

INSIDE THIS ISSUE

2 Moyamoya:
Specialized
Care for a Rare
Cerebrovascular
Disease

4 Spinal Vascular
Malformations:
Early Interventions
and Importance of
Proper Diagnosis

5 Stem Cell
Treatment After
Spinal Cord Injury:
The Next Steps

Glioblastoma: Seeking Personalized Care Through Radiomics

Mayo Clinic is working to individualize treatment for glioblastoma through advanced imaging and mathematical modeling. A principal focus of these efforts is better use of temozolomide. Although it has been the standard-of-care glioblastoma chemotherapy for more than a decade, the drug's optimal use in individuals hasn't been elucidated.

"The current treatment is homogenized — a standard strategy of six cycles of adjuvant temozolomide for every patient. We believe we might be able to personalize that approach," says Kristin R. Swanson, Ph.D., director of the Mathematical Neuro-Oncology Laboratory at Mayo Clinic in Phoenix/Scottsdale, Arizona.

The laboratory's researchers recently found that temozolomide has a greater effect on nodular tumors than on diffusely invasive tumors, suggesting that patients with less invasive tumors might benefit from additional cycles of the drug. That work builds on the laboratory's earlier discoveries of differences in the molecular mechanisms of glioblastoma tumors in men and women.

"Although we have known that the incidence of glioblastoma is higher in men and that they generally succumb more quickly than women, we haven't known why. This work takes us a step further in personalizing glioblastoma treatment," says Maciej M. Mrugala, M.D., Ph.D., medical director of the Comprehensive Multispecialty Neuro-Oncology Program at Mayo Clinic's campus in Arizona.

Personalized treatments require biomarkers of disease. In the absence of a glioblastoma biomarker, clinicians must rely on MRI. The Mathematical Neuro-Oncology Laboratory seeks to go beyond MRI to provide quantifiable measures of an individual's brain cancer.

"Having a radiomic biomarker of glioblastoma that would allow us to deeply interrogate a tumor — and not just look at it anatomically on the MRI — would be very valuable," Dr. Mrugala says. "Dr. Swanson's models have been able to predict tumor response to various treatments, which brings us closer to that goal."

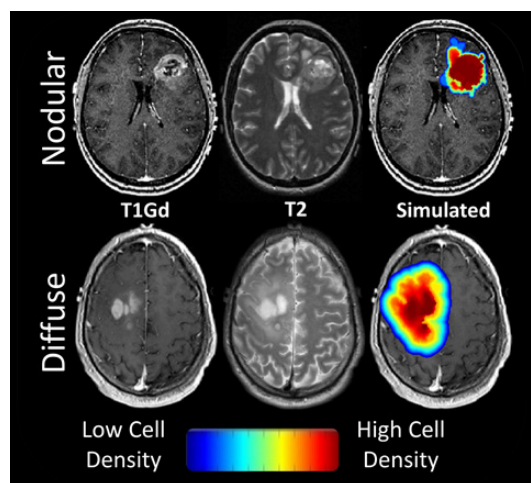


Figure. Gadolinium-enhanced T1-weighted and T2 fluid-attenuated inversion recovery images show differing levels of density in glioblastoma tumors. Less color is apparent in the nodular tumor in the top row, while greater color illustrates the higher volume of tumor cells found on biopsy of the diffuse tumor shown in the bottom row.

Quantifying individual tumor behavior

The temozolomide study compared gadolinium-enhanced T1-weighted and T2 fluid-attenuated inversion recovery images taken before and after adjuvant treatment. The images were used



Kristin R. Swanson, Ph.D.

to determine volumetric changes in imaging abnormalities and to calculate a tumor invasion metric based on mathematical modeling.

As described in the March 2020 issue of *PLOS One*, nodular tumors tended to respond more favorably to adjuvant temozolomide, in terms of both volumetric change and patient outcomes (Figure). “The less invasive the tumor looks, the greater the decrease in tumor volume and the longer the patient will have a sustained response to temozolomide,” Dr. Swanson says.

She notes that the greater response in nodular tumors might be due to higher concentrations of temozolomide in the tumor core, where the blood-brain barrier is likelier to be compromised compared with surrounding tissue. “In a diffuse glioblastoma, the tumor cells have migrated so far that the blood-brain barrier is still intact in those regions,” Dr. Swanson says. “The drug is not going to get there.”

