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Neurosciences Update

Neurologic Surgery and Clinical Neurology News

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Surgery for Malignant and Primary Spinal Column Tumors

INSIDE THIS ISSUE

Tumors of the bony spinal column may require resection and stabilization to improve patient outcome, reduce the risk of paralysis, and reduce pain. Michelle J. Clarke, MD, a neurosurgeon at Mayo Clinic in Rochester, Minnesota, with specialized training in spinal column and spinal cord tumors, notes that the goal in metastatic spinal tumors is often palliative. The goal in some primary bone tumors, such as chordoma of the spinal column, is to effect a cure.

Metastatic Tumor Resection

Dr Clarke points out that the occurrence of metastatic spine tumors is becoming increasingly common as the number of cancer survivors grows. It is estimated that vertebral masses develop in approximately 40% of cancer patients and 10% to 20% have spinal cord compression. Metastatic spinal tumors can cause fractures, pain, and neurologic dysfunction from spinal cord compression. Advances over the past 15 years have improved outcomes in the surgical approaches taken to manage metastatic tumors. Often, surgery is followed by adjuvant radiotherapy. The goal of surgery is to reduce pain and improve function by removing the tumor, decompressing the spinal cord, and stabilizing and reconstructing the spine (Figure 1).

"The purpose of surgery is to maintain or improve the patient's quality of life," says Dr Clarke.

At Mayo Clinic, the criteria for surgical candidacy include the type of tumor and the patient's expected survival rate (ie, 3 to 6 months or more) and current functional and overall health status. Occasionally, metastatic tumors are identified before loss of function, but for patients with a sudden onset of weakness or paralysis, the window of opportunity to restore function is very short—usually, 14 to 48 hours. Patients who live at a distance from Mayo Clinic may be flown to the clinic by Mayo's emergency medical helicopter service for immediate evaluation.

Chordoma Resection

Chordomas are slow-growing primary malignant bone tumors that can reach enormous proportions (Figure 2). Although far more rare than metastatic tumors, chordomas represent the most common primary malignant tumors of the sacrum and the mobile spine. Symptoms are often insidious in onset and their cause undiagnosed for months to years, until the tumor is so large that it disrupts function. Depending on their location, chordomas can cause pain and sensory and motor abnormalities, as well as bowel, bladder, or sexual dysfunction; airway obstruction; and swallowing difficulties. They can become large enough to compress

