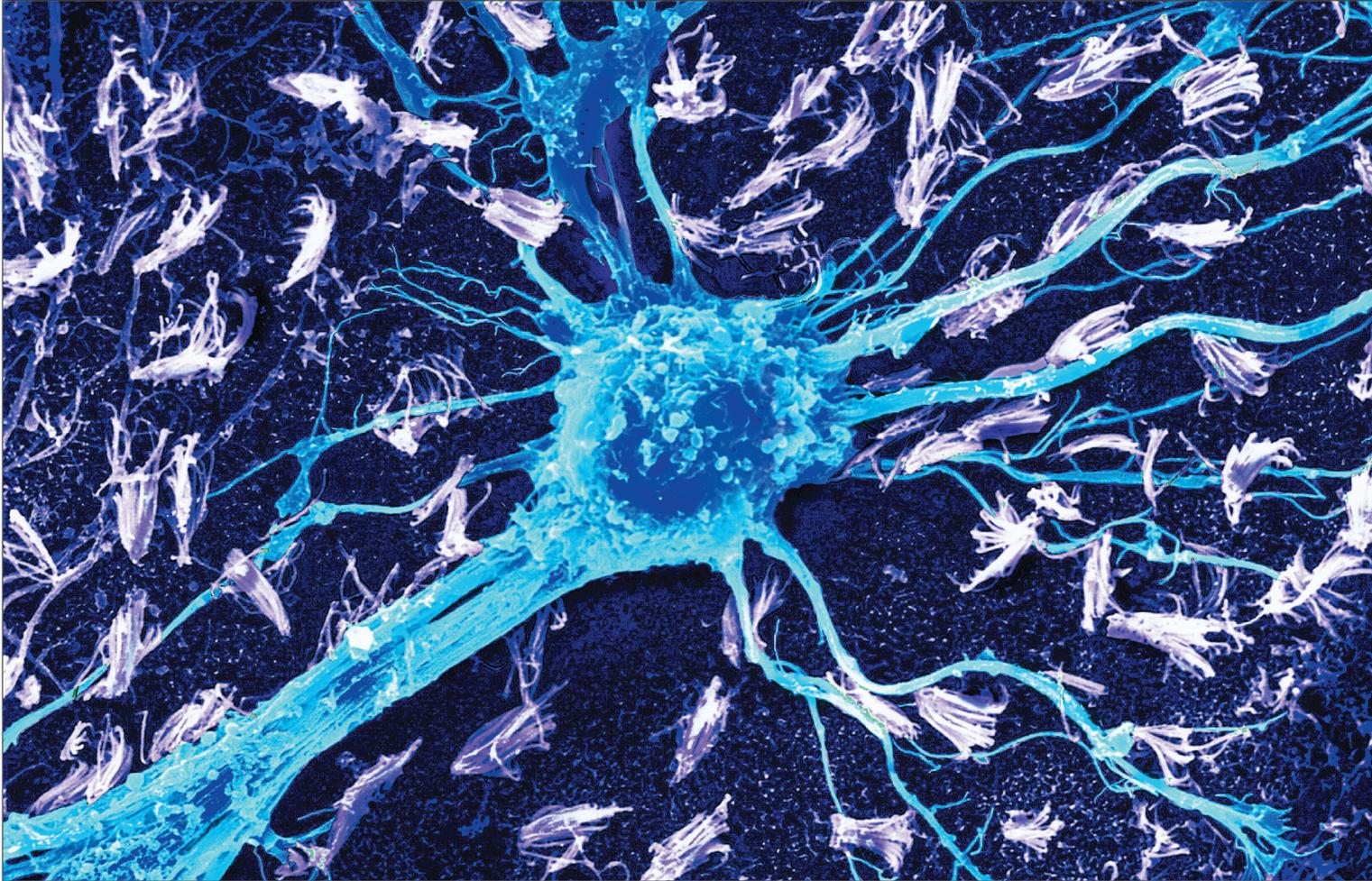




# NewYork-Presbyterian Neurology and Neurosurgery

## 2019 Report on Clinical and Scientific Innovations



**Weill Cornell  
Medicine**

**NewYork-  
Presbyterian**



**COLUMBIA**

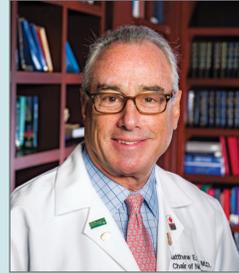
## Leadership



**Richard Mayeux, MD, MSc**  
Neurologist-in-Chief  
NewYork-Presbyterian/  
Columbia University  
Irving Medical Center



**Robert A. Solomon, MD**  
Neurosurgeon-in-Chief  
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**Matthew E. Fink, MD**  
Neurologist-in-Chief  
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Weill Cornell Medical Center



