

cnsq IS THE OFFICIAL NEWSMAGAZINE OF THE CONGRESS OF NEUROLOGICAL SURGEONS

CongressQuarterly

WINTER 2022

CNS IN TRANSLATION

FROM
DISCOVERY
TO THE
BEDSIDE



Congress of
Neurological
Surgeons

6 Up and Coming Technologies
and Therapies in
Cerebrovascular Neurosurgery

16 The Physician Scientist:
Balancing Private Practice and
Academic Interest

CO-EDITORS:

Co-Editor: Ellen L. Air, MD
Co-Editor: Clemens M. Schirmer, MD
Vice-Editor: Theresa Williamson, MD

EDITORIAL BOARD:

Rushna Ali, MD
Hoon Choi, MD, PhD
Rimal Dossani, MD
Aladine Elsamadicy, MD
Jeremy Hosein, MD
Michael Lawton, MD
James P. Caruso, MD
Khoi D. Than, MD
Scott D. Wait, MD
Han Yan, MD

MANAGING EDITOR:

Michele Hilgart

DESIGNER:

CameronRush, Inc.

CONGRESS OF NEUROLOGICAL SURGEONS 2020-2021 OFFICERS

PRESIDENT:

Nicholas C. Bambakidis, MD

PRESIDENT-ELECT:

Elad I. Levy, MD

VICE-PRESIDENT:

Alex A. Khalessi, MD

SECRETARY:

Martina Stippler, MD

TREASURER:

Daniel J. Hoh, MD

PAST-PRESIDENT:

Brian L. Hoh, MD

CEO

Regina Shupak
contact: 847-240-2500 or
info@cns.org

CONGRESS OF NEUROLOGICAL SURGEONS MISSION STATEMENT:
The Congress of Neurological Surgeons exists to enhance health and improve lives through the advancement of neurosurgical education and scientific exchange.

Congress Quarterly is the official newsmagazine of the Congress of Neurological Surgeons, located at 10 North Martingale Road, Suite 190, Schaumburg, IL 60173. Members of the Congress of Neurological Surgeons may call 847.240.2500 with inquiries regarding their subscription to *Congress Quarterly*.

© 2022 by the Congress of Neurological Surgeons. No part of this publication may be reproduced in any form or language without written permission from the publisher. Published free of charge for the Congress membership with additional distribution. Send address changes to Congress Quarterly, 10 N. Martingale Road, Suite 190, Schaumburg, IL 60173.



Congress of
Neurological
Surgeons

EDITOR'S NOTE



Ellen L. Air, MD, PhD
2021-22 Editor

It was invigorating to at last gather with colleagues in Austin for the 2021 CNS Annual Meeting. The innovation on display across all aspects of neurosurgery reflects the commitment and talent of many. In the process of highlighting new discoveries, dialogue ensues with cross-fertilization of ideas. Discoveries from wet-labs, animal studies, computational modeling, clinical trials, and observational studies are all pieces in a puzzle whose final picture is advancement in patient care.

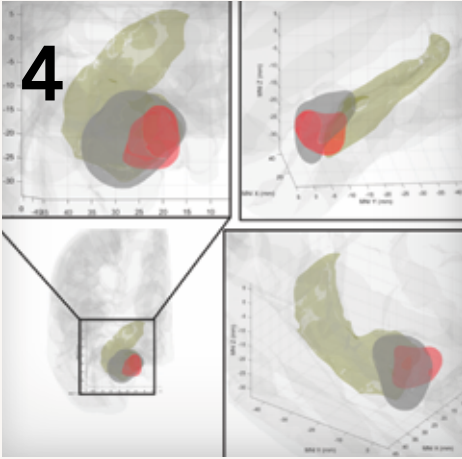
Inspired by this, we present many of the ways CNS members translate scientific discovery to the bedside. Peter Yang and Jennifer Strahle share a poignant example of a child whose life has been directly improved through translational research. The development of endoscopic third ventriculostomy and choroid plexus coagulation for treatment of congenital hydrocephalus has made life without shunting possible. Similarly, Rory Goodwin puts the impact of identifying molecular markers in spinal metastases into focus through the experience of a patient whose treatment was directly impacted. Sameer Sheth and colleagues are translating network analysis of intracranial recordings to optimize stimulation for depression. David Dornbos and colleagues from the Cerebrovascular section highlight several technology advancements that are changing patient care and outcomes. Critically, both articles emphasize how collaboration across subspecialties can lead to novel treatments for challenging clinical problems.

Beyond the specific advancement of identifying the amygdala as critical to apnea in SUDEP, the inaugural NINDS/CNS Foundation K12 Getch Awardee, Brian Dlouhy, reveals the impact of this award on his career. It is an excellent reminder of how CNS members amplify their impact through support of the CNS Foundation. Mohamad Bydon and colleagues from the Tumor Section provide another example of our collective impact. Developed through NeuroPoint Alliance, two Quality Outcome Databases have been built to leverage our combined experience to improve the treatment of brain tumors. These have been specifically designed to capture the information most critical for neurosurgeons.

For those who thought their circumstances precluded contribution or didn't know to get started, the articles by Mick Perez-Cruet and John Pracyk expand our horizons. Each provides unique, first-hand, insight and reminds us there are many ways to move ideas to action, regardless of public/private/academic/community moniker.

It has been a great honor co-edit the *Congress Quarterly* this past year with Martina Stippler. I am excited to be joined by Clemens Schirmer as Co-Editor and Theresa Williamson as Vice-Editor to carry forward this publication. We are committed to maintaining Dr. Stippler's high standards and to bringing you engaging articles that inform your practice and reflect the diversity of our community.

CONTENTS



Editor's Note

Ellen Air

President's Message

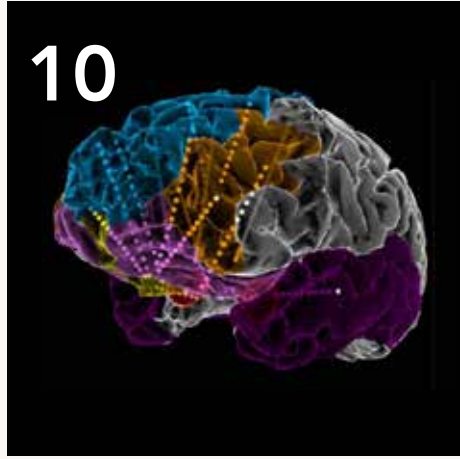
Nicholas C. Bambakidis

CNS IN TRANSLATION

- 4** The Impact of the CNS/NINDS Getch Scholar Award on My Career and Research: Answering a century old question – what causes loss of breathing during seizures?
Brian Dlouhy

- 6** From Discovery to Bedside: Up and Coming Technologies and Therapies in Cerebrovascular Neurosurgery
David Dornbos, Kunal Vakharia and Clemens Schirmer

- 8** Genetics in Metastatic Spine Disease: Understanding the Implications of Molecular Markers in Clinical Practice
C. Rory Goodwin



- 10** Deep Brain Stimulation for Severe, Treatment-resistant Depression

Sameer A. Sheth

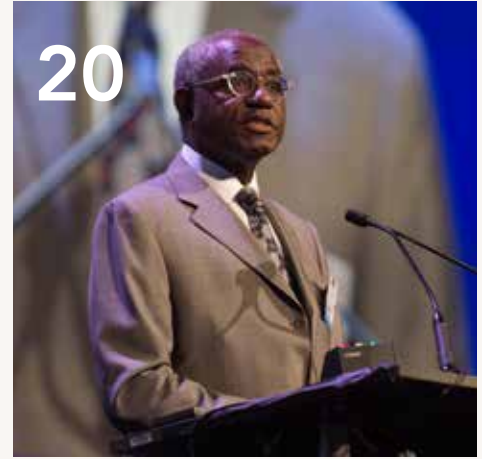
- 12** Quality Registries in Neurosurgical Neuro-Oncology
Mohamad Bydon, Giorgos D. Michalopoulos and Jason P. Sheehan

- 14** Endoscopic Third Ventriculostomy with Choroid Plexus Cauterization (ETV+CPC) for Pediatric Hydrocephalus: One Patient's Experience
Peter Yang and Jennifer Strahle

- 16** The Physician Scientist: Balancing Private Practice and Academic Interest
Mick Perez-Cruet

- 18** Cultivating a Nonclinical Career to Deliver Global Therapeutic Solutions
John B. Pracyk

- 20** Journal Feature: *Neurosurgery*—Shaping Clinical Practice Through Translational Research
Matthew J. McPheeters and Nelson M. Oyesiku



FOUNDATION UPDATE

- 23** CNS Foundation Update

INSIDE THE CNS

- 26** Washington Committee Report
Katie O. Orrico

CNSQ INSIDE BACK COVER

Images in Neurosurgery

PRESIDENT'S MESSAGE



Nicholas C. Bambakidis, MD
President, Congress of
Neurological Surgeons

As I settle back into my practice after returning from the CNS Annual Meeting in Austin, I can't help but reflect on the tremendous strength and resilience of this organization. We stand here after two of the most difficult years of our professional careers and the Congress of Neurological Surgeons is not only celebrating a record number of new online educational product launches over the past two years, but we also found a way to safely gather our members for five days of groundbreaking science, engaging speakers, and critical conversations about the future of our specialty and patient care. This outstanding meeting was the culmination of two years of planning by our Scientific Program Committee, working in conjunction with the Joint Sections and our other educational partners, as well as months of research into new safety measures, best practice benchmarking, and meticulous implementation of these procedures by our staff—beginning with our initial return to live education at the CNS Leadership Institute in May and building in the weeks and hours leading up to the kickoff in Austin.

These live meeting successes are just one measure of the CNS' remarkable strength as an organization. We are also stepping into a new partnership with Wolters Kluwer Health this year for the publication of our flagship journal, *Neurosurgery*, as well as *Operative Neurosurgery* and *Neurosurgery Open*. This partnership brings leadership, advanced digital solutions, and expertise in medical society publishing that will help us build upon the incredible reach our journal portfolio has achieved in recent years and expand access and engagement across all titles. At the same time, we are welcoming a new Editor-in-Chief, Dr. Doug Kondziolka. Dr. Kondziolka brings a great deal of passion and creativity to this role,



Dr. Bambakidis presents the CNS Resident Award during the recent Annual Meeting in Austin.

and given his demonstrated commitment to innovation, he is the perfect leader to continue the transformative work our current EIC, Dr. Nelson M. Oyesiku, cultivated during his 12-year tenure.

Our online education portfolio continues to expand, both in content and accessibility. We recently launched the new CNS+ app, which provides easy, one-stop access to many of CNS' most valuable resources, including publications, webinars, Guidelines, NEXUS, podcasts, case of the month and more. We also relaunched Nexus with a new user interface, making it easier to find a case like yours and review the approach, positioning, incision, operation, post-op, outcome and pearls/pitfalls. And we rolled out an online



Dr. Bambakidis accepts the gavel from 2021 CNS President, Brian Hoh, during the Annual Business Meeting in Austin.

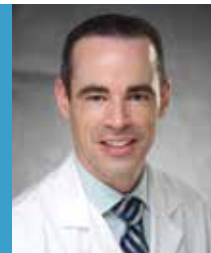
> I AM HONORED TO BE ENTRUSTED WITH LEADING THE CNS IN 2022 AS WE CONTINUE TO RETURN TO NORMALCY, OR AT LEAST TRANSITION TO A NEW NORMAL. I AM COMMITTED TO BUILDING UPON OUR RECENT SUCCESSES AND CONTINUING TO PURSUE BOLD AND INNOVATIVE PRODUCTS, SERVICES AND COLLABORATIONS ON BEHALF OF OUR MEMBERS AND OUR SPECIALTY. <

learning subscription option that gives members access to our extensive catalog of live and archived webinars, including more than 75 new offerings developed over the past two years. Together, these improvements make it easier than ever for our members to find timely insights relevant to their practice, right from their home, office, or mobile device.

The CNS is also fortunate to have developed great partnerships with some of the most respected organizations in our specialty—the American Board of Neurological Surgeons and the Society of Neurological Surgeons (SNS)—as well as with the CNS Foundation, which itself has experienced significant growth over the past few years. These partnerships, along with our healthy financial position,

have given us the necessary support to continue innovating and taking risks on behalf of our members.

