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Disclosures

Jorge Gonzalez-Martinez, MD, PhD, is a consultant for Zimmer Biomet. Pascal Zinn, MD, PhD, receives grant research support from UPMC startup funds. Marco Capogrosso, PhD, has received grant research support from GTX Medicals. Robert Friedlander, MD, MA, is a consultant for NeuBase Therapeutics and DiFusion Inc., and receives grant research support from the NIH and Clear Thoughts Foundation. All other contributing authors report no relationships with proprietary entities producing health care goods or services.

Instructions

To take the CME evaluation and receive credit, please visit UPMCPhysicianResources.com/Neurosurgery and click on the course *Neurosurgery News February 2021*.

Personalized Glioblastoma Management: Challenges and Prospects

by Pascal O. Zinn, MD, PhD

The current glioblastoma multiforme (GBM) treatment paradigm remains static in the face of this rapidly, and ever-evolving, niche-rich type of brain cancer. Irrespective of our expanding knowledge of GBM, prognosis and survival rates have only minimally improved over the last two decades. Currently, the median survival rates following surgical resection and chemoradiation are less than two years in 97% of patients. Moreover, median survival rate for patients who undergo supportive treatment without substantial medical or surgical interventions is only four months.

A number of factors are responsible for such grim prognoses. The most significant of those are thought to be rapid growth, a heterogeneous cellular micro-environment, and the diverse mutational landscape of GBM promoting glioma stem cell propagation and a highly invasive nature of cellular spread precluding complete surgical resection. Given the uniform failure of current therapy facing off against this “multiform” disease, it urges us to explore more individualized biological and disease adaptable GBM treatment paradigms to address each patient’s unique type of cancer in a hyper-personalized fashion over time.

Targeted Therapy

This type of therapy is based on targeting specific molecular structures within GBM cells and hence downstream signaling pathways. Other examples of possible targets in GBM are angiogenesis, epigenetic modifiers (e.g., DNA methylation), and immune

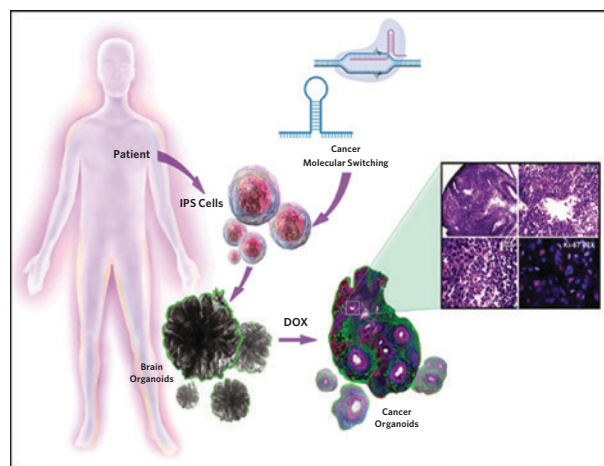


Figure 1. *In vitro* humanoid brain organoid cancer model toward a personalized high-throughput brain cancer co-clinical paradigm.

modulation. Such therapies can be tailored to each GBM patient and the cancer’s unique molecular profile.

Pharmacogenomics

The relationship between pharmacotherapy including chemotherapy and the chromosomal characterization of gliomas has been established. Pharmacogenomics is becoming an integral part in GBM post-surgical management. Currently, MGMT is used as a genetic marker that can predict temozolomide response and prognosis in general.

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Free Online CME

To take the CME evaluation for this issue, visit our education website: UPMCPhysicianResources.com/Neurosurgery.

Affiliated with the University of Pittsburgh School of Medicine, UPMC Presbyterian Shadyside is nationally ranked in neurology and neurosurgery by *U.S. News & World Report*.

