Neurofibromatosis Clinic: A Team for Lifelong Care

7-Tesla MRI: Pioneering Use for Patient Care

CREST-2 Update: Enrolling Patients for Optimal Care

Neurosurgery Registry for Continuous Improvement of Care and Quality of Life

Mayo Clinic has launched a neurosurgery registry designed to further improve patient safety and outcomes. The registry records detailed surgical and patient-reported outcomes for every neurosurgical procedure performed at Mayo Clinic (Figure).

“Our goal is for the data to inform and direct patient care, in the sense that we use the data to further improve outcomes,” says Mohamad Bydon, M.D., a neurosurgeon at Mayo Clinic in Rochester, Minnesota, and the registry’s medical director. “As one of the largest-volume neurologic surgery practices, we have the capacity to affect best practices and standards of care and to share what we learn with others.”

The registry augments Mayo Clinic’s parallel effort to collect samples of every resected brain tumor for genetic analysis and biobank storage. “Mayo Clinic has a strong commitment to individualized medicine. The more data we collect on patients — in terms of clinical presentation, blood work and biomarkers — the better able we are to find treatment paradigms tailored to specific patients,” says Selby G. Chen, M.D., a neurosurgeon at Mayo Clinic in Jacksonville, Florida.

Grounded in Mayo Clinic’s commitment to evidence-based care, the registry covers all neurosurgeries performed at Mayo’s campuses in Minnesota, Florida and Arizona, as well as at the Mayo Clinic Health System sites in Mankato, Minnesota, and Eau Claire and La Crosse, Wisconsin. Launched in mid-2016, the registry...
includes information from patient surveys in addition to complete clinical and surgical records. “We expect that information from the registry will inform patient selection for various procedures as well as our pre-surgery guidance to patients about possible surgical outcomes,” Dr. Chen says.

Patient input is a key component of the registry. “Historically, health care providers have judged outcomes. The registry makes the patient a partner in these assessments,” says Bernard R. Bendok, M.D., chair of Neurosurgery at Mayo Clinic in Phoenix/Scottsdale, Arizona. “Discussions about quality of life have been somewhat ignored in health care. At Mayo Clinic, we want to stay ahead of the curve by measuring and assessing quality of life, educating ourselves and also patients on these issues, and changing course where appropriate.”

Dr. Bendok notes that a 30-minute clinical follow-up a year after neurosurgery isn’t sufficient to assess quality of life. “You can’t just ask a couple questions in the clinic and be done,” he says. “Quality of life is a complicated issue. But there are now rigorous, validated surveys that ask the right questions.”

Obtaining that detailed information can yield insights that ultimately guide treatment decisions. Dr. Bendok offers a hypothetical example of a patient with a tumor who can expect the same medical outcome, in terms of length of life, after treatment with surgery or radiation.

“If radiation requires daily visits to the clinic for 40 days, and causes fatigue and deteriorated social life, then surgery might provide better quality of life,” he says. “In addition, with detailed patient surveys, we can drill down on why patients might feel their quality of life is not as good after radiation treatments. Was it the fatigue, or perhaps hair loss or pain? To improve quality of life, we need to measure it.”

The registry also enhances Mayo Clinic’s team approach to patient care. For example, many patients with spinal conditions also experience depression.

“We utilize very specific modules and parameters to assess overall health, including mental health. There are occasions when patients need additional clinical assessment and intervention prior to consideration of a surgery,” says Jamal McClendon Jr., M.D., a neurosurgeon at Mayo Clinic’s campus in Arizona.

Information collected in the registry is already having an impact on aspects of Mayo Clinic’s practice, such as the length of patients’ hospital stays. “With the help of colleagues from the Kern Center for the Science of Health Care Delivery and practice leadership, we are using the data to inform our opioid usage for the treatment of pain and sharing that data to help guide treatment throughout Mayo,” Dr. Bydon says.

“Mayo Clinic has a strong commitment to evidence-based care,” he adds. “Our goal is to continuously improve outcomes to benefit our patients.”

