

**INSIDE SPRING 2015**

**3** NewYork-Presbyterian Hospital Expands Expertise in Brain Cancer

**5** Clinical Trials Update: NeuroNEXT

**SAVE THE DATE**

**25th Annual Course:  
A Comprehensive Review  
of Movement Disorders  
for the Clinical Practitioner**

July 26-30, 2015

St. Regis Hotel  
Aspen, Colorado

For more information:  
(212) 305-3334 or  
cme@columbia.edu

**SAME DAY  
APPOINTMENT SERVICE  
FOR NEW PATIENTS**

For rapid access to a neurological specialist for patients requiring immediate evaluation, call:

**NewYork-Presbyterian/  
Columbia**  
(646) 426-3876

**NewYork-Presbyterian/  
Weill Cornell**  
(212) 746-2596

NewYork-Presbyterian  
Neurology and Neurosurgery  
ranks #2 in the nation.



## Skull Base Surgery: An Evolving Specialty for Complex Tumors

Skull base surgery continues to evolve as advances in minimally invasive and microsurgical techniques, as well as high quality imaging, are greatly improving the prognosis for tumors that arise from the brain, the lining of the brain, the bones of the skull, or the pituitary gland. Over the last decade, the refinement of endoscopic techniques and instrumentation are allowing neurosurgeons to visualize and excise lesions that could previously only be accessed through large, open surgeries.



"The traditional method that we had developed to enter the area underneath the brain and around arteries and cranial nerves involved opening up the side of the head, drilling out a lot of bone, and reaching around to access the tumor," says **Theodore H. Schwartz, MD**, David and Ursel Barnes Professor of Minimally Invasive Neurosurgery, Weill Cornell Medical College, and Director of Anterior Skull Base and Pituitary Surgery and the Epilepsy Imaging Laboratory at Weill Cornell. Dr. Schwartz is one of the nation's foremost neurological surgeons specializing in brain tumor and epilepsy surgery. "As you can imagine, that kind of surgery carries a lot of risks. There is the potential for causing damage to critical nerves and arteries that are along the pathway to the tumor. It also involves a long hospitalization period."

"Tumors at the base of the skull or tumors of the ventricle have always been difficult to access," says **Jeffrey N. Bruce, MD**, Co-Director of the Brain Tumor Center and Director of the Bartoli Brain

**"NewYork-Presbyterian had the first center in the New York area, as well as one of the first centers in the world, to develop and build a comprehensive program in minimally invasive skull base and pituitary surgery. We are able to take out very large, challenging tumors in locations that are difficult to reach."**

**– Dr. Theodore H. Schwartz**

Tumor Research Laboratory at NewYork-Presbyterian/Columbia University Medical Center. Dr. Bruce is a leading authority on complex tumors of the brain and skull base specializing in the surgical treatment of gliomas, meningiomas, pituitary tumors, skull base tumors, cranio-pharyngiomas, and pineal tumors. "These tumors are problematic because they tend to invade the blood vessels and nerves that are normally found along the base of the skull. Though they are generally benign and slow growing for the most part, they don't respond well to other forms of treatment such as radiation and chemotherapy. So the only really viable treatment option is a surgical one. This has forced us to come up with better ways to approach them surgically and to innovate new techniques to access these areas in a less invasive manner and operate through smaller corridors within and around the brain."

### Accessing the Brain through the Nasal Passages

More than a decade ago, Dr. Schwartz and Weill Cornell otolaryngologist, **Vijay K. Anand, MD**, were among the first in the country to help develop and refine the endoscopic endonasal approach (EEA), a minimally invasive surgical technique in which surgeons use an endoscope to operate through the nose and frontal sinuses to reach tumors in the anterior skull base.

