Beyond the Status Quo: Technical Advances in Neurosurgery

Mayo Clinic offers the latest technology in neurosurgery to maximize patient safety and outcomes. Technical advances are thoughtfully integrated into all aspects of neurosurgical care, from workup and diagnosis through surgery and postoperative care.

“Mayo Clinic is never satisfied with the status quo. We use the latest technology to improve patient outcomes and quality of life,” says Alfredo Quinones-Hinojosa, M.D., chair of Neurosurgery at Mayo Clinic in Jacksonville, Florida.

Technical advances at Mayo Clinic include:

- Deep brain stimulation (DBS) and sub-threshold cortical stimulation
- Laser ablation to treat focal epilepsy
- Focused ultrasound to treat essential tremor
- The first clinical 7-tesla MRI scanner in North America approved by the Food and Drug Administration (FDA)
- Magnetic resonance elastography (MRE) to determine intracranial tumor consistency
- Intraoperative navigation and awake craniotomy to lower risk and maximize the resection of lesions
- Presurgical simulations to enhance the safety of procedures
- Cryoablation, laser ablation and other minimally invasive approaches for tumor treatment
- Cutting-edge treatments for endovascular conditions

Before adopting new technologies, Mayo Clinic assesses the impact on patient care. “It’s important to embrace new technology. But it’s equally important to avoid investing in technologies that don’t improve patient care in a meaningful way,” says Bernard R. Bendok, M.D., chair of Neurosurgery at Mayo Clinic in Phoenix/Scottsdale, Arizona.

Mayo Clinic also has a technology development manager to facilitate the translation of neurosurgeons’ ideas and innovations into patient care. “Our approach is to take a step back and consider the unmet needs of patients, the existing therapies or tools we have to treat these patients, and what an innovation might provide to advance the practice and patient care,” says Justin T. Koepsel, Ph.D., a technology and intellectual property development manager at Mayo Clinic in Rochester, Minnesota. “When we identify innovative solutions, Mayo has the expertise to translate from concept to practice, with a rich history of entrepreneurship and industry partnership.”

Enhanced capability to treat epilepsy

Mayo Clinic is at the forefront of new technologies that advance care for patients with medically refractory epilepsy. “There are very few epilepsies that we can’t treat,” says Jamie J. Van Gompel, M.D., a neurosurgeon at Mayo Clinic’s campus in Minnesota.

DBS of the anterior nucleus of the thalamus, recently approved by the FDA for the treatment...
DBS of the anterior nucleus of the thalamus increases connectivity in the default mode network, raising the threshold for seizure propagation (Figure 1, see page 1). The researchers note that an inhibitory effect on the hippocampus may also contribute to seizure suppression. In a separate study, Mayo researchers describe a novel use of Fast Gray Matter T1 Inversion Recovery (FGATIR) MRI to improve visualization of the input into the mammillothalamic tract, which may be the true effective site of treatment.

Chronic subthreshold stimulation of the cortex, which acts earlier than conventional neurostimulation devices to prevent seizure onset, is another treatment pioneered at Mayo. “We’re describing new approaches for DBS that we think can have significant benefits for patients. A better understanding of the mechanism of action will also potentially improve DBS targeting,” Dr. Van Gompel says.

Imaging innovations
Mayo Clinic has long been an early adopter of new imaging technology. The 7-tesla MRI allows for enhanced visualization of pituitary tumors, multiple sclerosis lesions and sources of seizure activity. MRE, which was developed at Mayo Clinic, is used in preoperative assessments to measure tumor consistency and adherence to surrounding tissue — information critical to guiding the surgical approach.

Sophisticated intraoperative navigation and awake craniotomies facilitate less-invasive surgeries. These techniques help lower the risk to eloquent motor and sensory tissue as well as the cortical speech area. Awake craniotomy is used for selected tumor and epilepsy resection and treatment of moyamoya disease.

“Awake craniotomy that is performed by experienced hands can result in more extensive resection, and shorter hospitalizations and better outcomes for patients,” Dr. Quinones-Hinojosa says. He is exploring an initiative aimed at improving the patient experience during awake surgery through music and eyeglasses that provide pleasant visualizations.