### Neurofibromatosis Clinic: A Team for Lifelong Care

Mayo Clinic’s Neurofibromatosis Clinic provides multidisciplinary care for children and adults with neurofibromatosis type 1 (NF1) and neurofibromatosis type 2 (NF2). Both Neurofibromatosis Clinic locations — at Mayo Clinic’s campuses in Phoenix/Scottsdale, Arizona, and Rochester, Minnesota — have been recognized by the Children’s Tumor Foundation as providing comprehensive care for people with neurofibromatosis.

“Neurofibromatosis is a complex genetic disorder that requires expertise to manage. We have created a team that understands this rare disorder and that is passionate about caring for these patients,” says Radhika Dhamija, M.B.B.S., a pediatric neurologist and geneticist who directs the Neurofibromatosis Clinic at Mayo Clinic’s campus in Arizona.

Both NF1 (Figure 1) and NF2 (Figure 2) are characterized by the presence of nerve sheath
tumors. Over time, NF1 and NF2 can cause wide-ranging complications that may not be limited to the nervous system.

“Managing these patients over a lifetime requires knowing what to expect from this rare genetic disorder, which impacts not only patients but also their families,” Dr. Dhamija says.

A “home” within Mayo Clinic
The Neurofibromatosis Clinic brings together specialists with experience managing both NF1 and NF2. Those specialists include:

- Neuro-oncologists
- Neurologic surgeons with expertise in brain tumors
- Neurologic surgeons with expertise in peripheral nerve surgery
- Neuro-otologists with experience removing tumors from the vestibular nerve
- Neuro-ophthalmologists
- Oncologists and radiation oncologists
- Otorhinolaryngologists
- Orthopedic surgeons
- Geneticists and genetic counselors

“The Neurofibromatosis Clinic functions as the patient’s ‘home’ within Mayo,” Dr. Dhamija says. “We start with an evaluation of the medical records and an initial visit with the patient. From there we can determine which particular specialists the patient needs.”

Appointments are coordinated so that patients can generally see every needed specialist in a single visit to Mayo Clinic. Brain and spinal MRI might be done along with vision and hearing tests, and genetic testing to confirm the diagnosis.

“Early diagnosis is especially important in children because they may not show symptoms initially,” Dr. Dhamija says. “Confirming a diagnosis of neurofibromatosis allows us to start early surveillance for complications.”

Mayo Clinic recommends annual checkups for patients with neurofibromatosis. “At these visits we go head to toe and talk about all of the issues that can arise with neurofibromatosis, including specific issues that can arise during pubertal growth, risks during pregnancy and heightened risk of breast cancer in young women with NF1,” Dr. Dhamija says. “We understand the complications that can happen throughout these patients’ lifetimes.”

Geneticists and genetic counselors work with patients to find other family members at risk of neurofibromatosis. “We draw very detailed pedigrees,” Dr. Dhamija says. “There are often other first-degree relatives who are at risk. We help them come to our Neurofibromatosis Clinic or can suggest other options.

“These patients tell us they want a physician who understands this rare disorder,” Dr. Dhamija adds. “When a patient with neurofibromatosis has questions that their primary care provider cannot handle, they can call us at Mayo. We build very healthy, long-term relationships with patients and their families with this rare disorder.”
The clinical use of 7-Tesla MRI enhances Mayo Clinic’s ability to manage epilepsy, certain brain and peripheral nerve tumors, and other neurological disorders. Mayo Clinic was the first center in North America to use clinical 7-Tesla MRI, after the Food and Drug Administration (FDA) approved the system in late 2017.

“The contrast and detail in particular clinical applications is exquisite,” says Kimberly K. Amrami, M.D., a radiologist at Mayo Clinic in Rochester, Minnesota. “We’re putting a lot of effort into developing usable, consistent protocols to apply this technology to a broad group of patients. Mayo Clinic’s goal is to make 7-Tesla MRI a tool that will solve problems for our patients.”

