Redefining the Term “Lesion” in Pediatric Epilepsy Surgery

by Mandeep S. Tamber, MD, PhD

Children with lesional epilepsy, whose seizures are due to the presence of a brain tumor or cortical or vascular malformation, have the best prognosis for long-term seizure freedom following epilepsy surgery. The epileptogenic lesion is viewed as the epicenter of the so-called epileptogenic zone, the area of brain responsible for the generation of focal seizures, and whose removal is necessary to achieve seizure freedom. Depending on the nature of the lesion and its location in the brain, long-term seizure freedom rates at Children’s Hospital of Pittsburgh of UPMC range from 70 to 90 percent.

That being said, a significant proportion of pediatric patients with refractory epilepsy are non-lesional in the sense that no structural lesion is visible on a dedicated high-resolution epilepsy protocol MRI. However, state-of-the-art imaging predicated on cerebral metabolism and cerebral blood flow — coupled with the judicious use of invasive neurophysiology (intracranial electrode recordings) — is changing the epilepsy surgery landscape by making previously non-lesional patients lesional. This is a critical distinction when it comes to predicting the outcome following epilepsy surgery, as the expected outcomes in non-lesional patients are, on aggregate, worse than those for lesional patients. Children’s Hospital is at the forefront of applying these cutting-edge modalities to the evaluation of patients referred for epilepsy surgery candidacy. For patients that have traditionally been classified as non-lesional, the goal of these detailed evaluations is to elevate the likelihood of seizure freedom so that cure rates are comparable to their lesional counterparts.

Prior to the institution of PET imaging, which detects alterations in cerebral metabolism, a patient was excluded from further surgical evaluation if their MRI did not disclose the presence of a lesion. At Children’s Hospital, PET imaging has been fully incorporated as a routine test during presurgical evaluations at our epilepsy center, with all patients undergoing PET imaging on the first day of their admission to our epilepsy monitoring unit. A recent review of our surgical series has identified several patients who had a negative MRI but were found to harbor a potential metabolic epileptogenic zone on PET imaging. These patients were brought to surgery first for further refinement of the borders of the epileptogenic zone (and nearby eloquent areas of cortex) using a period of invasive electrode monitoring, and then for their cortical resection. All of these patients have gone on to achieve an excellent post-resection seizure outcome (Figure 1).

For those patients with both a negative MRI and PET scan, additional imaging is required to facilitate the identification of a well-localized seizure focus that may be amenable to resection. Non-invasive imaging of cerebral blood flow, both at baseline and at the time of a clinical seizure (subtraction

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Chairman’s Message

Neurosurgical Uncertainty

Uncertainty is a certain fact we deal with in everyday life. As neurosurgeons, we deal with uncertainty in almost everything we do. Our patients expect us to make the most accurate decisions and provide reasonable recommendations regarding their care. With uncertainty at so many levels, how do we know we are making the right decision? There is uncertainty as to the natural history of many of the life-threatening diseases we evaluate and treat, in the outcome of procedures we perform, and even in the safety of medications and durability of implants we use.

Uncertain natural history. A portion of our patients present with incidental findings, which may be asymptomatic. Examples include unruptured aneurysms and unruptured arteriovenous malformations (AVMs). As long as they do not rupture, they are for the most part benign. However, their rupture is frequently catastrophic and not uncommonly fatal. Much information has been generated over the years on their natural history, but significant uncertainty remains. In particular, even though the yearly chance of bleeding from these lesions is low, over the long-term the risk may be significant, particularly for young patients. Should a particular asymptomatic, but potentially lethal, lesion be treated or observed? How do we know which approach is better in the short- and long-term?

Uncertainty of treatment. Many of the diseases we manage can be treated using a variety of different approaches. For example, a brain tumor may be observed, treated with radiosurgery, treated with a biopsy and then chemotherapy or radiation, treated with an endoscopic approach, or treated with an open craniotomy. We are fortunate to work at an institution where we can offer all of these options to our patients. Many of these options were either developed or popularized at the University of Pittsburgh. How do we know which approach is better in the short- and long-term?

Uncertainty of medications or devices. Given the competitive free market we live in, we are constantly bombarded with a broad variety of choices pertaining to medications for our patients, as well as devices to be used as implants during a procedure. There are many different kinds of shunts, pedicle screws, and aneurysm clips. There are many different types of antibiotics or antiepileptic drugs. How do we choose? How do we know which one is really better? How do we know which medication or device is better in the short- and long-term?

