance criteria, patients are eligible to undergo PET. If PET results meet the criteria for ipsilateral increased oxygen extraction, then arteriographic criteria must be met for a patient to be eligible for randomization.

Says Dr Atkinson: "Early referral upon symptoms of carotid occlusion is, of course, essential. But when it's not possible, or if the patient's physician is not sure what to do, then we'd like to talk with the referring physician on the phone or see the patient to perform the basic evaluation here. We can give these patients the best treatment available and also determine if they're eligible to participate in COSS if they are so inclined."

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