Chairman's Message

Innovation and Inspiration



As I look back on 2020 — and forward to 2021 — two words come to mind that are not frequently associated with a global pandemic: innovation and inspiration. While we are all painfully aware of the impact of the restrictions, closures, and recommendations, less recognized are the remarkable ways in which health care delivery has been reengineered in response to this global health crisis. As a result of these advances, the

University of Pittsburgh Department of Neurological Surgery was well-positioned to continue to provide care for emergent and non-emergent patients despite the challenges posed by COVID-19. Increased use of technology, staff redeployment, and patient and provider flexibility all combined to ensure that any patient requiring neurosurgical treatment was able to receive care.

To continue availability for all patients when in-person visits were problematic, a rapid and broad-based expansion of telemedicine capabilities was accomplished. Telemedicine has long been available in our department, often utilized for patients requiring follow-up. New patients, however, were rarely, if ever, evaluated in this way. Upgrades to existing technology, as well as the integration of

new tools, permitted department physicians to provide expert evaluation and treatment to all patients that required care.

In addition to ensuring uninterrupted outpatient access, comprehensive mitigation efforts were undertaken in each of our hospitals to enable continued state-of-the-art care for both emergent and non-emergent patients. Social distancing, masking, and handwashing, augmented by robust COVID-19 testing capabilities, served to provide a safe care environment for both patients and staff.

I know that we all welcome an end to COVID-19 and a return to a new normal. I am grateful that through the commitment, expertise, and innovative spirit of the faculty and staff of the University of Pittsburgh Department of Neurological Surgery, we are all weathering this storm. We look forward to 2021 knowing that we met the needs of our patients during these unprecedented times. We will make use of the lessons learned in 2020 as we continue to provide world-class care no matter what the New Year brings.

Robert M. Friedlander, MD, MA

*Chairman and Walter E. Dandy Professor of Neurological Surgery
Co-Director, UPMC Neurological Institute*

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The Stereotaxic Exploration of the Epileptic Brain

by Jorge Gonzalez-Martinez, MD, PhD

One of the main goals of epilepsy surgery is the complete resection (or complete disconnection) of the cortical areas responsible for the primary organization of the epileptogenic activity. This area is also known as the epileptogenic zone (EZ). As the EZ can eventually overlap with functional cortical areas (eloquent cortex), preservations of these necessary brain functions is another goal of any surgical resection in patients with medically refractory epilepsy.

As successful resective epilepsy surgery relies on accurate preoperative localization of the EZ, a pre-surgical evaluation is necessary to obtain the widest and most accurate spectrum of information from clinical, anatomical, and neurophysiological aspects, with the ultimate goal of performing an individualized resection for each patient. The non-invasive methods of seizure localization and lateralization (scalp EEG, imaging, MEG, etc.) are complementary and results are interpreted in conjunction, in the attempt to compose a localization hypothesis of the anatomical location of the EZ. When the non-invasive data is insufficient to define the EZ, extra-operative invasive monitoring may be indicated. Stereo electroencephalography (SEEG) is one of the extra-operative invasive methods that can be applied in patients with medically refractory focal epilepsy in order to anatomically define the EZ and the possibly related functional cortical areas.

History and Basic Principle Related to the SEEG Methodology

The SEEG method was originally developed by Jean Talairach and Jean Bancaud during the 1950s and was mostly used in France and later in Italy, as the method of choice for invasive mapping in refractory focal epilepsy.

In France, after the development of the stereotactic techniques and frames, which were applied initially for abnormal movement disorder surgery, Talairach devoted most of his activity to the field of epilepsy. Bancaud joined Talairach in 1952 and the new methodology created by both physicians led them to depart very quickly from the current approaches. Wilder Penfield and colleagues at the Montreal Neurological Institute did likewise.

Talairach's ultimate goal was to implement a working methodology for a comprehensive analysis of morphological and functional cerebral space. His atlas on the telencephalon, published in 1967, perfectly illustrates the new anatomical concepts for stereotaxis.