"We enter through a natural orifice, or a natural corridor, namely the nostrils," says Dr. Schwartz. "Now we can perform surgery with basically no incisions whatsoever that in the past had required

*(continued on page 2)*



COLUMBIA UNIVERSITY

College of Physicians  
and Surgeons



Weill Cornell Medical College

## Skull Base Surgery: An Evolving Specialty for Complex Tumors *(continued from page 1)*



*Dr. Theodore H. Schwartz*

the largest opening in the side of the head, drilling out enormous amounts of bone, and retracting the brain. We think about endoscopic cranial base approaches as a combination of three factors: a target, a cranial base approach, and a nasal corridor.”

In developing their surgical plan, Dr. Schwartz and his colleagues address: “Where are we going, how will we get there, and where do we start,” says Dr. Schwartz. “This approach increases our ability to remove tumors and lesions in critical areas at the base of the skull or top of the spine, reduces our complication rate, and gets our patients home more quickly.”

**“Our goal has been to develop surgical techniques that make the areas in the brain that once were inaccessible more accessible, and then once you get there enable you to remove the tumors more aggressively.”**

**– Dr. Jeffrey N. Bruce**

“All the incisions are made in the nose. There are no scars on the face. There are no scars in the mouth, and the healing process is much faster,” says Dr. Bruce, who adds that the endoscopic approach complements other techniques, including microsurgery in which the neurosurgeon can operate using a microscope to visualize the smallest of brain and spine structures. “We may use the microscope for the majority of cases but then use the endoscope to complement areas of the surgery that are not as accessible by the microscope or vice versa. It requires knowing all the benefits and limitations of each approach and being able to incorporate that into the treatment that would provide the maximum outcome.”

### Defining Innovation in Skull Base Surgery

Dr. Bruce believes innovation lies in the refinement of all of these different approaches and the ability to use multiple techniques. “What has changed in minimally invasive surgery and why

patients have better outcomes is that we have narrowed the exposure needed to take these tumors and lesions out by using a combination of a microscope, an endoscope, and gamma knife radiosurgery,” he notes. “There are many times where we will see a tumor and remove the part that is easy to remove and know that the more difficult and dangerous part to remove can be left behind and treated with gamma knife later on. It’s a matter of having experts in all of the treatment options available so that they can be tailored for the individual patient and their specific problem.”



*Dr. Jeffrey N. Bruce*

According to Dr. Bruce, systems have also been devised to avoid the use of fixed retractors, which can be traumatic to the brain, and instead employing dynamic retraction with the use of handheld instruments that limits the risk of retractor-induced tissue injury.

Both Drs. Schwartz and Bruce stress that advances in intraoperative imaging techniques have contributed greatly to the surgeon’s ability to view highly detailed pictures of the tumor target site. “Imaging is critically important. The use of intraoperative navigation helps us with our surgical approaches,” says Dr. Schwartz. “We use MRI scanning, as well as 3-D endoscopes; our team at Weill Cornell was integral in the development of that particular technology.”

“In addition, stereotactic guidance allows us to use smaller openings and also to identify where the tumor has extended to so that we can ensure we are getting a complete removal as much as possible,” says Dr. Bruce.

“The success of these surgeries is also based on the experience of doing case after case after case, encountering all types of situations to develop more and more expertise, and continually increasing the ability to handle larger and more complicated tumors,” adds Dr. Schwartz, who in 2013 received the Pituitary Network Association’s highest honor – the Gentle Giant Award – for making great strides in the field of pituitary surgery.

*(continued on page 5)*

# NewYork-Presbyterian Hospital Expands Expertise in Brain Cancer

## Dr. Howard Fine Leads New Brain Tumor Center at NewYork-Presbyterian/Weill Cornell

**Howard A. Fine, MD**, an internationally renowned brain tumor expert, has joined NewYork-Presbyterian/Weill Cornell Medical Center as Director of the Brain Tumor Center and Chief of the newly established Division of Neuro-Oncology in the Department of Neurology at NewYork-Presbyterian/Weill Cornell. Dr. Fine also serves as Associate Director for Translational Research in the Sandra and Edward Meyer Cancer Center at Weill Cornell Medical College.

