New Standards of Care for Brain Tumors

As a center of excellence for neurology and neurosurgery, Mayo Clinic offers innovative approaches for patients with primary brain cancers and metastatic brain tumors. Mayo Clinic neuro-oncologists are setting new standards of care for patients with brain cancer, with a focus on not only halting tumor growth and progression but also maximizing patients’ quality of life during and after treatment.

Resecting ‘inoperable’ brain tumors

Mayo Clinic is able to resect tumors from deep and delicate regions of the brain (Figure 1) using awake surgery, advanced intraoperative monitoring — including intraoperative neuropsychology and MRI — and other advanced imaging and surgical strategies (Figure 2).

“We are routinely able to help patients enjoy many more years of high quality of life when they were told elsewhere that their tumors were inoperable, that they only had a short time to live or would require very high doses of brain radiation, since nothing else could be done,” says Terence (Terry) C. Burns, M.D., Ph.D., a consultant in Neurosurgery at Mayo Clinic in Rochester, Minnesota. “The best treatment for most brain tumors is to start by surgically removing as much tumor as is safely possible.”

Dr. Burns sometimes sees patients whose lesions were considered incidental findings or believed to be growing so slowly that they could simply be watched. “Unfortunately, it’s often not until the previously slow-growing low-grade glioma has transformed into an aggressive

Figure 1. On the left, MRI of a 36-year-old patient shows a large insular glioma. On the right, MRI immediately after gross total resection at Mayo Clinic shows the extent of tumor removal. The surgery was performed with the patient awake, using intraoperative neuropsychology to ensure the preservation of adjacent structures important for higher level cognitive function. The patient walked out of the hospital two days after surgery with no neurological or cognitive deficits.

Figure 2. On the left, MRI images of a 34-year-old triathlete show a pineal meningioma. The patient had undergone two prior surgeries at a major academic medical center. Less than 25 percent of her tumor could be removed, and most of what was removed grew back within six months. The patient came to Mayo Clinic with severe fatigue and rapid cognitive decline, expecting to undergo high doses of radiation for her “inoperable” tumor. On the right, MRIs after surgery at Mayo Clinic show a very small amount of tumor — less than 3 percent of the pre-surgery mass — that the Mayo Clinic neurosurgeon left at the junction between the Galen vein and straight sinus, as surgical removal risked a potentially catastrophic venous infarct. The patient subsequently had focused Gamma Knife radiosurgery treatment for the residual tumor, avoiding the risk of delayed complications from brainstem radiation. She is now preparing to resume triathlons.
glioblastoma that patients finally make it to Mayo,” he says. “It’s devastating to see patients who could have had much better outcomes had they been seen at Mayo sooner.”

**Imaging and treatment for tumor progression**

To identify tumor progression — and to distinguish it from radiation necrosis or inflammation — Mayo Clinic uses combined PET scan and MRI (Figure 3).

“This technology, which is not commonly available, gives us more reliable information to assess not only the structure of the lesion but also its metabolic activity,” says Maciej M. Mrugala, M.D., Ph.D., a consultant in Neurology at Mayo Clinic in Phoenix/Scottsdale, Arizona. “Any patient with suspected radiation necrosis or tumor progression can be referred to Mayo for a PET-MRI scan.”

Mayo Clinic also offers treatment options for the spread of tumor to the cerebrospinal fluid and subarachnoid space. Although leptomeningeal carcinomatosis (Figure 4) has become more prevalent among cancer patients, diagnosis is frequently delayed and the condition untreated. Mayo neuro-oncologists have experience recognizing and treating the condition.

“We don’t have a cure, but we do have options that can prolong life and delay devastating neurologic symptoms,” Dr. Mrugala says.

The primary treatment option is chemotheraphy administered into the patient’s spinal fluid. Mayo generally uses an intraventricular approach with an Ommaya reservoir, rather than lumbar puncture. “The Ommaya reservoir is more comfortable for the patient and allows the physician to sample spinal fluid without repeated spinal taps,” Dr. Mrugala says.

