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Disclosures

Nduka Amankolor, MD, Johnathan Engh, MD, Paul Gardner, MD, and Georgios Zenonos, MD, have reported no relationships with proprietary entities producing health care goods or services.

Instructions

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Stereotactic Dilatable Port Surgery for Brain Tumors Implementing the Next Generation of Minimally Invasive Brain Surgery

by **Johnathan A. Engh, MD**

The UPMC Department of Neurological Surgery has been at the forefront of the development of minimally invasive neurosurgical procedures for decades. Examples include the popularization of microvascular decompression surgery for cranial nerve disorders, the Gamma Knife® radiosurgery program, and the Endoscopic Endonasal Approach for brain tumors and lesions. Similarly, the Neuroendoport® program at UPMC, formally established in 2008, has facilitated the removal of deep-seated and intraventricular brain tumors with minimal brain dissection.

The central guiding principle of the Neuroendoport program is that all brain surgery causes some degree of iatrogenic trauma and that brain trauma may lead to surgical morbidity. Therefore, the port surgery apparatus is designed to minimize cortical and subcortical trauma whenever the brain cortex must be traversed to approach a tumor. Our technique involves the image-guided placement

of a small cylindrical conduit through which the tumor is removed. The tube evenly distributes retraction forces on the surrounding brain and does not require a wider brain dissection to work in deep spaces. Since the program was established, hundreds of tumors have been removed using this method, and our port surgery techniques have been taught to numerous physicians all over the world.

Despite these advances, substantial opportunities for improvement of port surgery remain. Regardless of its small size, the port requires a small craniotomy for placement, and the cannulation process can inflict shear injury on the surrounding brain, as the port is passed over a bullet-shaped dilator (see Figure 1). In order to improve upon these limitations, we have established a stereotactic-guided technique for placement of a dilatable brain port. This initiative has been backed by the innovative practice committee of the University of Pittsburgh, and it is intended to be used as a stepping stone to the placement of even smaller brain ports that can be placed through a burr hole craniostomy.

The dilatable port technique uses a Backlund stereotactic brain needle (Elekta, Inc.) as an entry conduit for a cigar-shaped balloon catheter. The brain needle is placed using stereotactic guidance, and then the balloon catheter is used to replace the inner cannula. Following removal of the outer cannula, the catheter is inflated, and the cylindrical port is then put into place. As a result, the shear injury from port placement is obviated. In addition, the inflation can be done over a prolonged period, maximizing the ability of the brain to adjust to the stretching of white matter fibers (see Figure 2 on Page 8).

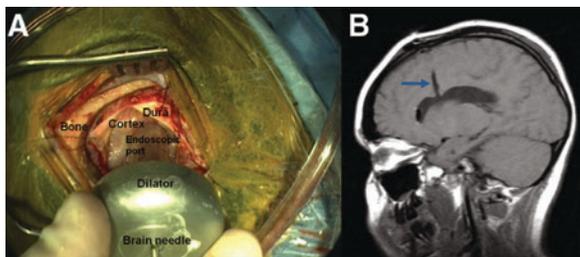


Figure 1. Illustration of shear injury caused by placement of an endoscopic port into the ventricle (left). The plastic port is placed over a bullet-shaped dilator through a small craniotomy (right). Sagittal post-operative T1-weighted MRI scan demonstrates a tract formed as a result of shear and direct compression caused by the small port.

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Chairman's Message

Playing with a Full Deck



Although I am not a poker player, I do know that you cannot properly play the game without a full deck of cards. Managing neurosurgical diseases — in particular in patients with brain tumors — requires a broad spectrum of approaches at your disposal, i.e., the full deck of options, in order to offer the most effective treatment. Treatment should maximize safety and efficacy while minimizing risk. The ideal goal is complete tumor removal — or as complete as is safely possible — with the least possible disruption of normal tissues, both on the surface and deep within the brain.

At UPMC, we offer a full spectrum of approaches for the management of brain tumors. Some important approaches are featured in this issue of *Neurosurgery News*.