With a nearly three-decade long career devoted exclusively to patients with brain tumors, Dr. Fine is establishing a state-of-the-art research and clinical program that will advance cutting-edge treatments for patients with these challenging diseases. Prior to joining Weill Cornell, the eminent clinician/researcher built two of the nation's leading neuro-oncology programs, the Dana-Farber Cancer Institute Center for Neuro-Oncology at Harvard Medical School and the Neuro-Oncology Branch at the National Institutes of Health. Dr. Fine most recently served as Deputy Director of the Cancer Center and Director of the Brain Tumor Center at NYU Langone Medical Center.



Dr. Howard A. Fine

Dana-Farber Cancer Institute and Harvard Medical School in Boston. He has served on the editorial boards of *Neuro-Oncology* and the *Journal of Clinical Oncology*. His numerous awards and honors include the Community Leadership Award for Service from the National Brain Tumor Society, the National Service to America Award, and the National Cancer Institute Director's Gold Star Award for vision, leadership, and advice in designing cancer programs for the future using neuro-oncology as a model.

In assuming his new position at Weill Cornell, Dr. Fine reflected on his distinguished career that began at a time when, he says, very little was known about brain tumors. "When I

first started, the field of neuro-oncology was several decades literally behind where we were in other tumors and cancers as far as our understanding of the biology of the tumors we were trying to treat, and even in areas as basic as how you conduct clinical research," says Dr. Fine. "It's fair to say we were basically in the dark ages. That's all dramatically changed. It is an exciting time now because we are on the cusp of developing a whole new generation of therapies based on our growing knowledge base of tumor biology. We have not only caught up to our colleagues working in the other fields of cancer and tumor, in many ways we also know more about brain tumors and their molecular and genetic causes than we do with many other tumors."

A prolific researcher, Dr. Fine has continuously led a basic and translational science laboratory and participated in more than 100 brain tumor clinical trials. He has also authored over 200 scholarly articles, reviews, and book chapters in subjects related to neuro-oncology and brain tumors, most recently *New Strategies in Glioblastoma: Exploiting the New Biology*, which was published in the February 2015 issue of *Clinical Cancer Research*.

"Glioblastomas are probably the single most lethal tumors, and these are the ones that I spent my career studying," says Dr. Fine. "There have been very few, if any, advances in this disease since we recognized it a century ago. The median survival is only about 15 months despite aggressive neurosurgery, radiation, and chemotherapy. However, with preclinical and biologic advances and a better infrastructure in place, the pharmaceutical industry and the private sector have become very interested. In the whole field, the wagons have been circled, the forces have been gathered, and I think we are really poised scientifically, politically, financially, and organizationally to make major inroads in the treatment of this disease."

According to Dr. Fine, the last five years have seen an explosion in the understanding of the genetic and molecular underpinnings of glioblastomas leading to renewed optimism about potential new therapeutic approaches. Several of the most promising include oncogenic signal transduction inhibition, angiogenesis inhibition,

**"In the whole field, the wagons have been circled, the forces have been gathered, and I think we are really poised scientifically, politically, financially, and organizationally to make major inroads in the treatment of glioblastoma."**

**— Dr. Howard A. Fine**

"The recruitment of Dr. Fine will be transformational for the Department of Neurology and the clinical neuroscience programs at NewYork-Presbyterian Hospital and Weill Cornell Medical College," says **Matthew E. Fink, MD**, Neurologist-in-Chief at NewYork-Presbyterian/Weill Cornell. "He brings knowledge and expertise to a specialized area that we have not pursued in the past, and he will help a key program, the Brain Tumor Center of the Meyer Cancer Center, fulfill its mission and vision."

"Dr. Fine will collaborate with our world-class neurosurgeons in translating research to the clinical setting, particularly in the area of precision and personalized therapies," says **Philip E. Stieg, PhD, MD**, Neurosurgeon-in-Chief at NewYork-Presbyterian/Weill Cornell. "Through these interdisciplinary collaborations, we hope to develop new, highly effective treatments for patients with difficult brain tumors."