The development of tools, adapted to a new stereotactic frame designed by Talairach and colleagues, allowed Talairach and Bancaud to propose the functional exploration of the brain by depth electrodes, allowing the exploration of both superficial



Figure 1. Intraoperative aspect of SEEG robotic implantation



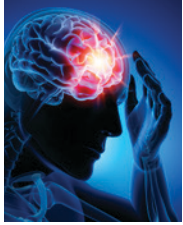
Figure 2. Intraoperative aspect of SEEG exploration, with depth electrodes inserted in percutaneous fashion, following an orthogonal orientation. Electrodes were inserted in the temporal and perisylvian cortical areas in a patient with medically refractory epilepsy. The extraoperative long-term monitoring revealed the presence of epileptiform activity in the lateral contacts of T' and U' electrodes, corresponding to the superior temporal gyrus. After SEEG guided resection, this patient achieved seizure freedom.

and deep cortical areas. The debut of SEEG was in 1957, when the first implantation of intracerebral electrodes for epilepsy was performed on May 3 at Saint Anne Hospital in Paris, France. By departing from the then current methods of invasive monitoring, such implantations allowed for the exploration of the activity of different brain structures and for the recording

(Continued on Page 4)

Rapid Blood Test Could Detect Brain Injury in Minutes

A blood protein test could detect the severity of head trauma in under 15 minutes, according to research published recently in the *Journal of Neurotrauma*.



By showing that glial fibrillary acidic protein (GFAP) can accurately determine the severity of a brain injury through a blood test, the research team working on this study, led by author **David Okonkwo, MD, PhD**, director of the Neurotrauma Clinical Trials Center at UPMC and professor of neurological surgery at the University of Pittsburgh School of Medicine, advanced the development of a point-of-care testing device designed to help clinicians assess traumatic brain injury (TBI) in minutes.

For the rapid test, the vision included using a hand-held device with a cartridge that would measure GFAP in a patient's blood. Researchers at Abbott Laboratories, a global health care company, will need to finalize the test for the i-STAT device, which already is used by the military and health care providers around the world to perform several common blood tests within minutes. The blood test would reveal a patient's GFAP level.

"This would eliminate guesswork in diagnosing TBIs and learn whether a person needs further treatment," said Okonkwo. "Whether you're testing a soldier injured in combat or testing a patient in a small rural hospital with limited resources, health care providers could have critical information they need — in minutes — to treat each patient's brain injury."

For this study, which expanded upon previous GFAP findings, researchers enrolled 1,497 people who sought care at one of the 18 Transforming Research and Clinical Knowledge in TBI (TRACK-TBI) level 1 trauma centers nationwide over four years. GFAP is a Food and Drug Administration-approved marker for ruling out whether a patient needs a head computed tomography (CT) scan within 12 hours after a mild TBI.

For years, scientists have studied blood tests involving GFAP. They also have studied a similar protein called S100B. Both proteins are released in the bloodstream in response to specific injuries, including TBI. But this study showed that GFAP substantially outperformed S100B as a TBI diagnostic marker.

"Knowing this protein can show the severity of a TBI through a simple blood test is promising when considering we can use a device that already is in widespread use in hospitals, doctors' offices and urgent care facilities. All we would need to do is add an extra cartridge to the device to analyze blood for the GFAP protein," said Okonkwo. He estimates this device could potentially decrease unnecessary CT scans by 20% or more, saving nearly \$100 million in medical expenses annually.

With support from the U.S. Army Medical Materiel Research and Development Command's U.S. Army Medical Materiel Development Activity, Abbott Point-of-Care and TRACK-TBI have begun a pivotal, FDA-regulated trial to validate the i-STAT to evaluate the effectiveness of Abbott's point-of-care blood test technology, using whole blood sample type.

This published study is a collaboration between the National Institutes of Health (NIH), the U.S. Department of Defense, the TRACK-TBI consortium, and Abbott Laboratories.

This work was supported with funding from the NIH National Institute of Neurological Disorders and the U.S. Department of Defense.