Dilatable port surgery provides an opportunity to surgically navigate deep into the brain, while minimizing trauma to normal intervening tissue. In previous issues, we have described how High Definition Fiber Tractography (HDFT) delineates normal white matter tracts, allowing for the ability to reduce their disruption as the neurosurgeon plans a surgical corridor to a lesion. Additionally, HDFT provides insight into the degree of

disruption caused by the tumor, allowing surgeons to optimize the resection. Endoscopic Endonasal surgery is an alternative approach, minimizing external incisions while allowing direct access to anterior skull base lesions.

For certain lesions, stereotactic radiosurgery provides an additional and, at times, complementary minimally invasive approach for the management of complex brain tumors. The newest addition to this technology described in this issue is the next generation Gamma Knife® Icon, which provides important advantages over the previous generation of Gamma Knife units.

Finally, at present, many tumors cannot be cured with surgery. Novel therapeutic approaches need to be developed to better diagnose and characterize the individuality of the tumor in order to biologically target it. At UPMC, we hold all the cards, allowing us to design and deliver treatment plans that maximize safety and efficacy.

Robert M. Friedlander, MD, MA

*Chairman and Walter E. Dandy Professor of Neurological Surgery
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Molecular Prognostication for Clival Chordomas

by Georgios Zenonos, MD, and Paul Gardner, MD

Chordomas are very rare, aggressive tumors with an incidence around one in one million annually. Because of difficulties associated with research of chordomas due to their rarity (lack of samples, scant research funding, etc.), this type of tumor has been characterized as an “orphan disease.” As such, the medical community’s understanding of the disease is lesser when compared with other diseases; consequently, no reliable molecular prognostication panel exists to guide clinical decision-making.

Chordomas are known to be extremely variable in their clinical behavior. Some chordoma patients have a nearly normal life span, whereas others rapidly succumb to their unrelenting tumor. The knowledge of how aggressive tumors are likely to behave after surgery or radiation would significantly impact patient counseling and treatment, including decisions about repeat surgery, observation, and high-dose radiation.

UPMC is a large-volume referral center for clival chordomas, which means that our physicians treat tumor patients on a regular basis. We have thus been able to prospectively evaluate a molecular prognostication panel based on 92 clival chordoma samples. This molecular prognostication panel consisted of Fluorescence in Situ Hybridization (FISH) for 1p36 and 9p21 deletions (see Figure 1); immunohistochemistry for Ki-67; and polymerase chain reaction-based studies for Loss of Heterozygosity (LOH) of 1p, 9p, 10q, and 17p. The aforementioned chromosomal loci are linked with several tumor suppressor genes (such as p16/CDKN2A, PTEN, TP53, etc.). The deletion of these loci is known to be associated with a less favorable prognosis in several other

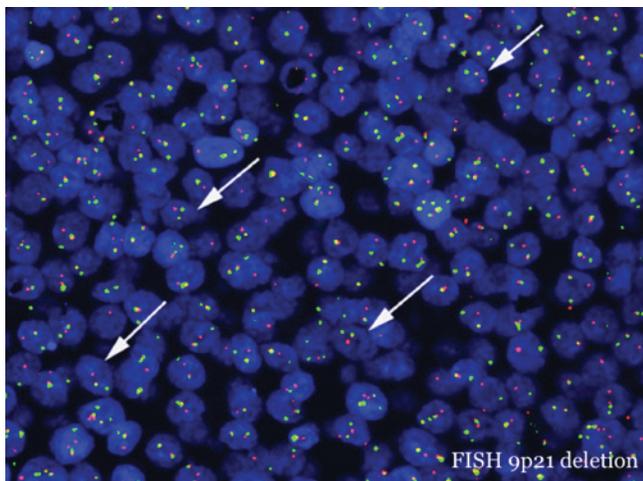


Figure 1. Fluorescence in Situ Hybridization (FISH) for 9p21 (p16/CDKN2A) deletions. As shown, chordomas are polyclonal tumors, and therefore not all the cells within the tumor share the same genetic aberration.

kinds of tumors. The primary endpoints of the study were freedom from radiographic progression after surgery and freedom from radiographic progression after radiation.