Dr. Fine received his medical degree at the Mount Sinai School of Medicine in New York City, completed an internship and residency in Internal Medicine at the University of Pennsylvania in Philadelphia, and a fellowship in Medical Oncology at the

## NewYork-Presbyterian/Columbia Brain Tumor Center Welcomes New Faculty

The Brain Tumor Center, co-directed by neurosurgeon **Jeffrey N. Bruce, MD**, Director of the Bartoli Brain Tumor Research Laboratory, and **Andrew B. Lassman, MD**, Chief of the Division of Neuro-Oncology at NewYork-Presbyterian/Columbia, has recently welcomed the following specialists.

**Fabio M. Iwamoto, MD**, has been appointed Deputy Director of the Division of Neuro-Oncology, charged with developing the Division's clinical and translational research components. Dr. Iwamoto has particular expertise in the diagnosis, management, and treatment of brain and spinal cord tumors, as well as neurological complications of cancer. Most recently he served as attending physician and an investigator at the Neuro-Oncology Branch, a trans-institute branch of the National Cancer Institute and National Institute of Neurological Disorders and Stroke, in Bethesda, Maryland. While there,



*Dr. Fabio M. Iwamoto*

Dr. Iwamoto was a principal investigator in early phase clinical trials for brain tumors and worked with laboratory and computational scientists in several translational projects in brain tumors.

Dr. Iwamoto earned his medical degree at the Federal University of Parana, Brazil, followed by a residency in neurology at NewYork-Presbyterian/Weill Cornell and a fellowship in neuro-oncology at Memorial Sloan Kettering Cancer Center.

**Teri N. Kreisl, MD**, whose clinical interests include primary brain tumors and metastatic disease affecting the central nervous system, joins the Division from the Neuro-Oncology Branch of the Center for Cancer Research at the National Cancer Institute where she was a Tenure Track Clinical Investigator with a research focus on molecular imaging in brain tumors. Dr. Kreisl also served as Fellowship Director and Medical Director for the Neuro-Oncology Branch. She



*Dr. Teri N. Kreisl*

served as principal investigator for numerous Phase 1 and 2 clinical trials for the treatment of primary brain tumors and will continue similar research efforts with the Division of Neuro-Oncology at Columbia University.

Dr. Kreisl earned her medical degree from Weill Cornell Medical College, followed by a residency in neurology at NewYork-Presbyterian/Weill Cornell where she became Chief Resident. Dr. Kreisl went on to pursue a fellowship in neuro-oncology at Memorial Sloan Kettering Cancer Center. She is board certified in neurology.

**Yazmín Odia, MD, MSc**, specializes in the diagnosis and management of primary central nervous system tumors, as well as metastatic brain tumors and neurologic complications of systemic cancers. She previously served as both clinical and research fellow in neuro-oncology and neurology consultant at the National Institutes of Health. She also has clinical trial and translational research experience through various NIH-funded training grants. Dr. Odia's current research focuses on the potential prognostic and predictive role of cMYC expression in gliomas using retrospective pathologic cohorts.

Dr. Odia completed her medical training at the University of Chicago, Pritzker School of Medicine, a Master of Science in Clinical Research at the Mayo Graduate School in Rochester, and a neurology residency at the Johns Hopkins Hospitals, where as Chief Resident she received both the Jay Slotkin Award for Excellence in Research and the Guy M. McKhann Award for Excellence in Teaching.



*Dr. Yazmín Odia*

### For More Information

Dr. Fabio M. Iwamoto • [fi2146@cumc.columbia.edu](mailto:fi2146@cumc.columbia.edu)  
 Dr. Teri N. Kreisl • [tnk2109@cumc.columbia.edu](mailto:tnk2109@cumc.columbia.edu)  
 Dr. Yazmín Odia • [yo2240@cumc.columbia.edu](mailto:yo2240@cumc.columbia.edu)

## Dr. Howard Fine *(continued from page 3)*

targeting canonical stem cell pathways in glioblastoma stem cells, and immunotherapy.