Additional authors on the study include Ross Puffer, MD, of UPMC and Mayo Clinic; Ava Puccio, RN, PhD, of UPMC; Esther Yuh, MD, PhD, John Yue, MD, Sabrina Taylor, PhD, Pratik Mukherjee, MD, PhD, and Amy Markowitz, JD, of UC San Francisco and Zuckerberg San Francisco General Hospital and Trauma Center; Ramon Diaz-Arrastia, MD, PhD, University of Pennsylvania; Frederick Korley, MD, PhD, of the University of Michigan; Kevin Wang, PhD, of the University of Florida; Xiaoying Sun, MS, Sonia Jain, PhD, of UC San Diego; and Geoffrey Manley, MD, PhD, of UC San Francisco.

The Stereotaxic Exploration of the Epileptic Brain *(Continued from Page 3)*

of the patients' spontaneous seizures. This was something that Penfield's method of investigation failed to achieve. In 1962, Talairach and Bancaud named the new technique and method "the Stereo-Electro-Encephalography."

The principles of SEEG methodology remain similar to the principles originally described by Talairach and Bancaud, which are based on anatomic-electro-clinical correlations (AEC) with the main aim to conceptualize the three-dimensional spatial-temporal organization of the epileptic discharge within the brain. The implantation strategy is individualized, with electrode placement based on pre-implantation hypotheses that takes

into consideration patient's seizures' electro-clinical correlations and their relation with a suspected lesion. The SEEG implantations are performed under robotic guidance, guided by precise pre-implantation hypothesis of localization (See Figure 1, Page 3). The pre-implantation AEC hypotheses formulation is the single most important element in the process of planning the placement of SEEG electrodes (See Figure 2, Page 3). If the pre-implantation hypotheses are incorrect, the placement of the depth electrodes will be inadequate and the interpretation of the SEEG recordings will not give access to the definition of the epileptogenic zone.

What Did You Do Today to Improve the Life of People with Spinal Cord Injury?

by Marco Capogrosso, PhD

Modern neurotechnologies hold promises to restore a variety of neural functions after neurological disorders.

For example, spinal cord stimulation (SCS), initially developed for the treatment of refractory pain, is now finding great momentum as a tool to restore movement after spinal cord injury. Due to the ancestral attraction that the human animal has always had with movement in connection with the concept of life, these applications are easily appealing to the large public. But how much of this glitter actually translates into clinical practice?

Unfortunately, translation of exciting pre-clinical results obtained in research laboratories into clinical settings must undergo a slow but necessary validation process. Rigorous federal procedures regulate the submission of clinical testing of new technologies as well as cost-driven opportunities of industrial partners that can produce new devices. Therefore, economic and societal interests clash in a complicated maelstrom that the scientist is definitively unprepared to navigate.

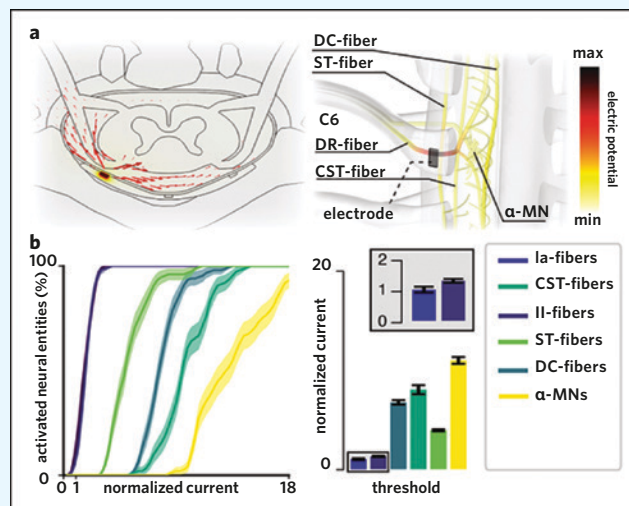
In our group, we believe that working as scientists in a clinical department allows a direct interaction with clinical leaders in the field. This helps steer the day-to-day compass of scientific discovery towards realistic clinical goals.