After a median follow-up of 45 months, we found a number of molecular markers to be predictive of a shorter progression-free survival (PFS) after surgery. The most important markers were a higher Ki-67, homozygous deletions of 9p21, and 1p deletions by FISH. Higher Ki-67 and homozygous 9p21 deletions were also predictive of a shorter PFS after radiation. The study also revealed a dose effect relationship between the molecular markers and prognosis. In other words, the degree to which each tumor carried a specific molecular aberration (e.g., 90% of tumor cells deleted for 9p21 vs. 5% of tumor cells deleted for 9p21) was associated with a different PFS curve (see Figure 2).

The results of the study carry important implications in day-to-day clinical practice. Being able to predict the behavior of a tumor is not only crucial for the correct counseling of patients, but it could also potentially steer an oncologist or surgeon toward recommending observation, radiation, or re-operation for residual tumors or recurrences. Such predictions may even lead a physician and patient to consider enrollment in clinical trials for chemotherapy. While prospective validation of this prognostication panel is needed to further elucidate its role in the management of chordoma patients, it can potentially reveal a critical missing piece in the understanding of this rare disease.

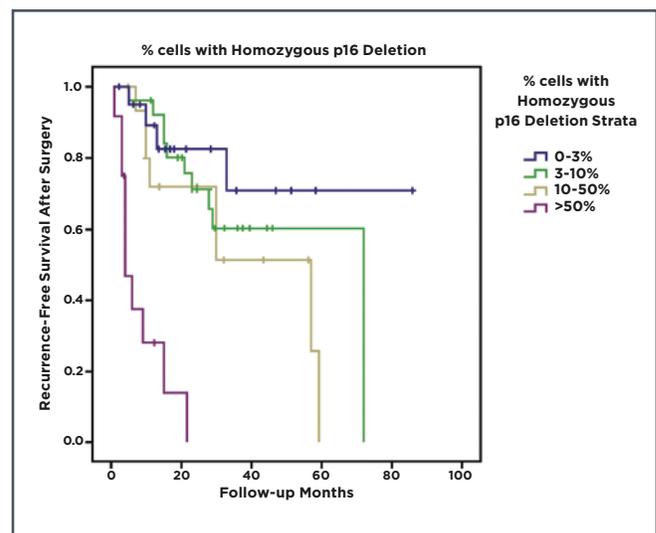


Figure 2. Kaplan-Meier curve showing a dose effect relationship between the percentage of tumor cells carrying the 9p21 (p16/CDKN2A) deletion and the progression-free survival after surgery.

Multidisciplinary Approach to Brain Tumor Treatment Produces Meaningful Results

by **Johnathan A. Engh, MD, and Nduka Amankulor, MD**

The Adult Neurosurgical Oncology Program at the UPMC Department of Neurological Surgery is dedicated to the optimal surgical management of patients with brain and spinal tumors. The program is closely associated with medical tumor specialists at the Hillman Cancer Center of UPMC. Under the leadership of **Johnathan Engh, MD, and Nduka Amankulor, MD**, the group of physicians has built a nationally recognized program. The team believes in an emphasis on positive patient outcomes through multidisciplinary care, innovative surgical techniques, translational research, and clinical trial participation.

The program relies on input from multiple physician groups, including neurosurgery, neuro-oncology, radiology, radiation oncology, and pathology, to create a care plan for each patient. Representatives from each of these disciplines meet at a weekly tumor board conference to discuss clinical cases and outcomes. In addition, group representatives meet each week to discuss clinical trials for cancer treatment and each month to discuss upcoming translational research initiatives. Patients have access to multiple physicians during a single appointment in our multidisciplinary clinic, further streamlining care. As a result, each patient receives a treatment plan that is rooted in medical evidence and tailored for their individual success.

Essential surgical competencies of the neurosurgical program include awake craniotomy, fluorescent-guided brain tumor resection, Neuroendoport® minimally invasive brain tumor surgery, Cyberknife® stereotactic radiosurgery, and minimally invasive spinal tumor surgery and fixation. These tools and processes facilitate maximal tumor removal with minimal neurologic morbidity, but they require appropriate application to suit the needs of each individual patient. Patients of the program who receive open surgery participate in an institutional tumor banking initiative, which has facilitated the harvest and molecular characterization of hundreds of brain tumors. The program also offers surgical, radiosurgical, and oncological clinical trials to appropriate patients.