To battle uncertainty, we must rely foremost on separating what is certain in each specific case. Based on specific facts, as well as our extensive clinical experience, we aim to provide the most appropriate options for our patients’ uncertain conditions. As the largest academic neurosurgery practice in the country, our faculty is extremely experienced and subspecialized. At the University of Pittsburgh Department of Neurological Surgery, we battle uncertainty with facts and experience, with the goal to optimize outcomes.

Robert M. Friedlander, MD
Chairman and Walter E. Dandy Professor of Neurological Surgery
Pediatric Division a Multifaceted Leader in Neurosurgical Care

The Pediatric Neurosurgery Division at Children’s Hospital of Pittsburgh of UPMC is a multifaceted leader in neurosurgical care, providing care for children with tumors, spinal deformities, cranial malformations, spasticity, and epilepsy. The division — led by Ian Pollack, MD, and including the work of full-time faculty members Elizabeth Tyler-Kabara, MD, PhD, Stephanie Greene, MD, and Mandeep Tamber, MD, PhD — has gained worldwide recognition for the treatment of pediatric brain tumors, cerebral palsy, and traumatic brain injury. The center’s neurosurgeons work closely with specialists in pediatrics, surgery, radiation therapy, oncology, physical therapy, orthopaedics, plastic surgery, critical care, and social services to maximize patient care.

Neuro-Oncology

Through its neuro-oncology program, the center provides comprehensive, multidisciplinary care for patients with brain and spinal cord tumors, in collaboration with the oncology and radiation therapy programs. Patients may be eligible for treatment in one of many innovative research protocols at Children’s Hospital. These protocols — several of which are unique to Children’s Hospital or available at only a few centers throughout the country — provide patients with access to new treatments and promising studies.

Dr. Pollack is the institutional principal investigator and chair of the neurosurgery committee in the Pediatric Brain Tumor Consortium, supported by the National Cancer Institute to perform cutting-edge clinical trials in children with brain tumors. He also serves as the principal investigator on several studies involving vaccine-based immunotherapy for children with challenging brain tumors, such as newly diagnosed brainstem and high-grade gliomas and recurrent low- and high-grade gliomas and ependymomas.

Dr. Tyler-Kabara has pioneered the use of endoscopic endonasal approaches to the skull base in the pediatric population. Children’s Hospital offers this minimally invasive approach to skull base pathologies even in children under the age of five. The clinical brain tumor program is augmented by NIH-funded, laboratory-based research initiatives examining molecular markers of prognosis and novel treatment strategies in children with brain tumors.

Pediatric Epilepsy Surgery

The Surgical Epilepsy Program is the only center in the region able to provide comprehensive evaluation and surgical treatment options for children with intractable epilepsy. Dr. Tamber, the lead epilepsy neurosurgeon, collaborates closely with epileptologists within the division of pediatric neurology. A comprehensive pre-surgical evaluation, using state-of-the-art neuro-imaging resources, is carried out to identify the specific site in the brain causing seizures, and to determine its relationship to important functional areas of the brain. Surgical candidates benefit from a full spectrum of treatment options ranging from lesionectomies (guided by intraoperative electrocorticography); tailored cortical resections following a period of invasive subdural EEG monitoring; corpus callosotomies; and hemispherectomies. Other patients may benefit from vagus nerve stimulation. Children’s Hospital has implanted more than 300 vagus nerve stimulators, making it one of the busiest programs in the country.

Movement Disorders

The Spasticity and Movement Disorders Clinic, led by Dr. Tyler-Kabara, is made up of a team of pediatric medical professionals who specialize in the comprehensive, multidisciplinary evaluation and treatment of children and young adults with spasticity and other movement disorders such as dystonia, chorea, athetosis, and tremor. The clinic was founded in 1986 by A. Leland Albright, MD, former head of CHP’s pediatric division. Dr. Albright was the first investigator in the United States approved by the FDA to study the use of intrathecal baclofen and the first doctor to perform deep brain stimulation for tremor dystonia resulting from cerebral palsy. The purpose of the clinic is to determine whether a patient would benefit from treatment with oral medications, intrathecal baclofen, selective dorsal rhizotomy, intramuscular BOTOX® injection, deep brain stimulation, or other therapies.