Mayo’s previous study on sex differences in glioblastoma outcomes — described in the Jan. 2, 2019, issue of *Science Translational Medicine* — applied a computational algorithm to male and female transcriptome data. In men receiving standard glioblastoma treatment, survival corre-

lated with the expression of cell cycle regulators. In women, survival correlated with the expression of integrin signaling pathway components.

“The biology of the tumor appears to be different in men and women,” Dr. Mrugala says. “That might be one reason females have potentially responded better to standard treatment.”

Future work might look for sex differences in temozolomide response. “We are finding reasons, based on our imaging and sex differences studies, to think about different strategies for treating glioblastoma,” Dr. Swanson says. “Our goal is to use the tools in our arsenal, such as temozolomide, to the best of our ability. That means taking a more personalized approach.”

For more information

Massey SC, et al. Image-based metric of invasiveness predicts response to adjuvant temozolomide for primary glioblastoma. *PLOS One*. 2020;15:e0230492.

Yang W, et al. Sex differences in GBM revealed by analysis of patient imaging, transcriptome, and survival data. *Science Translational Medicine*. 2019;11:eaa05253.



Maciej M. Mrugala, M.D., Ph.D.

Moyamoya: Specialized Care for a Rare Cerebrovascular Disease



Rabih G. Tawk, M.D.

Although rare, moyamoya disease can have devastating consequences, triggering strokes and seizures in children and adults. Mayo Clinic’s approach utilizes a multidisciplinary moyamoya clinic to provide timely evaluation and treatment for this complex disorder.

“The moyamoya clinic is a one-stop shop where patients can be seen in a single day by experts in vascular neurology and vascular neurosurgery. During the same clinic visit, these specialists discuss the diagnosis and generate a treatment plan,” says Rabih G. Tawk, M.D., a neurosurgeon and co-director of the moyamoya clinic at Mayo Clinic in Jacksonville, Florida.

As a high-volume center, Mayo Clinic has experience and expertise in rare conditions. Moyamoya disease is a progressive disorder characterized by blockage in the distal internal carotid artery and adjacent blood vessels. The name moyamoya means “puff of smoke” in Japanese, and describes the appearance of the tangle of tiny blood vessels formed to compensate for the blockage.

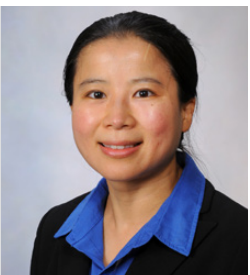
Moyamoya disease can occur at any age, but symptoms are most common in children ages 5

to 10 and adults ages 30 to 50. The first symptom is usually stroke or recurrent transient ischemic attack, especially in children, whose symptoms might be mistakenly attributed for months.

“It can be devastating for a young patient when stroke happens, especially when that person is at risk of recurrent stroke or even cerebral hemorrhage,” says Michelle P. Lin, M.D., M.P.H., a stroke neurologist and co-director of the moyamoya clinic at Mayo’s campus in Florida.

The cause of moyamoya disease is unknown, although the disease is most common in East Asia and a genetic component is suspected. Some patients have moyamoya syndrome, defined as moyamoya caused by an underlying condition such as vasculitis, atherosclerosis or a blood-clotting disorder. Moyamoya syndrome is usually unilateral.

To facilitate current and future research, Mayo Clinic has a biobank with blood samples collected from patients with rare disorders, including moyamoya. “We have a long-term commitment to understanding moyamoya disease and to improving treatment for patients,” Dr. Tawk says.



Michelle P. Lin, M.D., M.P.H.

Finding subtle indicators of disease

Early diagnosis and treatment of moyamoya disease are essential to prevent debilitating stroke and seizures. But diagnosis is challenging, as moyamoya disease has many mimics. “Unless you’re an expert, moyamoya is difficult to detect. The indicators of disease can be subtle,” Dr. Tawk says.

Physicians should consider referring a patient to moyamoya specialists if the patient has had recurrent strokes and has signs of large vessel cerebrovascular disease. Other signs — which can be especially helpful in a patient whose stroke has gone undiagnosed — include unilateral vasculopathy, headache and cognitive decline.