The FDA approval covers clinical use of 7-Tesla MRI scans of the knee and brain. Mayo Clinic is using the system in selected patients to image peripheral nerves in the knee, to visualize tumors, microhemorrhages and multiple sclerosis (MS) lesions, and to locate seizure-origin sites in people with drug-resistant focal epilepsy (Figure). For that type of epilepsy, surgical resection is often curative when structural lesions are well-defined on MRI — but surgery is much less successful in patients with normal imaging.

“The 7-Tesla MRI has demonstrated its potential to uncover abnormalities that aren’t detected using MRI with lower magnet strengths. Patients with drug-resistant focal epilepsy who have a normal 1.5-Tesla or 3-Tesla MRI and who are considering surgical resection should have a 7-Tesla MRI,” says Gregory A. Worrell, M.D., Ph.D., a neurologist at Mayo Clinic’s campus in Minnesota. “The 7-Tesla MRI might also benefit patients who are being considered for the implantation of intracranial electrodes for brain stimulation.”

### Defining characteristics

The 7-Tesla MRI provides enhanced detail in cortical imaging, reducing blurring between gray and white matter. “Since the signal to noise ratio is more than doubled, what is invisible or a little ambiguous in a 3-Tesla MRI can be much more clearly defined on the 7-Tesla system,” Dr. Amrami says.

As a result, small MS plaques and their relationship to cerebral veins are more clearly visible on 7-Tesla MRI, facilitating earlier diagnosis. In addition, the stronger magnetic field enhances the prominence of magnetic susceptibility effects, which can be useful in the diagnosis of tiny intracranial bleeds or other diseases of cerebral blood vessels.

“With the 7-Tesla MRI, we can detect subtle traumatic brain injury or tiny hemorrhages caused by hypertension or amyloid angiopathy that would be difficult or impossible to see on other scanners,” says Kirk M. Welker, M.D., a neuroradiologist at Mayo Clinic’s campus in Minnesota.

Functional MRI is similarly enhanced. “Detecting small changes in brain blood flow is much easier at 7 Tesla and allows us to generate more-accurate functional maps to avoid injuring critical brain areas during tumor removal or seizure surgery,” Dr. Welker says.

When used to image the knee, 7-Tesla MRI can guide decision-making for peripheral nerve surgery. “At 7-Tesla strength, we can start to see individual nerve bundles, which is very useful if a problem doesn’t affect an entire nerve,” Dr. Amrami says. “When a cyst is associated with the nerve coming from the knee or superior tibiofibular joint, we can actually see the joint connection and the tiny nerve that innervates the joint much better than at 3 Tesla.”

### Figure

MRI scans of a patient with medically refractory epilepsy provide a comparison of image quality at 7-Tesla and 3-Tesla. Focal cortical dysplasia (arrows) is more clearly visible in the 7-Tesla image on the left than in the 3-Tesla image on the right.
CREST-2 Update: Enrolling Patients for Optimal Care

Kevin M. Barrett, M.D., a neurologist at Mayo Clinic in Jacksonville, Florida, answers questions about the CREST-2 study comparing methods of stroke prevention. Mayo Clinic is the clinical coordinating center for this multicenter, randomized study sponsored by the National Institute of Neurological Disorders and Stroke (NINDS).

Q: Is CREST-2 still enrolling patients?
Yes — we’ve already randomized more than 1,100 patients into the study, but our target recruitment is 2,480 patients. At this point in the trial, we have a lot of momentum, with more than 120 centers in North America currently enrolling patients. We’re continuing to enhance our recruitment efforts nationwide, not only in neurological practices but also in primary care, cardiology and vascular surgery offices across North America.

Q: What are the criteria for enrollment?
CREST-2 is designed to identify the optimal approach for stroke prevention in patients with high-grade asymptomatic carotid stenosis (Figure). We’re recruiting men and women who:
• Are ages 35 and older
• Have 70 percent or greater narrowing of at least one carotid artery
• Lack other serious medical complications

Q: What are the potential benefits for patients who enroll in CREST-2?
Because of the current uncertainty with respect to the optimal approach to stroke prevention, we feel that the best treatment for patients with high-grade asymptomatic carotid stenosis is enrollment in CREST-2.