It is against the backdrop of this historic success, growth and accomplishment that I step into my new role as CNS President. I am honored to be entrusted with leading the CNS in 2022 as we continue to return to normalcy, or at least transition to a new normal. I am committed to building upon our recent successes and continuing to pursue bold and innovative products, services and collaborations on behalf of our members and our specialty. Most of all, I am looking forward to serving and re-connecting with all of you, our members over the coming year and at our next meeting in San Francisco. Thank you for this incredible opportunity. 🍷



Brian Dlouhy, MD

The Impact of the CNS/NINDS Getch Scholar Award on My Career and Research: Answering a century old question – what causes loss of breathing during seizures?

It was an honor and privilege to be named the first NINDS/CNSF Getch K12 Scholar. To be the first and only (at the time) awardee brought great responsibility. As a resident, I remembered attending the CNS Annual Meeting in 2011 when Christopher Getch, MD presided over and was honored as the President of the CNS. Although I did not know Dr. Getch, he appeared to have done things “right” in his life and career – evidenced by his beautiful family celebrating his time atop a successful year in the CNS. To hear of his untimely death just months later was startling and saddening to me.

I didn’t know it at the time, but just a few years later, the prestigious K12 award named in Dr. Getch’s honor would help launch my neurosurgeon-scientist NIH funded career. My NINDS/CNSF Getch K12 research focused on understanding the pathogenesis of sudden unexpected death and developing novel treatment strategies to prevent such death.

The award brought critical grant funding for my research as a young faculty member at the University of Iowa where my neurosurgeon-scientist career began. It provided me not just funding for resources in my lab, but it allowed me time to pursue my goals. Most importantly, it validated the importance of my research and early findings on sudden death. I wanted to prevent such sudden tragic deaths, especially ones that affect the young, those in the prime of their lives.

My research path began with a simple question but one that had gone unanswered for over a century – what causes loss of breathing during seizures? This question appeared to lay at the fundamental cause of sudden unexpected death in epilepsy (SUDEP), a devastating and relatively common event in those with intractable epilepsy.

SUDEP is the death of a seemingly healthy person with epilepsy for whom no other cause of death is found. And when I say, “healthy individual,” I’m referring to the fact that the patient hasn’t experienced trauma or a drowning and there has been no associated episode of status epilepticus. The patient hasn’t had a myocardial infarction or aneurysm rupture. In fact, a post-mortem examination does not reveal a structural or toxicological cause for death. This is the criteria for SUDEP. These deaths are often unwitnessed, but it is believed that SUDEP invariably occurs due to a seizure and the rare, witnessed cases suggest this.

Tragically, SUDEP is the most common cause of death in patients with medically intractable epilepsy. It affects the young and is second only to stroke in number of years of potential life lost. Sudden unexpected death is 24 times greater in young adults with epilepsy than the general population. In a cohort study of children with epilepsy, these individuals were found to have a 7% cumulative risk of dying suddenly within 40 years. Over this 40-year period, SUDEP accounted for 38% of all deaths.

Increasing evidence suggests that the primary mechanism in SUDEP is seizure induced respiratory inhibition. In rare observed cases of SUDEP in epilepsy monitoring units, a seizure typically proceeded a period of respiratory dysfunction which ultimately led to terminal central apnea (centrally mediate loss of breathing). Consistent with this possibility, nonfatal seizures, both focal and generalized, are often associated with apnea and oxygen desaturation. Previously, many had believed that SUDEP was either from airway obstruction or were primarily cardiac in origin. It’s only been recent that the loss of breathing induced by seizures has been found to be central in origin. Patients are often found prone, face down without apparent struggle and often after sleep.

To determine the cause of apnea during seizures, we took advantage of our own neurosurgical patients undergoing intracranial electrode monitoring for seizure focus localization. All patients had continuous respiratory monitoring during their 1-2 week stay in the hospital while electrodes recorded seizure activity.

In our initial cohort of adult epilepsy patients, we found that when seizures spread to the amygdala, apnea was induced. The observations suggested that the amygdala might be responsible for inhibiting breathing during seizures. To investigate that possibility, we used the same contacts of the implanted electrodes where the seizure activity co-occurred with apnea to electrically stimulate the amygdala. Strikingly, when the amygdala was stimulated, apnea was immediate in onset and persisted until stimulation ended. Importantly, patients could overcome the apnea when asked to breathe or speak, indicating that respiratory motor output pathways and musculature remained functional, and suggesting that the more likely explanation for the apnea was loss of brainstem mediated automatic breathing. These findings have now been repeated in over 30 intractable epilepsy patients including children as young as 3 and adults as old as 59. To test whether the amygdala's role in respiratory inhibition was unique to patients with epilepsy, we studied a patient without epilepsy undergoing language mapping during resection of a temporal lobe tumor. Consistent with our findings in epilepsy patients, stimulation of the amygdala in this patient elicited apnea, suggesting that a normal physiologic function of the amygdala is brainstem respiratory inhibition. Together these findings established a functional connection between the amygdala and brainstem respiratory centers.

In studying these 30+ patients, we have been able to ask many questions about the amygdala's role in brain control of breathing. Stimulation of both the right and left amygdala can induce apnea, suggesting that there is not a laterality to the amygdala's respiratory inhibition. Moreover, similar effects are seen in children as young as 3 as well as adults, suggesting that a connection between the amygdala and brainstem respiratory network is established in humans prior to age 3, either in early postnatal development or in utero.

Because the amygdala is composed of numerous nuclei that serve different functions, we hypothesized that specific locations within the

amygdala may be responsible for stimulation-induced apnea. In a cohort of epilepsy patients, we used high density amygdala depth electrodes with closely spaced contacts to map the amygdala's effect on breathing. Across patients, apnea was most consistently observed when stimulation spanned the medial portion of the amygdala and included the basal nuclei of the amygdala. Using a machine-based learning algorithm based on respiratory effects from 45 stimulation sites in the patients' brains and 210 stimulation trials, we identified a focal region of the amygdala that consistently inhibited respiration. Because this site in the amygdala inhibits respiration, we call this focal subregion the Amygdala Inhibition of Respiration (AIR) site. It includes the medial subregion of the basal nuclei, as well as nearby areas.

One of the most interestingly findings that has been observed in all patients studied to date is that patients are completely unaware that they have stopped breathing, do not struggle, and express no desire to breathe. This is despite stimulations and apneas that have lasted up to 1 minute. Thus, the amygdala may not just inhibit respiration but also the dyspnea associated with loss of breathing. These findings appear consistent with the lack of struggle exhibited by those who die of SUDEP from loss of breathing.

Although the amygdala appears critical for seizure-induced loss of breathing and potentially SUDEP, we have expanded our work to further understand how the entire forebrain controls breathing. This research could lead to better understanding

numerous diseases and developing novel treatments to help prevent or treat them. These include sudden unexpected death in epilepsy (SUDEP), sudden infant death syndrome (SIDS), primary respiratory disorders, and anxiety related disorders.

There are far too many people here to thank that have supported and mentored me and now work with me to help those whose lives are tragically lost both suddenly and without warning. I thank all of you! Importantly, I want to thank the CNSF and the Foundation for the National Institutes of Health (FNIH) for my initial support, for this award has changed my entire research career path. Hopefully 40 years from now, I can write in an update that we have developed cures for the conditions above and we can prevent sudden deaths such as those that occur in epilepsy. ■

The NINDS/CNSF Getch K12 Scholar Award, supported by the CNS Foundation in partnership with the CNS, the National Institutes of Health, and the National Institute of Neurological Disorders and Stroke, is a biennial award providing unparalleled support for a young neurosurgeon scientist beginning their clinical research for two years at their home institution. To date, the CNS Foundation, through a generous donation from the CNS, is the proud supporter of three NINDS/CNSF Getch K12 Scholars. To learn more or make a donation in support of the award visit foundation.cns.org.



David Dornbos III, MD



Kunal Vakharia, MD

Clemens Schirmer, MD,
PhD

From Discovery to Bedside: Up and Coming Technologies and Therapies in Cerebrovascular Neurosurgery

Cerebrovascular neurosurgery has rapidly evolved over the last several years, expanding into new territories. The adoption of endovascular techniques has opened new avenues to care for our patients and collaborate with other specialties. Translational research carries the bench-to-bedside paradigm from early basic science and animal models to initial device development in models and simulation environments. With the tremendous increase in neurosurgical funding through NIH, CV section, and industry-funding mechanisms, cerebrovascular research developed novel, groundbreaking advances and innovations. These new advances have expanded into other traditionally non-vascular spaces, changing paradigms of patient care.

New Therapeutics in Ischemic Stroke

As the role and indications of mechanical thrombectomy continue to expand, management of acute ischemic stroke continues to be rolled into the care of cerebrovascular neurosurgeons. While alteplase has been the gold standard in stroke for several decades, tenecteplase (a more fibrin-specific and longer-acting agent) has shown recent promise with enhanced functional outcomes and improved reperfusion when followed by mechanical thrombectomy. Newer agents are also on the horizon focusing on additional targets within the thrombotic cascade. For example, a reversible RNA aptamer designed to target von Willebrand factor has been found to limit thrombosis and lead to enhanced arterial recanalization following thrombotic occlusion. Following successful preclinical and translation studies, this novel agent has already been introduced in phase 1 clinical trials in healthy volunteers.

The role of artificial intelligence (AI) has become ubiquitous in triage and patient identification for large vessel occlusion acute ischemic stroke. Automated CT perfusion has been in routine practice for several years and continues to expand its clinical applicability. AI-enabled detection of large vessel occlusion has seen a rapid increase in growth and adoption across many centers given its ability to rapidly identify thrombectomy candidates, decrease transfer delays, and improve time to revascularization (**Figure 1**). As these algorithms become more refined and their use more widespread, this will continue to improve the care of ischemic stroke patients.

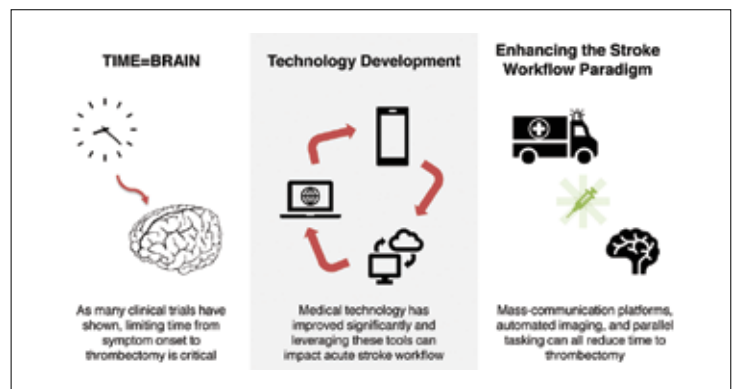


Fig. 1: Reused from Yaeger, KA, *et al.*, Emerging Technologies in Optimizing Pre-Intervention Workflow for Acute Stroke, *Neurosurgery*, Volume 85, Issue suppl_1, by permission of Oxford University Press on behalf of the Congress of Neurological Surgeons.

Spanning the Interdisciplinary Divide

Stroke care is a well-known example of interdisciplinary collaboration. Neuro-oncology and neurosurgery have worked in symbiosis for many years. However, with new oncologic therapies available based on genetic sequencing and patient-tailored treatments, moving past the ideology of surgical resection, radiation, and chemotherapy alone leads to a constantly changing landscape. Although intra-arterial (IA) delivery of chemotherapeutic agents to the brain in preclinical animal models was introduced in the 1950s, there has been a paucity of improvements over the years. Infusing high concentrations of chemotherapeutic agents with the ability to cross the blood-brain-barrier (BBB) while limiting toxicity to the patient remains a challenge.

Retinoblastoma remains a beacon of hope for intra-arterial therapy. A particular success story, IA therapy for retinoblastoma started in 1955 with internal carotid artery infusion of nitrogen mustard and triethylenemelamine. Coupling advances in chemotherapy with endovascular microcatheter technology, selective ophthalmic artery infusions have allowed much higher chemotherapy doses to penetrate the blood-retina barrier and significantly increased survival for these patients. Paralleling this success, emerging methodologies underlie the potential marriage of interdisciplinary care for glioblastoma.