Mayo Clinic also has the capability to simulate disease behavior and complex surgeries via computer and 3D-printed models of patients’ anatomy. “This allows us to assess various options in a risk-free environment and to help patients make the most well-informed decisions possible,” Dr. Bendok says. “Simulating diseases and operations also allows for device innovation. Our neuroscience innovation and simulation center is creating new devices and approaches that we hope will serve patients well.”

Tumor and endovascular treatments
Mayo Clinic strives to provide minimally invasive approaches whenever appropriate. Cryoablation is used to treat selected tumors in the spine and skull base — an approach that can be particularly helpful if the patient has had previous surgery in the area. Laser ablation can be used to treat recurrent tumors.

Surgery using a tubular retractor system can substantially lower the risk of damaging eloquent tissue during the removal of certain lesions (Figure 2). “This is a challenging procedure. But we have the appropriate teams and tools to remove tumors through a tube without performing a large craniotomy,” Dr. Quinones-Hinojosa says.
For patients with intracranial aneurysms, Mayo’s neurosurgeons offer modified eyebrow incisions, endoscopic skull base surgery, and transnasal and transcranial endoscopy, aided by neuronavigation technology. “We are now treating aneurysms that were once thought to be untreatable,” Dr. Bendok says. “Because of our depth and breadth of expertise, we have neurovascular surgeons who can perform whatever a patient with an endovascular condition needs — including extracranial to intracranial bypass, coiling, stenting or microvascular procedures.

“Mayo Clinic’s focus is always on doing what is best for patients,” he adds. “Our hope is that increasingly effective neurosurgical technology and interventions will help alleviate suffering and improve quality of life.”

Cavernous Angiomas: Infrastructure for Future Drug Trials

Kelly D. Flemming, M.D., a neurologist at Mayo Clinic in Rochester, Minnesota, answers questions about Mayo’s work to facilitate clinical trials of candidate therapeutics for these rare but disabling cerebrovascular abnormalities (Figure).

Q: Why is Mayo Clinic participating in a multicenter effort to improve treatment for cavernous angiomas?

Currently, the only treatments for brain cavernous angiomas are observation and surgery. Both provoke understandable anxiety, and patients often ask if there’s another option.

Brain cavernous angiomas with symptomatic hemorrhage are rare — there are fewer than 200,000 cases in North America today — but they can re-bleed and pose a heavy burden of neurological disability. What’s especially difficult for patients is that although we know what percentage of people with certain cavernous angiomas will re-bleed, we can’t yet tell if a specific patient is likely to bleed again.

Because cavernous angioma is a rare disease, multiple centers need to work together to achieve adequate patient numbers so we can solve the puzzle as to why these abnormalities form, why some are symptomatic and others aren’t, and which patients might benefit from treatments other than surgery.

Q: When might clinical trials of new therapies start?

A number of candidate therapeutics have emerged that will require clinical trials, probably in the next one to five years. Drugs have been tested in animal models of cavernous angioma and have been found to reduce the leakiness of the malformation and reduce lesion burden.

Q: What preparation is needed for future multicenter clinical trials?

It’s important to develop an infrastructure for these future clinical trials. The ability to screen, enroll and risk-stratify people with symptomatic cavernous angioma has never been assessed prospectively at multiple sites. Imaging and laboratory biomarkers and outcomes instruments need to be evaluated for their reliability and harmonized at multiple sites.

Q: How is Mayo Clinic helping to build that infrastructure?

We are participating in a multicenter clinical trial readiness study, funded by the National Institutes of Health, to construct workable models for future therapeutic trials.

Mayo Clinic’s contribution to the clinical trial readiness study is severalfold. We’ll be the lead center evaluating the re-bleed risk in patients enrolled to determine if imaging biomarkers or patient-reported outcomes should be used as endpoints in clinical trials. The imaging that we’re investigating is specialized MRI — dynamic contrast-enhanced quantitative perfusion (DCEQP) and quantitative susceptibility mapping (QSM). DCEQP and QSM provide information about the leakiness of the cavernous angioma and the iron content.

In addition to Mayo Clinic, the other institutions involved are the University of Chicago, Johns Hopkins University, Barrow Neurological Institute, the University of New Mexico, the University of Utah and the University of California, San Francisco.

Q: What strengths does Mayo Clinic bring to this NIH-funded research?