CREST-2 is designed as two parallel clinical trials — one comparing treatment with intensive medical management alone versus intensive medical management combined with carotid endarterectomy, the other comparing intensive medical management alone versus intensive medical management combined with carotid angioplasty and stenting. The aim is to measure treatment differences between intensive medical therapy alone and intensive medical therapy plus carotid revascularization.

We’re also following cognitive outcomes in patients enrolled in CREST-2. It might be that one of the approaches in the study is better at preserving cognition in these patients.

Q: How does the structure of CREST-2 help ensure that participants receive optimal care?
CREST-2 is unique because it builds upon the experience of CREST — the multicenter Carotid Revascularization Endarterectomy Versus Stenting Trial. Like CREST, CREST-2 uses rigorous credentialing of proceduralists before their participation to ensure that the patients receive optimal surgical care as well as optimal medical care.

Most of our CREST-2 clinical sites have experience providing both carotid endarterectomy and carotid angioplasty and stenting. But if a center happens to specialize in one type of carotid revascularization, the center can still participate in CREST-2. The parallel structure of CREST-2 helps augment the ability of sites to participate and ensure that participants who

A leader in neuroimaging
Mayo Clinic has a distinguished history of imaging. In 1973, Mayo Clinic was the first center in North America to use CT. Mayo was an early adopter of MRI and the first center in the United States to use clinical 3-Tesla MRI, as well as a leader in the use of positron emission tomography.

“We’re now exploring ways to expand our use of 7 Tesla to improve patient care,” Dr. Amrami says. “The 7-Tesla system is unique among our 40 MRI scanners, and provides us with an exciting new set of capabilities for diagnosing disease. We’re actively working to learn which groups of patients stand to benefit the most from a 7-Tesla scan.”

The 7-Tesla system is less suitable for imaging certain structures near the skull base, such as the inferior temporal lobes, pituitary gland or internal auditory canal. “Bone and air in the skull base cause a greater degree of imaging artifact at 7 Tesla than at lower field strengths,” Dr. Welker says. “Our medical physicists are investigating potential solutions to these problems so they may be less of a concern in the future.” In addition, safety constraints for implanted metal objects in the body are much greater for 7-Tesla MRI.

Kevin M. Barrett, M.D.
have carotid revascularization are treated by experienced providers.

CREST-2 also has ongoing oversight from an independent Data Safety and Monitoring Board. At CREST-2’s most recent review, the board found no safety concerns for patients in the study and was enthusiastic about our continuing it.

**Q: How have the CREST-2 protocols been updated?**

We’re keeping pace with the changes occurring in routine clinical practice with respect to intensive medical therapy and neuro-imaging. Over the course of the study, the protocols for CREST-2 procedures have been modified to incorporate the newest generation of lipid-lowering medications and contemporary neuro-imaging studies. We want to ensure that the study results are informative and relevant.

**Q: What strengths does Mayo Clinic bring to this large, NINDS-funded research?**

As the clinical coordinating center for CREST-2, we’re drawing on our experience as a coordinating center for CREST. We’re also taking advantage of our large footprint in North America, and the relationships across the Mayo Clinic campuses in Arizona, Florida and Minnesota. Our historical and institutional experience puts us in a position of leadership.

**Figure.** Illustration shows the process by which carotid artery disease leads to stroke.
Research Highlights in Neurology and Neurosurgery

Long-Term Outcomes for Survivors of West Nile Neuroinvasive Disease
Mortality and early disability for patients with West Nile neuroinvasive disease (WNND) are high, but long-term data on the outcomes for severely affected patients are lacking. In a study with retrospective review of records and prospective telephone follow-up, Mayo Clinic researchers found that WNND survivors with severe early disability can recover functional independence in the long term. The researchers identified 26 patients with WNND who were treated at Mayo Clinic from 1999 to 2016. Among them, 15 percent died during their initial hospitalization and a total of 23 percent had died after a median follow-up of 73 months. However, nearly 80 percent of survivors had minimal or no disability on long-term follow-up. Patients who required mechanical ventilation had a worse prognosis, but most of them experienced substantial recovery in the long term. The findings indicate that intensive support during the acute phase, and extensive rehabilitation efforts after hospital discharge, can often result in good functional recovery, even if such recovery is slow. (Hawkes MA, et al. Outcomes in patients with severe West Nile neuroinvasive disease. Critical Care Medicine. 2018;46:e955.)