Disruption of the BBB with osmotic agents is effective and reversible. Pairing osmotic agents with IA therapy has helped limit side effects while increasing permeability into tumor beds. The potential of merging IA therapy with focused ultrasound targeted biologics and stem cell delivery of oncolytic viruses along with endovascular super-selective IA infusions bridges this interdisciplinary gap while also making step-by-step progress towards more expanded clinical trials.

Exploring New Frontiers in Brain-Computer Interfaces

Restoration of function remains the goal of many of our efforts. Many translational advancements bring different multidisciplinary endeavors together and culminate to open new doors and move therapy in alternate directions. Endovascular stent-electrode technology to facilitate delivery of brain-computer interface technology is a recent example of this type of transformative change. While the stent-electrode may have initially started nearly four decades prior, this technology has evolved, finding a more suitable option for long-term viability. Although SEEG and other implantable devices have historically allowed for good mapping, endovascular neural interfaces in animals have also been shown to get similar responses. This technology coupled with computational modeling to determine potential deep brain stimulation targets has shown multiple potential sources for endovascularly targeted interfaces.

This push for intravascular technology brought on a new generation of trials focused on long-term implantable and safe solutions. Although direct brain and cortical mapping initially seemed to be the most straightforward approach, it did not limit the long-term potential for gliosis. However, as endovascular techniques have become more pervasive, venous procedures and delivery of venous stents have gained substantial traction. Recently, Oxley *et al.* has formalized a method of cerebral venography with implantation of a venous stent-electrode in sheep that has translated into an NIH grant, clinical trials, and now first-in-human experience is underway (Figure 2).

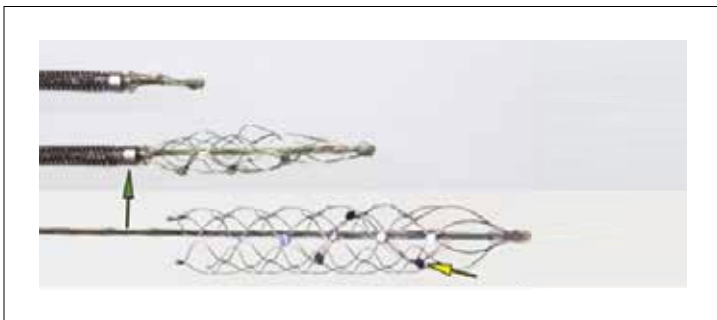


Fig. 2: Reused from Martini, ML, *et al.*, Sensor Modalities for Brain-Computer Interface Technology: A Comprehensive Literature Review, *Neurosurgery*, Volume 86, Issue 2, by permission of Oxford University Press on behalf of the Congress of Neurological Surgeons

Innovative Device Development

The innovative milieu around endovascular neurosurgery continues to expand interventional tools at a rapid pace. With new devices rolling out in clinical trials and coming to market, the abilities and opportunities to improve patient outcomes are continuously evolving. For example, while the results of the WEB-IT trial were published just over two years ago, bringing intra-saccular devices into the mainstream, newer generation devices have subsequently been introduced, allowing treatment of aneurysms as small as 3 mm (Figure 3). In addition, further miniaturization of endovascular devices has also been introduced in ischemic stroke with newer generation retrievers designed to be used in vessels as small as 2.5 mm. These advances are allowing treatment for patients that would previously have not been afforded endovascular care.



Fig. 3: Reused from Pierot, L, *et al.*, Endovascular WEB Flow Disruption in Middle Cerebral Artery Aneurysms: Preliminary Feasibility, Clinical, and Anatomical Results in a Multicenter Study, *Neurosurgery*, Volume 73, Issue 1, by permission of Oxford University Press on behalf of the Congress of Neurological Surgeons

Additional translational advances are improving the safety profile in endovascular care of both intracranial aneurysms and stroke treatment. For example, while flow diversion technology has been utilized for nearly ten years in the United States, the addition of surface modification agents (such as phosphate choline polymers) can decrease thromboembolic risks associated with their use. Further, improved hydrophilic glide technology and catheters uniquely designed for radial access continue to push the envelope to enhance the safety profile of neurointerventional procedures.

Conclusion

Recent translational advances in cerebrovascular neurosurgery have shattered paradigms, moved the field into new areas, and increased cross-collaboration with other neurosurgical subspecialties. Transformative discoveries and new devices are rapidly evolving the field and what cerebrovascular neurosurgery has to offer, but most importantly, is providing improved and safer solutions for our patients. ■



C. Rory Goodwin, MD,
PhD

Genetics in Metastatic Spine Disease: Understanding the Implications of Molecular Markers in Clinical Practice

A 60-year-old female with Crohn's disease presents with multiple visceral and skeletal lesions, and a large lung mass that was biopsied and found to be non-small cell lung cancer. The patient has a Bilsky Grade 2 metastatic lesion at T5 with frank instability (Spinal instability neoplastic score 14), and had been bedbound for week, but had relatively good lower extremity strength. The patient was seen at an outside hospital, where the decision was made to refer the patient to hospice based on the lung cancer diagnosis and extent of the systemic disease. The family requested a second opinion to evaluate for any other potential options.

The incidence of spine metastases in late stage cancer is quite high with up to 70% of patients having metastatic spine disease (MSD) at autopsy¹. Spinal metastases are associated with a wide array of debilitating symptoms including significant back or bone pain, pathologic fractures, and instability. It has been reported that approximately 10% of cancer patients will experience symptomatic metastatic spinal disease, with epidural spinal cord compression (ESCC) among the most concerning sequelae of the disease process^{2,3}. Compression of the spinal cord in the setting of malignancy may lead to weakness, paresthesia, bladder dysfunction,

> SPINAL METASTASES HAVE HISTORICALLY BEEN VIEWED AS A MARKER OF END-STAGE DISEASE. BRIDGING THE GAP IN OUR UNDERSTANDING OF THE MOLECULAR MECHANISMS AND PATHOPHYSIOLOGY UNDERLYING THE PROGRESSION OF METASTATIC DISEASE WILL ALLOW CLINICIANS TO BETTER PREDICT THE BEST OVERALL TREATMENT PARADIGMS FOR PATIENTS THAT CAN INFLUENCE QUANTITY AND QUALITY OF LIFE, AS WELL AS IMPROVE NEUROLOGIC FUNCTION, AND OVERALL TUMOR AND PAIN CONTROL. <

and paralysis –all of which significantly impact a patient's quality of life in their remaining years⁴⁻⁷. While the incidence and prevalence of spine metastases have recently increased secondary to improved detection, screening, and treatment, there is a paucity of research aimed at better understanding and thereby effectively treating this disease process.

Classical decision making paradigms, such as NOMS, allow for the systematic evaluation of patients diagnosed with spinal metastasis to determine the most appropriate treatment regimen for a given patient. The NOMS paradigm is broken down into four main criteria including neurologic status, oncologic sensitivity to radiation, biomechanical stability of the spine, and systemic disease burden, with the goal of optimizing clinical outcomes and quality of life for patients diagnosed with spine metastasis⁸. With the advent of next generation sequencing platforms, immunotherapies, and targeted therapeutics, future work should aim to rapidly expand and modify these paradigms to incorporate these molecular targets and inhibitors into clinical decision-making. In general, multiple cancer types rely on molecular subtyping to define the appropriate management paradigm and predict the treatment response⁹. In lung cancer, EGFR mutations and c-Met mutations are shown to be important in treatment response, whereas hormone status is the key driver for prostate cancer, through androgen receptor modulation, and breast cancer through estrogen/progesterone/HER-2 receptor pathways. Melanoma is largely dictated by the BRAF mutation status, and renal cell carcinoma is influenced by receptor tyrosine kinase inhibitors or VEGF inhibitors. Furthermore, immunotherapies have demonstrated dramatic survival benefit for wide array of cancer types. These targeted therapies actually provide argument for surgical treatments that will maintain performance status and improve neurologic dysfunction, thus allowing patients to remain eligible for systemic treatments (good performance status is often a requirement for various treatments and clinical trials). It also argues for more minimally invasive approaches given that the systemic therapies can more effectively treat disease, obviating the need to perform aggressive resections aimed at tumor control.

Revisiting the case above, the patient was transferred to our institution for second opinion, and on presentation, her performance status remained poor with generalized lower extremity weakness and an inability to ambulate. A repeat biopsy was obtained to examine the molecular markers and determine if she would be a candidate for a clinical trial versus other therapies and this revealed an EGFR mutation and as well as favorable expression of PD-L1. Given these markers would predict a positive response to an EGFR inhibitor and immunotherapy treatment, the patient was offered surgical decompression and stabilization followed by stereotactic radiosurgery

and placed on an immunotherapeutic agent. Following inpatient rehabilitation, the patient was able to walk within 4 weeks. She was also started on an EGFR inhibitor, with regression of the visceral and skeletal disease and good systemic control one year later.

Spinal metastases have historically been viewed as a marker of end-stage disease¹⁰. Bridging the gap in our understanding of the molecular mechanisms and pathophysiology underlying the progression of metastatic disease will allow clinicians to better predict the best overall treatment paradigms for patients that can influence quantity and quality of life, as well as improve neurologic function, and overall tumor and pain control. As clinicians develop and refine prognostic algorithms to determine optimal treatment strategies for individual patients, knowledge of the relevant molecular markers for spine metastasis patients could provide valuable insights as to patients that will maximally benefit from surgery, radiation, systemic treatments, and/or other interventions.

References

- 1 Tseng, C.L., et al., Spine Stereotactic Body Radiotherapy: Indications, Outcomes, and Points of Caution. *Global Spine J*, 2017. 7(2): p. 179-197.
- 2 Maccauro, G., et al., Physiopathology of spine metastasis. *Int J Surg Oncol*, 2011. 2011: p. 107969.
- 3 Barzilai, O., et al., Association of neurologic deficits with surgical outcomes and health-related quality of life after treatment for metastatic epidural spinal cord compression. *Cancer*, 2019. 125(23): p. 4224-4231.
- 4 Honore, P., et al., Osteoprotegerin blocks bone cancer-induced skeletal destruction, skeletal pain and pain-related neurochemical reorganization of the spinal cord. *Nat Med*, 2000. 6(5): p. 521-8.
- 5 Kozlow, W. and T.A. Guise, Breast cancer metastasis to bone: mechanisms of osteolysis and implications for therapy. *J Mammary Gland Biol Neoplasia*, 2005. 10(2): p. 169-80.
- 6 Cossigny, D.A., et al., An in vivo mouse model of intraosseous spinal cancer causing evolving paraplegia. *J Neurooncol*, 2013. 115(2): p. 189-96.
- 7 Goodwin, C.R., et al., Molecular Markers and Targeted Therapeutics in Metastatic Tumors of the Spine: Changing the Treatment Paradigms. *Spine (Phila Pa 1976)*, 2016. 41 Suppl 20: p. S218-S223.
- 8 Laufer, I., Rubin, DG, Lis, E, Cox, BW, Stubblefield, MD, Yamada, Y, Bilsky, MH, The NOMS framework: approach to the treatment of spinal metastatic tumors. *Oncologist*, 2013. 18(6): p. 744-51.
- 9 Goodwin, C.R., et al., Clinical Decision Making: Integrating Advances in the Molecular Understanding of Spine Tumors. *Spine (Phila Pa 1976)*, 2016. 41 Suppl 20: p. S171-S177.
- 10 Jayarangaiah, A. and P. Theetha Kariyanna, Bone Metastasis, in *StatPearls*. 2020, StatPearls Publishing Copyright © 2020, StatPearls Publishing LLC.: Treasure Island (FL).