Cavernous angiomas are rare, even for general neurologists and neurosurgeons. Mayo Clinic’s campus in Minnesota has been designated a Center of Excellence by the Angioma Alliance, a patient advocacy group. As a major neurological center, Mayo Clinic has the patient volume, clinical expertise and research capability to study this rare condition.
Spinal Oncology: Multidisciplinary Approach for Complex Care

Mayo Clinic has the multidisciplinary, subspecialized expertise to manage care for people with even the most complex intradural and vertebral tumors, including both primary and metastatic disease (Figure). Depending on the type of tumor, treatment at Mayo might involve multidisciplinary en bloc resection, minimally invasive surgery, separation of the tumor from the spinal cord or proton beam therapy. These approaches are available at all three Mayo Clinic campuses.

“Spinal oncology problems can be very complicated and truly require a multidisciplinary team. When a patient comes to Mayo Clinic, his or her case is evaluated by a team that includes a neurological radiologist, medical oncologist, radiation oncologist and spinal surgeon. Other specialists are involved as needed. We then discuss our recommendations with the patient and tailor a unique treatment plan for that individual,” says Matthew T. Neal, M.D., a neurosurgeon at Mayo Clinic in Phoenix/Scottsdale, Arizona.

Spinal tumors are often aggressive and debilitating, causing significant pain and rapid development of neurological problems. Patients can progress to paraparesis, which typically affects bowel and bladder function and increases the risk of decubitus ulcers, deep vein thrombosis and pneumonia.

“These patients have tremendous quality-of-life issues. We have a group of surgeons with the expertise to treat these tumors aggressively when appropriate,” says Maziyar A. Kalani, M.D., a neurosurgeon at Mayo Clinic’s campus in Arizona.

Mayo Clinic’s expertise in spinal oncology encompasses all types of spinal tumors. If a tumor-related syndrome is suspected, geneticists are part of the treatment team. Mayo Clinic has a Neurofibromatosis Clinic and a von Hippel-Lindau Clinic with the range of specialists needed to manage patients with these syndromes.

Mayo Clinic also has neurosurgeons who subspecialize in spinal surgery. “Some types of spinal tumors are encountered very infrequently. Subspecialized training in spinal surgery is a very big advantage in treatment of these complex spinal cases,” says Jamal McClendon Jr., M.D., a neurosurgeon at Mayo’s campus in Arizona.

At Mayo, a multidisciplinary care team considers surgical and nonsurgical options for each patient, based on the type and location of the spinal tumor. “In some cases, when we know that radiation treatment is not very effective, we may be more aggressive resecting a tumor. We routinely use image-guidance technology, which can help maximize tumor removal and

Figure. A and B. Sagittal and axial T2 MRIs show a large metastatic lesion involving the thoracic cavity, ribs, spine and epidural space in a 67-year-old man with metastatic renal cell carcinoma. The patient experienced intractable back and thoracic radicular pain. After a preoperative embolization procedure to reduce the blood supply to the tumor, Mayo Clinic neurosurgeons worked with colleagues in cardiothoracic surgery to maximally debulk the tumor and stabilize the spine with T5–T11 instrumentation. C and D. Postoperative anteroposterior and lateral X-rays show the surgical results. The patient has remained ambulatory, and his preoperative pain symptoms have improved. He continues to receive adjuvant treatments.
Vascular Pathologies and Alzheimer’s Disease: Probing Genetic Pathways

Mayo Clinic is investigating genetic pathways that may contribute to both vascular pathologies and Alzheimer’s disease. Funded by the National Institutes of Health (NIH), the research involves analysis of changes at the cellular level as well as whole-brain tissue, in an effort to discover biomarkers and potential therapies for Alzheimer’s disease.

“We’ve known for some time that the risk factors that lead to cerebrovascular disease — such as hypertension, high cholesterol and diabetes — also increase the risk of dementia, particularly Alzheimer’s disease. We need to identify the pathways that may be influencing both before we can generate new therapies for Alzheimer’s,” says Nilufer Ertekin-Taner, M.D., Ph.D., a neurologist and neurogeneticist at Mayo Clinic in Jacksonville, Florida.

Mayo’s research, funded by two grants totaling about $9.3 million, is part of a major NIH venture known as the Molecular Mechanisms of the Vascular Etiology of Alzheimer’s Disease (MOVE-AD) Consortium. The multicenter effort seeks to build a nuanced model of Alzheimer’s disease that more accurately reflects its many causes and pathways.