For instance, we have been working on the development of SCS technology for the restoration of arm movement in people with arm paralysis. The proximity and continuous discussions with clinical investigators and the daily reality of clinical practice highlighted two critical factors that must be accounted for to translate our research to clinical practice:

- The optimal neural targets of SCS must be identified to define precise implantation procedures for the cervical spine.
- The technology used to tune, control, and deliver SCS must be kept simple for it to be practical for patients, clinicians, and caregivers.

These seemingly very practical points tamper with profound questions on the mechanisms of motor control and how electrical pulses modify the activity of spinal circuits to produce movements. Failure to address such questions can only lead to the definition of cumbersome and sub-optimal technical solutions likely relying on unpractical trial and error tuning procedures.

For this reason, we focused the activity in our laboratory on building a bridge between basic research in neural engineering and clinical stakeholders. We are studying the mechanisms of interaction between electrical stimulation and the spinal circuits to design simple, optimal technologies that leverage anatomical



Combined Finite Element/Neural Model of the macaque cervical spinal cord. In (a), voltage and current densities induced by an epidural electrode located lateral above the posterior spinal root C6; right panel the electric potential projected on the three-dimensional trajectories of major afferent and efferent myelinated fibers: DC dorsal columns, DR Dorsal Roots, CST Cortico Spinal Tract, ST spinocerebellar tract, α -MN axons of alpha motoneurons. In (b), number and threshold of neural elements recruited at different current amplitudes normalized to the threshold of C6-Ia-afferents.

and physiological properties of neural circuits to maximize efficacy. In a recent pre-clinical study in monkeys, we combined computer simulations and electrophysiology to decipher the optimal neural target of SCS of the cervical spinal cord for the recovery of arm movements after spinal cord injury. We found that electrodes with lateral contacts can engage single dorsal roots and thus specific arm motoneurons via monosynaptic excitatory pathways with a high degree of reproducibility across subjects. We are now ready to translate these pre-clinical results in humans and verify if a simple technological solution can induce complex hand movements in people with arm paralysis.

We strongly believe that basic research and engineering must go hand in hand with clinical research if we seriously want to tackle unsolved clinical challenges of neurological disorders and help patients with neurological deficits.

My post-doc mentor Grégoire Courtine used to randomly drop by my desk to ask, “What did you do today to improve the life of people with spinal cord injury?”

Let’s keep this question in mind during our daily life as basic researchers and mentors of new generations of investigators.

Trigeminal Neuralgia

by Raymond F. Sekula Jr., MD, MBA

A man begins supper with his wife and takes a bite of bread. He immediately notes a feeling of “electricity” spreading throughout one side of his face. Almost as soon as the pain has struck, it has vanished. He remembers a similar feeling in his hand and arm while playing with an electrical outlet as a child. In that instance, however, his mother explained the cause and how to avoid a similar experience. Although he does not know it, this episode of facial pain represents the beginning of a journey that may or may not end well.

In the Center for Brainstem and Cranial Nerve Disorders, we are working to better understand which patients with trigeminal neuralgia (TN) can benefit from surgical intervention. We know that patients with classical trigeminal neuralgia (cTN) fare better than those with other types of TN. Information gleaned from a detailed history (i.e., a short conversation between patient and physician) allows the physician to make a diagnosis of cTN. Patients with cTN describe sharp, intermittent facial pain usually lasting for a few seconds or less and never longer than a minute or so. This pain does not encompass the posterior third of the scalp or the ear. Triggers include innocuous stimuli such as light touch, wind, or chewing. Attacks may occur numerous times each day with periods (i.e., days to months) of remission. Sensory deficit (i.e., orofacial numbness) is not a related symptom. Most patients with cTN will wince (i.e., the so-called “tic doloieux” or painful spasm) with pain. All patients with cTN will benefit from a neurosurgical consultation. Approximately 85% of patients with cTN will have evidence of vascular