Sameer A. Sheth, MD,
PhD

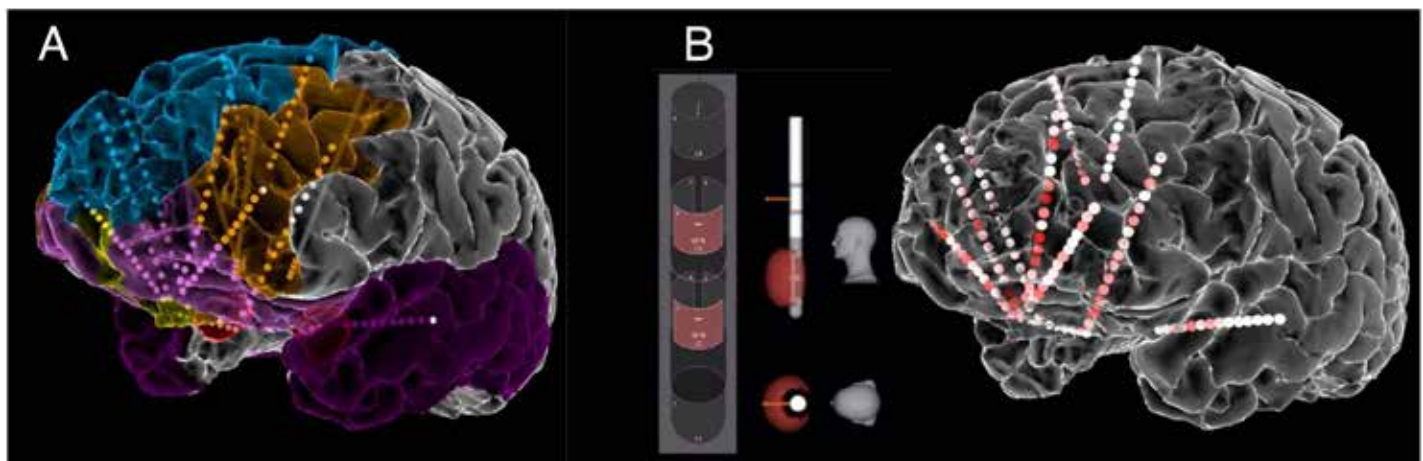
Deep Brain Stimulation for Severe, Treatment-resistant Depression

The Presidential addresses by Drs. Steve Kalkanis and Brian Hoh at our recent Annual Meeting provided a welcome opportunity for us to reflect on aspects of our chosen field that we hold dear. Dr. Kalkanis's emphasis on the amazing contributions of each of our specialties inspired in the standing-room-only audience a sense of great kinship and promise for the future. Dr. Hoh's insistence on professionalism reminded us of the awesome responsibility we have to treat our patients thoughtfully, with attention to their individual needs and concerns. Examples of such innovative and personalized approaches abound in our rapidly evolving field. Here, I share one example of ongoing work in functional neurosurgery, a specialty of ours experiencing rapid growth accelerated by tremendous scientific progress.

Neuromodulation may be defined as the targeted application of external energy (whether electrical, mechanical, optical, etc.)

to engage the nervous system in a therapeutically effective manner. Doing so non-invasively carries the advantage of greater palatability and acceptance from patients but suffers from the major disadvantage of non-specificity. Thriving neurosurgical programs in movement disorder and epilepsy surgery evidence the great efficacy we have when neuromodulation is delivered with surgical precision. Our surgical targets are high-priced real estate, with benefits imparted by higher accuracy and costs associated with off-target spillover of stimulation.

I believe we are entering an era in which our quest for precision is pushing previous limits. Our efforts to date have focused on delivering therapeutic neuromodulation (e.g., deep brain stimulation, DBS) via surgically implanted devices, which provide the aforementioned specificity and accompanying efficacy. The information from which this specificity is derived, however, is typically attained through



Stereo-EEG informed deep brain stimulation for severe, treatment-resistant depression. A) Implant strategy for the first participant in our trial showing the stereo-EEG electrodes sampling frontotemporal regions including dorsolateral prefrontal cortex (PFC) (blue), ventrolateral PFC (orange), ventromedial PFC (yellow), orbitofrontal cortex (pink), lateral temporal lobe (violet) and medial temporal lobe (red). **B)** Stimulation on one of the DBS leads (left subcallosal cingulate) using the contact configuration shown (frequency 130 Hz, pulse width 180 microsec, amplitude 5 mA) produced the depicted activity pattern (red indicates higher power in gamma band oscillations). This stimulation configuration represents one of several hundred tested to determine brain network responses to DBS.

non-invasive strategies. Examples include functional MRI, diffusion tensor imaging tractography, electroencephalography (EEG), magnetoencephalography, etc. The sole counterexample is the field of epilepsy surgery, in which it is common to base therapeutic decisions on intracranial recordings from surgically implanted diagnostic electrodes. This intracranial diagnostic platform, common in epilepsy surgery programs across the globe for decades, is nearly unheard of outside of epilepsy surgery.

Our group has adopted this intracranial approach to derive a precise, individualized understanding of network activity in patients with severe, treatment-resistant depression. The societal burden of this disorder is vast, and the need for improved therapy is urgent. Presumably these factors motivated successful funding for the effort by NIH (BRAIN Initiative UH3 NS103549) and approval by the U.S. FDA (IDE G180300). Co-leads of this project with me are Nader Pouratian, MD, PhD, chair of neurosurgery at the University of Texas Southwestern, and Wayne Goodman, MD, chair of psychiatry at the Baylor College of Medicine. Our project takes the epilepsy surgery approach of temporary intracranial evaluation and applies it to the goal of understanding not seizure ictus and spread but rather activity patterns associated with mood regulation and cognition.

Subjects in the trial are implanted with DBS leads targeting key regions that have a previous evidence base of success: the region of the ventral portion of the anterior limb of the internal capsule and the region of the subcallosal cingulate. Both of these regions are thought to be “hubs” of networks regulating emotion and cognition that are well-connected to other involved frontotemporal cortical and subcortical regions. We implant the therapeutic DBS leads in these hubs and also implant temporary stereo-EEG electrodes (as is done routinely in epilepsy surgery) in the downstream network regions. The subject is then kept in the inpatient monitoring unit for several days while we conduct a series of studies to measure her/his brain network activity across a range of mood states and in response to stimulation. The goal of this effort is to leverage these precious intracranial data to derive bespoke stimulation parameters that are individualized to the patient, with the hope that this degree of precision drives improved and more consistent outcomes. The first subject in our trial has done remarkably well. His depressive episode was in its fifth year when he enrolled. A highly intelligent young man

> THE GOAL OF THIS EFFORT IS TO LEVERAGE THESE PRECIOUS INTRACRANIAL DATA TO DERIVE BESPOKE STIMULATION PARAMETERS THAT ARE INDIVIDUALIZED TO THE PATIENT, WITH THE HOPE THAT THIS DEGREE OF PRECISION DRIVES IMPROVED AND MORE CONSISTENT OUTCOMES. <

of Puerto Rican descent, he was completely disabled by depression, unable to engage in his demanding job in risk management, unable to maintain social relationships, often unable to even get out of bed. He tolerated this first-of-its-kind surgery well. Our analysis of the intracranial data produced DBS stimulation parameters that led to remission of symptoms over just a few months. To confirm that his response was related to stimulation and was not a sham (placebo) response, we performed a double-blinded gradual withdrawal of stimulation amplitude. His symptom severity steadily increased during this tapering period until he met escape criteria, at which point we reinstated open-label DBS delivery, and he again achieved remission. He has regained his interest in pleasurable activities, is successful at work, enjoys relationships, and is thrilled to have become a father recently. For more details on these results and the trial, please see our recent publication (Sheth *et al. Biological Psychiatry*, <https://doi.org/10.1016/j.biopsych.2021.11.007>)

Our ability to deliver effective neuromodulatory therapy is largely limited by our understanding of the networks we are trying to engage. As we tackle increasingly challenging neurological and psychiatric disorders, approaches such as these will provide this necessary understanding. I believe that the thoughtful application of creative solutions will drive further upward inflection of our field’s success and influence in the coming years. ■



Mohamad Bydon, MD

Giorgos D. Michalopoulos,
MDJason P. Sheehan, MD,
PhD

Quality Registries in Neurosurgical Neuro-Oncology

Background

Neuro-oncology encompasses a heterogeneous mixture of pathological entities, treated with a broad spectrum of surgical and radiotherapeutic modalities. Assessing outcomes and evaluating the quality of care delivery has been particularly challenging yet necessary. Responding to the call, the NeuroPoint Alliance (NPA) has instituted two national quality registries, one focusing on stereotactic radiosurgery (SRS) and one on brain tumor surgery. These registries were built based on the successful model of the Spine modules of the Quality Outcomes Database (QOD), characterized by the following features: multi-institutional participation, prospective collection of data, and long-term patient follow-up. The narrow focus of these registries compared to administrative databases (e.g., the National Inpatient Sample – NIS) and broad-spectrum surgical registries (e.g., the American College of Surgeons National Surgical Quality Improvement Program – ACS-NSQIP) allows for significantly more granular and accurate analyses and conclusions. The SRS registry and Tumor QOD are currently utilized to compare institutional with national surgical benchmarks, evaluating the quality of care among the participating sites. Equally significantly, the registries provide a valuable resource of data for research purposes.

The SRS Registry

The most common indication for SRS is benign and malignant brain tumors. High-quality evidence is essential to improve the selection, technique, and outcomes of patients undergoing SRS. Also, practice variations exist for the use of SRS throughout the U.S. and, more broadly, the world. While SRS has been performed for more than 50 years, the vast majority of published studies were single-center, retrospective cohort studies. These studies were often limited by the inherent selection biases of the clinicians at that center, a uniformity to the device typically used to deliver SRS, and low statistical power.

Recognizing these challenges to a rapidly growing part of neurosurgery practice, a national SRS registry was launched by the American Association of Neurological Surgeons in 2014. The registry is currently comprised of 21 sites accruing data from across the U.S. Since that time, more than 4,153 SRS patients and 6,980 events have been included in the registry, which is now overseen by the NPA. The registry prospectively collects patient and tumor attributes, radiosurgical treatment parameters, neuro-imaging studies of the SRS treatment and relevant studies, and patient-related clinical outcomes (**Figures 1-3**). Aggregation and analysis of the data can occur at the site level and also across the entire SRS registry cohort. In leading journals such as the Journal of Neuro-Oncology and the Journal of Neurosurgery, multiple studies have been published

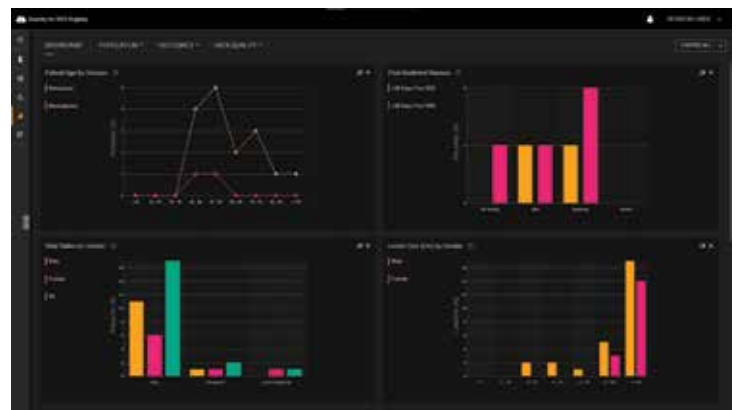


Figure 1: Analytics Dashboard for the Stereotactic Radiosurgery Registry

to date looking at the registry and brain tumor-related patient outcomes, including those treated with brain metastasis. The registry also allows for an individual neurosurgeon to review outcomes and for a site to assess practice variations and any relevant opportunities for improvement (**Figure 1**). Through big data initiatives such as this prospective registry, the Tumor Section has been able to advance the field in meaningful ways. The value of these registries will likely only expand in the years to come.