Far-reaching impact

Mayo Clinic’s MOVE-AD research takes a novel approach, with parallel work occurring in patients and in laboratory models.

Under the initial grant, Mayo’s Genetics of Alzheimer’s Disease and Endophenotypes Laboratory, led by Dr. Ertekin-Taner, is analyzing brain tissue and blood samples from living patients with Alzheimer’s disease and varying levels of cerebrovascular pathology. The information about gene expression obtained from the patient samples is used to build mathematical models of the diseases. The mathematical models are then tested in laboratory animal and cell models developed in Mayo’s Neurobiology of Alzheimer’s Disease laboratory, led by Guojun Bu, Ph.D., who with Dr. Ertekin-Taner is a co-principal investigator on the NIH grants.

The Mayo researchers received an additional NIH grant in 2017 to investigate gene expression at the single-cell level. “We are generating a lot of data from whole-brain tissue. But in a disease as complex as Alzheimer’s, it’s critical for us also to understand the cell-specific changes,” Dr. Ertekin-Taner says. “We hope to identify the specific cell base changes in the brain that play a role in the vascular risk factors and also contribute to Alzheimer’s disease. We expect that looking at single cells will also allow us to capture an even larger number of changes than we see with whole-brain tissue.”

The single cells will be derived from fresh brain tissue from patients who have neurosurgery performed by Alfredo Quinones-Hinojosa, M.D., chair of Neurosurgery at Mayo’s campus in Florida and a co-investigator on this second grant.

Proton beam therapy is also a treatment option, particularly for tumors resistant to traditional radiotherapy. Proton beam therapy allows radiation delivery to conform more closely to the tumor.

“We are fortunate to have subspecialized expertise from our radiation and medical oncologists who help formulate the treatment plan, whether surgery is needed or not,” Dr. Neal says.

After surgery and adjuvant therapy, physiatrists work with patients to optimize pain control and rehabilitation. Long-term follow-up care is available at all three Mayo Clinic campuses.

“With every patient, our goal is to provide not only compassionate care but the highest quality of care,” Dr. Neal says.

Jamal McClendon Jr., M.D.

Nilufer Ertekin-Taner, M.D., Ph.D.

Alfredo Quinones-Hinojosa, M.D.
NIH grant. With patient approval, Mayo Clinic collects for research the tissue that otherwise would be discarded after neurosurgery.

“This research is very important for developing biomarkers that can allow us to design new therapies for a devastating disease,” Dr. Quinones-Hinojosa says. “This is the strength of Mayo Clinic — we partner with patients to take care of them and to find cures for their diseases so we can share our knowledge with the world.”

Working in parallel with the patient-samples research, Dr. Bu will perform single-cell data analysis in mouse models. “To our knowledge, this single-cell work is unprecedented,” Dr. Ertekin-Taner says. “Identifying specific cell-based expression changes is a major question not just in Alzheimer’s disease but also in other neurological conditions. Our data will inform the field in general, with impact far beyond our own project.”

Mayo Clinic’s breadth of expertise allows for its participation in major initiatives such as M’OVE-AD. “Team science can only happen where there are multidisciplinary teams, each of which is at the top of its game,” Dr. Ertekin-Taner says. “Our patients trust that we are going to be able to make a difference for these diseases — if not for them, then for the community. All of our work is laser focused on moving the field forward.”

**Figure.** Mayo Clinic’s research into genetic pathways of vascular pathologies and Alzheimer’s disease starts with gathering information about patient phenotypes and genomic data. That information is used to build mathematical models that are subsequently tested in laboratory animals and cell models, with the ultimate goal of developing therapies to benefit patients.