Exploration of a few specific cases the program has taken on illustrates the advantages of the multidisciplinary approach to patient care. Figure 1 outlines the case of a young adult international patient who was referred to UPMC for a brain tumor causing complex partial seizures. An MRI scan revealed a contrast-enhancing tumor within the non-dominant parahippocampal gyrus. Although deep-seated tumors such as this are often excellent candidates for Neuroendoport surgery, the lesion's close proximity to the skull base raised concern for the safety of brain cannulation in this scenario. Therefore, the patient was offered a subtemporal approach to the tumor with

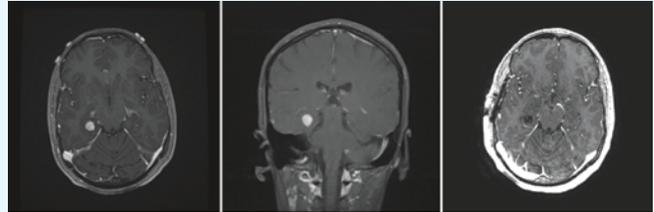


Figure 1. A 25-year-old patient with new-onset partial complex seizures was found to have a discrete, enhancing mass lesion in the right parahippocampal gyrus on contrast-enhanced MRI scans (left and middle). Using fluorescein for intraoperative tumoral visualization, the tumor was completely excised (right).

augmentation of tumor visualization using the Yellow 560nm microscope light filter (Carl Zeiss Meditec AG). This technique can help to distinguish tumors from the surrounding white matter when viewed under a specialized operating microscope filter, facilitating maximal tumor resection. A complete resection was achieved in this case; pathology was consistent with a pilocytic astrocytoma, and the patient returned home with no neurological deficits.

Figure 2 illustrates the case of a 75-year-old man with an esophageal adenocarcinoma who, after a screening PET scan, was found to have a mass in the cerebellum. Subsequent MRI scans confirmed a 3 cm metastasis with mild effacement of the

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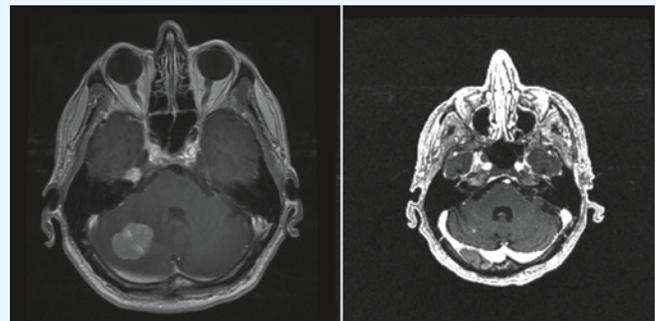


Figure 2. In this 75-year-old patient, pre-procedural (left) and six months post-procedural (right) axial contrast-enhanced T1 weighted MRI scans demonstrated a sizable right cerebellar metastasis from esophageal adenocarcinoma and a remarkable response to fractionated radiosurgery using the Cyberknife. This particular treatment protocol is specifically designed for large tumors.

Brain Tumor Treatment *(Continued from Page 4)*

fourth ventricle. Normally, such lesions require surgical resection. However, in light of the patient's age and lack of symptoms, he underwent Cyberknife radiosurgery in three separate doses, tailored to treat larger tumors for which such an approach is normally not safe. A six-month follow-up MRI demonstrated a remarkable response to treatment, with a 3 mm area of residual enhancement. The patient had no untoward effects from the therapy and was able to avoid open brain surgery as a result.

Figure 3 illustrates a 32-year-old patient who presented with a generalized seizure and was found to have a non-enhancing, expansile mass within the premotor cortex. Given his young age and a presumptive diagnosis of low-grade glioma, he underwent magnetoencephalography (MEG) with pre-surgical mapping under the direction of **Ajay Niranjani, MD**. The MEG clearly demonstrated that the tumor was within the supplemental motor area, abutting the motor cortex. An awake craniotomy was performed with cortical mapping, confirming the findings of the MEG and allowing for radiographic tumor resection. The tumor was an oligodendroglioma. The patient had transient motor deficits that resolved due to accurate mapping of the motor cortex. He is now on observation status with serial MRI scans.