Vascular Anomalies

Patients with vascular anomalies such as aneurysms, arteriovenous malformations, cavernous malformations, and moyamoya syndrome are managed by Dr. Greene. Select patients undergo further evaluation at the department’s Center for Image-Guided Neurosurgery with L. Dade Lunsford, MD, for possible radiosurgical treatment; angiography by Brian Jankowitz, MD, for further definition of anomalies and possible embolization of feeding vessel.
Pediatric Vascular Anomalies

by Stephanie Greene, MD

In the Vascular Anomalies Clinic, we provide multidisciplinary care for children with a variety of vascular malformations, such as hemangiomas and venous and lymphatic malformations. It is one of the largest centers in the country for management of vascular anomalies. The clinic involves specialists from plastic surgery, dermatology, interventional radiology, general pediatrics, hematology, general surgery, cardiology, orthopaedics, otolaryngology, ophthalmology, neurology, and neurosurgery.

Treatment for PHACES Syndrome

Children with PHACES syndrome are managed through the clinic. Their hemangiomas are treated medically or with laser therapy. The peak incidence of stroke secondary to moyamoya syndrome in children with PHACES is in the first year of life, so children are monitored closely during this time with serial MRIs and neurologic examinations.

PHACES Syndrome
The acronym stands for:

- Posterior fossa anomalies
- Large segmental facial hemangiomas
- Arterial lesions
- Cardiac abnormalities
- Eye abnormalities
- Ster nal lesions or supraumbilical raphe

Moyamoya syndrome is a progressive narrowing of the distal internal carotid arteries and proximal anterior and middle cerebral arteries, producing a decrease in cerebral blood flow (Figure 1). Ischemic attacks precipitated by hyperventilation or dehydration can produce infarction. The treatment for moyamoya syndrome is surgery.

A pial synangiosis, or indirect internal-to-external carotid artery bypass, is offered to children in this age group.

This surgery entails dissecting a portion of the superficial temporal artery out of the scalp and suturing it down to the pia, the innermost layer of the leptomeninges. A pial synangiosis allows the formation of collateral vascular supply to the brain from the superficial temporal artery, with a gradual improvement in symptoms over the first few months following surgery. These patients are maintained on low-dose aspirin for life.

Case Study: Epidural Vascular Malformation

A recent patient managed through the Vascular Anomalies Clinic was an 18-year-old woman with an epidural vascular malformation communicating with a posterior mediastinal mass through two thoracic neural foramina (Figure 2). She had an enlarging syrinx extending from C6-T4 that produced paresthesias and neurogenic claudication. The syrinx was presumed to be secondary to venous hypertension or direct compression of the spinal cord by the malformation.

The mediastinal mass was injected with contrast by the interventional radiologist, allowing the mass to be defined as venous and not lymphatic. A hematologist ruled out a hypercoagulable state, as is commonly seen in patients with venous malformations, and determined that the patient would not need perioperative anticoagulation. The mediastinal mass had previously been biopsied with significant bleeding, and it had recurred over six years’ time. It was decided that decompressing her spinal cord was the most pressing concern, and the mediastinal mass would be best treated by sclerotherapy after the spinal surgery. She underwent a C6-T5 osteoplastic laminectomy and fusion to expand her spinal canal, with resection of the venous malformation along the length and width of the exposed thecal sac. The thecal sac began to pulsate at the termination of the resection, evidence that normal flow of CSF had been restored. She was discharged to the rehabilitation unit for reconditioning, with no new neurological deficits. Follow-up imaging obtained six weeks after surgery revealed a dramatic improvement in the syrinx.
Spasticity and Movement Disorders

by Elizabeth Tyler-Kabara, MD, PhD

One of the biggest misconceptions about children with movement disorders is that they are intellectually impaired. In reality, children with movement disorders are often of average or above-average intelligence, but due to the disruptive nature of their disorder, they may suffer from communication disorders, learning disabilities, attention deficit hyperactivity disorder (ADHD), obsessive-compulsive disorder (OCD), and other neurobehavioral disorders.

Our team treats the whole child, not just the disorder, by carefully coordinating surgical and medical treatment with a host of other rehabilitative and support services that address all of the child’s clinical needs.

Common Movement Disorders Among Children Include:

- **Spasticity**: An involuntary muscle tightness and stiffness that occurs in about two-thirds of people with cerebral palsy (CP) and in many who suffer severe head injuries. The medical definition of spasticity is a velocity-dependent, increased resistance to passive muscle stretch. In other words, when a muscle affected by spasticity is stretched by someone else, it is harder to move the muscle than normal, and the faster one pushes, the harder the muscle is to move.