In addition to standard chemotherapies, Mayo Clinic uses intrathecal monoclonal antibodies — trastuzumab for metastatic breast cancer and intrathecal rituximab for lymphomatous meningitis. Craniospinal radiation might be another option, in select patients. “This is a very toxic treatment, but that can be decreased with proton beam therapy,” Dr. Mrugala says. Proton beam therapy is available at Mayo Clinic’s campuses in Arizona and Minnesota.

“Any cancer patient — whether the disease is melanoma, leukemia, lymphoma, or a solid tumor in the breast or lung — is at risk of leptomeningeal carcinomatosis. Physicians should consider leptomeningeal carcinomatosis when they see a patient with cancer who is developing neurologic symptoms that cannot be easily explained, and refer the patient to a center of excellence,” Dr. Mrugala says.

**Optimizing radiation strategies for metastatic brain tumors**

Whenever possible, Mayo Clinic uses targeted radiation treatment, such as proton beam therapy or stereotactic radiosurgery. However, even focused radiation can cause radiation necrosis, which can lead to severe brain swelling and require further treatments or surgery. An upcoming clinical trial seeks to optimize radiation strategies for patients who undergo surgery for metastatic brain tumors.

Stereotactic radiosurgery is currently used after tumor resection to reduce recurrence of tumor from malignant cells “spilled” during surgery. “However, that strategy isn’t perfect,” Dr. Burns says. “Some tumor cells may escape quite a distance from the original site, yet treating a larger area of surrounding tissue with radiation increases the risk of radiation necrosis and cognitive sequelae.”

Retrospective evidence suggests that if tumor cells are neutralized with radiation before surgery, there is a lower risk of viable cells escaping during surgery into the surrounding brain or cerebral spinal fluid, as well as a lower risk of radiation necrosis. The clinical trial will compare outcomes for patients who have stereotactic radiosurgery before and after metastatic tumor resection.

“So far, there are very few centers that offer stereotactic radiation prior to surgery. Radiation remains more of an afterthought once the tumor is out,” Dr. Burns says. “We will determine if preoperative stereotactic radiosurgery should become the new standard of care for these patients.”

**Clinical trials and online consultations**

Mayo Clinic has a wide array of clinical trials for patients with primary brain tumors or brain metastases. Online consultations with Mayo Clinic neurologists and neurosurgeons also are available. (See contact information on page 8 or www.MayoClinic.org/medicalprofs.)

Among planned clinical trials is an evaluation of a Mayo Clinic test to assess the genetic risk of glioma. Using quantitative imaging machine learning, Mayo Clinic radiologists have developed algorithms to predict the presence of genomic variations associated with glioma, based
on a patient’s MRI. The predictive testing builds on Mayo Clinic’s previous discovery of tumor biomarkers that define five biologically distinct glioma tumor groups.

“We’re beginning to find that we can predict the presence of these molecular groups in patients by machine learning,” says Daniel H. Lachance, M.D., a consultant in Neurology at Mayo Clinic’s campus in Minnesota.

An initial clinical trial is planned for patients seen at Mayo Clinic for idiopathic focal epilepsy. Mutations in isocitrate dehydrogenase are associated with that disease as well as long-term risk of glioma.

“We want to use the genomic test and the machine learning to preoperatively predict glioma risk because that information can affect a surgeon’s thinking about how much lesion to remove,” Dr. Lachance says.

Stalling molecular motors of glioma
Another avenue of research involves inhibitors of enzymes known as molecular motors, which appear to play a role in both the proliferative and invasive cellular processes of glioma cells. “We’re using a variety of genetic approaches to target some of these enzymes in mouse models of glioma. We’ve got some promising leads,” says Steven S. Rosenfeld, M.D., a neurologist at Mayo Clinic in Jacksonville, Florida.

Preclinical work focuses on using existing drugs to optimize treatment of glioma in mouse models. “We have evidence that the cells’ ability to proliferate and invade are linked — if you wrestle with one, you inadvertently stimulate the other,” Dr. Rosenfeld says. “We think these molecular motors are involved in both processes, so they present a potentially effective target.”