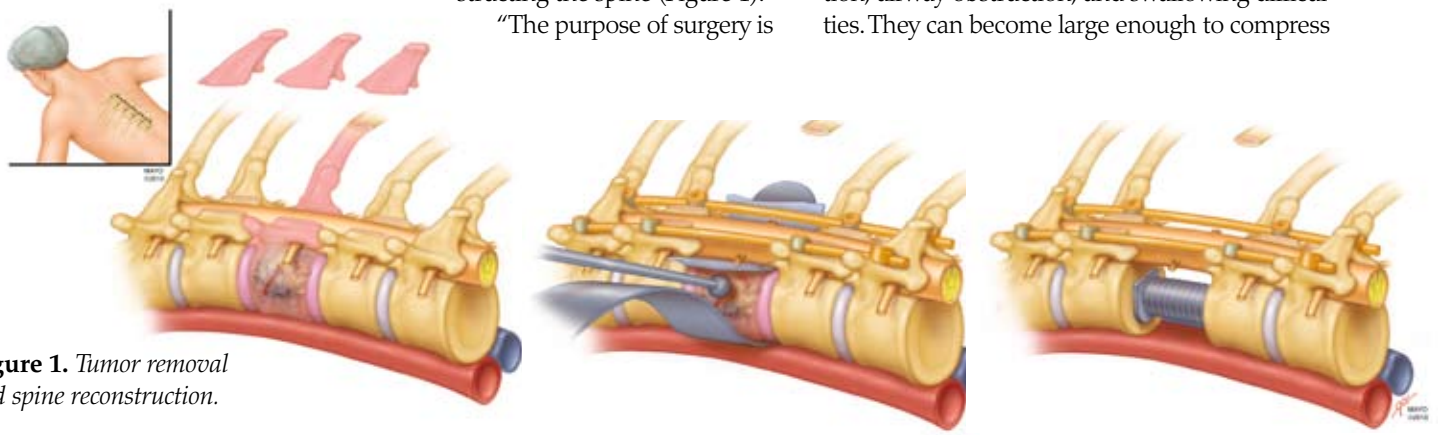


Figure 1. *Tumor removal and spine reconstruction.*

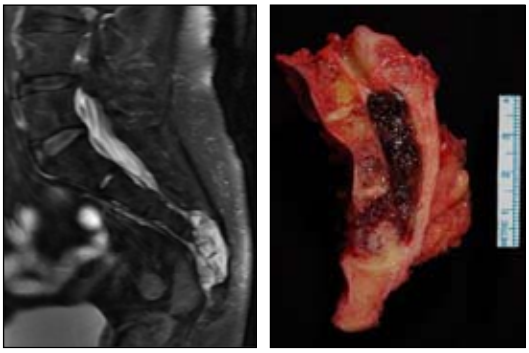


Figure 2. *MRI scan (left) and postsurgical specimen (right) of a sacral chordoma that was resected en bloc.*

vital structures, such as the aorta or vena cava.

Perhaps the most important thing about chordomas is that they are encapsulated tumors. Dr Clarke, who has had specialized training in resecting chordomas, points out that if a neurosurgeon tries to debulk or break the tumor up in surgery, the tumor will spread. However, if the entire tumor is removed as an intact whole, recurrence is less likely. She adds that anything more than a needle biopsy risks recurrence. Thus, it is critical that the tumor be removed as a single mass, even when the tumor has gigantic proportions. The procedure is provided at only a few medical centers in the world and typically involves a radical en bloc resection.

Depending on the location of the tumor, such a surgery may involve thoracic, orthopedic, cardiac, general, and plastic surgeons in addition to the neurosurgeon. Surgery may take place over several days, during which the site is prepared, the entire tumor removed in one encapsulated mass, and the spine reconstructed. Such a procedure requires several days of coordinated efforts among multiple team members and, following surgery, the services of a pain management team and rehabilitation specialists.

Michelle J. Clarke, MD

In addition to problems stemming from their unusual size, chordomas can metastasize to other organs. Without surgery, chordomas are fatal in approximately 50% to 70% of patients. Resecting a large chordoma as an encapsulated whole can be extremely challenging. However, as Dr Clarke points out, major en bloc resections of this type can be done with the kind of specialized expertise and interdisciplinary team effort that is characteristic of Mayo Clinic's practice.

Although spinal tumor removal may require a major surgical procedure, according to Dr Clarke, patient surveys show that patients are pleased with the outcome. For patients with chordoma, surgery can be lifesaving. For appropriately selected patients with metastatic spine tumors, surgery can make a marked difference in quality of life.

Abnormal Bone Fusion: Research and Management of Craniosynostosis at Mayo Clinic

Although brain growth is not complete until about 20 years of age, two-thirds of it occurs in the first two years of life. Following birth, the cranial sutures maintain separation of the calvarial bones as the skull accommodates the growing brain. The expanding brain also stimulates new bone deposits at the contact edges of the sutures. If one or more of the sutures are fused at birth, the skull will expand into the abnormal head shapes and facial distortions that characterize craniosynostosis.

In simple craniosynostosis, a single suture is fused. Complex or syndromic craniosynostosis involves the fusion of multiple sutures. More than 180 hereditary syndromes, such as Crouzon, Pfeiffer, and Apert syndromes, manifest craniosynostosis. Some of these syndromes are associated with developmental delays, a restricted airway, and protruding eyes.

Abnormal head shape in infants can also be caused by positional plagiocephaly, a much more common and benign condition that can be addressed through nonsurgical intervention with the aid of physical and occupational therapy. Treatment may involve repositioning the infant during sleep, frequent head turning, the wearing of a helmet until the head is reshaped and, when torticollis is present, stretching exercises.

The incidence of craniosynostosis is 1 in 2,500 live births. Of those cases, only 6% are complex or syndromic. Fusion of the sagittal suture is the most common form of simple craniosynostosis, accounting for 40% to 60% of cases. It occurs predominantly in males and is characterized by an elongated skull, bitemporal narrowing, and frontal and occipital bossing (Figure). The flat, asymmetrical head shape in positional plagiocephaly is sometimes confused with posterior unilateral lambdoid synostosis, a subtype of craniosynostosis.