- **Dystonia**: The second most common movement disorder. It is characterized by sustained muscle contractions that result in twisting movements and abnormal postures and is present in 25 to 35 percent of people with CP. It may begin in childhood, adolescence, or adulthood, and may affect only one region of the body, such as the neck, in which case it is called focal dystonia. It can occur in adjacent body regions (segmental dystonia), one side of the body (hemidystonia), or the entire body (generalized dystonia). Dystonia may also occur after head injuries or as an isolated problem.

- **Athetosis**: A slow, writhing motion of the fingers and hands that occurs in approximately 5 percent of people with CP. Athetosis was a common diagnosis a few years ago, but now many people previously diagnosed as having athetosis are considered to have dystonia. We believe the two disorders are different, in that athetosis affects muscles of the fingers, hands, and around the mouth, causing slow, twisting, writhing motions that are more continuous than dystonic movements.

- **Chorea** (pronounced “korea”): An involuntary, abrupt, rapid, brief, and unsustained irregular movement that is sometimes described as “dance-like.” Chorea occurs in 5 percent of people with CP.

- **Ataxia**: An abnormality of coordination. It particularly affects walking; gait is typically very unsteady.

- **Myoclonus**: A sudden, shock-like twitching of muscles without a rhythm or pattern.

- **Tremor**: An involuntary trembling movement.

It is important to remember that people may have more than one movement disorder at one time; the combination of spasticity and dystonia is particularly common.

Why These Problems Occur (Pathophysiology)

Muscle tone — the state of muscle contraction — is controlled by two factors: inhibitory (relaxing) signals coming down from the brain into the spinal cord, causing the release of a chemical, GABA, which makes the muscles relax; and excitatory (stimulating) signals coming from the muscles into the spinal cord, telling themselves to contract. If the balance between those two is normal, muscle tone is normal.

Spasticity is caused by damage to parts of the brain that send the messages for GABA to be released. The damage may occur anywhere along the pathway, from the brain to the brainstem to the spinal cord. The end result is the same: deficiency of GABA and a relative excess of excitatory impulses.

The cause of dystonia is not understood nearly as well as the cause of spasticity. It is thought to be due to damage to the basal ganglia, deep structures in the brain that adjust the amount of movement that occurs when people tell a muscle to move. The cause of athetosis is probably similar.

Chorea is due to damage to a different region of the basal ganglia, so that output from a structure called the internal globus pallidus is less than normal.

Diagnosis and Evaluation

Patients are evaluated individually by each of the team members. Each specialist performs a separate evaluation that gives the team several different perspectives and helps determine treatment recommendations. Prior imaging and evaluations are reviewed, and current equipment and bracing is evaluated by our therapists. After evaluation, team members meet to discuss findings and to develop recommendations for the patient and family.

Treatment Options

The Spasticity and Movement Disorders team strives to precisely understand family and patient goals in determining all treatment options. These goals are a key factor in any treatment plan.

The main indications for treating movement disorders include:

- To improve function.
- To facilitate care.
- To retard or prevent the development of contractures, and occasionally, to reduce pain.

If function improvement is key, the team evaluates the child for muscle tone, trunk strength, underlying muscle strength,
Pediatric Division a Multifaceted Leader in Neurosurgical Care (Continued from Page 3)

vessels; and assessment by a vascular neurologist for management of seizures, dystonia, and coagulopathies that may be identified during the course of the evaluation process. Patients with vascular problems involving more than one organ system, or those with syndromes such as Sturge-Weber or PHACES, are seen in the multidisciplinary Vascular Anomalies Clinic.

Collaboration and Research

The division is an integral collaborator in the Cleft-Palate and Craniofacial Center in the management of children with craniofacial disorders. Because children with complex craniosynostosis often require a staged approach to the treatment of their cranial, midfacial, and lower facial deformities, close multidisciplinary follow-up is maintained throughout childhood and adolescence in order to optimize long-term functional and cosmetic outcome.

The division is also actively involved in the Brain Trauma Research Program, the Fetal Diagnosis and Treatment Center, and the Brachial Plexus Program. In conjunction with a team of specialists at Magee-Womens Hospital of UPMC, Dr. Greene has established a program to treat babies with myelomeningocele, or spina bifida, with in utero surgery here in Pittsburgh. Babies who are not candidates for in utero surgery for a variety of reasons undergo conventional closure of the defect within several days of birth. These children are seen throughout childhood by a multidisciplinary team of medical professionals in the Spina Bifida Clinic at Children's Hospital of Pittsburgh of UPMC, one of the largest such clinics in the country.