Conventional angiogram, which is the diagnostic test of choice, might show the extent of occlusive disease and the characteristic puff of smoke appearance of small blood vessels. “These findings are suggestive of moyamoya disease. But further testing is needed to determine if the patient has moyamoya or a mimic,” Dr. Lin says.

Mayo Clinic uses several state-of-the-art diagnostic tests, starting with comprehensive cerebral angiogram. The imaging is evaluated by specialists with experience in this rare condition. “We have seen several patients in our clinic who had imaging done elsewhere and were managed for prolonged periods, but moyamoya was missed,” Dr. Tawk says.

High-resolution MRI of the cerebral blood vessel walls is also performed, to help differentiate moyamoya from vasculitis and atherosclerosis. That distinction is crucial, as the treatment pathways for moyamoya disease differ significantly from the approaches to vasculitis and atherosclerosis.

“Each of these diseases has a very distinct pattern on the vessel walls,” Dr. Lin says. “The spatial resolution in our MRI is so high that we can literally see different layers of the blood vessel walls — it’s almost like looking at a slide through a microscope.”

In addition, the moyamoya clinic routinely performs functional MRI with carbon dioxide challenge, to evaluate changes in cerebral hemodynamics. “It’s like a stress test to the brain,” Dr. Lin says.

Patients with impaired cerebrovascular reserve who “fail” the stress test are at higher risk of stroke or recurrent stroke. “These are important pieces of individualized clinical findings that help guide timing of bypass surgery versus medical treatment,” Dr. Lin says.

Personalized treatment

Test results and the clinical work-up are used to generate an individual treatment plan (Figure). “The presentation of moyamoya disease varies,