Management of Craniosynostosis at Mayo Clinic

Craniosynostosis management at Mayo Clinic is conducted by an interdisciplinary team whose members vary depending on the type of cranio-

synostosis involved. All patients with craniosynostosis are seen by the departments of pediatric neurosurgery, plastic surgery, and medical genetics. To care for patients with syndromic craniosynostosis, the team may also include the departments of pediatric neurology, pediatric otorhinolaryngology, ophthalmology, physical medicine and rehabilitation, and speech pathology.

Differential Diagnosis

Nicholas M. Wetjen, MD, a pediatric neurosurgeon at Mayo Clinic in Rochester, Minnesota, notes that although there is no upper age limit for a referral, the optimal time is between one and two months of age. The diagnosis is based on a physical examination and imaging studies. The goal is to differentiate normal from abnormal growth patterns and positional plagiocephaly from craniosynostosis and to identify craniosynostosis subtype. Dr Wetjen says that he prefers to meet and get to know a patient's family, even if it is just to offer reassurance, to monitor the child, or to help the family avoid an unnecessary procedure.

Surgical Management

Dr Wetjen and his colleagues have determined that when surgery is required, the optimal age is between four and six months, although surgical reshaping can be done at any age. In all cases of craniosynostosis, the bones have a tendency to grow together again, but simple craniosynostosis rarely requires a second procedure. Dr Wetjen notes, "Our patients with simple craniosynostosis tend to do very well. We usually do a single operation and see them for follow-up a few times in the first year and again after five years. We rarely have to operate again. Those with syndromic or complex craniosynostosis may require more than one procedure and are actively monitored for a wide range of potential problems by our comprehensive management team."

During surgery, a pediatric neurosurgeon removes bone at the suture site, and a plastic surgeon conducts the reconstruction and remodeling of the head. In some cases, surgery may be performed endoscopically. According to Dr Wetjen, the endoscopic outcomes are similar to the standard surgical procedure, but endoscopy requires that the patient wear a helmet for approximately a year postsurgery.

Abnormal Bone Growth Research

What causes cranial sutures to fuse before birth? Dr Wetjen and Jennifer Westendorf, PhD, a scientist in the departments of orthopedic surgery and biochemistry and molecular biology at Mayo Clinic in Minnesota, have been collaborating over the past year to understand more about the mechanism of premature bone fusion. It is thought that bone at the cranial sutures grows in response to signals from the dura mater and that in craniosynostosis, gene mutations alter the signal or signaling process. In 15% of craniosynostosis cases, the genetic mutation is known. Dr Westendorf and colleagues are in the process of developing a genome-wide approach to identify other gene mutations.

Nicholas M. Wetjen, MD, and Jennifer Westendorf, PhD

Dr Westendorf explains that determining the molecular basis of premature bone fusion will provide insights into craniosynostosis and bone formation in general. This knowledge could impact other skeletal diseases and disorders, such as osteoporosis and fracture repair. Dr Wetjen adds that their research may also contribute to the design of structural scaffolding to improve reshaping of the head in craniosynostosis. Their research utilizes what would have been waste tissue—the bone that is removed during surgery for craniosynostosis. Drs Westendorf and Wetjen are pleased to note that all of the families coming to Mayo for craniosynostosis surgery over the course of the project have been eager to participate in it.