In summary, the Adult Neurosurgical Oncology Program is fortunate to have a wide range of tools to treat tumor patients and a team of physicians with the expertise to use them. Through individualized application of these tools, we aim to achieve optimal outcomes for each patient as we strive to improve the field of neurosurgical oncology.

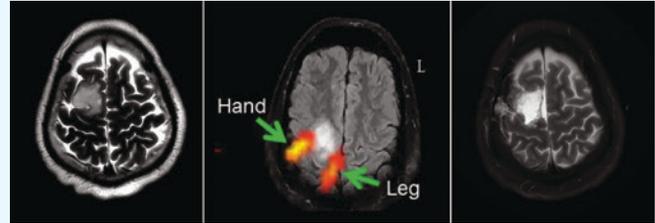


Figure 3. A young patient with a new generalized seizure was found to have an expansile mass within the right frontal lobe (left). Pre-operative magnetoencephalography for brain mapping demonstrated that the lesion was immediately anterior to the motor areas for the hand and the leg, suggesting that the tumor involved the supplemental motor area (middle). The tumor was removed with the patient awake, using cortical mapping to identify and preserve motor cortex and radiographically resect the tumor without causing permanent motor deficits (right).

Gamma Knife Icon: Next-Generation Brain Radiosurgery

UPMC Presbyterian physicians began performing brain radiosurgery with the next-generation Gamma Knife® Icon stereotactic radiosurgery system (SRS) on May 24, 2016. UPMC is the first hospital in the region and the third institution in the United States to treat patients using this revolutionary device.

The Gamma Knife provides physicians with a minimally invasive alternative for treating brain tumors and other neurologic conditions once considered inoperable. The computer-driven, bloodless system is optimal for the treatment of vascular malformations; complex, newly diagnosed, or residual skull base tumors; trigeminal neuralgia; and severe movement disorders.

Icon, the most advanced Gamma Knife system, uses MRI and other radiological imaging to identify and target exact problem locations within the brain to ensure precise dosage distribution to the appropriate area. The system's innovative technology allows for standard, frame-based fixation of the cranium as well as the frameless, mask-based system. With Icon, an entire radiosurgery procedure can be completed in a single outpatient visit.

"UPMC's history of innovation in radiosurgery began in 1987 when we installed North America's first Gamma Knife unit," says **L. Dade Lunsford, MD**, director of the UPMC Center for Image-Guided

Neurosurgery. Since then, more than 14,000 patients have been treated with the Gamma Knife by Dr. Lunsford and his staff at UPMC Presbyterian.

"Each of the five previous generations of Gamma Knife units has improved efficiency and allows us to provide a highly effective option for the many patients who receive treatment each year at UPMC," Dr. Lunsford says. "With the option of a frame-based or frameless approach for non-invasive cranial immobilization, Icon gives us a new way to treat a wide array of complex neurological conditions."



Leksell Gamma Knife Icon

News & Notes

UPMC Passavant to Host Spine Symposium

The first-ever UPMC Spine Symposium, hosted by the UPMC Passavant Spine Center, will be held October 28, 2016 at Cumberland Woods Village in Allison Park, Pa. Specialists in neurosurgery, orthopaedic spine surgery, diagnostic imaging, sports medicine, rehabilitation, and pain medicine will cover a variety of topics including the treatment of back and neck pain, spine disorders, spine injuries, and other back and neck problems.

Matt El-Kadi, MD, PhD, chief of neurosurgery at UPMC Passavant, is the symposium chair, while **Adam Kanter, MD**, chief of Spine Services at UPMC Presbyterian and director of UPMC's Minimally Invasive Spine Program, is the symposium's scientific program co-chair, along with **Suehun Ho, MD**, medical director of UPMC Physical Medicine and Rehab, North.

For more information about the symposium, please contact Caitlin Colkitt at 724-720-4544 or Julie Hehman at 412-647-9275.

UPMC Neurosurgeons Named Best Doctors

Twenty-one UPMC neurosurgeons from the department were named as some of the region's leading doctors in their field in a national survey published locally in *Pittsburgh Magazine*.