**Who’s New, What’s New**

Matthew T. Neal, M.D., recently joined the Department of Neurological Surgery at Mayo Clinic in Phoenix/Scottsdale, Arizona. Dr. Neal practices general neurologic surgery but has a particular focus on minimally invasive spinal surgery. Mayo Clinic is committed to minimally invasive approaches to spinal surgery whenever appropriate. Learn more about Dr. Neal and Mayo Clinic’s approach to minimally invasive spinal surgery at medprofvideos.mayoclinic.org.
Research Highlights in Neurology and Neurosurgery

Unified System for Staging Lewy Body Disorders

There are multiple neuropathological staging systems for the neurodegenerative disorders characterized by Lewy bodies, including Parkinson’s disease and dementia with Lewy bodies. But the Unified Staging System for Lewy Body Disorders (USSLB) is the first system to allow for nearly complete classification of all such disorders. Mayo Clinic researchers and colleagues found that the USSLB provides clear rules for classification, eliminating the arbitrary classification of borderline cases. The researchers used the Arizona Study of Aging and Neurodegenerative Disorders database to correlate motor and nonmotor clinical findings with the presence of Lewy-type synucleinopathy (LTS) in postmortem studies using the USSLB. The 280 cases in the study were categorized into one of five USSLB stages:

- **Stage I:** olfactory bulb only (8.6 percent of cases studied)
- **Stage Ila:** brainstem predominant (15.4 percent)
- **Stage Iib:** limbic predominant (13.6 percent)
- **Stage III:** brainstem and limbic (31.8 percent)
- **Stage IV:** neocortical (30.7 percent)

Subjects with stages III and IV died at a younger age. Clinically, 25.7 percent of the 280 subjects were cognitively normal, 8.6 percent had mild cognitive impairment and 65.7 percent had dementia. Multiple measures of motor parkinsonism and cognitive impairment, as well as hyposmia and probable rapid eye movement sleep behavior disorder, correlated with increasing USSLB stage. (Adler C, et al. Unified Staging System for Lewy Body Disorders: Clinicopathologic correlations. Presentation at: American Academy of Neurology Annual Meeting; 2018; Los Angeles, Calif.)

Seizure Semiologies and AED Therapy in LGI1-Ab Autoimmune Epilepsy

The role of anti-epileptic drug (AED) therapy in leucine-rich glioma-inactivated-1 ligand antibody (LGI1-Ab) autoimmune epilepsy (AE) is underemphasized and unclear. To characterize seizure semiology and the utility of AED therapy in this disease, Mayo Clinic researchers retrospectively reviewed the records of 56 Mayo Clinic patients who were LGI1-Ab-positive and who presented with seizures. Among those patients, 49 (88 percent) had more than one seizure type. The most common seizure semiologies were faciobrachial dystonic (experienced by 63 percent of patients studied), focal impaired awareness (52 percent), generalized tonic-clonic and focal aware nonmotor (both 50 percent). Thirty-eight patients in the study (68 percent) became seizure-free: 29 (76 percent) after treatment with immunotherapy, five (13 percent) with AEDs alone and four (11 percent) with AEDs after immunotherapy. Patients with faciobrachial dystonic seizures were more likely to respond to immunotherapy than to AEDs. There was no difference in the rates of response between immunotherapy and AEDs in patients who didn’t experience faciobrachial dystonic seizures. AEDs with sodium channel blocking properties were more likely than other AEDs to confer seizure freedom. (Lamb C, et al. Seizure semiologies and effects of anti-epileptic drugs in patients with leucine-rich glioma-inactivated-1 ligand antibody (LGI1-Ab) autoimmune epilepsy. Presentation at: American Academy of Neurology Annual Meeting; 2018; Los Angeles, Calif.)

Stem Cell Therapy for MSA Boosts Neurotrophic Factors

Recent insights into pathophysiological mechanisms in multiple system atrophy (MSA) suggest a critical role for neurotrophic factor deprivation. Mesenchymal stem cells (MSCs) have been shown in preclinical studies to secrete these factors. Mayo Clinic researchers have found that intrathecal administration of MSCs in people with MSA results in a marked, dose-dependent increase of neurotrophic factors in spinal fluid. The researchers recently completed a phase I/II dose-escalation trial using intrathecal MSC administration in MSA. Spinal fluid from 24 patients undergoing intrathecal delivery of adipose-derived autologous MSCs as part of that trial was collected at baseline as well as one and four weeks after MSC administration. Nerve growth factor (NGF) was undetectable or detectable only at low levels at baseline. Although there was no significant increase following MSC administration at the lowest dose-tier, NGF increased more than hundredfold by one week after MSC administration, with well-detectable levels for all patients in the medium-dose tier, and even higher levels in the high-dose tier. NGF levels decreased but remained markedly elevated four weeks after MSC administration. Brain-derived neurotrophic factor (BDNF) and glial-derived neurotrophic factor (GDNF) were undetectable at baseline but became detectable in one patient in the low-dose group after MSC administration. BNF was detectable in nine patients and GDNF in eight patients in the medium- and high-dose groups after MSC administration. (Singer W, et al. Intrathecal administration of autologous mesenchymal stem cells in multiple system atrophy results in growth factor spike. Presentation at: American Academy of Neurology Annual Meeting; 2018; Los Angeles, Calif.)