Confronting radiation-induced brain injury
As principal investigator in Mayo Clinic’s Regenerative Neurosurgery and Neuro-Oncology Laboratory, Dr. Burns leads a team developing regenerative strategies to optimize neurological function and quality of life for patients with brain tumors. While improved treatments might lengthen life spans, survivors often must live with the cognitive sequelae of radiation-induced brain injury.

“Survivors of medulloblastoma can end up with an IQ 25 points lower than it should be, due to the long-term effects of radiation treatment,” Dr. Burns says. “Children could have the most to gain from our regenerative strategies, since radiation-induced demyelination can worsen over time.”

However, radiation also severely affects adults. “I hear people say, ‘My wife’s brain tumor is under control, but she has just not been the same person since brain radiation.’ As part of a team that treats tumors with radiation, we feel a strong obligation to understand and better treat radiation-induced brain injury,” Dr. Burns says.

At Mayo Clinic, patients undergoing brain radiation have neuropsychological testing to measure cognition at baseline and after treatment. Mayo Clinic is also leading clinical trials aimed at better understanding and preventing cognitive deficits from brain radiation — work strengthened by Mayo’s clinical and research expertise in Alzheimer’s disease, demyelinating diseases and brain aging.

“Our studies of the brain’s inflammatory cells suggest that brain radiation may accelerate aging-like changes in the brain,” Dr. Burns says.

Mayo Clinic researchers led a multicenter trial that demonstrated that memantine, used to reduce symptoms of Alzheimer’s disease, improves cognition after brain radiation. Other therapies, ranging from anti-aging drugs to oligodendrocyte progenitor cells, are being studied preclinically. Mayo Clinic’s Center for Regenerative Medicine is designing a regenerative neuro-oncology service line to facilitate translational research and ensure patients receive services they need for late effects of cancer therapy.

“We need to take care of the whole patient,” Dr. Burns says. “Depression, anxiety, fatigue and cognitive problems are all extremely common among patients with brain tumors, and the effects of brain radiation can worsen these. If we’re only focused on the brain tumor itself, and ignore the rest of the patient, we haven’t provided optimal care.”

Awake Craniotomy for Tumor Resection in Motor and Sensory Tissue
Awake craniotomy, which allows for maximal tumor resection while preserving functional tissue, has become an established approach for the removal of tumors in the cortical speech area of the brain. Mayo Clinic neurosurgeons are expanding their use of awake craniotomy to resecting tumors in eloquent motor and sensory tissue.

Typically, awake craniotomy is avoided in those areas, due to the risk of intraoperative seizures. However, Mayo Clinic neurosurgeons have demonstrated expertise with this approach, offering better outcomes for patients and lower
costs than tumor resection performed under general anesthesia.

“As a tertiary referral center, Mayo Clinic can invest in the multidisciplinary teams that allow us to perform these complex procedures,” says Alfredo Quinones-Hinojosa, M.D., chair of Neurosurgery at Mayo Clinic in Jacksonville, Florida. “What separates us from any other center is the Mayo system of care — a multidisciplinary approach, with strong investment in people and technology that ensures patient safety is at the forefront.”

Avoiding seizures
Mayo Clinic’s awake craniotomy protocol seeks to minimize the intensity of current used for cortical and subcortical stimulation, while not compromising the reliability of stimulation mapping. In surgery involving eloquent motor tissue, the primary motor region is targeted to determine a minimum current intensity necessary to elicit a clinical response.

Reported rates of stimulation-induced intraoperative seizures during an awake craniotomy range from 2.2 to 21.9 percent, with 70 to 86 percent of those seizures occurring during resections of tumors involving the frontal lobe perirolandic region. However, a study published in *Neurosurgery* reported that intraoperative seizures occurred in just two of 27 (7.4 percent) awake craniotomy surgeries performed by Dr. Quinones-Hinojosa (Figure) to treat perirolandic gliomas. In both cases, the seizures were rapidly controlled, and the surgeries continued.