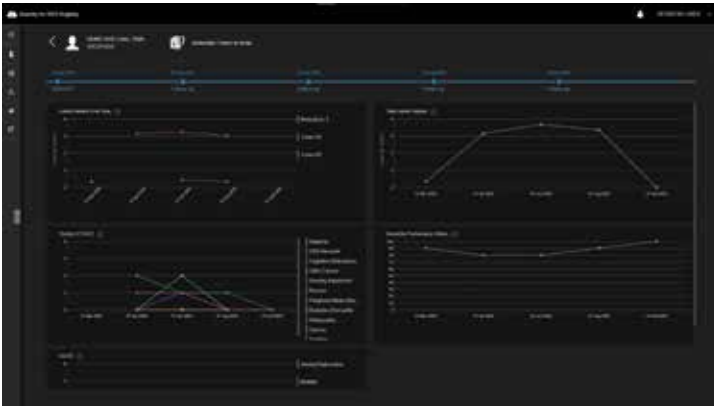


Figure 2: Patient Dashboard for the Stereotactic Radiosurgery Registry

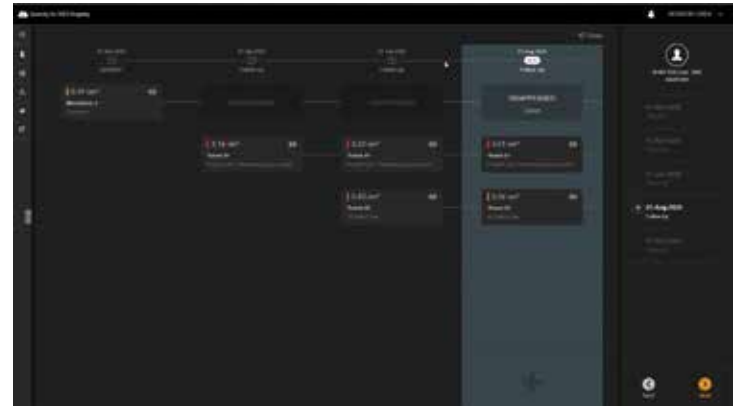


Figure 3: Tumor Monitoring Tools in Brainlab's Qentry for the Stereotactic Radiosurgery Registry

The Tumor QOD

Instituted in February 2019, the Tumor QOD currently includes 1,804 patients from nine participating sites, with eight more sites currently initiating participation. The caseload of the registry is predominantly comprised of high-grade gliomas, meningiomas, metastases, pituitary tumors, and schwannomas – all histopathological diagnoses are represented by International Classification of Diseases for Oncology (ICD-O) codes. Professional abstractors prospectively collect all variables via evaluation of electronic medical records and patient interviews.

An important feature of the Tumor QOD that distinguishes it from other registries is its granularity in surgical parameters. More than 40 operative variables are captured in the registry, providing a detailed illustration of surgical techniques and equipment used during tumor resection. These variables include – but are not limited to – surgical approach, neuromonitoring, imaging and navigation, fluorescence, and brachytherapy. Another advantage of this registry is its focus on patient-reported outcomes. All patients undergoing elective tumor resection are interviewed prior to surgery and complete a quality-of-life questionnaire, a process also repeated at all follow-up time points. Patient-reported outcomes are of particular significance in evaluating the quality of care multidimensionally, and insights from this registry are anticipated to be valuable in quality surveillance and neuro-oncological surgery research. The Tumor QOD also provides a detailed illustration of the patients' preoperative and postoperative clinical status in the form of a detailed list of clinical symptoms. The resolution of prior symptoms and the emergence of new ones after surgery is an unprecedented quality measure for registries of this scale.

> THE CONTINUOUS ENROLLMENT OF PATIENTS CONSTANTLY INCREASES THE POPULATION THAT CAN BE POTENTIALLY STUDIED VIA THESE REGISTRIES. SOON, THESE TWO REGISTRIES WILL CONSTITUTE AN INVALUABLE SOURCE OF DATA, EVEN FOR SOME RARE AND UNDER-STUDIED DISEASE MODALITIES. <

Future Directions

The participating sites are continuously increasing in number. In the future, the two registries are expected to provide a more representative illustration of clinical standards across the United States. International participation is also anticipated: institutions from Latin America and Asia are currently in the registration process for the Tumor QOD.

The continuous enrollment of patients constantly increases the population that can be potentially studied via these registries. Soon, these two registries will constitute an invaluable source of data, even for some rare and under-studied disease modalities.

Finally, the SRS and Tumor QOD have overlapping fields of interest, mainly intracranial metastatic disease and schwannoma. One of the NPA's upcoming endeavors is to facilitate "cross-talking" between the two registries so that patients enrolled in both registries can be identified and studied more accurately. ■



Peter Yang, MD



Jennifer Strahle, MD

Endoscopic Third Ventriculostomy with Choroid Plexus Cauterization (ETV+CPC) for Pediatric Hydrocephalus: One Patient's Experience



Nova with her parents, Jessica and Steve, and brother Owen

In pediatrics, hydrocephalus primarily affects infants under one year of age, often related to myelomeningocele or premature birth. The traditional treatment for hydrocephalus is cerebrospinal fluid (CSF) shunting. Life-time complications of CSF shunts are numerous and expensive, with annual hospital charges of nearly \$2.0 billion in the U.S. alone, accounting for 3.1% of all pediatric hospital charges. As shunt complications also adversely impact quality of life, it is not surprising that surveys of families with children affected by hydrocephalus have shown a desperate desire for shunt-free treatment options.

Patient Highlight: Nova was born at term with an open myelomeningocele who underwent surgery for closure on day-of-life one. She recovered well from surgery, but several weeks later, she began developing signs of hydrocephalus. Her family had been counseled in a prenatal visit by our team about the diagnosis of myelomeningocele and association with hydrocephalus, but now had to make a difficult decision regarding treatment. Our team discussed that CSF shunting and endoscopic third ventriculostomy with choroid plexus cauterization (ETV+CPC) were two treatment options. Nova's family recognized that although shunting is the more common and established procedure, they were in favor of a surgery to treat hydrocephalus while potentially avoiding the problems associated with implanted hardware. They wanted to give her a chance to be shunt-free. At six weeks of age, Nova underwent an ETV+CPC procedure at St. Louis Children's Hospital in which the floor of the third ventricle and the membrane of Liliequist were fenestrated to connect CSF compartments and the choroid plexus within both lateral ventricles was cauterized. She recovered well.

> ENDOSCOPIC THIRD VENTRICULOSTOMY WITH CHOROID PLEXUS CAUTERIZATION MAY REDUCE OVERALL CSF PRODUCTION AND IMPROVE CSF CIRCULATION, AND IS A PROMISING SHUNT-FREE TREATMENT OPTION FOR INFANT HYDROCEPHALUS <



Nova at five and a half months old

Since surgery nearly six months ago, Nova has not had any signs of hydrocephalus and has met all her major developmental milestones. Her family has told us that they are happy with her progress and are cautiously optimistic about her having undergone a definitive treatment for hydrocephalus without the need for a shunt.

In combination, ETV+CPC may reduce overall CSF production and improve CSF circulation, and is a promising shunt-free treatment option for infant hydrocephalus. Over the years, the Hydrocephalus Clinical Research Network (HCRN), a committed group of 14 North American pediatric neurosurgical centers with a long track-record of collaborative clinical research, and others including Dr. Benjamin

Warf, have shown ETV+CPC to be a safe alternative to shunting in select infants. However, as the function of the choroid plexus is nuanced and multifactorial (including being recently recognized to play a role in clearing CSF solutes), the long-term effects of ETV+CPC are not known. Conversely, shunting may deplete CSF of important trophic factors. Currently, the cognitive outcome of ETV+CPC compared to shunt placement is not well-described. We have found that most families, such as Nova's, would accept the risks of ETV+CPC for the chance to be free of having a shunt, but only if ETV+CPC does not lead to a noticeable sacrifice in cognitive outcome compared to shunting. Moreover, motor outcomes, language outcomes, surgical complications, and MRI findings that relate to brain development and hydrocephalus are also important factors to consider when comparing the two surgeries.

To study these outcomes in an unbiased way, Drs. David Limbrick, John Kestle, Abhaya Kulkarni, and Richard Holubkov received NIH funding to conduct a multi-center randomized controlled trial, Endoscopic versus Shunt Treatment of Hydrocephalus in Infants (ESTHI) comparing ETV+CPC and shunt in infants with hydrocephalus. Our center is excited to be recruiting new patients and is encouraged by the collegial collaboration between high-volume peer institutions. We hope that the results of this trial will help guide decisions for the treatment of hydrocephalus in infants. ❏



Mick Perez-Cruet, MD,
MS

The Physician Scientist: Balancing Private Practice and Academic Interest

In its most basic form, translational research transforms scientific discoveries made in the laboratory into cost-effective clinical treatments, like penicillin, bone morphogenic protein for use in spinal fusion, and gamma knife to apply focused radiation to tumors. Most of these advances are made in a university setting with the resources and personnel capable of carrying out labor-intensive scientific experiments, and neurosurgeons interested in conducting translational research often choose an academic track that can provide help and protected time to conduct scientific studies. Though there are advantages to being a purely academic clinician, there are also advantages to being in private practice. The advantage of being in private practice is autonomy and the ability to practice independently. Private practice neurosurgeons can own ancillary services, operate at multiple hospitals, and own intellectual property that does not belong to an academic institution. However, a private practitioner must do a sufficient number of cases to support him or herself, and with reimbursement declining, this can be a real challenge. In addition, research funding is limited and extremely difficult to obtain. An R01 grant, which is multi-year research requiring millions of dollars funding, is usually only provided to large academic centers.

Translational laboratory research is not for everyone. To conduct this type of research, one has to understand the scientific method and laboratory techniques, and technologies that can perform this type of research. Collaboration is essential, and without it, true scientific experiments published in high-impact journals are unlikely. I began my

scientific interest while doing field research on reef systems in Costa Rica during college. This resulted in a publication. After college, I conducted shark tumor research at Mote Marine Laboratory in Sarasota, Florida, and earned a Masters in Chemistry from the University of South Florida in Tampa. My thesis research discovered the red tide toxin that causes human asthmatic respiratory attacks during a red tide outbreak. During my masters, I would often oversee medical students perform laboratory experiments. What I quickly realized was that many were not interested or dedicated enough to complete investigations. Thus there appeared a need for clinician-scientist in medicine. This ultimately led to my interest in medicine and being a physician-scientist. I do encourage all physicians to have at least some exposure to science as it makes one a better critical thinking clinician. The art of clinical diagnosis is not far removed from scientific investigation.

Once I started a practice, I began meeting with basic science researchers. The collaboration between basic science and clinical researchers is critical and extremely valuable to conduct successful translational research. The basic scientist PhDs bring fundamental knowledge of biological processes and experimental techniques that fuels the technological innovations. The clinical researcher MDs bring along knowledge of medical conditions that require treatments. Working together, they can be a productive and successful research team. My research and clinical interest lead me to investigate intervertebral disc regeneration using stem cell technology.

Though I had always been interested in spinal cord regeneration, the obstacles to practical research in this area seemed daunting. Stem cell-based disc regeneration appeared more likely to result in clinical treatment. I began researching with Dr. Rasul Chaudhry, Director of the Stem Cell and Regenerative Institute at Oakland University, Rochester, Michigan. I knew that it was up to me to keep this collaboration going. I made time for research meetings and provided research support through my practice. We helped fund several very hard-working and outstanding Masters and PhD graduate students and together worked closely to foster and guide them through their research. My knowledge of the clinical condition of intervertebral disc degeneration and my basic science background, in combination with Dr. Chaudhry's knowledge of stem cell biology, was critical for our successful collaboration that produced basic science and preclinical findings published in high impact journals.

However, taking bench research to the market is a whole other area. I have been successful in writing a number of patents. The patent protects the intellectual property and adds value, making it worth the effort for a business person to bring the technology to market. It is costly to bring technology to the market, and without the opportunity to regain investments, a basic science idea is unlikely to make it to the market. In order to get these products to market, collaboration is established with business leaders. My first product to market was the Bonebac Press. This product allows the surgeon to collect bone from the surgical site and use it as



Figure 1. A. The Bonebac Press (Thompson MIS, Salem, New Hampshire) used to collect morselized autograph from the surgical site during minimally invasive lumbar decompression. **B.** Use of the Bonebac TLIF system to inject the morselized autograph into the disc space using a proprietary bone injection system where the autograph is injected through the implant holder to fill the disc space. **C.** Post-operative image showing complete fusion at the L3-4 interbody space using the Bonebac TLIF system in combination with bone harvested using the Bonebac Press.

a fusion material. I understood that direct patient bone has the highest probability of achieving an effective fusion. This was followed by a device, the Thompson MIS TLIF System, that allows for this bone to be used to fill the disc by injecting it through the device holder and around the implant. Using this method, the disc can be fully packed with a significant amount of morselized autograph achieving a very high fusion rate. Our clinical success has been validated using this system. (Figure 1)

Ultimately, I would like to see our basic science stem cell-based intervertebral disc research result in a method to restore the biologic integrity of the degenerated disc. I think this can only be achieved by first restoring the height of a degenerated collapsed disc. To this end, I have patented a disk distractor that allows for the slow restoration of disc height. This would act like a tissue expander placed under the skin used for reconstructive plastic surgery or the Ilizarov bone extender used to elongate long bones. The tension of the Annulo device would, over time, restore the disc height. The nucleus pulposus could then be reconstituted using nucleus pulposus cells differentiated from human umbilical cord mesenchymal stem cells. (Figure 2)

In essence, the clinical scientist interested in translational research and private practice

autonomy must be able to collaborate effectively. I am blessed to have an excellent private practice, Michigan Head and Spine Institute, supporting my research efforts. MHSI is a multi-specialty practice with over 20 neurosurgeons. MHSI owns ancillary services, including an ambulatory surgery center, MRI and CT imaging, and rehabilitation center. My partners cover my service when I am at meetings presenting our research accomplishments. In addition, I have an outstanding collaboration with Dr. Rasul Chaudhry, who is an absolute joy to work with. His incredible basic science

research mind and my clinical acumen make us an exceptional team capable of taking cost-effective bench research to the clinical arena: Translational research. 