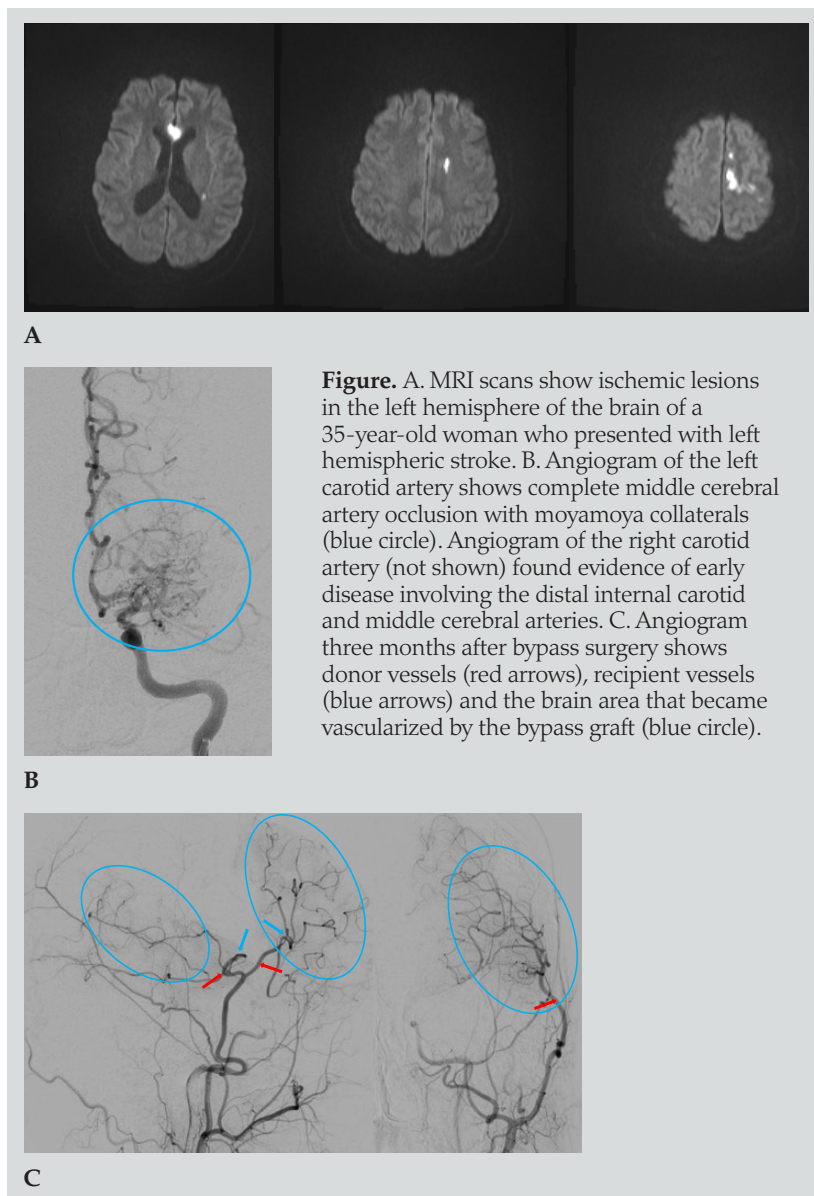


Figure. A. MRI scans show ischemic lesions in the left hemisphere of the brain of a 35-year-old woman who presented with left hemispheric stroke. B. Angiogram of the left carotid artery shows complete middle cerebral artery occlusion with moyamoya collaterals (blue circle). Angiogram of the right carotid artery (not shown) found evidence of early disease involving the distal internal carotid and middle cerebral arteries. C. Angiogram three months after bypass surgery shows donor vessels (red arrows), recipient vessels (blue arrows) and the brain area that became vascularized by the bypass graft (blue circle).

and management has to be individualized to each patient,” Dr. Tawk says.

Medical management includes the use of blood thinners, blood pressure medications, cholesterol lowering medications and immunosuppressants. “We’re treading a very fine line,” Dr. Lin says. “As stroke neurologists, it’s important to individualize each patient’s stroke and bleeding risks, particularly in patients with moyamoya, as they are at increased risk of both.”

For example, patients who are poor metabolizers of the blood thinner clopidogrel — an estimated 14% of the population — have an increased risk of stroke. “At our moyamoya center, we routinely check if a patient is a clopidogrel responder versus a nonresponder, and titrate the blood thinness with the anti-platelet level,” Dr. Lin says.

Surgery involves direct or indirect revascularization. Mayo Clinic neurosurgeons are able to

perform combined direct and indirect revascularization to provide optimal surgical outcomes while minimizing complications. "Patients do best when the surgery is individualized to meet their needs," Dr. Tawk says.

Collaboration between neurosurgeons and stroke neurologists is also key, particularly for patients with moyamoya syndrome. In one recent case, Dr. Lin identified thyrotoxicosis in a patient with moyamoya.

"We performed unilateral bypass surgery, which immediately reduced the patient's risk of stroke," Dr. Tawk says. "Then, by treating the underlying pathology, we stopped additional injuries to the blood vessels on the contralateral brain."

Individuals with moyamoya disease require lifelong care. The moyamoya clinic performs regular follow-up imaging to determine if a patient's vascular bypass has matured. If a bypass regresses and patients continue to have symptoms, additional surgery might be needed. Patients can receive initial or follow-up care at any Mayo Clinic campus, as all three academic campuses have cerebrovascular specialists with experience in moyamoya.

"Mayo is unique in that our colleagues throughout the system help one another," Dr. Tawk says. "Patients have the expertise of not just an individual physician but many experts who come together to recommend what can best help that individual."

Spinal Vascular Malformations: Early Interventions and Importance of Proper Diagnosis



W. Oliver Tobin, M.B., B.Ch., B.A.O., Ph.D.

W. Oliver Tobin, M.B., B.Ch., B.A.O., Ph.D., a neurologist, and Giuseppe Lanzino, M.D., a neurosurgeon, at Mayo Clinic in Rochester, Minnesota, discuss spinal vascular malformations.

What makes a spinal vascular malformation unique and difficult to treat?

Spinal vascular malformations encompass a range of disorders that often result in an intermittent or progressive myelopathy. Standard magnetic resonance imaging (MRI) may not identify the vascular abnormality and can be normal in the early stages of the disorder. The myelopathy can be exercise dependent initially and can spontaneously remit. However, if not identified, it can lead to a progressive disabling myelopathy, which is difficult to reverse even after correction of the spinal vascular abnormality. A negative formal spinal angiogram does not completely exclude a spinal vascular malformation, as there is a large range of abnormalities that extend throughout the length of the spine and beyond into the cerebral vasculature and pelvic vasculature.