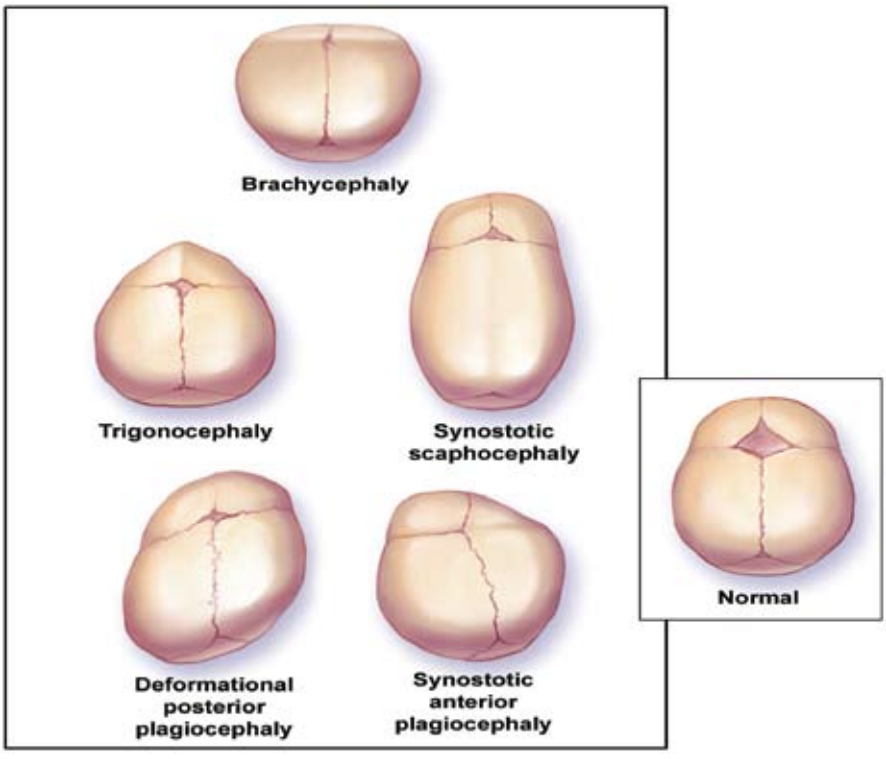


Figure. *Craniosynostosis compared with normal bone fusion.*

Mayo Clinic in Florida Designated an NAEC Level 4 Epilepsy Center

Jerry J. Shih, MD, and William Tatum, DO

Mayo Clinic Hospital at Mayo Clinic in Jacksonville, Florida, (MCF) has been designated a Level 4 Epilepsy Center by the National Association of Epilepsy Centers (NAEC). Level 4 centers are capable of providing care for the most complex cases. Services at MCF have advanced to include 3-Tesla dedicated brain MRI protocols; an innovative epilepsy monitoring unit (EMU); specialized nursing care; neuropsychological services, including intracarotid amobarbital or methohexital procedures; neurosurgical support, including intracranial EEG and resective surgery; and investigational and available forms of neurostimulation.

The comprehensive epilepsy center at MCF, directed by Jerry J. Shih, MD, includes an EMU that has expanded to five beds and is adjacent to the neurophysiology laboratory in the new hospital (Figure). In addition, mobile video-EEG monitoring capability allows technicians in the EMU to monitor patients in the neurosurgical intensive care unit who are at risk for seizures or have undergone epilepsy surgery. Intraoperative MRI is also available. William Tatum, DO, director of the EMU, notes that the new facilities provide optimal coordination between inpatient and outpatient evaluations for epilepsy and other seizure disorders.

Complex Diagnosis in the EMU

Patients in the EMU are safely monitored in a controlled environment with comprehensive monitoring and neurologic nursing care while their routine doses of antiepileptic drugs are tapered. Continuous video-EEG monitoring provides an opportunity to make definitive diagnoses and treatment changes not available from routine, shorter-duration EEG.

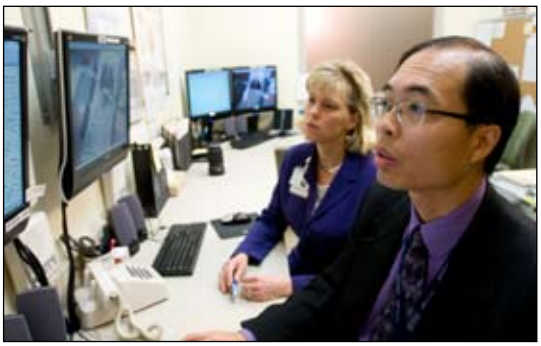


Figure. *The epilepsy monitoring unit at the new Mayo Clinic Hospital in Jacksonville, Florida.*