References

- 1 Perez-Cruet M, Beeravolu N, McKee C, et al. Potential of Human Nucleus Pulposus-Like Cells Derived From Umbilical Cord to Treat Degenerative Disc Disease. *Neurosurgery*. 2019 Jan 1;84(1):272-283.
- 2 Beeravolu N, McKee C, Alamri A, et al. Isolation and Characterization of Mesenchymal Stromal Cells from Human Umbilical Cord and Fetal Placenta. *J Vis Exp*. 2017 Apr 3;(122).
- 3 Beeravolu N, Brougham J, Khan I, et al. Human umbilical cord derivatives regenerate intervertebral disc. *J Tissue Eng Regen Med*. 2018 Jan;12(1):e579-e591.
- 4 Beeravolu N, Khan I, McKee C, Dinda S, Thibodeau B, et al. Isolation and comparative analysis of potential stem/progenitor cells from different regions of human umbilical cord. *Stem Cell Res*. 2016 May;16(3):696-711.
- 5 McKee C, Perez-Cruet M, Chavez F, Chaudhry GR. HYPERLINK Simplified three-dimensional culture system for long-term expansion of embryonic stem cells. *World J Stem Cells*. 2015 Aug 26;7(7):1064-77.

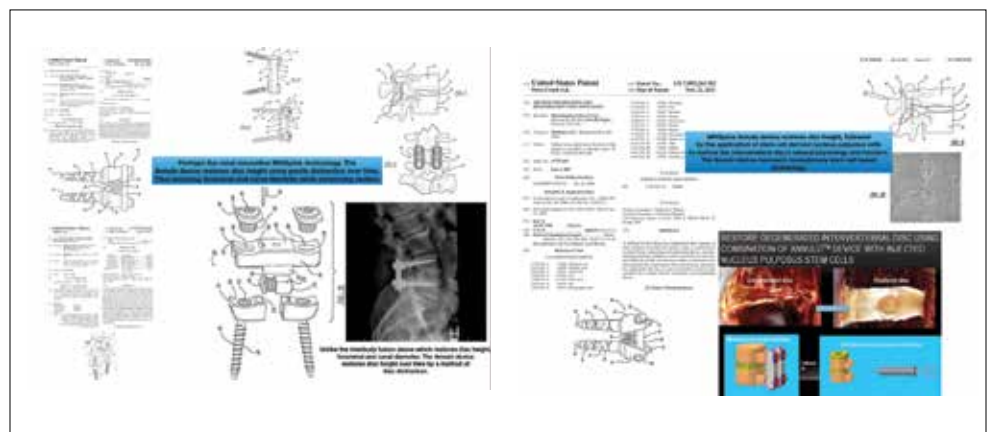


Figure 2. Example of translational research efforts. Patents of Annulo disc height restorative technology combined with stem cell-based nucleus pulposus restoration could lead to biologic regeneration of the degenerated intervertebral disc to treat debilitating spinal disorders.



John B. Pracyk, MD,
PhD, MBA, FACS

Cultivating a Nonclinical Career to Deliver Global Therapeutic Solutions

Several years ago, at the CNS Annual Meeting, I delivered a keynote presentation about transitioning from neurological surgery into the medical technology industry. I found it curious that not a single question was asked during the presentation, but upon stepping down from the stage, I was met by a line of fellow neurological surgeons, including several department chairs. I spent the better part of an hour answering their questions about how they might architect the next chapter in diversifying their own careers. Clearly, these surgeons were concerned about how they would be perceived should they express interest in making a move publicly. But make no mistake, the interest in exploring a career in industry was there.

Fast forward through 20 months of dealing with COVID and the resulting pandemic burn out, and that smoldering interest is now ablaze. According to a recent Medscape survey, 22% of physicians are expressing an interest in transitioning to a nonclinical role.¹

While we begin our neurosurgical careers as individual contributors treating one patient at a time, we also have the very real opportunity to multiply our impact exponentially by helping advance the delivery of therapeutic solutions to patients worldwide. In this article, I'm going to highlight opportunities to have that kind of global impact while possibly launching your own career transition.

Teaching Faculty for an Industry Course

We all attend society and industry sponsored instructional courses, so why not try your hand at teaching one of them? In addition to sponsoring societal courses, the medical technology industry is known to host their own professional education courses on the safe and effective use of their products. Perhaps start locally or regionally and then ascend to national courses. The format can be a didactic instructional course lecture (ICL) or a hands-on demonstration in a laboratory setting with simulators or cadavers.

This is an excellent way to explore what it is like to work within the constraints of a highly regulated industry. While partnering

with you as a faculty instructor, the company will be assessing your potential as an emerging thought leader, innovator, educator, or health system executive. In the new world of teaching virtually, it is easier than ever to have a global reach from the comfort of your office or home.

Expert Consultant or Advisory Board Member

Consulting with industry on a service-level contractual basis might be the next step after teaching. The medical technology industry is eager for thoughtful practitioners who are developing their own voice and can effectively communicate a fresh perspective in a specific therapeutic area. The topics are plentiful and include emerging trends, therapies for difficult-to-treat disease states, challenges with current medical technologies and pharmaceuticals, and identifying true unmet medical needs that are not satisfactorily being addressed.

Digital is an exploding area and artificial intelligence is of practical importance, not only for clinical decision support but also for the wealth of data residing within the electronic health records of health systems and integrated delivery networks globally. We are learning that there is a tidal wave of "exhaust data" emitted from medical devices that may just translate into a competitive edge for the future. For those with deep analytical skills, it's all about capture, interpretation, and application.

Traditional clinical research focusing on the safety and performance of the devices are another avenue that can be accomplished via industry sponsored trials or grant support through investigator-initiated studies. The new European Medical Device Regulation has spawned significant need to substantiate the clinical value of products in the jurisdictions that require the CE mark. Much of that work will take place outside of the European Union and will take the form of post-market clinical trials where the products are already launched.

For those surgeon leaders with administrative experience, Health Economics & Market Access (HEMA) is an adjacency to clinical practice that also holds great potential. Before transitioning into industry, I spent over a decade immersing myself in the business side of developing multidisciplinary, collaborative care delivery models that included clinic operations, service line optimization, new revenue realization, as well as building out the value analysis committee for supply chain purchasing decisions.

Advisory Board memberships present a great opportunity to help industry better understand how recent market conditions are impacting care delivery. In addition, practice considerations, reimbursement landscape, environmental impact, and site-of-care delivery that is now migrating outside the traditional hospital are all opportunities to share your expertise. Health inequities in access to care and clinical outcomes are cogent topics that need to be factored into industry sponsored research.

Disclosure:

Dr. John Pracyk is a full-time employee of the Olympus Corporation.

Going for Gold – Becoming a Design Surgeon

For a select few, the role of designing medical technologies represents the crowning achievement for the practicing neurological surgeon. With this level of contribution, the surgeon will have built themselves a reputation as a global thought leader who will attract companies interested in scientific collaboration to bring new technologies to market. Typically, this level of partnership involves an exchange of ideas that are defined as unique intellectual property that can be defended and protected through a method or device patent. In exchange for this intellectual property, monetary compensation takes the form of royalties derived from the sale of the product. You need to be mindful of all the legal complexities to make sure that it meets health care compliance, conflict of interest, and fair market value considerations, just to name a few.

In specialties outside of neurological surgery, some surgeons may use only one brand of product their entire career, which limits one's ability to work with different manufacturers. In neurological surgery, some of the most successful design surgeons have worked with many industry partners over their careers. The design surgeon concept is unique to the medical technology industry. In pharmaceuticals and biotech, the current trend is to attract successful researchers (molecular biologists, oncologists, immunologists, and pharmacologists) from academia for the clinical development programs of the drug or biologic.

Incubators and External Innovation Ecosystems

Today, the large pharmaceutical and medical technology companies are cultivating external innovation ecosystems that will underwrite and drive a significant portion of their inorganic growth, as embodied via licensing, distribution, and outright mergers and acquisitions.

Most medical device manufacturers are prepared to partner with a young startup anywhere along the following continuum: research collaborations > equity investments with specified deliverables and milestones > licensing and distribution agreements > outright acquisition with subsequent integration into the strategic company.

This has been perfected in the biotech and pharmaceutical arena and is now making its way to medical technologies. For the entrepreneurial minded that have the wherewithal to launch an entire company, this represents a viable path and exit strategy for the thousands of companies that are being formed in the technology transfer sections of academia and for-profit healthcare entities.

Innovation centers are being set up by corporate venture capital entities in pharmaceuticals and medical technology companies alike, with being virtual and others with brick-and-mortar incubator facilities. Entry to these highly competitive, incubators is often earned by successfully outcompeting other startups in a "Shark Tank" style competition where hundreds of companies contend for 3-5 coveted residences. The days of a surgeon with an idea on the

back of an envelope are long gone. For this new paradigm, the invention needs to be de-risked, having successfully completed a proof of principle "killer experiment" before an industry strategic partner will be interested.² The time horizon expectation for most acquisitions to become financially accretive to the bottom line is shortening. Some companies will pay more to take less risk or alternatively get in early and assume more risk for a lower cost of entry. It is not uncommon for outside financing professionals to help the startup companies secure the requisite capital to accomplish their preliminary clinical trials so a strategic suitor can accomplish a pivotal trial for a pharmaceutical or a technology, if necessary. Indeed, the stakes are much higher, and a significant amount of financial commitment is required for this route. It is not for the faint of heart nor the basement innovation hobbyist.

Conclusion

So why did those surgeons at my keynote presentation prefer to keep their interest under wraps? I suspect it could be an underlying feeling of desertion that causes them to be uncertain about displaying any public interest in industry. Perhaps they are hesitant because of all the time invested personally by themselves, and by their spouses, families, faculty mentors, and surgical colleagues that helped shape their successful careers in one of the most technically challenging and personally demanding surgical specialties. There are indisputable heroics in neurological surgery, and maybe we simply don't want to turn our back on the hero.

But a professional life can have many iterations. Just as in our field, we use therapeutic devices from many brands; we can impact medicine across a range of capacities. At our core, we want to continue to learn, grow, and contribute meaningfully. Although my own entry into industry leveraged my neurosurgical career, today I derive significant accomplishment in mastering the complexities of many as seven different therapeutic areas as the Global Chief Medical Safety Officer at Olympus Corporation. My work is as exciting today as when I first started my career—fulfilling, rewarding, and challenging.

Each day I leverage the diverse experiences gained along the many paths described in this article to create therapeutic solutions that satisfy unmet medical, clinical, and patient safety needs. Ultimately, it's about innovation that materially improves the work and lives of billions worldwide - practitioners, providers, payors, policy makers, and most importantly, our patients. ■

References:

1. Lehmann, C. *Medscape Non-Clinical Careers Report*. October 8, 2021.
2. Hait, W., Stoffels, P. A primer for academic entrepreneurs on academic-industrial partnerships, *Nature Communications*, 12: 5778, October 1, 2021.