Giuseppe Lanzino, M.D.

What is Mayo Clinic's approach to the diagnosis and treatment of spinal vascular malformations?

We use a multidisciplinary approach to the evaluation of myelopathy and of suspected spinal vascular malformations. A carefully coordinated evaluation is completed by experts in neurology, neuroradiology, neurosurgery, physical medicine and rehabilitation, urology, and other fields to identify the cause for the myelopathy and determine a treatment plan.

As noted in a 2018 article in *Neurology*, almost 1 in 5 patients who are referred to Mayo Clinic for evaluation of an idiopathic myelopathy are identified as having a vascular myelopathy.

Why is early intervention or treatment important?

In a 2016 *American Journal of Neuroradiology* (AJNR) article, Mayo Clinic researchers noted that early identification and treatment of vascular myelopathy is critical for good patient outcomes. We also know that people with a longstanding dural arteriovenous fistula with an associated myelopathy have a poor prognosis for recovery.

Have there been any recent technological advancements or other innovations that have helped further enhance the treatment of this malformation?

Mayo Clinic noted, in research published in the *Journal of Neurosurgery* in 2017 and the *Journal of NeuroInterventional Surgery* in 2016, that enhanced diagnostic tools allow us to see distinct patterns on MRI that can identify dural arteriovenous fistula (Figure). Also, some spinal vascular malformations once considered extremely rare, such as epidural spinal arteriovenous fistulas, are now being recognized in an increasing number of patients due to improved diagnostic tools and enhanced knowledge and better understanding.

When should a physician refer a patient for treatment or a second opinion for spinal vascular malformation treatment?

Any patient with a myelopathy of uncertain origin should be referred for secondary evaluation. After

evaluation at Mayo Clinic, only a very small proportion of patients initially referred with a diagnosis of idiopathic transverse myelitis were thought to be idiopathic following the evaluation. Many of these patients underwent treatment, including 1 in 5 patients who underwent treatment for a vascular myelopathy. We also know from our research published in *AJNR* in 2016, that even after a negative spinal angiogram, patients should be referred for an evaluation, as we have found that of all patients with a delayed diagnosis, approximately 20% had a nonrevealing spinal angiogram in the course of their initial evaluation.

At Mayo Clinic, who would be part of a care team for a patient with spinal vascular malformation? Why is this distinction important?

We have a close collaboration among all the teams at Mayo Clinic. This enables us to be very coordinated on all necessary appointments and have test results available quickly. Since we work together as a multidisciplinary team, we are able to provide that expert, individualized care to every person who seeks our expertise. We have the experience, knowledge, state-of-the-art research and laboratory facilities, and advanced technology, and we are constantly innovating to continually best meet the needs of the patients.

For more information

Zalewski NL, et al. Evaluation of idiopathic transverse myelitis revealing specific myelopathy diagnoses. *Neurology*. 2018;90:e96.

Brinjikji W, et al. Clinical outcomes of patients with delayed diagnosis of spinal dural

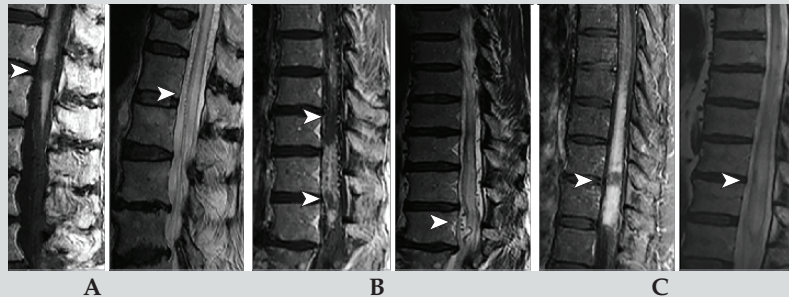


Figure. Imaging of three patients with spinal dural arteriovenous fistulas (dAVFs) illustrates a distinct pattern that can identify dAVFs on MRI. A-C, left panels. Arrows indicate a T1-weighted gadolinium enhancement pattern with abrupt pieces of contrast enhancement missing. A-C, right panels. Arrows in the accompanying sagittal T2-weighted imaging show possible subtle flow voids in the first patient (A), prominent tortuous flow voids in the second patient (B) and no flow voids in the third patient (C), whose spinal dAVF was recognized only at the time of durotomy. Imaging reprinted with permission from *JAMA Neurology*.

arteriovenous fistulas. *American Journal of Neuroradiology*. 2016;37:380.