**Philip E. Stieg, PhD, MD**  
Neurosurgeon-in-Chief  
NewYork-Presbyterian/  
Weill Cornell Medical Center



**NewYork-Presbyterian  
Neurology and Neurosurgery  
Ranks #4 in the Nation**

**NewYork-Presbyterian  
A Top 5 Hospital in the Nation**



**New York's #1 Hospital  
19 Years in a Row**

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# Welcome

Dear Colleague:

We are pleased to bring you our *2019 Report on Clinical and Scientific Innovations in Neurology and Neurosurgery*. The Departments of Neurology and Neurosurgery at NewYork-Presbyterian continue to lead in the diagnosis and treatment of neurological diseases and disorders, with nationally and internationally recognized faculty practicing at the forefront of their specialties. Their efforts are strengthened and supported by the exceptional clinical, scientific, and educational resources made possible by NewYork-Presbyterian's affiliation with two renowned medical schools – Columbia University Vagelos College of Physicians and Surgeons and Weill Cornell Medicine. Our vast academic medical enterprise affords our physicians and surgeons important opportunities for conducting research that, in turn, drives progress in neurological and neurosurgical care.

In this year's report, we present work that is underway in glioblastoma, one of the deadliest forms of cancer. At the basic science level, our researchers continue their investigations to better understand the role of genetics in Alzheimer's disease. We also include updates on new applications for high-intensity focused ultrasound for an expanding range of conditions, as well as the latest treatments for complex epilepsy cases. In addition, our efforts in helping patients with debilitating spinal disease are highlighted.

NewYork-Presbyterian is proud to be a destination of choice for patients who seek out our expertise and experience in neurology and neurosurgery from the metropolitan area, across the country, and around the world. We are committed to continue pursuing progress in the labs and at the bedside to achieve the best possible outcomes and quality of life for our patients.

Sincerely,



**Steven J. Corwin, MD**  
*President and  
Chief Executive Officer  
NewYork-Presbyterian*



**Lee Goldman, MD**  
*Dean of the Faculties of  
Health Sciences and Medicine  
and Chief Executive  
Columbia University  
Irving Medical Center*



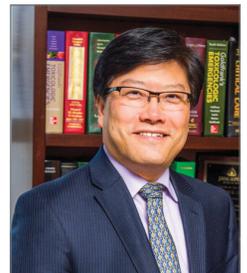
**Augustine M.K. Choi, MD**  
*Stephen and Suzanne Weiss Dean  
Weill Cornell Medicine*



Dr. Steven J. Corwin



Dr. Lee Goldman



Dr. Augustine M.K. Choi

# Measures of Distinction

## Clinical Care

**159**

Neurologists

**44**

Neurosurgeons

**11,349**

Adult and Pediatric Discharges

**6,673**

Surgical and Endovascular Procedures

Adult and Pediatric Patient Discharges  
in Key Specialties

**2,979**

Stroke and  
Cerebrovascular

**2,596**

Epilepsy

**1,723**

Spine

**967**

Neuro-Oncology

**134**

Inpatient Neuro Beds

**32**

Neuro ICU Beds

**27**

Epilepsy Monitoring Beds

**Advanced Certification  
as a Comprehensive  
Stroke Center**

The Joint Commission

**Two Level 4  
Comprehensive  
Epilepsy Centers**

National Association of Epilepsy Centers

## Research

**>\$74.6 million**

received from the National Institutes  
of Health and other major organizations

**398**

clinical trials and studies conducted by  
140 researchers

## Graduate Medical Education

**91 residents**

in neurology and neurosurgery residency  
programs

**48 fellows**

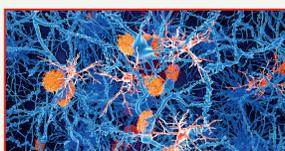
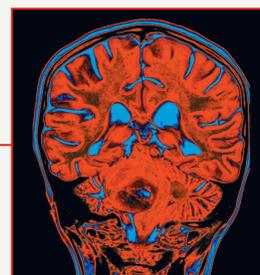
in fellowship programs that include:

- Clinical Neurophysiology
- Endovascular Neurosurgery
- Epilepsy
- Interventional Neuroradiology
- Minimally Invasive Endoscopic Skull Base
- Minimally Invasive Spinal Surgery
- Movement Disorders
- Multiple Sclerosis
- Neurocritical Care
- Neurology
- Neuro-Oncology
- Neurosurgery
- Vascular Neurology
- Vascular Neurosurgery

# Innovations at a Glance

Parallel programs in neurology and neurosurgery at NewYork-Presbyterian/Columbia University Irving Medical Center and NewYork-Presbyterian/Weill Cornell Medical Center strengthen and extend our ability to offer the most advanced technologies, newest therapies, and interdisciplinary approaches for the most challenging brain, neurological, and spinal disorders.