“Successful surgery of this type requires a very large team — neurosurgeons with expertise in awake craniotomy, neurologists, neuroanesthesiologists, neuroradiologists and experienced nurses,” Dr. Quinones-Hinojosa says.

This depth of subspecialized expertise facilitates rapid identification of impending intraoperative seizure. “We take an active approach to intraoperative monitoring of brain function at Mayo Clinic in an attempt to identify patterns on the electrocortico gram that may portend a greater risk of impending seizures when superficial or deep brain stimulation is performed,” says William Tatum, D.O., a consultant in Neurology at Mayo Clinic’s campus in Florida.

“Any seizure that occurs in the operating room is immediately treated to rapidly terminate it and prevent it from recurring,” he adds. “Having a prearranged protocol for neurophysiological monitoring, together with open communication in the OR, ensures the best possible care for patients. Coordination and combined expertise during the surgical procedure is critical not only to optimize the extent of resection and limit morbidity but also to avert potential risk of intraoperative seizures.”

Improving outcomes
The *Neurosurgery* study also documented improved outcomes in the patients who had awake craniotomy compared with 31 matched case-control patients who had perirolandic glioma resection under general anesthesia:

- Total resection achieved in seven patients (25.9 percent) in the awake craniotomy group versus two (6.5 percent) in the general anesthesia group
- Mean delayed Karnofsky performance scale (KPS) score of 93.3 for the awake craniotomy group versus 89.7 for the general anesthesia group
- Mean delayed KPS score of 91.1 for the general anesthesia group (mean follow-up time of 28 months)

A separate study by Dr. Quinones-Hinojosa and colleagues published in *Neurosurgery* comparing cost associated with awake craniotomy versus general anesthesia during resection of perirolandic region tumors found that the total inpatient expense per patient was $34,804 for the awake craniotomy group and $46,798 for the general anesthesia group. The study concluded that the costs of additional personnel and equipment for awake craniotomy were offset by better postoperative status and shorter hospitalization — a mean length of stay of 4.12 days compared with 7.61 days for the general anesthesia group.

“Our studies show that with awake craniotomy, you resect more tumor, the patients do better, and the overall health bill is less,” Dr. Quinones-Hinojosa says.

Another potential advantage of awake craniotomy may be avoidance of cancer cell migration during surgery. “Just recently we have begun to realize that anesthesia might have a deleterious effect on this cell migration, possibly by inhibiting the immune system,” Dr. Quinones-Hinojosa says.

To enhance guidance during brain tumor resection, Mayo Clinic has pioneered combining awake surgeries with high-field intraoperative MRI. “This gives us the best possible functional guidance — motor and speech mapping — and image guidance, allowing us to safely resect tumors that would be difficult to remove without causing harm otherwise,” says Ian F. Parney, M.D., Ph.D., a consultant in Neurosurgery at Mayo Clinic in Rochester, Minnesota.

In addition to tumor resection, treatment for cavernomas, small arteriovenous malformations (AVMs) and select patients with moyamoya disease is often performed at Mayo Clinic with awake surgery.
“It allows us to map white matter around cavernous vascular malformations and AVMs, and to resect epileptogenic tissue that would have been left behind otherwise,” says Bernard R. Bendok, M.D., chair of Neurosurgery at Mayo Clinic’s campus in Phoenix/Scottsdale, Arizona. “For moyamoya disease, awake surgery may lower the risk of ischemic complications by reducing hemodynamic compromise and giving the anesthesia and surgical teams immediate feedback that can prompt hemodynamic interventions.”

Selecting patients
Patient selection is key to successful awake craniotomy in areas of eloquent tissue. Contraindications for awake craniotomy include communication problems, developmental delay, age under 12 years, uncontrolled coughing, severe dysphagia, hemiplegia and less than antigravity motor function. Dr. Quinones-Hinojosa stresses the importance of building a relationship of trust with the patient. “Patients put their lives in my hands. So before I take them to the operating room, I always explain exactly what I’m going to do,” he says. “If you develop these relationships, patients have faith in the team. Our anesthesiologists also do a beautiful job with nerve blocks in the scalp, so patients are comfortable and have no pain.