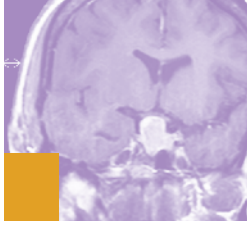
Video-EEG monitoring is known for the advantages it provides in classifying and characterizing seizures in patients with drug-resistant epilepsy. In a recent study on seizure classification in a series of patients with absence seizures observed in more than 1,000 video-EEG monitoring sessions, Dr Tatum and colleagues described a unique type of electroclinical, generalized epilepsy syndrome with polyspike onset absence seizures that had implications for treatment resistance (*J Clin Neurophys*. 2010;27[2]:93-9). Video-EEG is also considered a gold standard for identifying patients who have received a misdiagnosis of epilepsy. For example, as of June 2010, more than 40% of the patients admitted to the MCF EMU with a diagnosis of epilepsy were found not to have the disease. In addition, video-EEG is a valuable tool for differentiating epilepsy from events that may be confused with seizures. In the November 24, 2009, issue of *Neurology*, Dr Shih and colleagues described a patient who had been given a previous misdiagnosis of Tourette syndrome on the basis of episodes of aggressive, apparent goal-directed gestures and profane verbalization. Video-EEG helped to identify the patient's condition as frontal lobe epilepsy, for which the patient was then successfully treated.

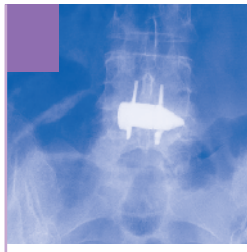
Imaging Advances

Subtraction ictal SPECT coregistered to MRI (SISCOM), an imaging protocol particularly useful for localization when MRI and EEG are not definitive, is available at MCF. Pioneered at Mayo Clinic in Rochester, Minnesota, SISCOM subtracts ictal SPECT studies from interictal studies, compares the two images, and coregisters the "difference image" with the patient's MRI. Statistical ictal SPECT coregistered to MRI (STATISCOM), a more advanced imaging protocol also developed at Mayo Clinic, compensates for subtle variations among serial SPECT images. It has been shown to localize the seizure focus in more patients with nonlesional MRI findings and to be better at correctly localizing the subtype of temporal lobe epilepsy (eg, mesial temporal, lateral neocortical) than SISCOM (*Neurology*. 2010;74[1]:70-6). STATISCOM will further enhance the comprehensive evaluation procedures available in the epilepsy center at MCF.

Overall, both Drs Shih and Tatum agree that among Mayo's most precious resources for patient care are the experienced EEG technologists and dedicated neuroscience nurses who serve the EMU. Together with members of the interdisciplinary team and sophisticated technology and techniques, MCF meets the standards of excellence representative of an NAEC Level 4 Epilepsy Center.

Research Highlights





Mild Cognitive Impairment More Common in Men

A Mayo Clinic study found that the prevalence of mild cognitive impairment was 1.5 times higher in men than in women. The research, part of the Mayo Clinic Study of Aging, also showed a prevalence rate of pls change to 16% in the population-based study of individuals aged 70 to 89 years without dementia who live in Olmsted County, Minnestoa. The study was published in the September 2010 issue of *Neurology*. Authors: R. Petersen, R. Roberts, D. Knopman, Y. Geda, R. Cha, V. Pankratz, B. Boeve, E. Tangalos, R. Ivnik, W. Rocca.

Inflammation Causes Some Postsurgical Neuropathies

A Mayo Clinic study found that nerve inflammation may cause the pain, numbness, and weakness following surgical procedures that is known as postsurgical neuropathy. An uncommon surgical complication, postsurgical neuropathy is typically attributed to compression or stretching of nerves during surgery. This new research shows that, in some cases, the neuropathy is actually caused by the immune system attacking the nerves and is potentially treatable with immunosuppressive drugs. The study was published in the September 2010 issue of *Brain*. Authors: P.J.B. Dyck, N. Staff, J. Engelstad, C. Klein, K. Amrami, R. Spinner, P.J. Dyck, M.A. Warner, M.E. Warner

New Insight Into the Cause of Common Dementia

Researchers at the Mayo Clinic campus in Jacksonville, Florida have found a clue about the mechanism through which some people develop frontotemporal lobar degeneration, a form of dementia that affects the brain areas associated with personality, behavior, and language. The scientists discovered a link between two proteins — progranulin and sortilin — that might open new avenues for the treatment. This form of dementia, which is currently untreatable, generally occurs at a younger age than other common neurodegenerative disorders such as Alzheimer's disease. This study was published in the November 2010 online issue of *American Journal of Human Genetics*. Authors: R. Rademakers, M. Carrasquillo, A. Nicholson, N. Finch, M. Baker, N. Rutherford, T. Hunter, M. DeJesus-Hernandez, G. Bisceglio, J. Crook, R. Petersen, N. Graff-Radford, S. Younkin.