Nasr DM, et al. Clinical presentation and treatment outcomes of spinal epidural arteriovenous fistulas. *Journal of Neurosurgery*. 2017;26:613.

Brinjikji W, et al. Spinal epidural arteriovenous fistulas. *Journal of NeuroInterventional Surgery*. 2016;8:1305.

Zalewski NL, et al. Unique gadolinium enhancement pattern in spinal dural arteriovenous fistulas. *JAMA Neurology*. 2018;75:1542.

Stem Cell Treatment After Spinal Cord Injury: The Next Steps

Following promising phase 1 testing, Mayo Clinic is launching phase 2 of a randomized clinical trial of stem cell treatment for patients with severe spinal cord injury. The clinical trial, known as CELLTOP, involves intrathecal injections of autologous adipose-derived stem cells.

“The field of spinal cord injury has seen advances in recent years, but nothing in the way of a significant paradigm shift. We currently rely on supportive care. Our hope is to alter the course of care for these patients in ways that improve their lives,” says Mohamad Bydon, M.D., a neurosurgeon at Mayo Clinic in Rochester, Minnesota.

The first participant in the phase 1 trial was a super responder who, after stem cell therapy, saw significant improvements in the function of his upper and lower extremities (Figure).

“Not every patient who receives stem cell treatment is going to be a super responder. Among the 10 participants in our phase 1 study, we had some nonresponders and moderate responders,” Dr. Bydon says. “One objective in our future studies is to delineate the optimal treatment protocols and understand why patients respond differently.”

In CELLTOP Phase 2, 40 patients will be randomized to receive stem cell treatment or



Mohamad Bydon, M.D.



Figure. Photograph shows the initial patient in CELLTOP Phase 1 (right), with Mohamad Bydon, M.D.



Anthony J. Windebank, M.D.

best medical management. Patients randomized to the medical management arm will eventually cross over to the stem cell arm.

Study participants must be age 18 or older and have experienced traumatic spinal cord injury within the past year. The spinal cord injuries must be American Spinal Injury Association (ASIA) grade A or B.

Reversing the microenvironment

The initial participant in CELLTOP Phase 1 sustained a C3-4 ASIA grade A spinal cord injury. As described in the February 2020 issue of *Mayo Clinic Proceedings*, the neurological examination at the time of the injury revealed complete loss of motor and sensory function below the level of injury.

After undergoing urgent posterior cervical decompression and fusion, as well as physical and occupational therapy, the patient demonstrated improvement in motor and sensory function. But that progress plateaued six months after the injury.

Stem cells were injected nearly a year after his injury and several months after his improvement had plateaued. Clinical signs of efficacy in both motor and sensory function were observed at three, six, 12 and 18 months following the stem cell injection.

“Our patient also reported a strong improvement with his grip and pinch strength, as well as range of motion for shoulder flexion and abduction,” Dr. Bydon says.

Spinal cord injury has a complex pathophysiology. After the primary injury, microenvironmental changes inhibit axonal regeneration. Stem cells can potentially provide trophic support to the injured spinal cord microenvironment by modulating the inflammatory response, increasing vascularization and suppressing cystic change.

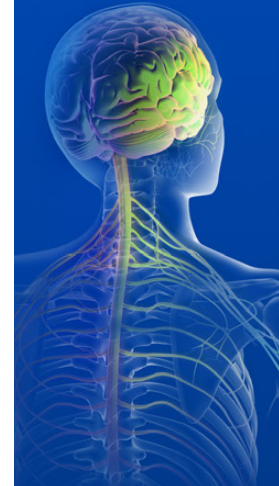
“In the phase 2 study, we will begin to learn the characteristics of individuals who respond to the therapy in terms of their age, severity of injury and time since injury,” says Anthony J. Windebank, M.D., a neurologist at Mayo’s campus in Minnesota and director of the Regenerative Neurobiology Laboratory. “We will also use biomarker studies to learn about the characteristics of responders’ cells. The next phase would be studying how we can modify everyone’s cells to make them more like the cells of responders.”