The list includes: **Adnan Abla, MD; Daniel M. Bursick, MD; Matt El-Kadi, MD, PhD; Johnathan Engh, MD; Juan C. Fernandez-Miranda, MD; Robert M. Friedlander, MD; Paul A. Gardner, MD; Peter C. Gerszten, MD; D. Kojo Hamilton, MD; Brian Jankowitz, MD; Adam S. Kanter, MD; L. Dade Lunsford, MD; Joseph C. Maroon, MD; Vincent J. Miele Jr., MD; Edward A. Monaco, MD, PhD; John J. Moossy, MD; Ajay Niranjana, MD; David O. Okonkwo, MD, PhD; Ian Pollack, MD; Mark Richardson, MD, PhD; Raymond Sekula Jr., MD; and Elizabeth Tyler-Kabara, MD, PhD.**

The list was compiled by Best Doctors®, founded in 1989 by Harvard Medical School physicians with the purpose of helping people get the right medical diagnosis and treatment.

Department Honors 2016 Chief Residents

A special black-tie graduation reception and dinner was held on June 18 at the Pittsburgh Golf Club honoring 2016 chief residents **Ali Kooshkabadi, MD**, and **Robert Miller, MD**, on their successful completion of the University of Pittsburgh's seven-year neurological surgery residency program.

Upon graduation, Dr. Miller will be joining New England Neurological Associates in Lawrence, Mass., while Dr. Kooshkabadi will be joining UPMC Altoona.

Congratulations

Residents in the University of Pittsburgh Department of Neurological Surgery selected **Raymond Sekula Jr., MD**, to receive the Best Faculty Teaching Award for 2015-16. **Ali Kooshkabadi, MD**, and **Robert Miller, MD**, were named co-recipients of the Best Resident Teaching Award as selected by department faculty.

Joseph Maroon, MD; Julian Bailes, MD; and Mark Lovell, PhD, were awarded the Lifetime Leadership Award for Concussion Research on June 11 at the Emerging Frontiers in Concussion Conference sponsored by the UPMC Sports Medicine Concussion Program.

PGY-2 resident **Nitin Agarwal, MD**, was selected as a Council of State Neurological Societies (CSNS) Socioeconomic Fellow for 2016-17.

Special Lectures and Appearances

L. Dade Lunsford, MD, was the Lars Leksell Lecturer at the University of California, San Francisco, on March 24.

David Okonkwo, MD, PhD, was a visiting professor at the Department of Neurological Surgery, University of Florida, on April 13-14. Dr. Okonkwo was also a faculty member for the AONeuro Neurotrauma course in Changsha, China, on April 22. Additionally, Dr. Okonkwo was a panelist discussing the future of neurotrauma clinical trials at the National Neurotrauma Symposium on June 29.

Partha Thirumala, MD, was a special speaker at the Pan Yangtze River Delta Neurosurgery Forum in Shanghai, China, on March 25.

Juan C. Fernandez-Miranda, MD, was the honored guest of the Endoscopic Endonasal Surgery Symposium organized in Hospital La Paz, Madrid, Spain, on June 28. He successfully performed live surgery demonstrating the Endoscopic Endonasal Approach for a complex skull base meningioma, which was broadcast to an audience of more than 100 neurosurgeons.

Raymond Sekula Jr., MD, hosted the TNA Facial Pain Association Regional Conference on April 23 at the University of Pittsburgh University Club.

Paul Gardner, MD, was an honored faculty member at the 4th National Yang-Ming University & Taipei Veterans General Hospital Endoscopic Endonasal Hands-On Skull Base Cadaver Dissection Course in Taipei, Taiwan, from July 21-23. Dr. Gardner was also appointed as a director-at-large to the North American Skull Base Society Board of Directors and a member of the Program Advisory Committee for the 2017 annual meeting.

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Neurosurgery Research Team Uncovers New Immune Escape Mechanism in Gliomas

by **Nduka Amankulor, MD**

Glioblastoma multiforme (GBM) continues to be a fatal disease with an average expected survival of only 18 months from initial diagnosis. Recent discoveries have shed light on the spontaneous genetic errors that give rise to these malignant neoplasms; however, until recently, it remained unclear why GBM cells escape immune detection in humans with normal immune system function.