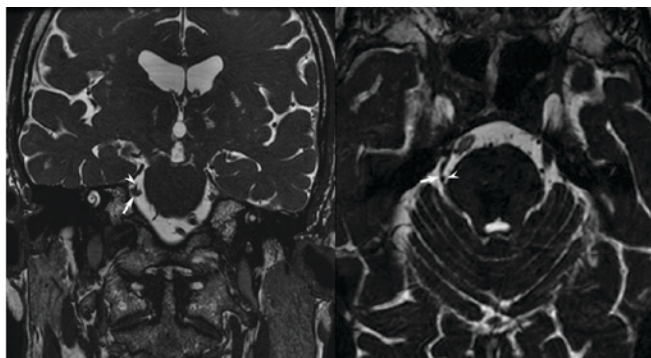


Figure 1. Severe NVC. (Left) Coronal SSFP image demonstrates the right superior cerebellar artery (white arrowhead) indenting the cranial surface of the right trigeminal nerve (white arrow). (Right) Axial SSFP image demonstrates the right superior cerebellar artery (white arrowhead) deviating the right trigeminal nerve (white arrow).

TN grading system score ^a	Estimated probability of long-term pain-free status, (95%CI)
5	93% (0.92 - 0.93)
4	76% (0.74 - 0.78)
3	44% (0.40 - 0.47)
2	16% (0.12 - 0.21)
1	4% (0.03 - 0.06)

^a Derived from adding points from 3 characteristic categories, points assigned as follows:

TN type		Response to carbamazepine or oxcarbazepine		Neurovascular contact	
Classical	1	Yes	1	Arterial deformation	3
Non-classical	0	No	0	Arterial contact	2
				Absent or venous contact	1

Table 1. We developed a readily applicable, quantitative grading system to aid patients and referring clinicians in understanding if microvascular decompression (MVD) is the optimal choice.

compression of the trigeminal nerve by high-resolution MRI T2 images. In our Center, we perform high-resolution imaging (Figure 1) on a higher MRI magnet (i.e., 3T) than found in community hospital MRI machines. Those patients with cTN without evidence of neurovascular conflict or an inability to tolerate a general anesthetic are referred for ablative procedures to the trigeminal nerve.

A patient's response to the antiseizure drug carbamazepine or oxcarbazepine provides helpful information for the clinician. Many patients report rapid relief of facial pain within just minutes of the first tablet or two of these drugs. While we do not fully understand why response to the drugs is an important predictor of response to neurosurgical intervention, we do know that it is important.

Note: Komal Eubanks, DNP, CRNP, also contributed to this article.

News & Notes

Gardner Named Peter J. Jannetta Professor

Paul A. Gardner, MD, neurosurgical director of the UPMC Center for Cranial Base Surgery, was appointed as the Peter J. Jannetta Endowed Chair in Neurosurgery at the University of Pittsburgh. In making the announcement, Department of Neurological Surgery chairman Robert Friedlander, MD, MA, said, “We are very proud of the work and accomplishments that Dr. Gardner has made here at the University of Pittsburgh. This chair acknowledgement is fitting of the impact that Paul has made in the field of minimally invasive brain surgery, ideally keeping with the innovative spirit of Peter Jannetta.”

Fridays with Friedlander

In the spring of 2020, the department inaugurated the *Fridays with Friedlander* webcast, hosted by department chairman **Robert Friedlander, MD, MA**. This weekly webcast presents updates on topical neurological surgery issues, and features department faculty giving brief talks on their specialty — followed by an interactive Q&A session. The webcasts are streamed live via Microsoft Teams. Links to past episodes and the upcoming schedule can be found at neurosurgery.pitt.edu/fridays-with-friedlander.

Maroon Receives Clinician of Courage Award

Joseph Maroon, MD, Heindl Scholar in Neuroscience at the University of Pittsburgh, received the 2020 UPMC Clinician of Courage Award, given to a UPMC physician who is thriving and/or serving as a leader within their community after having faced and overcome adversity. To further honor Dr. Maroon, after awarding the courage award, UPMC renamed the award “The Joseph Maroon UPMC Clinician of Courage Award” for future recipients.