- ▶ Demonstrated in an animal model that a pump implanted in the abdomen to deliver a chronic infusion of a drug was successful in killing glioma cells and is now being tested in humans
- ▶ Participated in a multicenter clinical trial investigating a novel combination approach of an adenovirus plus an immune checkpoint inhibitor for treatment of recurrent glioblastoma or gliosarcoma

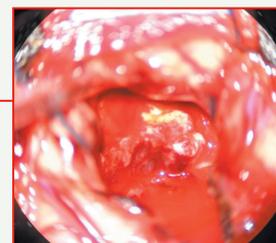


- ▶ Isolated two specific proteins in the microglia implicated in Alzheimer's disease and subsequently identified small molecules with therapeutic potential that would involve disrupting the binding of these proteins

- ▶ Further advanced the application of high-intensity focused ultrasound for essential tremor and tremor-dominated Parkinson's disease, with additional studies underway for non-invasively delivering gene therapies to the brain
- ▶ Investigated new methods to treat refractory epilepsy, including MR-guided laser interstitial thermal ablation
- ▶ Conducted a preliminary study indicating that close analysis of EEG data revealed that nearly 1 in 7 brain-injured ICU patients showed evidence of hidden consciousness just days after injury and may help predict recovery potential



- ▶ Evaluated the capability of Gleolan to distinguish residual tumors from normal brain matter during surgery for high-grade glioma
- ▶ Pioneered middle meningeal arterial embolization for symptomatic chronic subdural hematoma as upfront treatment in lieu of surgical evacuation when conservative management has failed



- ▶ One of only four sites in the United States using the ROSA neurosurgical robot as part of a clinical trial to administer gene therapy to children with mucopolysaccharidosis type IIIA, a rare congenital disorder

# Glioblastoma

## Enhancing Convection-Enhanced Delivery



Dr. Peter D. Canoll and Dr. Jeffrey N. Bruce

“There are many drugs that are very effective at killing glioma cells, at least in the laboratory, but in order to get enough of the drug into the brain, you have to give a high enough dose, which causes too much toxicity in the rest of the body,” says **Jeffrey N. Bruce, MD**, Director, Bartoli Brain Tumor Research Laboratory, and Co-Director, Brain Tumor Center, at NewYork-Presbyterian/Columbia University Irving Medical Center. “Overcoming the blood-brain barrier poses an additional challenge by limiting the systemic delivery of therapeutics to the tumor.”

While studies have shown that prolonged infusion in small amounts improves survival, intracerebral convection-enhanced delivery (CED) has been limited to short durations due to a reliance on externalized catheters. “One of the problems in our earlier studies was that the catheters needed to be hooked up to a pump at the side of the bed, and we could only give the drug for about four days for fear of infection,” notes Dr. Bruce.

To address this, Dr. Bruce and his colleagues developed a novel drug delivery strategy that utilizes a microinfusion pump to establish a positive pressure gradient in the brain via an implanted catheter. The pump could be implanted in the abdomen to facilitate chronic infusion and is controlled by Bluetooth. This CED strategy has been pioneered in the Bruce and Canoll laboratories with basic studies to select appropriate anti-tumor agents, preclinical testing in animal models, and a phase 1 clinical trial in patients with recurrent malignant gliomas.

The researchers tested the delivery system in a porcine model. The infusion was tolerated without serious adverse events and a large volume of distribution was achieved. Following extensive preclinical studies, a phase 1 dose escalation trial of topotecan by CED was performed in patients with recurrent malignant gliomas with clinical, radiographic, and neuropsychological testing for toxicity and anti-tumor response. “We turned the pump on for two days and then off for five days for four rounds of treatment over a month,” says Dr. Bruce. “Median survival and median time to progression and at six months compared favorably with the best standard treatment available for this tumor group. The pilot study, the first of its kind, was recently completed and was successful in all patients.”