In the vast majority of immune-competent humans, newly formed cancer cells are detected and eradicated by the immune system using a biological program known as immune surveillance. Most newly formed tumor cells accumulate intracellular stress (oncogenic stress) from a high burden of genetic errors. Oncogenic stress promotes the production of an immune “kill-me” signal that spurs innate immune cells known as natural killer (NK) cells to identify and destroy new malignant tumor cells.

In a series of experiments performed in the UPMC Department of Neurological Surgery laboratory, our team of physicians discovered that many gliomas disable the immune “kill-me” signal, which means NK cells do not seek out and destroy the malignant cells. Importantly, experiments showed that immune “kill-me” signals are immediately disarmed upon the induction of isocitrate dehydrogenase (IDH) mutations in human gliomas. IDH mutations are known to enable glioma cell proliferation, but this mutation’s inherent immune escape properties were unknown until our recent findings. Thus, our studies establish that IDH mutant gliomas employ a nefarious two-for-one process to acquire both proliferative potential and immune escape properties simultaneously.

In additional studies, our group discovered that the glioma’s “kill-me” signal/NKG2D ligand expression is disabled in IDH

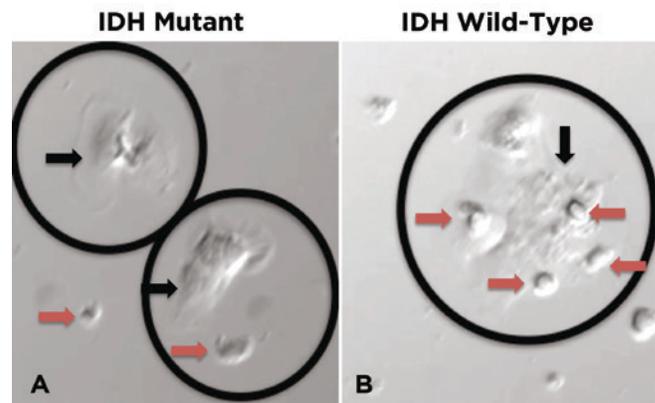


Figure 1. A) IDH mutant glioma cells (black arrows, left panel), which lack immune “kill-me” signals, do not attract NK cells (red arrows); B) Non-IDH gliomas, which contain NKG2D “kill-me” signals, are recognized and destroyed by NK cells.

mutant gliomas using a biological process known as hypermethylation. Fortunately, hypermethylation can be reversed with pharmacological agents known as demethylating agents, many of which are FDA-approved for hematologic malignancies. Indeed, our studies show that treating IDH mutant glioma cells with demethylating agent 5-aza-2'-deoxycytidine enables re-expression of NKG2D ligands and eradication of glioma cells by innate immune NK cells. As a result of our studies, 5-aza-2'-deoxycytidine is emerging as a potential therapeutic target in IDH mutant gliomas, and clinical trials utilizing this agent are being planned at the UPMC CancerCenter.

News and Notes *(Continued from Page 6)*

In the News

L. Dade Lunsford, MD, was featured July 11 in a *Pittsburgh Tribune Review* article that told the story of how a former patient’s life-saving experience with the Gamma Knife® expert inspired a career in medicine.

PGY-3 resident **Benjamin Zussman, MD**, wrote an op-ed article on drug and opioid abuse prevention for neurosurgeryblog.org, published on June 8.

Mark Richardson, MD, PhD, was noted in a June 2 feature article in Oregon’s *The Bulletin* that explained how Parkinson’s disease patients are finding relief through deep brain stimulation surgery.

Dr. Richardson was also featured in an April 27 *Journal of Neurosurgery* podcast discussing the neurobiology of deep brain stimulation. Additionally, Dr. Richardson was featured on the KDKA-TV *Evening News* on July 12 for a story discussing how deep brain stimulation can help patients with obsessive-compulsive disorder.