Magnetic Stimulation for Migraine Prevention
Migraine affects more than 38 million people in the United States and is the leading cause of neurological disability. Medications are often associated with suboptimal efficacy and tolerability. Single pulse transcranial magnetic stimulation (sTMS) is a noninvasive, safe, and well-tolerated diagnostic and treatment modality that modulates the electrical environment of neurons in the superficial layers of the cortex. The treatment has been shown to be effective in the acute treatment of migraine with aura. In a multicenter study, Mayo Clinic researchers and colleagues found that sTMS may be a safe and effective treatment option for the prevention of migraine. Study participants completed a one-month baseline headache diary followed by three months of treatment: four pulses twice daily as preventive treatment and three pulses repeated up to three times as acute treatment during an attack. The participants recorded daily headache status, and medication and device use. Mean reduction of headache days compared to baseline was measured over the final 28 days of treatment; that endpoint was then compared to a statistically derived placebo estimate. Among the 220 study participants, 46 percent experienced a reduction in the number of headache days of greater than 50 percent. There were also significant reductions in disability and in the number of days of acute medication use. The most common adverse events were lightheadedness, tingling and tinnitus, each of which was reported by less than 4 percent of study participants. No serious adverse events were reported. (Starling AJ, et al. A multicenter, prospective, single arm, open label, observational study of sTMS for migraine prevention [ESPOUSE study]. Cephalalgia. 2018;38:1038.)

Neuromodulation Enables Independent Stepping After Complete Paraplegia
Mayo Clinic previously reported a clinical case in which epidural electrical stimulation (EES) restored the ability to stand and control step-like activity in a patient with complete sensorimotor paralysis of the lower extremities due to spinal cord injury. Since then, dynamic task-specific training in the presence of EES of lumbosacral spinal networks — termed multimodal rehabilitation (MMR) — was performed for 43 weeks by the patient and resulted in:

- Bilateral stepping on a treadmill, independent from trainer assistance or use of a body-weight support system
- Independent stepping over ground while using a front-wheeled walker with trainer assistance at the hips to maintain balance
- Independent standing

The researchers report that over the course of MMR, they discovered that two interleaved EES programs enabled bilateral control of leg functions via independent adjustment of active electrodes and voltage intensities within each program. The researchers suggest that the dynamic MMR paradigm may have re-educated spinal neural networks associated with locomotor activities. The outcomes support the concept that spinal neuromodulation with sensorimotor rehabilitation facilitate the functional reorganization of the supraspinal-spinal connectome to recover functions lost to spinal cord injury. (Gill ML, et al. Neuromodulation of lumbosacral spinal networks enables independent stepping after complete paraplegia. Nature Medicine. In press. Video at: http://medprofvideos.mayoclinic.org/videos/epidural-stimulation-enables-motor-function-after-chronic-paraplegia.)

To read more about Mayo Clinic neurosciences research and patient care, visit http://www.mayoclinic.org/medical-professionals.
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2019 courses

January
2019 Mayo Clinic Advancements in Surgical & Medical Management of the Spine
Jan. 13-17, 2019
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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, Fla.

March
Mayo Clinic Headache Symposium: Creating Migraine Warriors
March 1-3, 2019
Mayo Clinic Education Center, Phoenix

2nd Annual Mayo Clinic Advances and Innovations in Complex Neuroscience Patient Care: Brain and Spine 2019
March 7-9, 2019
Enchantment Resort, Sedona, Ariz.

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 Clinic Center, Rochester, Minn.

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

November
Parkinson's Disease and Other Movement Disorders 2019
Nov. 15-16, 2019
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Mayo Clinic in Jacksonville, Florida
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Website: https://ce.mayo.edu/neurology-and-neurologic-surgery

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

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3. Brain, spinal cord or peripheral nerve tumors
4. Epilepsy with indications for surgery
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