“We used to say not all parts of the brain are eloquent. It turns out that there are many more eloquent parts than what we thought,” Dr. Quinones-Hinojosa adds. “One day, awake surgery will be done for all gliomas. That’s the way we’re moving.”

For more information


Tissue Biopsy for Identifying Early Parkinson’s

Mayo Clinic researchers and colleagues have found that submandibular gland needle biopsies can identify Lewy type alpha-synucleinopathy in people with Parkinson’s disease of less than five years’ duration. The finding has implications for research enrollment criteria: The accuracy of clinical diagnosis of early Parkinson’s disease may be as low as 50 percent, and a peripheral tissue biopsy could confirm diagnosis for patients enrolling in clinical trials.

“A peripheral tissue diagnostic test for early Parkinson’s, similar to what we have for cancer, would be extremely valuable for trials looking at neuroprotective therapies,” says Charles H. Adler, M.D., Ph.D., a consultant in Neurology at Mayo Clinic in Phoenix/Scottsdale, Arizona. “A definitive diagnosis before study enrollment avoids exposing patients who do not have Parkinson’s unnecessarily to invasive treatments, and powers the accuracy of the trial. Many potential therapies for early Parkinson’s have failed in human trials. One reason for that might be that some people enrolled in the studies don’t actually have Parkinson’s disease.”

Published in the February 2016 issue of Movement Disorders, the peripheral synucleinopathy study was cited by the journal as its 2016 Best Research Article. The study was performed by the Arizona Parkinson’s Disease Consortium, whose principal members are Mayo Clinic’s campus in Arizona and Banner Sun Health Research Institute. It didn’t address the issue of patients who don’t yet have signs of Parkinson’s disease on examination but who might go on to develop the condition.

Potential gold standard
In the study, submandibular gland needle biopsies (Figure) were performed on 25 patients with early Parkinson’s disease (mean disease duration of 2.6 years) and 10 control participants. Six participants with Parkinson’s disease and one control participant had inadequate glandular tissue. Tissue staining for phosphorylated alpha-synuclein was positive in 14 of 19 participants with Parkinson’s disease (74 percent) and 2 of 9 (22 percent) of control participants.

“The false-positives might be true false-positives, or they might represent prodromal Parkinson’s disease,” Dr. Adler says.

The tissue biopsy isn’t intended for current routine clinical use at this time. In the absence of definitive clinical diagnosis, treatment is routine for patients with suspected early Parkinson’s disease because the oral medications generally don’t have permanent side effects.

In addition to facilitating clinical trials, the biopsy test may benefit genetic and epidemiologic research of Parkinson’s disease. “By providing definitive diagnosis, the biopsy test could eventually serve as a gold standard for biomarker studies, short of autopsy confirmation,” Dr. Adler says.

Figure. Photograph shows a needle biopsy of the submandibular gland. Photo reprinted with permission from Neurology. 2014;82:859.
Future directions
The researchers plan to investigate whether a tissue biopsy test might aid diagnosis of prodromal Parkinson’s disease — potentially in patients with nonmotor conditions, such as anosmia or rapid eye movement sleep behavior disorder, that often predate Parkinson’s disease. Mayo Clinic’s campus in Arizona is also participating in the Systemic Synuclein Sampling Study (S4), funded by the Michael J. Fox Foundation. S4 is comparing biopsies of submandibular gland, colon and skin tissue, as well as cerebrospinal fluid, blood and saliva, to identify biomarkers for Parkinson’s disease.

“Mayo Clinic is committed to this type of translational research,” Dr. Adler says. “There is synergy between our neurologists and our otorhinolaryngology colleagues who perform the biopsies. Although the submandibular gland biopsy test is primarily a research tool now, we’re working to eventually bring it to the clinic.”

For more information

Referral Center for Endovascular Treatment of Acute Stroke

Mayo Clinic’s campus in Minnesota offers a unique level of endovascular treatment for acute stroke, with not only excellent door-to-groin puncture and perfusion metrics (Figure) but also 24/7 coverage by highly experienced neurointensivists.