Joseph Maroon, MD, was mentioned May 12 in a number of media outlets across the country discussing the Gordie Howe Initiative, the first clinical trial of its type to use adult stem cells to regenerate and preserve brain cells in brain injury patients in the United States. Dr. Maroon is an advisor on the trial named after the late hockey legend who underwent stem cell treatments in Mexico in his battle to fight the effects of a stroke.

Stereotactic Dilatable Port Surgery for Brain Tumors *(Continued from Page 1)*

The new technique is compatible with both frame-based and frameless iterations of Neuroendoport surgery. It has been successfully utilized in a number of cases (see Figure 3). Long-term clinical outcomes and MRI studies of the port tract will be compared to cases performed with standard cannulation technique to determine the degree of iatrogenic injury from the port placement. This new technique is envisioned as a stepping

stone to more versatile application of the port technique through even smaller openings in the skull.

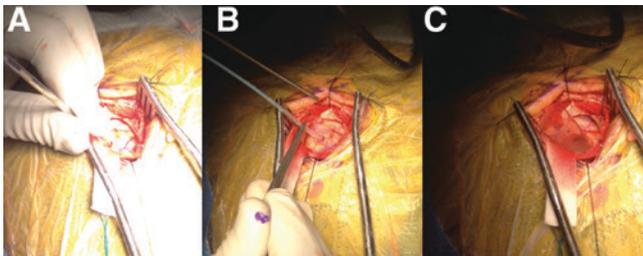


Figure 2. Demonstration of a new method of brain cannulation for the Neuroendoport technique. A Backlund stereotactic brain needle is placed through the cortex, aiming at the target lesion (A). The inner cannula of the Backlund needle is replaced with a cigar-shaped balloon catheter. This catheter is then slowly inflated with saline (B) to create a tract for placement of the endoscopic port (C), through which tumor removal is performed.

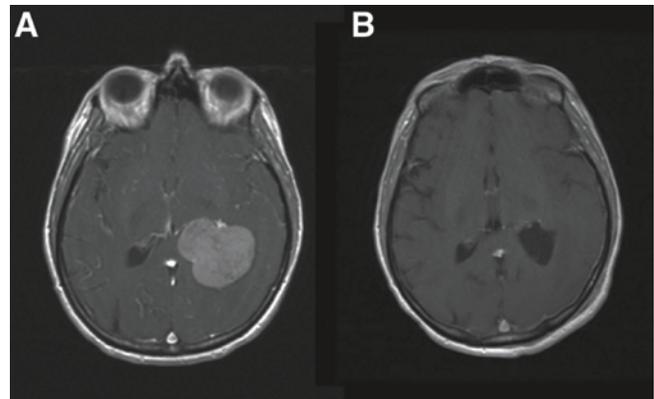


Figure 3. A 60-year-old right-handed woman presented with speech difficulty, headaches, and a 5 cm meningioma of the left trigone of the lateral ventricle (A). A frameless, stereotactic, transparietal approach for placement of an endoscopic port was used to facilitate tumor resection. Complete resection of the meningioma was achieved (B) with resolution of the patient's pre-operative symptoms.

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A world-renowned health care provider and insurer, Pittsburgh-based UPMC is inventing new models of patient-centered, cost-effective, accountable care. It provides nearly \$900 million a year in benefits to its communities, including more care to the region's most vulnerable citizens than any other health care institution. The largest nongovernmental employer in Pennsylvania, UPMC integrates 60,000 employees, more than 20 hospitals, more than 500 doctors' offices and outpatient sites, and a 3 million-member Insurance Services Division, the largest medical and behavioral health services insurer in western Pennsylvania. Affiliated with the University of Pittsburgh Schools of the Health Sciences, UPMC ranks No. 12 in the prestigious *U.S. News & World Report* annual Honor Roll of America's Best Hospitals. UPMC Enterprises functions as the innovation and commercialization arm of UPMC, while UPMC International provides hands-on health care and management services with partners in 12 countries on four continents. For more information, go to UPMC.com.

UPMC is proud to be the only hospital in western Pennsylvania to be named to *U.S. News & World Report's* prestigious national Honor Roll for excellence in 15 specialty areas, including neurology and neurosurgery. For more information about our programs, continuing medical education, Video Rounds, news, and events, please visit UPMCPhysicianResources.com/Neurosurgery.