Gardner, Stefko Co-Edit Orbit Surgery Volume

UPMC Center for Cranial Surgery neurosurgical director **Paul Gardner, MD**, along with **S. Tonya Stefko, MD**, director of the Oculoplastic, Aesthetic and Reconstructive Surgery Service at the UPMC Eye Center, are co-editors of a new volume on skull base orbital surgery published by Thieme Publishers through the *Journal of Neurological Surgery Part B: Skull Base* journal series. The volume is comprised of 16 comprehensive and detailed articles on orbital approaches — the gateway to the skull base — from some of the most prominent neurosurgeons, otolaryngologists, orbital surgeons, neuroradiologists, and pathologists in the world.

Abou-Al-Shaar Co-Authors Surgical Handbook

Third-year resident **Hussam Abou-Al-Shaar, MD**, is co-author of a medical reference guide, *The Surgical Handbook*, published by Thieme Publishers. “The book serves as a great resource for medical students and junior residents interested in surgical specialties, especially neurosurgery,” noted Dr. Abou-Al-Shaar. “It includes algorithms on the management of common emergencies across different surgical disciplines.”

Media and Special Appearances

David O. Okonkwo, MD, PhD, was a guest on WESA 90.5 (NPR) *The Confluence*, December 3, along with Ryan Shazier, discussing recovery from spinal cord injury and the Ryan Shazier Fund for Spinal Rehabilitation to help others in their recoveries. Dr. Okonkwo was also a guest on *OneMind Brain Waves*, September 17, a podcast featuring interviews with notable mental health experts and brain scientists.

Joseph Maroon, MD, provided the keynote address at the 7th Annual 2020 Neuro-Oncology Brain Tumors Symposium, held at the University of Pennsylvania Abramson Cancer Center, October 30, 2020.

Pascal O. Zinn, MD, PhD, presented the September lecture — “The Making of Brain: Toward Personalized Bio-Adaptable Brain Cancer Therapy” — in the University of Pittsburgh Senior Vice Chancellor’s Research Seminar Series.

Congratulations

Raymond F. Sekula Jr., MD, MBA, and **Parthasarathy D. Thirumala, MD**, were both promoted to professor of neurological surgery at the University of Pittsburgh.

Diane Carlisle, PhD, was promoted to associate professor of neurological surgery.

Gary Kohanbash, PhD, director of the Pediatric Neurosurgery ImmunoOncology Laboratory (PNIO) at the University of Pittsburgh, was awarded a \$50,000 Discovery Grant for innovative research and development from the American Brain Tumor Association for his research project “Theranostic Antibody for Improving Immunotherapy and Immune Monitoring in Glioma.”

Chief resident **Nitin Agarwal, MD**, was selected to receive the inaugural University of Pittsburgh School of Medicine Distinguished Junior Mentor Award.

First-year resident **Prateek Agarwal, MD**, was elected to the American Association of Neurological Surgeons’ Young Neurosurgeons Committee. The committee provides a channel for young neurosurgeons to impact the direction of neurosurgery and helps develop future leaders of the field.

Chief resident **Jeremy Stone, MD**, was named a winner of the 2020 UPMC Medical Education LEAP Award for Patient Safety and Quality Improvement for his paper “Improved Patient Satisfaction Through Adoption of the Transradial Approach Compared to the Transfemoral Approach for Diagnostic Angiography.”

Chief resident **Nima Alan, MD**, was named recipient of the 2020 North American Spine Society (NASS) Young Investigator Clinical Research Grant Award for his research project “Quantitative Tractography of Spinal Cord White Matter Pathways to Assess Severity of Clinical Presentation in Cervical Spondylotic Myelopathy.”