Matthew J. McPheeters,
MD, MBA



Nelson M. Oyesiku,
MD, PhD

Journal Feature: Neurosurgery – Shaping Clinical Practice Through Translational Research

Since the CNS published first published *Clinical Neurosurgery*, which today serves as the official register of the CNS Annual Meeting, the Congress has been fortunate to work in partnership its members to provide the neurosurgical community a preeminent journal dedicated translating the science of neurosurgery into clinical practice. In the first publication of *Clinical Neurosurgery* in 1955, then editor-in-chief, Raymond K. Thompson, described the purpose of the journal, “to present a chronicle having a two-fold purpose. First, to honor one or more scientists in the field of the neurological sciences and to have him present some of his original studies. Secondly, to record for the future and for those not members of the Society the valuable ideas of those men who have contributed to the success of the program.”¹

Over the ensuing 67 years numerous scientific discoveries have transformed the field of neurosurgery, yet the focus of *Neurosurgery*, the official journal of the CNS first published in 1977, and its relationship with the CNS remain largely unchanged. The past two years have been trying times throughout healthcare consistent only in their unpredictability. As many surgeons and scientists found themselves with more time at home, they utilized this time to submit an unprecedented volume of manuscripts for publication. In this issue of *Congress Quarterly*, we look at the role *Neurosurgery* continues to play in shaping the clinical practice of neurosurgery through translational research by reviewing



a selection of promising translational studies published in *Neurosurgery* over the past year.

Radiotherapy, Temozolomide, and Antiprogrammed Cell Death Protein 1 Treatments Modulate the Immune Microenvironment in Experimental High-Grade Glioma²

The poor prognosis and relatively rapid progression of high-grade gliomas (HGG), makes HGG one of the most difficult

diagnoses managed by neurosurgeons. As such, the development of effective treatments, specifically in immunotherapy, is a common area of study in translational neurosurgery. Despite this, the effect of radiation therapy, chemotherapy, and immunotherapies on immune biology is not well understood. In the February issue of *Neurosurgery*, Riva and colleagues published a mouse model to better understand the treatment effects of HGG on immune biology.

NEUROLOGICAL SURGERY

PUBLICATIONS

The authors focused their efforts on radiation therapy (RT), conventional chemotherapy (temozolomide; TMZ), and the immunotherapy anti-programmed death protein 1 (α PD1) and the study included both monotherapies and combination therapies. Several immunologic markers were studied as well as survival. The results demonstrated RT, TMZ, and α PD1 to be effective in stimulating the innate immune system, with RT having the most robust effect. Similarly, RT was effective at stimulating the adaptive immune system, while TMZ required combination therapy for such a response. Surprisingly, although α PD1 did stimulate the innate immune system, it had no significant effect on the adaptive immune response in monotherapy or combination therapy and did not provide additional survival benefit.

While the study findings demonstrated a negative result for the target immunotherapy, α PD1, the study will continue to play a role in the development of effective therapies for HGG. In the future, researchers will be able to use this model to assess the immune biology effects of new immunotherapies for HGG.

PD-1+ Monocytes Mediate Cerebral Vasospasm Following Subarachnoid Hemorrhage³

Later in the year, another article published in *Neurosurgery* by Jackson and colleagues again studied the programmed death protein 1 (PD-1), but in a very different neurosurgical setting. For individuals who survive the initial injury of cerebral aneurysm

rupture, delayed ischemic injury secondary to cerebral vasospasm results in significant morbidity and mortality. The physiology underlying cerebral vasospasm is complex and poorly understood but is linked to underlying inflammation. Given recent data demonstrating the anti-inflammatory effect of α PD1 in oncology research, the authors hypothesized that PD-1+ monocytes could be used as a marker for cerebral vasospasm and that α PD1 therapy would decrease cerebral vasospasm in the setting of subarachnoid hemorrhage (SAH).

To test their hypothesis, the authors devised two separate experiments. In the first a mouse model was used to induce cerebral vasospasm via endovascular internal carotid artery perforation to produce severe SAH. The authors then administered an α PD1 and measured arterial wall thickness and luminal diameter as measures for vasospasm in the mice who received and did not receive the α PD1. They found that administration of α PD1 significantly reduced the vasospasm. Additionally, to further strengthen their findings, the authors performed an additional test in which the mice were given PD-1 blocking antibodies prior to injury and treatment with the α PD1, which abrogated the effect of the α PD1. The second experiment assessed the association between PD-1+ monocytes in peripheral blood with radiographic vasospasm. Six consecutive patients with aneurysmal SAH were assessed with serial serum PD-1+ monocyte levels and transcranial dopplers. In the two patients

who developed cerebral vasospasm, the radiographic findings were preceded by a significant increase in number of circulating PD-1+ monocytes.

The authors refer to their study design as “bench-to-bedside,” as the α PD1 treatment response was tested only in the animal model, whereas patients were studied observationally with a tangentially related study design to logically connect the results. Despite the low number of enrolled patients, the robust study results in combination with existing α PD1 therapies provides an exciting future for this area of research on cerebral vasospasm and future therapy. ■

References

- 1 Thompson, R. K., Jackson, I. J., Christoferson, L. A., Strewler, G. J. & Weaver, E. N. Preface. *Neurosurgery* 1, v-v (1955).
- 2 Riva, M. et al. Radiotherapy, Temozolomide, and Antiprogrammed Cell Death Protein 1 Treatments Modulate the Immune Microenvironment in Experimental High-Grade Glioma. *Neurosurgery* 88, E205–E215 (2020).
- 3 Jackson, C. M. et al. PD-1+ Monocytes Mediate Cerebral Vasospasm Following Subarachnoid Hemorrhage. *Neurosurgery* 88, 855–863 (2020).

NEW!

MARCH 24, MARCH 31, APRIL 7, 2022



CNS

Neurosurgical Emergencies

Virtual Course



Earn up to 12.25 CME

Join us for a new course on state-of-the-art diagnosis, workup, and first-line treatments for neurosurgical emergencies. This fast-paced course focuses on emerging technologies that are changing the field, including advances in stroke management, the emerging role of TXA in intra-cerebral hemorrhage, the ever-changing landscape of anticoagulation, and more! Enhance your learning through small-group breakout discussions and case-based learning.

View the agenda and register at cns.org/trauma

Course Directors



Martina Stippler



David Okonkwo

FOUNDATION UPDATE



CNS

Foundation

CNS Annual Meeting Showcases the CNS Foundation's Growth and Impact!

Welcoming New CNS Foundation Board Members



Members of the CNS Foundation Board: Left to Right: Front Row: Courtney Johnson (CNSF Director), Scott Simon, Joseph Phelps, Alexander Khalessi (CNSF Co-Chair), Martina Stippler (CNSF Co-Chair), Sarah Woodrow, Gita Barry, Nicholas Bambakidis (CNS President), Daniel Hoh (CNSF Treasurer) **Back Row:** Brian Nahed, Paul Gardner, Elad Levy (Past CNSF Chair, CNS Chair-Elect), Clemens Schirmer, David Crawford



Thanks to donors like Mark Krinock and his wife, the CNS Foundation raised more than \$24,000 during the CNS Annual Meeting Silent Auction.

The CNS Foundation says “Thank you” to Elad Levy, “Welcome” to new members of the Board.

The CNS Foundation Board expressed heartfelt appreciation to Elad Levy for his three years of dedicated service as Chair of the CNS Foundation. New Co-Chairs are Martina Stippler and Alexander Khalessi. Also approved, the expansion of the Board to include representatives from each neurosurgical subspecialty, as well as the Members-At-Large of the CNS Executive Committee.

CNS Foundation Board 2022

Alexander Khalessi, MD, MBA
CNS Foundation Operations Chair
CNS Vice President

Martina Stippler, MD
CNS Foundation Strategic Chair
CNS Secretary

Nicholas Bambakidis, MD
CNSF Board member
CNS President

Brian Hoh, MD, MBA
CNSF Board member
CNS Past President

Ricardo J. Komotar, MD
CNSF Board member

Brian V. Nahed, MD, MSc
CNSF Board member
CNS EC member

Daniel Hoh, MD
CNS Foundation Treasurer
CNS Treasurer (2021-2023)

Elad I. Levy, MD, MBA
CNS Foundation Chair and Secretary
CNS President-Elect

Clemens M. Schirmer, MD, PhD
CNSF Board member
CNS EC member

Regina Shupak
CNS Foundation Ex-officio Board Member
CNS CEO

David B. Crawford, CFA
CNSF Board member

Gita Berry, MBA
CNS Foundation Advisory Board

CNS Member-At-Large Appointees

Ellen Air, MD
Tiffany Hodges, MD
Akash Patel, MD
Laura Snyder, MD
Anand Veeravagu, MD
Khoi Than, MD

Section Appointees

Sarah Woodrow, MD, WINS
Julie Pilitsis MD, PhD, ASSFN
Ruth Bristol, MD, Pediatric
Paul Gardner, MD, Tumor
Jeremy Phelps, MD, CSNS
Scott Simon, MD, Cerebrovascular
Section on Spine and Peripheral Nerves - Pending
Trauma Section - Pending
Pain Section - Pending

Babacar Cisse, second NINDS/CNS GetchK12 Scholar presented, “The role of E proteins in the regulation of the proliferation and stemness of glioma stem cells,” at the CNS Annual Meeting on October 19th, 2021.

“The micro-environment plays critical roles in progression, response to therapy, and recurrence of GBM. Therefore, determining the roles and mechanisms of action of key constituents of GBM micro-environment will contribute to the development of more effective therapies.”



“The Getch K12 award has provided us with critical and much needed support at the right time. We are grateful!”

– Babacar Cisse

Interview with **Matthew Pease**, Inaugural Data Science Scholar

Matthew Pease speaks about his year as the inaugural 2020-2021 CNS Data Science Scholar.

"It was a phenomenal opportunity to receive this grant. It really cemented my interest in machine learning and data science for my career. There are not a whole lot of people doing this type of research in neurosurgery, so I hope to expand this in our field." ([Read the entire interview.](#))

Dr. Pease's goal was to investigate how data science may be applied in neuro-oncology to determine treatment options for brain tumors.



CNS Foundation Fitness Challenge during the CNS Annual Meeting *Fun for all the Early morning risers!*



HIIT Competition Fundraiser Participants



Erg Competition Fundraiser participants



CNSF Co-Chair congratulates
*Future Women Leaders
in Neurosurgery Scholarship*
winners Sylvia Shitsama and
Beverly Cheserem during the
CNS Annual Meeting.

(Not pictured, Kimberly Huang)

INSIDE THE CNS



Washington Committee Report



Katie O. Orrico, Esq

Prior Authorization Reform Legislation Gaining Steam in Congress

On Oct. 20, the Improving Seniors' Timely Access to Care Act ([S. 3018](#)) was introduced in the U.S. Senate. Sponsored by Sens. **Roger Marshall**, MD, (R-Kan.), **Kyrsten Sinema** (D-Ariz.) and **John Thune** (R-S.D.), this bipartisan legislation would help



Senator Roger Marshall, MD, (R-Kan.) is leading the way in the U.S. to pass legislation to improve prior authorization in the Medicare Advantage program.

protect patients from unnecessary delays in care by streamlining and standardizing prior authorization under the Medicare Advantage program. The CNS and the AANS issued a [press release](#) endorsing the Senate bill. Additionally, the neurosurgical groups signed an Alliance of Specialty Medicine [letter](#) supporting this legislation.

Meanwhile, identical legislation introduced in the House of Representatives earlier this year has reached a significant milestone by garnering enough co-sponsors to pass Congress' lower chamber. If the bill is brought forward for a vote, the more than 250 bipartisan co-sponsors are more than enough to pass the House. The CNS and the AANS celebrated this turn of events by issuing a [press release](#) expressing enthusiasm for the progress of [H.R. 3173](#).

Following introduction of S. 3018, on Oct. 28, Sens. **Sherrod Brown** (D-Ohio) and **John Thune** (R-S.D.) spearheaded a letter to CMS Administrator **Chiquita Brooks-LaSure** calling for improvements to the prior authorization process. Signed by 29 U.S. Senators, the bipartisan letter encourages the agency to streamline prior authorization protocols across government health programs, including Medicare Advantage, to make them more efficient. The CNS and

the AANS issued a [press release](#) expressing support for the Senate letter.

Simultaneously with the Senate letter, the CNS and the AANS joined the [Regulatory Relief Coalition](#) (RRC) in a [letter](#) to CMS encouraging CMS to assess all utilization review programs — including prior authorization, step therapy and AUC for imaging — and to take appropriate action to improve and streamline these programs. The letter pointed out that the previous administration issued a proposed rule to, among other things, reduce provider and patient burden by adopting an electronic prior authorization program in Medicaid, the Children's Health Insurance Program (CHIP) and the individual health insurance markets. The RRC urged the agency to finalize this rule and expand it to include the Medicare Advantage program. The coalition hopes to meet with CMS officials later this fall.