“Physicians who send acute stroke patients to us can expect them to be in the angiographic suite and undergoing treatment in less than 30 minutes from arrival,” says Alejandro A. Rabinstein, M.D., a consultant in Neurology at Mayo Clinic in Rochester, Minnesota. “A consultant in neurocritical care is present for the entire procedure, and our rates of complete or nearly complete reperfusion exceed 80 percent.”

In addition to being a certified comprehensive stroke center, Mayo Clinic’s campus in Minnesota ranks No. 1 for neurology and neurosurgery in the U.S. News & World Report Best Hospitals rankings. The Joint Commission commended Mayo in 2017 for ensuring that consultants directly manage endovascular care for all patients with acute stroke.

Between two-thirds and three-fourths of patients with acute stroke who are seen at Mayo Clinic’s campus in Minnesota are referred from other centers. Patients can be transferred by Mayo One, an emergency helicopter service that flies within a 150-mile radius of bases at the Rochester campus of Mayo Clinic, Mankato Regional Airport in Mankato, Minnesota, and Chippewa Valley Regional Airport in Eau Claire, Wisconsin. Telemedicine consultations also are available to identify patients who would benefit from endovascular therapy.

“As acute stroke and neurocritical care consultants, we evaluate the patients via telestroke at the referring emergency department and assist the transportation team while the patients are in transit. We receive the patients as they arrive at the hospital; we are in the endovascular suite during the entire intervention; we take the patients to the intensive care unit after the procedure, and we communicate with the families throughout the process,” Dr. Rabinstein says. “In addition, all of our endovascular specialists have at least 15 years of experience.”

The benefit of endovascular revascularization performed at high-volume hospitals has been demonstrated. In a study published in the May 2017 issue of Stroke, Mayo Clinic researchers found that both mortality rate and mortality index were significantly lower for patients transferred to high-volume centers compared with patients directly admitted to low-volume hospitals. The findings suggest that the benefits of treatment at high-volume centers may outweigh the potential detrimental effect of the time delay for hospital transfer.

“Transferring patients to high-volume hospitals, where there is expertise to do everything possible to maximize recovery, makes a very big difference for functional outcomes,” Dr. Rabinstein says. “At Mayo we have performed recanalization within 19 minutes of the patient’s arrival at our hospital. We have oiled the process so that we are not only very likely to get the vessel open but the tissue reperfused in a manner that allows for reduction in the size of the stroke.”

For more information
Neurovascular Manifestations of Takayasu Arteritis

Takayasu arteritis (TA) is a rare, large-vessel vasculitis that presents with symptoms related to end-organ ischemia. Although extracranial neurovascular manifestations of TA are well-established, little is known about the intracranial manifestations. Researchers at Mayo Clinic in Rochester, Minnesota, have found that intracranial vascular abnormalities aren’t rare in patients with TA who present with neurological symptoms. The researchers reviewed the records of patients with TA treated at Mayo Clinic from 2001 to 2016 who had intracranial or cervical vascular imaging or both. Among the 79 patients who met the study criteria, the most common neurological symptoms were headache (experienced by 32.9 percent of patients studied) and dizziness (experienced by 15.2 percent of patients studied). The patients’ imaging was evaluated for the presence of vascular abnormalities, including intracranial or extracranial stenosis, vessel-wall thickening, dissection, subclavian steal syndrome, aneurysms, infarcts, and hemorrhages. Among patients who had intracranial vascular imaging, five (6.5 percent) had intracranial vasculitis, three (3.9 percent) had intracranial aneurysms, three (3.9 percent) had acute large-vessel occlusion, and one (1.3 percent) had reversible cerebrovascular constriction syndrome. Among patients who had cervical vascular imaging, 42 (53.1 percent) had some degree of narrowing of the common carotid artery and 18 (22.8 percent) had narrowing of the internal carotid arteries. (Bond K, et al. Intracranial and extracranial neurovascular manifestations of Takayasu arteritis. Presentation at: American Academy of Neurology Annual Meeting; 2017; Boston.)