CELLTOP illustrates Mayo Clinic’s commitment to regenerative medicine therapies for neurological care. “Our findings to date will be encouraging to patients with spinal cord injuries,” Dr. Bydon says. “We are hopeful about the potential of stem cell therapy to become part of treatment algorithms that improve physical function for patients with these devastating injuries.”

For more information

Bydon M, et al. CELLTOP clinical trial: First report from a phase I trial of autologous adipose tissue-derived mesenchymal stem cells in the treatment of paralysis due to traumatic spinal cord injury. *Mayo Clinic Proceedings*. 2020;95:406.

Research Highlights in Neurology and Neurosurgery



Progressive Dysexecutive Syndrome: Identifying a Type of Alzheimer's in Younger People

Mayo Clinic researchers have defined a form of Alzheimer's disease characterized by dysfunction in core executive functions and relatively young age of onset. Although atypical dysexecutive variants of Alzheimer's disease have been reported, no diagnostic criteria exist for a progressive dysexecutive syndrome. Mayo's proposed criteria are based on a retrospective review of 55 patients who presented with a clinically defined progressive dysexecutive syndrome, and who underwent F-fluorodeoxyglucose-positron emission tomography (PET) and testing for Alzheimer's disease biomarkers. Sixty-two percent of participants were female. The mean age of reported symptom onset was 53.8 years, while the mean age at diagnosis was 57.2 years. Participants and informants commonly referred to initial cognitive symptoms as "memory problems," but upon further inquiry described problems with core executive functions of working memory, cognitive flexibility and cognitive inhibitory control. Multidomain cognitive impairment was evident in neuropsychological testing, with executive dysfunction most consistently affected. The frontal and parietal regions that overlap with working memory networks consistently demonstrated hypometabolism on PET. Cerebral spinal fluid or neuroimaging biomarkers were consistent with Alzheimer's disease pathophysiology. The researchers propose that this progressive dysexecutive syndrome should be recognized as a distinct clinical phenotype. They note that nearly all study participants were affected during their productive working years at symptom onset, and that initial misdiagnosis of this understudied clinical presentation was common. (Townley RA, et al. Progressive dysexecutive syndrome due to Alzheimer's disease: A description of 55 cases and comparison to other phenotypes. *Brain Communications*. 2020;2:fcaa068.)

Standardized Relative CBV Has Similar Predictive Power to Normalized Relative CBV in High-Grade Gliomas

Perfusion MRI measures of relative cerebral blood volume (CBV) can distinguish recurrent tumor from posttreatment radiation effects in high-grade gliomas. Currently, relative CBV measurement requires normalization based on user-defined reference tissues; however, a recently proposed method of relative CBV standardization eliminates the need for user input. Mayo Clinic researchers have found that standardized relative CBV achieves similar performance compared with normalized relative CBV. To compare the predictive performance of the two methods, the researchers analyzed 112 image-localized biopsies from 38 previously treated patients with high-grade gliomas undergoing further resection for new contrast-enhancing lesions concerning for recurrent tumor versus post-treatment radiation effects. The percentage of histologic tumor content versus post-treatment radiation effects were quantified for each sample. Spatially matched normalized and standardized relative CBV metrics and fractional tumor burden were also measured in each biopsy. Analysis of the measurements demonstrated that histologic tumor content, at the level of image-localized biopsies, can be predicted by fundamental relative CBV metrics, as well as a fractional tumor metric that has been shown to correlate strongly with global tumor content as a predictor of overall survival. The researchers note that the use of relative CBV would be an important step toward optimizing workflow and achieving consensus on methodology. (Hoxworth JM, et al. Performance of standardized relative CBV for quantifying regional histologic tumor burden in recurrent high-grade glioma: Comparison using normalized relative CBV using image-localized stereotactic biopsies. *American Journal of Neuroradiology*. 2020;41:408.)