Aggressive Surgery Is Best for Children With Brain Tumors

A Mayo Clinic study found that children with low-grade brain tumors (gliomas) who undergo aggressive surgery to completely remove the tumor have an increased chance of overall survival. If complete removal is not possible, adding radiation therapy to a less complete surgery provides patients with the same outcomes as a complete removal. This study was presented at the Society for Neuro-Oncology Annual Scientific Meeting on November 21, 2010. Authors: N. Laack, S. Khwaja, N. Wetjen, P. Brown.

Seizure Generation in Brain Is Isolated From Surrounding Brain Regions

Mayo Clinic researchers found that areas of the brain generating seizures in individuals with epilepsy are functionally isolated from surrounding brain regions. The researchers speculate that this functional separation may represent an electrophysiologic signature and a useful means of mapping epileptic brain regions. This study was presented at the American Epilepsy Society Annual Meeting on December 4, 2010. Authors: G. Worrell, C. Warren, S. Hu, S. Stead, B. Brinkmann, and M. Bower.

To read more about Mayo Clinic neurosciences research and patient care, visit www.mayoclinic.org.

Here, There, and Everywhere: Telemedicine Robot Delivers Stroke Care

In a rural hospital in the Arizona desert, a five-foot robot leaves an elevator, navigates down the hall around personnel and equipment, enters a patient's room, and comes to a stop at the bedside. Two hundred miles away, Bart M. Demaerschalk, MD, a neurologist at Mayo Clinic in Phoenix, drives the robot. It is his face on the screen and his voice that greets the patient. With the aid of the on-site robot, Dr Demaerschalk begins his neurologic examination (Figure 1). Separated geographically, the robot and the Mayo telestroke team act in real time, and together they are taking telemedicine to the next level.

Serving the Underserved

About 40% of the US population lives in counties without a hospital actively engaged in acute stroke care. A gap exists between the number of certified stroke centers and stroke specialists and the need for stroke expertise in both urban and rural settings. Internationally, most strokes occur in underdeveloped or developing nations where specialized stroke care is often not available.

Rapid evaluation and intervention in acute stroke are critical. The administration of tissue plasminogen activator (tPA) in the first 4½ hours, for example, can limit the amount of brain injury in ischemic stroke. Yet, tPA is underutilized by hospitals that lack stroke expertise. The American Stroke Association estimates that only 5% to 10% of eligible patients in the United States receive tPA. Other immediate decisions include whether the patient needs to be transferred to a primary stroke center for further intervention, such as the evacuation of a brain hemorrhage or surgical management of a brain aneurysm.

Bart M. Demaerschalk, MD

In 2007, Mayo Clinic neurologists addressed this gap in Arizona by providing stroke telemedicine to the rural communities of Yuma and Kingman. In a hub-and-spoke model, Mayo neurologists at the hub in Phoenix use a two-way audiovideo platform and a remotely controlled camera to conduct patient examinations and consultations with emergency department physicians at the affiliate hospital. Neuroradiographic images, laboratory reports, electrocardiograms, and vital signs can be reviewed by the stroke specialist via the Internet, and triage decisions can be made.

Since the telestroke program's inception, Mayo Clinic in Arizona has added the robot, and the telestroke team has conducted more than 400 telestroke examinations. Before the telestroke program, virtually all rural stroke patients were transferred to a primary or comprehensive stroke center. But now, with telestroke consultation, only 30% of patients examined by Mayo telestroke physicians are transferred. The remaining 70% have been able to stay in their communities with the support of their family, local physicians, and care providers. That 70% represents a commensurate savings in the human and economic cost of unnecessary ground or air ambulance transport.

Figure 1. *Dr Bart Demaerschalk operates a remotely controlled robot telemedicine platform, which allows him to assess and treat a patient with acute stroke in a rural hospital in an underserviced community hundreds of miles away.*

The Robot

On-site training by Mayo physicians and administrative personnel includes training nurses in the affiliate hospital to provide some physical support to the robot. They are trained to conduct the examination sensory functions and reflexes and to help position robotic extensions, such as an ophthalmoscope, otoscope, and stethoscope, for the neurologist at the hub site to conduct the physical examination.