Personalized Glioblastoma Management *(Continued from Page 1)*

3D Culture and Brain Organoid Cancer Modeling

In vitro brain modeling has become an expanding field of research since the introduction of humanoid brain organoids in 2013. While most published brain organoid research describe the application of organoid technology in developmental and neurodegenerative disorders, few studies have illustrated application of such technology in GBM research by creating a GBM organoid model — either by coculturing GBM stem cells with induced pluripotent stem cells or by means of genetic engineering inducing de novo formation of cancer within the organoid.

Challenges and Prospects

Despite all efforts, no personalized GBM treatment has been clinically implemented to date. The need for rapid and cost efficient personalized in vitro GBM therapy trials is apparent. In vitro humanoid brain organoid cancer models are the most apparent, robust, and realistic choice toward a personalized high-throughput brain cancer co-clinical paradigm (See Figure 1, Page 1). We envision a patient-derived 3D in vitro cancer model system, recapitulating each patient GBM as well as serving as a bio-factory used to test and train different therapeutic agents (e.g. oncolytic viruses). At the University of Pittsburgh Department of Neurosurgery and the UPMC Hillman Cancer Center, a promising co-clinical trial model (Figure 2) is being developed that envisions leveraging

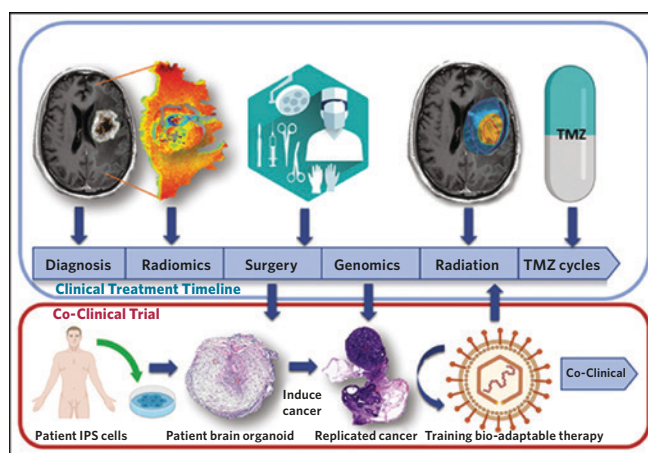


Figure 2. Clinical trial model leveraging personalized patient derived brain cancer systems.

personalized patient derived brain cancer systems to serve as therapy training avatars to boost tropism of oncolytic virus therapy. This model is a bio-adaptable therapy that continuously evolves to address the ever-evolving cancer landscape and anticipate cancer mutations in the model system before actually happening in the patient setting — a “minority report” of cancer therapy.

Free Online CME

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A \$21 billion health care provider and insurer, Pittsburgh-based UPMC is inventing new models of patient-centered, cost-effective, accountable care. The largest nongovernmental employer in Pennsylvania, UPMC integrates more than 90,000 employees, 40 hospitals, 700 doctors' offices and outpatient sites, and a 3.9 million-member Insurance Services Division, the largest medical insurer in western Pennsylvania. In the most recent fiscal year, UPMC contributed \$1.4 billion in benefits to its communities, including more care to the region's most vulnerable citizens than any other health care institution, and paid more than \$800 million in federal, state, and local taxes. Working in close collaboration with the University of Pittsburgh Schools of the Health Sciences, UPMC shares its clinical, managerial, and technological skills worldwide through its innovation and commercialization arm, UPMC Enterprises, and through UPMC International. *U.S. News & World Report* consistently ranks UPMC Presbyterian Shadyside among the nation's best hospitals in many specialties and ranks UPMC Children's Hospital of Pittsburgh on its Honor Roll of America's Best Children's Hospitals. For more information, go to UPMC.com.

UPMC Presbyterian Shadyside is proud to be the only hospital in western Pennsylvania to be nationally ranked in neurology and neurosurgery by *U.S. News & World Report*. For more information about our programs, continuing medical education, news, and events, please visit UPMCPhysicianResources.com/Neurosurgery.