The Brachial Plexus Program, run through the division of pediatric plastic surgery, manages infants with obstetric injuries to the brachial plexus in a collaborative fashion with specialists from neurosurgery, plastic surgery, orthopaedic surgery, and physical and occupational therapy. Children's Hospital is one of a handful of centers in the country that has a dedicated multidisciplinary clinic for these patients. Patients with peripheral nerve tumors or injuries are seen by Dr. Greene outside of the Brachial Plexus Program.

Dr. Tamber has worked to include Children's Hospital in several large multi-center clinical networks that are dedicated to the study of common pediatric disorders. Children's Hospital is a member of the Hydrocephalus Clinical Research Network, a group of seven premier pediatric neurosurgical departments in North America that is dedicated to designing and undertaking field-changing prospective research into pediatric hydrocephalus. In addition, Children's Hospital has been selected as a member institution in the Park-Reeves Syringomyelia Research Consortium, a group dedicated to solving important clinical problems within the realm of Chiari malformation and syringomyelia. Dr. Tamber is the institutional principal investigator for both of these endeavors.

Pediatric Epilepsy Surgery

(Continued from Page 1)

SPECT imaging) and/or non-invasive imaging of the electrical activity of the brain in the period between seizures (MEG), may be required. Both modalities are available at Children's Hospital and allow us to achieve excellent surgical outcomes (Figure 2).

Pediatric epilepsy surgery over the past few decades has demonstrated that improved patient outcomes through diagnostic and therapeutic advances can be achieved. In parallel, these advances, especially as they relate to improvements in our diagnostic performance, allow us to offer the possibility of improved outcomes to more patients.

Fellowship in Pediatric Neurosurgery

In addition to having a vibrant clinical and research program, the Pediatric Neurosurgery Division at Children's Hospital of Pittsburgh of UPMC has a longstanding commitment to the education of residents, fellows, and faculty physicians. The pediatric neurosurgery fellowship, one of the most active in the country, has trained 16 post-residency fellows during the last 21 years, many of whom have gone on to academic positions at other centers throughout the country.

Figure 2. Representative images from a patient with a normal preoperative structural MRI study (A) and no asymmetry seen on metabolic PET imaging (B), but with a presumed epileptogenic focus in the right frontal lobe visualized on subtraction SPECT imaging (C). After a period of invasive monitoring with surface and depth electrodes, this patient went on to undergo a right frontal cortical resection (D). Pathology was cortical dysplasia. The child is seizure-free approaching one year postoperatively.
Maroon Climbs Mt. Kilimanjaro

Joseph Maroon, MD — clinical professor of neurosurgery, Heindl Scholar in Neuroscience at the University of Pittsburgh, and noted sports medicine expert — reached the summit of Mt. Kilimanjaro February 26, in the first ever climb of Africa’s tallest mountain by 10 amputees, serving as the expedition’s medical advisor.

Dr. Maroon praised his fellow climbers, saying, “I was with three individuals with no legs, one individual with both legs amputated and an arm, and another with no arms — a 19-year-old young man who was born with no arms. To see these individuals climb over steep rocks and terribly difficult trails, to reach this, was one of the most inspiring things I’ve seen.”

The expedition was the centerpiece of the Live Free Foundation’s “No Limits Freedom Tour,” a trek across Africa, that included Tanzania, Johannesburg, and Cape Town. On the tour, the expedition members presented lectures and athletic events at various community centers, disabled centers, and orphanages with the message of overcoming obstacles whether you are physically disabled or not.

Mt. Kilimanjaro, located in Tanzania’s Kilimanjaro National Park, is the highest mountain in Africa and the highest free-standing mountain in the world. It stands at 19,341 feet above sea level.

Congratulations

Desiree Playso-Doyle, division administrator, received the American College of Healthcare Executives Senior Level Healthcare Executive’s Regent Award in December. The award recognizes ACHE members who have made significant contributions to the advancement of healthcare management excellence.

Jonet Vacsulka, RN, Gamma Knife® nurse coordinator, received UPMC’s 2013 Dignity and Respect Champion Award for her efforts in building and sustaining a work environment in which everyone feels included, valued, and appreciated. The award recognizes and honors UPMC staff for their commitment to the UPMC core value of dignity and respect, creating the best experience for patients, families and employees.

Parthasarathy D. Thirumala, MD, was promoted to clinical associate professor of neurological surgery and neurology in February.

Adam S. Kanter, MD, was promoted to associate professor of neurological surgery in February.

Special Lectures and Appearances

Peter C. Gerszten, MD, MPH, was a guest speaker at the Brooke San Antonio Military Medical Center on February 25, where he spoke about the latest advancements in the treatment of symptomatic lumbar disc herniations for active military personnel.