Neuromuscular complications in solid tumor cohort treated with PD-1 inhibitors

There have been increasing reports of neuromuscular complications among patients with solid tumors who have PD-1 inhibitor therapy. Researchers at Mayo Clinic in Rochester, Minnesota, have found that immune-mediated neuromuscular adverse events from this therapy are diverse, can affect any part of the nervous system and have an unpredictable time of onset. In a retrospective chart review, the researchers identified 347 Mayo Clinic patients who received pembrolizumab or nivolumab for the treatment of solid tumors. Eight of the patients (2.3 percent) had subacute onset of neurological complications occurring after a median 5.5 cycles of PD-1 inhibitor therapy. Complications included neuropathy, necrotizing myopathy, cerebellar ataxia and retinopathy. Five patients had treatment with steroids, and two received intravenous immunoglobulin. Seven patients improved; one patient with severe necrotizing myopathy died. The researchers note that although these complications are relatively rare, they are likely to occur with increasing frequency as PD-1 inhibitors become widely used. The neurological deficits found in the study can evolve rapidly and may be life-threatening. However, with prompt recognition and treatment, neurological outcomes are generally favorable. (Kao J, et al. Neuromuscular complications occurring in solid tumor cohort treated with PD-1 inhibitors. Presentation at: American Academy of Neurology Annual Meeting; 2017; Boston.)

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Biomarkers of Cognition in Aging Patients With MS

Advanced MRI techniques used in imaging myelin of brain parenchyma aren’t myelin specific. In contrast, amyloid tracers such as Pittsburgh compound-B (PiB) have recently been shown to target myelin, indicating that positron emission tomography (PET) with PiB may be a candidate to image demyelinating diseases. Researchers at Mayo Clinic in Rochester, Minnesota, studied the association of cognitive function with thalamic volume, lobar cortical thickness, cortical PiB-PET, and white matter PiB binding as a potential myelin marker in an aging population with multiple sclerosis (MS). In the population-based Mayo Clinic Study of Aging, 24 of 4,869 patients had MS; among them, 16 had brain MRI and 12 had PiB-PET. Controls from the same cohort were matched by age and sex. Quantitative image analyses were performed using automated image processing pipelines. Compared with controls, patients with MS had lower cognitive z-scores for memory and language, smaller thalamic volumes, and thinner temporal and frontal cortices. Thalamic volume loss was associated with decreased attention-executive performance. PiB uptake was reduced in areas of white matter hyperintensities compared with normal-appearing white matter in participants with MS and in control participants. Reduced PiB uptake in areas of white matter hyperintensities was associated with decreased visuospatial performance in participants with MS. There was no difference in global cortical PiB standardized uptake value ratios between participants with MS and control participants. The researchers conclude that thalamic atrophy correlates with lower attention-executive function in aging patients with MS, and likely reflects white matter injury in thalamo-cortical projections. As a potential measure of white matter injury, PiB-PET images correlate with visuospatial processing and may reflect injury to association area connectivity. (Zeydan B, et al. Pittsburgh Compound-B PET and MRI biomarkers of cognition in aging MS patients. Presentation at: American Academy of Neurology Annual Meeting; 2017; Boston.)

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Oct. 24-25, 2017
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**Sleep and Stroke 2017**
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Epilepsy and EEG in Clinical Practice 2017
Nov. 9-11, 2017
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**Mayo Clinic Multidisciplinary Spine Care Conference 2017**
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The Fairmont Orchid, Waimea, Hawaii

**Mayo Clinic Cerebrovascular Update & Controversies: Neurology and Neurosurgery 2018**
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Four Seasons, Las Vegas

Information and registration

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**Contact Us**
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Mayo Clinic Neurosciences Update is written for physicians and should be relied upon for medical education purposes only. It does not provide a complete overview of the topics covered and should not replace the independent judgment of a physician about the appropriateness or risks of a procedure for a given patient.

**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