To read more about Mayo Clinic neurosciences research and patient care, visit [http://www.mayoclinic.org/medical-professionals](http://www.mayoclinic.org/medical-professionals).
Expedited Patient Referrals to Mayo Clinic
Departments of Neurology and Neurologic Surgery

While Mayo Clinic welcomes appointment requests for all neurologic and neurosurgical conditions, patients with the following conditions are offered expedited appointments:

1. Cerebral aneurysms
2. Cerebral or spinal arteriovenous malformations
3. Brain, spinal cord or peripheral nerve tumors
4. Epilepsy with indications for surgery
5. Carotid disease

Resources
MayoClinic.org/medicalprofs
Clinical trials, CME, Grand Rounds, scientific videos and online referrals

Contact Us
Mayo Clinic welcomes inquiries and referrals, and a request to a specific physician is not required to refer a patient.

Phoenix/Scottsdale, Arizona
844-292-8343 (toll-free)

Jacksonville, Florida
888-508-9912 (toll-free)

Rochester, Minnesota
844-627-7684 (toll-free)

Information and registration
Mayo Clinic in Rochester, Minnesota
Phone: 800-323-2688 (toll-free) or 507-284-2509
Email: cme@mayo.edu

Mayo Clinic in Jacksonville, Florida
Phone: 800-462-9633 (toll-free) or 904-953-0421
Email: cme-jax@mayo.edu

Mayo Clinic in Phoenix/Scottsdale, Arizona
Phone: 480-301-4580
Email: mca.cme@mayo.edu

Website: https://ce.mayo.edu/neurology-and-neurologic-surgery

Education 2018-2019 Neurology and Neurologic Surgery Continuing Medical Education Programs

2018 courses

**October**
- Mayo Clinic Neuroscience and Oncology Innovation Summit 2018
  - Oct. 18-20, 2018
  - The Ritz-Carlton Key Biscayne, Miami Key Biscayne, Fl.
- Mayo Clinic 10th Annual Stroke and Cerebrovascular Disease Review 2018
  - Oct. 25-27, 2018
  - The Ritz-Carlton, Amelia Island, Fla.

**November**
- Mayo Clinic Convergence Neuroscience 2018
  - Nov. 8-10, 2018
  - The Ritz-Carlton, Amelia Island, Fla.
- Microsurgical Approaches to Aneurysms and Skull Base Diseases 2018-November
  - Nov. 15-17, 2018
  - Mayo Clinic Simulation Center, Jacksonville, Fl.
- 3rd Annual Epilepsy and EEG in Clinical Practice 2018
  - Nov. 15-17, 2018
  - The Ritz-Carlton Orlando Grande Lakes Orlando, Fl.
- Mayo Clinic Multidisciplinary Spine Care Conference 2018
  - Nov. 16-17, 2018
  - The Ritz-Carlton, Amelia Island, Fl.

2019 courses

**February**
- Mayo Clinic Multiple Sclerosis and Autoimmune Neurology 2019
  - Feb. 8-9, 2019
  - Mayo Clinic Education Center, Phoenix

**February-March**
- Mayo Clinic Electromyography (EMG), Electroencephalography (EEG), and Neurophysiology in Clinical Practice 2019
  - Feb. 24-March 2, 2019
  - The Ritz-Carlton, Amelia Island, Fl.

**March**
- Principles of Pain Management and Palliative Care: Essential Tools for the Clinician 2019
  - March 18-22, 2019
  - JW Marriott Desert Springs, Palm Desert, Calif.

**June**
- 8th Quadrennial International Conference on Vestibular Schwannoma and Other CPA Tumors: Advancing Care through Ideas and Innovation 2019
  - June 18-21, 2019
  - Mayo Civic Center, Rochester, Minn.

**July**
- Neurology in Clinical Practice 2019
  - July 18-21, 2019
  - Hilton Hawaiian Village Waikiki Beach Resort Honolulu