In addition to gathering information through patient interaction, the stroke specialist can test speech, language, and other cognitive functions by projecting diagrams, words, and sentences onto the robot's screen. Through this interaction at the bedside, the Mayo physician can assess the cognitive and behavioral status. Dr Demaerschalk says that although initially surprised, patients and families adapt within about five minutes to this form of health care delivery. The robot, informally known as Bart2-D2, begins to assume human qualities, and people respond as if the physician was in the room.

Program Expansion

The Mayo Clinic Telestroke Network has grown to include seven affiliate hospitals in Arizona, including one in Phoenix (Figure 2). Seven more hospitals will be added in the next 12 months. The program has also expanded from a regional to a national service. Dr Demaerschalk and his team worked with their clinical and administrative counterparts in the department of neurology at Mayo Clinic in Florida to bring telestroke to Florida. Since its inception in May 2010, the Mayo Clinic program in Florida has already provided 60 telestroke consults to an affiliate hospital in Titusville. Plans are underway at Mayo Clinic in Minnesota to provide telestroke services to affiliate hospitals in the Mayo Health System, which reaches communities in Minnesota, Wisconsin, and Iowa.

Is There a Smartphone Application for That?

Initially, telestroke service was delivered to and from large, stationary workstations. Now, the telestroke robot can access any area in the affiliate hospital and can be activated from a laptop computer at the hub hospital, or even from the physician's home, with the same level of privacy and security as in the hospital. The robot can go on rounds and conduct follow-up visits as needed. The next step under investigation by Dr Demaerschalk and colleagues is the use of smartphone technology. With a smartphone application, the robot could be activated even more easily from anywhere in the world, eliminating the need to access a computer and a wireless setup.

Here, There, and Everywhere

In January 2010, Dr Demaerschalk and the Mayo Clinic stroke telemedicine team were awarded the first Mayo Clinic Connect, Design, and Enable Innovation Award. The goal of the award is to facilitate innovation, collaboration, and transformation of the way health care is experienced and delivered. Dr Demaerschalk points out that neurology is particularly well suited to telemedicine because "so much of what we do is listening and observing; interacting with patients; testing consciousness, cognitive skills, language, vision, motor and sensory function, movement, coordination, balance, and gait; and evaluating diagnostic data, such as neuroimaging studies and electrophysiologic reports (eg, EEG), all of which can be done from a distance. By synthesizing that information, we can come up with a diagnosis and a management plan—one that in many cases can be implemented in the local community."

Not surprisingly, the telestroke teams have been asked by affiliate hospitals to extend their telemedicine services beyond stroke to other neurologic disorders. By providing specialized care to distant communities, the telestroke teams are helping Mayo Clinic meet one of its key goals for the 21st century—that of providing medical expertise "here, there, and everywhere" there is a need.

Figure 2. *Mayo Clinic Hospital in Phoenix, Arizona, is the hub hospital that provides emergency stroke care via telemedicine to seven affiliate spoke hospitals in the Mayo Clinic Telestroke Network.*

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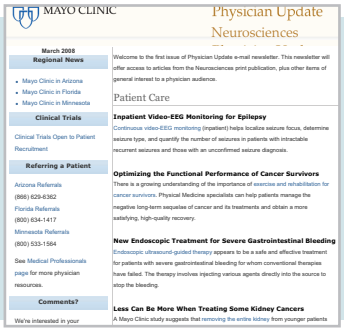
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Welcome to the first issue of Physician Update e-mail newsletter. This newsletter will offer access to articles from the Neurosciences print publication, plus other items of general interest to a physician audience.

Patient Care

Inpatient Video-EEG Monitoring for Epilepsy
Continuous video-EEG monitoring (inpatient) helps localize seizure focus, determine seizure type, and quantify the number of seizures in patients with intractable recurrent seizures and those with an unconfirmed seizure diagnosis.

Optimizing the Functional Performance of Cancer Survivors
There is a growing understanding of the importance of exercise and rehabilitation for cancer survivors. Physical Medicine specialists can help patients manage the negative long-term sequelae of cancer and its treatments and obtain a more satisfying, high-quality recovery.

New Endoscopic Treatment for Severe Gastrointestinal Bleeding
Endoscopic ultrasound-guided therapy appears to be a safe and effective treatment for patients with severe gastrointestinal bleeding for whom conventional therapies have failed. The therapy involves injecting various agents directly into the source to stop the bleeding.

Less Can Be More When Treating Some Kidney Cancers
A Mayo Clinic study suggests that removing the entire kidney from younger patients

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