“There is another element of this research that is unprecedented in its efforts,” says **Peter D. Canoll, MD, PhD**, Director of Neuropathology at Columbia. “At the time of catheter placement and following treatment, many MRI-localized biopsies of the patient’s brain tissue are taken from the tumor and the surrounding infiltrated areas. Each of those biopsies is then analyzed for tumor content using immunohistochemical and molecular analyses. With two sets of biopsies pre- and post-treatment for each patient, we can directly assess the effects of the treatment in different areas of the tumor.” Furthermore, in collaborations with **Peter A. Sims, PhD**, Director, Columbia Single Cell Analysis Core, they are testing the effects of topotecan on surgical samples using single cell sequencing analysis.

“If we find a population of cells pre-treatment that have disappeared post-treatment, it’s very good evidence that they are being targeted by the drug,” says Dr. Canoll. “Because the analysis of the tissue is so comprehensive, it addresses another major obstacle. These are spatially and genetically heterogeneous tumors, so sampling these tumors is an unmet challenge. Most everything we know comes from a single piece of tissue. By taking biopsies from multiple areas and documenting their locations, we have been able to create a very large data set that not only captures the heterogeneity of each person’s tumor, but also allows us to make predictions about the unsampled areas of the tumor.”

“When we look at the tissue, it shows that the approach is working,” says Dr. Bruce. “It’s killing the tumor cells and it’s safe for the normal cells.”

# Glioblastoma

## Will Immunotherapy Play a Role?

“Glioblastoma, unlike lung cancer and some other solid tumors like melanoma, does not typically respond to immunotherapy,” says **Rohan Ramakrishna, MD**, a surgical neuro-oncologist with NewYork-Presbyterian/Weill Cornell Medical Center. “For example, in lung cancer, you have proteins expressed, such as PDL1, that correlate with a response to immunotherapy. Unfortunately, glioblastoma does not respond to immunotherapy in a way that correlates with PDL1 expression. Moreover, GBM does not appear to be intrinsically immunogenic given its relatively low mutational load and associated low neoantigen expression. It is thought that tumors with high mutational burdens have significantly elevated numbers of neoantigens that make it possible for the immune system to recognize the tumor and eliminate it. Therefore, GBM doesn’t appear to be intrinsically responsive to immunotherapy via checkpoint inhibition, at least in trials conducted so far.”

Despite these challenges, neuro-oncologists and neurosurgeons are not deterred in their pursuit of immunotherapy approaches that can surmount the unique treatment obstacles presented by malignant tumors within the brain. “Although we don’t have the data yet to be confident, the effect of neoadjuvant immunotherapy on GBM is an exciting area to look into and the immunosuppressive microenvironment remains a potential target for treatment,” notes Dr. Ramakrishna, who serves as Co-Director of the William Rhodes and Louise Tilzer-Rhodes Center for Glioblastoma at NewYork-Presbyterian and the Director of the Brain Metastases Clinic at Weill Cornell. “Some recent studies have shown that immunotherapy via checkpoint inhibition alters the tumor microenvironment and causes

genetic changes in the tumor itself, despite mixed clinical results. This is definitely an area to potentially exploit.”

At Weill Cornell Medicine, Dr. Ramakrishna is the Principal Investigator of the CAPTIVE trial. This innovative phase 2 clinical trial for recurrent glioblastoma evaluates a combination of DNX-2401, a genetically modified common cold virus,

followed by pembrolizumab, an immunotherapy given every three weeks for up to two years or until disease progression. “When you inject the virus into the tumor, it triggers an immune response against the tumor,” he says. “The dying tumor cell releases signals and generates neoantigens that stimulate the immune system to kill additional tumor cells. By selectively replicating within cancer cells, but not normal cells, the virus sets off a chain reaction of tumor cell killing and further spreads the oncolytic virus to adjacent tumor cells. A week after the virus injection the patient starts treatment with pembrolizumab that activates an immune response against tumor cells.”

Preliminary results demonstrated that the combination of the two agents is well tolerated and associated with promising survival. The trial recently closed enrollment and results are now being processed.



Dr. Rohan Ramakrishna

### “Pink Drink” Paves the Way in Glioma Surgery

Gleolan (aminolevulinic acid hydrochloride) is one of the newest tools for use in glioma surgery. The optical imaging agent when given orally has a remarkable ability to pass through the blood-brain barrier and penetrate a tumor. Viewed under blue light during surgery, Gleolan, which was FDA approved in 2017, fluoresces as a hot pink indicator distinguishing tumor cells from healthy brain tissue. **Theodore H. Schwartz, MD**, Co-Director of Surgical Neuro-Oncology at Weill Cornell, has used

the agent on several patients undergoing surgery for glioblastoma. “The ability to identify the full extent of a tumor is invaluable for resecting an aggressive tumor, particularly glioblastoma,” says Dr. Schwartz. “Often in these tumors, we cannot tell if there are small amounts of residual tumor. Using Gleolan, we can now see tumor cells that were previously invisible. In all my cases, post-operative MRI scans showed that the entire tumor had been removed.”