L. Dade Lunsford, MD, was the honored guest at the Texas Association of Neurological Surgeons Annual Meeting in San Antonio, Texas, February 27-28, giving the Samuel Hassenbusch Lecture.

Juan Fernandez-Miranda, MD, was a special invited guest of the North American Skull Base Society, February 14-16 in San Diego, lecturing on 3D surgical approaches to the posterior skull base during the meeting’s plenary sessions.

Ian Pollack, MD, gave the keynote lecture at the Pediatric Neuro-Oncology Symposium sponsored by MD Anderson Children’s Cancer Hospital, in Houston, Texas, February 28-March 1.

In the News

Dr. Maroon’s climb of Mt. Kilimanjaro received extensive coverage in February and March in various media outlets including the Pittsburgh Tribune-Review, the Pittsburgh Post-Gazette, the KDKA Radio 1020 Morning News, the KDKA TV-2 Evening News and steelers.com among others.

Robert Friedlander, MD, MA, commented on the relationship between ALS and head trauma in a December 17 Pittsburgh Tribune-Review article reporting on an NCAA lawsuit involving concussions.

Stephanie Greene, MD, commented on the arteriovenous malformation surgery of a 14-year-old patient in the March 5 edition of the Pittsburgh Tribune-Review.

David O. Okonkwo, MD, PhD, commented on a promising new formulation of progesterone used in traumatic brain injury research in an NBC.com article in March.

Deep Brain Stimulation Symposium

An overview of DBS for Parkinson’s disease, tremor, dystonia, epilepsy, and OCD.

September 19, 2014 • 8:00 a.m. to 4:30 p.m. • University Club, University of Pittsburgh
For more info or to register call 412-864-1839, or visit neurosurgery.pitt.edu/dbs2014.
Open to physicians, physician assistants, nurses, patients, family members, and community advocates.
Glioma Therapeutics: Researching Novel Treatments

by Kimberly A. Foster, MD

When neurosurgeons diagnose and treat patients with malignant glioma, the current common therapies include surgery, chemotherapy, and radiation. These modalities together attempt to treat cancer via cytoreduction, nonspecifically halting cellular processes of DNA metabolism and cell division. Resistance to such treatment is significant and largely due to aberrant activation of survival signaling pathways, rendering glioma cells refractory to programmed cell death, or apoptosis. Thus, prognosis for patients remains extremely poor, and novel treatment approaches are needed.

Recent trends in cancer therapeutics aim to exploit agents that can disrupt specific oncogenic signaling processes. Researchers now understand that cancer is “smart” and has many modes of resistance. Blocking one key signaling pathway is usually insufficient to promote cellular death.

The Glioma Therapeutics Laboratory of Ian Pollack, MD, applies novel, rationally designed combinations of molecularly targeted agents to inhibit multiple pathways of survival in a panel of genotypically defined glioma cells and primary tumor cell lines. Researchers in Dr. Pollack’s lab examine a variety of drugs, including tyrosine kinase inhibitors, death receptor activators, epigenetic modifiers, and small molecules that regulate important pro-survival and pro-apoptotic proteins. Ideally, such therapies cross the blood-brain barrier, do not kill healthy neurons or glia, and can induce cancer cell death at clinically achievable doses.

This work helps elucidate the molecular basis for tumorigenesis and uncover causes for differential clinical sensitivity to therapy. The study of cancer now looks beyond basic tumor histology. As researchers continue to understand the unique genomic alterations of each patient’s tumor, they can implement strategies that match individual patients with specific treatments to which they are more likely to respond. Ultimately, based on in vitro studies, these drugs can be applied to in vivo models of glioma and translated into clinically useful therapies.

Dr. Pollack’s lab includes the work of myself, David Premkumar, PhD, and Esther Jane, PhD, both research assistant professors with the University of Pittsburgh Department of Neurological Surgery. Second-year University of Pittsburgh medical student Alejandro Morales also contributes to the program. Lab facilities are located in the Rangos Research Center at the Children’s Hospital of Pittsburgh of UPMC campus.

Spasticity and Movement Disorders (Continued from Page 5)

It is important to realize that some treatment is recommended for almost all patients but that surgical treatment is not recommended for everyone. Some patients are too young or too small for surgery, or they can be effectively treated by oral medications or intramuscular injections. Occasionally, it is not clear which treatment would be most appropriate; in that case, the team often asks to re-evaluate the child after a specific time period.