"Glioblastomas are incredibly complex genetic tumors," says Dr. Fine. "I don't think we are going to find one single gene that is going to turn off these tumors, but rather that there are biochemical pathways that drive them. I believe the answer will lie in understanding these critical pathways and identifying how to block them. This will likely involve several drugs hitting different points along that pathway or maybe even concurrent pathways."

Having founded and led prestigious brain tumor programs

in both government and academia, Dr. Fine sees this point in his career as pivotal. "The Weill Cornell Brain Tumor Center will offer its patients the highest level of comprehensive state-of-the-art care delivered by nationally renowned clinical experts from multiple disciplines. We will define our success by how far we can move the field forward scientifically and make a major difference for patients."

### For More Information

Dr. Howard A. Fine • [haf9016@med.cornell.edu](mailto:haf9016@med.cornell.edu)

## Clinical Trials Update: NeuroNEXT

The Network for Excellence in Neuroscience Clinical Trials, NeuroNEXT, was created to conduct studies of treatments for neurological diseases through partnerships with academia, private foundations, and industry. The network is designed to expand the capability of the National Institute of Neurological Disorders and Stroke to test potential new therapies, increase the efficiency of clinical trials, and respond quickly as new opportunities arise to test promising treatments. Karen Marder, MD, MPH, and Claudia Chiriboga, MD, MPH, are co-principal investigators, and Claire Henchcliffe, MD, DPhil, is site PI at Weill Cornell. Joyce Moran, CCRC, is NeuroNEXT Project Manager.

### NN103: A Phase 2 Trial of Rituximab in Myasthenia Gravis

Myasthenia gravis (MG) is an autoimmune disorder of neuromuscular transmission with an estimated annual incidence of about 1 to 2 per 100,000. Common symptoms include a drooping eyelid, double vision, slurred speech, difficulty chewing and swallowing, weakness in the arms and legs, chronic muscle fatigue, and difficulty breathing. Despite current therapies a subset of patients remains medically refractory or has intolerable medication adverse effects. The purpose of the study is to find out the effect and safety of a new use of the drug rituximab in MG patients who are on prednisone.

#### For More Information

Columbia University Medical Center  
Principal Investigator: Thomas H. Brannagan, MD  
Coordinator: Jacqueline Scoon, MD, MPH  
Email: js4462@cumc.columbia.edu

Weill Cornell Medical College  
Principal Investigator: Jonathan M. Goldstein, MD  
Coordinator: Lauren Langford, LCSW  
Email: langfordl@hss.edu

### NN104: A Multicenter, Phase 2 Study of 3K3A-APC with tPA in Ischemic Stroke

Currently, the only approved treatment in the U.S. for ischemic stroke is a drug called recombinant tissue plasminogen activator (rtPA or tPA), indicated for intravenous administration within three hours of onset of the stroke. The drug is designed to break down blood clots to restore blood flow to the brain. In some patients, however, tPA can cause internal bleeding and other complications.

This multicenter, Phase 2 study uses a continual reassessment method to determine the safety, tolerability, and activity of 3K3A-APC, a recombinant variant of human activated protein C (APC), in combination with tPA, in subjects with moderately severe acute hemispheric ischemic stroke. The cytoprotective properties of 3K3A-APC may be useful in protecting ischemic brain tissue from further damage, while avoiding an increase in the chance of treatment-related bleeding. The study intervention will be administered as a 15-minute infusion every 12 hours for up to 5 infusions. Four dose levels will be considered for this trial. Approximately 100 participants, ages 18 to 80 years old, will be enrolled and followed for 90 days.