House Members Urge Action on Medicare Payment Cuts

On Oct. 14, a bipartisan group of 247 members of Congress [wrote](#) to House Speaker **Nancy Pelosi** (D-Calif.) and Republican Leader **Kevin McCarthy** (R-Calif.) urging action to prevent steep Medicare payment cuts scheduled to take

> PRIOR AUTHORIZATION IS ANOTHER TACTIC THAT HEALTH PLANS ARE USING TO CUT COSTS, BUT ITS RAMPANT OVERUSE IS NOW CAUSING INAPPROPRIATE DELAYS AND DENIALS OF MEDICAL TREATMENTS THAT OUR SENIORS NEED OUR PATIENTS SUFFER FROM PAINFUL AND LIFE-THREATENING NEUROLOGIC CONDITIONS SUCH AS BRAIN TUMORS, DEBILITATING DEGENERATIVE SPINE DISORDERS, STROKE AND PARKINSON'S DISEASE. WITHOUT TIMELY MEDICAL CARE, OUR PATIENTS OFTEN FACE PERMANENT NEUROLOGIC DAMAGE, AND SOMETIMES DEATH.<

—John K. Ratliff, MD, Chair, Washington Committee

effect on Jan. 1, 2022. The letter expressed concerns these cuts could have serious financial consequences for physicians who are already under financial distress due to the sustained COVID-19 pandemic.

The AANS and the CNS issued a [press release](#) thanking Reps. **Ami Bera**, MD, (D-Calif.) and **Larry Bucshon**, MD, (R-Ind.) for leading this effort. The neurosurgery organizations continue to lead the [Surgical Care Coalition](#) (SCC) and its campaign to prevent these cuts. Incorporating messages from surgeons across the country into its campaign, the SCC recently featured a [message](#) from CNS Vice President **Alexander A. Khalessi**, MD.

Neurosurgery Urges CMS to Increase Global Surgical Code Values

On Oct. 28, the CNS and the AANS joined the American College of Surgeons and other surgical groups in a [letter](#) to CMS urging the agency to increase global surgery code post-operative evaluation and management (E/M) values. The letter follows up on issues raised during a Sept. 7 meeting the societies had with CMS. Washington Committee and Coding and Reimbursement Committee leaders, **John K. Ratliff**, MD, and **G. Edward**

Vates, MD represented neurosurgery at this meeting. In 2021, the values for new stand-alone E/M office visit codes were increased, but CMS refused to increase the E/M portion of the 10- and 90-day global codes. The letter emphasized that this omission disrupts the relativity of the Medicare Physician Fee Schedule and inappropriately undervalues these codes.

Biden Administration Publishes Additional Surprise Billing Regulations

On Sept. 30, the Biden Administration [issued](#) an [interim final rule](#) (IFR) — the third in a series to implement the [No Surprises Act](#) and curb the practice of surprise medical billing. Among other things, the IFR provides a process to settle out-of-network (OON) rates between providers and payers. The regulation establishes the federal independent dispute resolution (IDR) process that providers and plans may use to determine payment rates for OON care after unsuccessful negotiations. The IFR establishes a de facto payment rate in contravention of the law, making the median in-network rate the default factor considered in the IDR process — which will drive down reimbursement for both OON and

in-network care and will likely exacerbate the problem of narrow provider networks.

Key members of Congress involved in negotiating the surprise billing law are demanding changes to the IFR before it takes effect on Jan. 1, 2022. One such [letter](#) to the Biden Administration — spearheaded by Reps. **Tom Suozzi** (D-N.Y.), **Brad Wenstrup**, DPM (R-Ohio), **Raul Ruiz**, MD, (D-Calif.) and **Larry Bucshon**, MD, (R-Ind.) and signed by 152 bipartisan members of Congress — points out that after extensive negotiations, Congress specifically rejected a benchmark rate.

In a [press release](#) supporting this Congressional letter, Washington Committee chair, **John K. Ratliff**, MD pointed out that “Congress enacted a thoughtful and balanced approach to protect patients from unanticipated medical bills for out-of-network care that also included a fair process for resolving billing disputes. Unfortunately, this rule directly conflicts with both the letter and intent of the law by prioritizing median in-network payment rates. It is therefore incumbent upon the Biden Administration to revise the new rules before they take effect on January 1.”

Cigna to Cover LITT Following Neurosurgery Position Statements

On Oct. 15, Cigna announced it would cover Laser Interstitial Thermal Therapy (LITT) for certain brain tumor, radiation necrosis and epilepsy indications. Following a meeting with Cigna medical directors in September, the Joint Section on Tumors and the American Society for Stereotactic and Functional Neurosurgery (ASSFN) released position statements regarding LITT for brain tumors, radiation necrosis and epilepsy. The documents included an analysis of current clinical literature for LITT and were cited by Cigna in their [policy document](#). 



CNS

Oral Board Review Course

FEBRUARY 12-13, 2022

Prepare for the ABNS Oral Board

Let expert faculty guide you in preparing with confidence for the final step in your certification with the CNS Oral Board Review Course.

Register at cns.org/oralboard!

This virtual, highly interactive course prepares you for the case-based nature of the ABNS exam with:

- Multiple learning formats
- One-on-one sessions with faculty
- Complimentary post-course quiz sessions

Course Directors



Akash J. Patel



Robert J. Spinner

IMAGES IN NEUROSURGERY

Laser Interstitial Thermal Therapy for Burnt-out Hippocampus Syndrome

A 36-year-old male with history of complex partial seizures occurring 1-2 times a week presented for evaluation of medically refractory epilepsy. The seizure semiology included altered consciousness, left head turning, and oral automatism. Neurological exam was unremarkable. His pre-surgical evaluation was most suggestive of a "burnt-out hippocampus syndrome" with scalp EEG onsets appearing in the right temporal lobe but contralateral to the side of mesial temporal sclerosis seen on MRI. MRI brain demonstrated left-sided mesial temporal sclerosis and reduced hippocampal size on the left (**Figure 1**). Ictal SPECT, and subsequent SISCOM (subtraction ictal single-photon emission CT co-registered to MRI) revealed increased ictal uptake in the left temporal lobe (**Figure 2**). Thus, MRI, SPECT as well as neuropsychological evaluation were all suggestive of left mesial temporal localization.

Patient underwent left mesial hippocampal ablation (**Figures 3 and 4**). Other than 2 atypical, immediate post-operative seizures, the patient remained seizure free on 1 year follow up and is currently being weaned off anti-epileptic medication. Burnt-out hippocampus syndrome is rare, occurring in about 7% of cases with mesial temporal lobe epilepsy. (1) This is seen in patients with a severely atrophic hippocampus. The extensive atrophy precludes sufficient ipsilateral neocortical recruitment, which prevents the generation of a sizeable surface discharge. Therefore, seizure propagation occurs via the hippocampal commissure to the contralateral temporal region prior to being detected on the ipsilateral side. ■

Submitted by: Mohamed Abouelleil, MD;
Rushna Ali, MD

Affiliation: Division of Neurosurgery, Spectrum Health Medical Group, Grand Rapids, MI

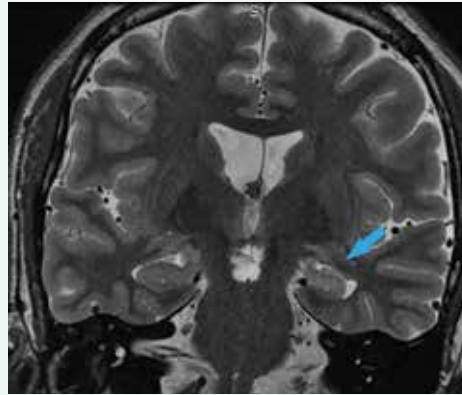


Figure 1: Coronal MRI demonstrating left hippocampal atrophy consistent with mesial temporal sclerosis (blue arrow).

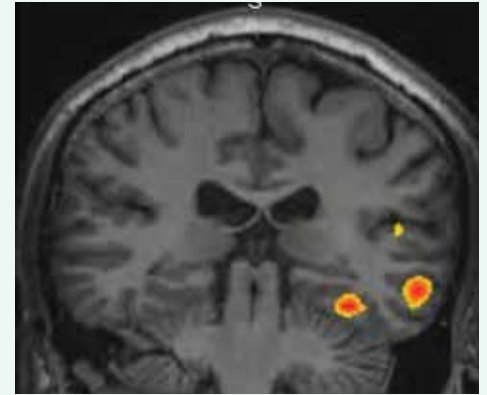


Figure 2: Coronal SISCOM revealing increased ictal uptake in the left temporal lobe.

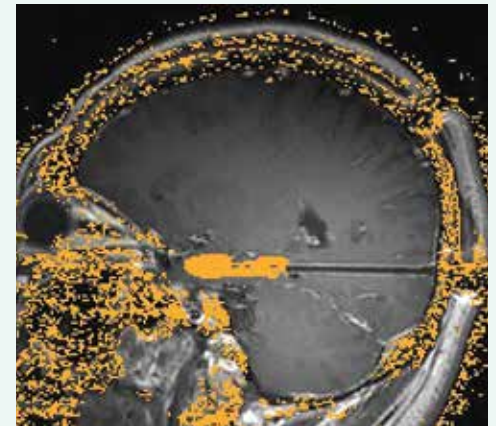
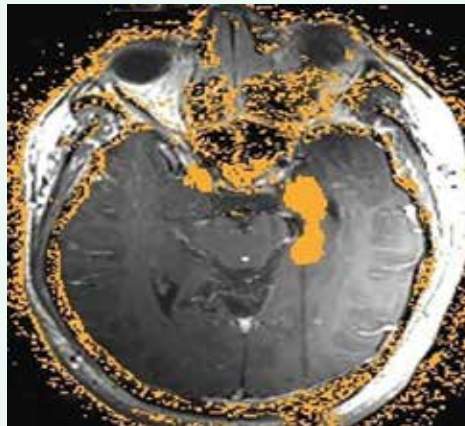


Figure 3a and 3b: MRI axial and sagittal view of intra-operative left mesial temporal ablation.

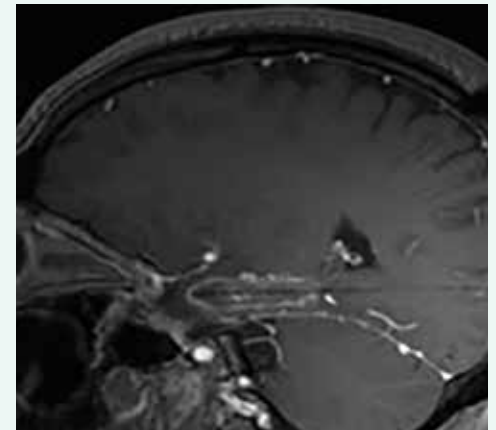
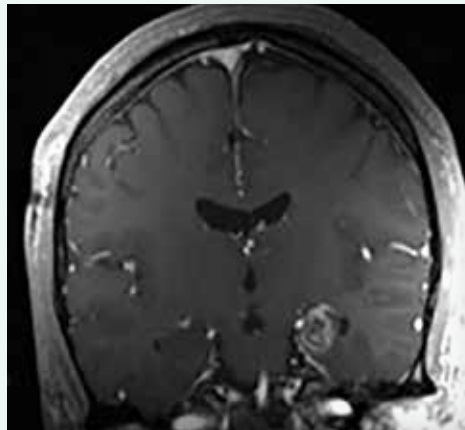


Figure 4a and 4b: MRI coronal and sagittal view post ablation of left mesial temporal lobe.



Congress of
Neurological
Surgeons

Congress Quarterly, 10 N. Martingale Road, Suite 190, Schaumburg, IL 60173.

SAVE THE DATE!



CNS | 2022 ANNUAL MEETING

SAN FRANCISCO, CALIFORNIA • OCTOBER 8-12, 2022

We hope you will be able to join us for the 2022 CNS Annual Meeting where you can expect a variety of data-driven science, first-rate speakers, and plenty of interactive learning opportunities. We are pleased to announce our 2022 Honored Guest presentation will be from Robert F. Spetzler of the Barrow Neurological Institute. Stay tuned for many more details in the coming months!



Register at cns.org/2022