Data From Randomized Study Support the Use of IgG to Treat Autoimmune Epilepsy

The management of autoimmune epilepsy currently centers on immunotherapies. However, the evidence base is limited to retrospective case studies and to expert opinions. In the first randomized double-blind placebo-controlled trial evaluating the efficacy of intravenous immunoglobulin (IVIg) in reducing seizure frequency, Mayo Clinic researchers presented data supporting the use of that immunotherapy. Study participants had seizures tied to one of two rare types of encephalitis: leucine-rich, glioma-inactivated 1 (LGI1)-immunoglobulin (IgG)-seropositive encephalitis or contactin-associated protein-like 2 (CASPR2)-IgG-seropositive encephalitis. The participants were randomized to receive IVIg or intravenous saline. After the blinded phase, the nonresponders in the placebo group received IVIg. The study's enrollment goal was 30 adults; however, due to slow enrollment, the study was terminated after 17 patients enrolled. Although the study didn't reach its statistically based sample size, administration of IVIg among the randomized participants was associated with a favorable responder rate compared with placebo, especially among individuals with LGI1-IgG. The efficacy of IVIg was further supported by the open label arm of the study, in which the majority of participants had a reduction in seizure frequency of at least 50% after six weeks of IVIg. The researchers note that their results must be interpreted with the caveat that the study didn't reach its originally selected sample size. (Dubey D, et al. Randomized placebo-controlled trial of intravenous immunoglobulin in autoimmune LGI1/CASPR2 epilepsy. *Annals of Neurology*. 2020;87:313.)

To read more about Mayo Clinic neurosciences research and patient care, visit www.MayoClinic.org/medical-professionals.

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Clinical trials, CME, Grand Rounds,
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Education 2021 Neurology and Neurologic Surgery Continuing Medical Education Programs

The current environment presents many challenges. Mayo Clinic's highest priority is patient and staff safety. We are taking every precaution to manage patient safety to the highest standard through universal masking, enhanced safety protocols, robust screening and COVID-19 testing strategies. Mayo Clinic has a long-standing history of helping our community in crisis while maintaining capacity to care for patients who need it most. We will continuously evaluate the circumstances at each of our sites and follow federal and state mandates to protect the safety of our patients, staff and community.

Find resources for providers and answers to questions on referrals and testing for COVID-19 on the Medical Professionals Resource Center at www.MayoClinic.org/medical-professionals/neurology-neurosurgery.

February

Mayo Clinic Multiple Sclerosis and Autoimmune Neurology Update 2021 — LIVESTREAM

Feb. 5-6, 2021

This course provides the latest clinically relevant updates on multiple sclerosis and autoimmune neurology. Mayo Clinic experts discuss evidence-based strategies for practical, multidisciplinary clinical management of patients with these neurologic disorders. Attendees learn about the latest clinical and laboratory research through didactic lectures, case vignettes, interactive Q&A sessions and open discussions with faculty.

March

Electromyography (EMG), Electroencephalography (EEG), and Neurophysiology in Clinical Practice 2021 — LIVESTREAM

March 14-20, 2021

This course offers a review and update of techniques and topics pertaining to the practice of clinical neurophysiology in the evaluation and diagnosis of a variety of neurological disorders. The course focuses on techniques and pitfalls, along with clinical correlation of various neurophysiological tests used for the evaluation of patients with peripheral nerve and neuromuscular disorders, epilepsy, central nervous system disorders and sleep disorders.

April

Mayo Clinic Sleep Medicine Update — LIVESTREAM

April 15-17, 2021

This CME course — the first from Mayo Clinic pertaining entirely to sleep medicine — is designed for established providers, new practitioners, physician assistants and nurse practitioners. The

faculty mirror the multidisciplinary approach to the practice of sleep medicine, and will draw on the wealth of cases from sleep centers at all three Mayo Clinic campuses. A pre-course session on fundamentals of sleep medicine will occur Thursday, April 15, 2021.

May

7th Annual Neuro and Intensive Care: Review, Workshops and Controversies 2021 — LIVESTREAM

May 6-8, 2021

This course is designed for medical providers who care for patients with neurological/neurosurgical emergencies, acute stroke and brain hemorrhage, acute brain injury, coma and disorders that require hospital, emergency department and intensive care unit (ICU) evaluation and management. The course will provide a mixture of didactic, case-based and evidence-based guideline review and workshops.

Information and registration

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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

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