#### For More Information

Columbia University Medical Center  
Principal Investigators: Jan Claassen, MD, PhD,  
and Randolph Marshall, MD, MS  
Coordinator: Cristina Faló, PhD  
Email: cf2427@cumc.columbia.edu

## Skull Base Surgery: An Evolving Specialty for Complex Tumors (continued from page 2)

"When we deal with these kind of complex tumors, the results we want to achieve are to avoid neurological deficits and preserve or restore quality of life," says Dr. Bruce. "Having the benefit of the wisdom and experience of the team is critical – the neurosurgeons, otolaryngologists, anesthesiologists, imaging specialists, the Neuro ICU group, residents, and rehabilitation specialists – who are readily available to address any problem that might arise and participate in the patient's care from preoperative planning and surgery to recovery and rehabilitation."

Sharing expertise in minimally invasive skull base surgery is a key component of both the Weill Cornell and Columbia programs. For the past 12 years, the Weill Cornell Brain and Spine Center has hosted a two-day *Advanced Endoscopic Skull Base and Pituitary Surgery* symposium attended by neurosurgeons from around the world. Dr. Schwartz and Dr. Anand have also contributed to the literature with the first textbook on endoscopic skull base surgery – *Practical Endoscopic Skull Base Surgery* – as well as *Endoscopic Pituitary Surgery: Endocrine, Neuro-Ophthalmologic, and Surgical Management*.

"Experience is a big determinant in outcome, both in choosing the right patients that need surgery and sometimes knowing when it is better for patients to not have surgery," says Dr. Bruce. "Having the experience to choose the best approaches and to make those judgments

when during any given operation there are literally so many decisions that are made second by second, minute by minute, is critical in optimizing the best outcome for each patient."

#### Reference Articles

Patel KS1, Raza SM, McCoul ED, Patrona A, Greenfield JP, Souweidane MM, Anand VK, Schwartz TH. Long-term quality of life after endonasal endoscopic resection of adult craniopharyngiomas. *Journal of Neurosurgery*. 2015 Apr 17:1-10. [Epub ahead of print]

Shoakazemi A, Evins AI, Burrell JC, Stieg PE, Bernardo A. A 3D endoscopic transtubular transcallosal approach to the third ventricle. *Journal of Neurosurgery*. 2015 Mar;122(3):564-73.

Khan OH, Anand VK, Schwartz TH. Endoscopic endonasal resection of skull base meningiomas: the significance of a "cortical cuff" and brain edema compared with careful case selection and surgical experience in predicting morbidity and extent of resection. *Neurosurgical Focus*. 2014 Oct;37(4):E7.

D'Amico RS, Kennedy BC, Bruce JN. Neurosurgical oncology: advances in operative technologies and adjuncts. *Journal of Neuro-Oncology*. 2014 Sep;119(3):451-63.

#### For More Information

Dr. Jeffrey N. Bruce • jnb2@cumc.columbia.edu  
Dr. Theodore H. Schwartz • schwarth@med.cornell.edu

## Advances in Neurology and Neurosurgery

NewYork-Presbyterian Hospital  
525 East 68th Street  
New York, NY 10065

[www.nyp.org](http://www.nyp.org)

NON-PROFIT ORG.  
US POSTAGE  
PAID  
STATEN ISLAND, NY  
PERMIT NO. 169

---

**Richard P. Mayeux, MD, MSc**

Neurologist-in-Chief  
NewYork-Presbyterian/  
Columbia University Medical Center  
[rpm2@cumc.columbia.edu](mailto:rpm2@cumc.columbia.edu)

**Robert A. Solomon, MD**

Neurosurgeon-in-Chief  
NewYork-Presbyterian/  
Columbia University Medical Center  
[ras5@cumc.columbia.edu](mailto:ras5@cumc.columbia.edu)

**Matthew E. Fink, MD**

Neurologist-in-Chief  
NewYork-Presbyterian/  
Weill Cornell Medical Center  
[mfink@med.cornell.edu](mailto:mfink@med.cornell.edu)

**Philip E. Stieg, PhD, MD**

Neurosurgeon-in-Chief  
NewYork-Presbyterian/  
Weill Cornell Medical Center  
[pes2008@med.cornell.edu](mailto:pes2008@med.cornell.edu)