# Alzheimer's Disease

## Targeting Molecules in Innate Immune Cells

In the Department of Neurology's Center for Translational and Computational Neuroimmunology at Columbia University Irving Medical Center, **Elizabeth M. Bradshaw, PhD**, Co-Director of Basic Research, has set her sights on microglia – the resident innate immune cells of the central nervous system – in the pathogenesis of Alzheimer's disease (AD).

“Genetic studies of AD directly implicate the involvement of the innate immune system,” says Dr. Bradshaw. “We have identified eight genetically associated proteins that may be working together in a tyrosine phosphorylation signaling pathway in innate immune cells. We now seek to identify the common interacting molecules of these eight proteins, which we believe function together in microglia and for which we already have strong supporting evidence of a shared pathway. Finding a binding partner shared by many genetically associated proteins may be an ideal therapeutic target for AD.”

“Our data will potentially provide a mechanistic answer of how these proteins function and, in doing so, increase an individual's risk of developing AD.”

– Dr. Elizabeth M. Bradshaw

If Dr. Bradshaw and her colleagues can validate that the proteins are phosphorylated and that the interactions occur *in situ* in the Alzheimer's disease brain, they can then dissect the signaling pathway *in vitro* to understand functional outcomes and isolate targets for intervention. One specific target of Dr. Bradshaw's investigations is the CD33 protein. “We found a very clear change in the amount of the protein on the surface of peripheral innate immune cells based on someone's genetic background,” says Dr. Bradshaw. “The influence of this genetic change related to how much full-length CD33 was expressed on the surface of innate immune cells. We then looked at functional outcomes and found a difference in peripheral monocytes, as well as monocytes that we polarized, to be more microglia-like in their ability to internalize amyloid beta (A $\beta$ ). We saw that this was associated with the genetic variation as well. The AD genetic risk led to more



Dr. Elizabeth M. Bradshaw

full-length CD33, as well as a decreased ability to internalize or to uptake the A $\beta$  (1-42) peptide, which is the major constituent of amyloid plaques in the brains of Alzheimer patients.”

The research team then wanted to better understand CD33 and how they could manipulate it therapeutically. “We know that full-length CD33 binds to sialic acid and that the genetic variation dictates how much of two different forms of CD33 you have – one can bind to sialic acid and one can't,” she says. “The genetic variation actually leads to more of the form that can bind to sialic acid.”

The researchers conducted an unbiased screen and identified proteins that were being bound to CD33 through sialic acid. “We focused on CD45, in particular, which is another immune-limited molecule only expressed in immune cells,” adds Dr. Bradshaw. “We are now working on understanding the relationship of these two proteins and to see if there is a possible therapy in creating small molecules that disrupts the binding of the two proteins.”

Dr. Bradshaw and her colleagues have since identified small molecules and antibodies that they think have therapeutic potential. With promising data from early *in vitro* studies looking at target engagement, funding has been provided to accelerate the development of a preliminary therapeutic first-round molecule. It's still early days and the small molecule needs to be optimized for therapeutic application, but their journey from hypothetical to probable has garnered much attention by the Alzheimer's disease community.

# Movement Disorders

## Realizing the Promise of MR-Guided HIFU

**Michael G. Kaplitt, MD, PhD**, a neurosurgeon and Director of Movement Disorders at the Weill Cornell Brain and Spine Center, was the first in New York to perform MR-guided high-intensity focused ultrasound (MRgHIFU), a noninvasive technology approved for use in essential tremor by the FDA in July 2016. Just three years later, Dr. Kaplitt and **J. Levi Chazen, MD**, a neuroradiologist who specializes in image-guided interventions, are continuing to advance potential applications of this novel therapeutic modality. “HIFU is transforming treatment by gaining access deep within the brain without harming healthy tissue, enabling surgeons to ablate targeted tissue without exposing the brain to the effects of ionizing radiation,” says Dr. Kaplitt.

“The most robust application in terms of cranial use is for essential tremor,” says Dr. Chazen. “Existing treatment options include medication as a first-line therapy and deep brain stimulation [DBS] when the tremor cannot be controlled medically. The drawback of DBS is that it requires a craniotomy and putting a probe deep into the brain. The patient also has to have a battery pack sewn under the skin very similar to a pacemaker for the heart.”



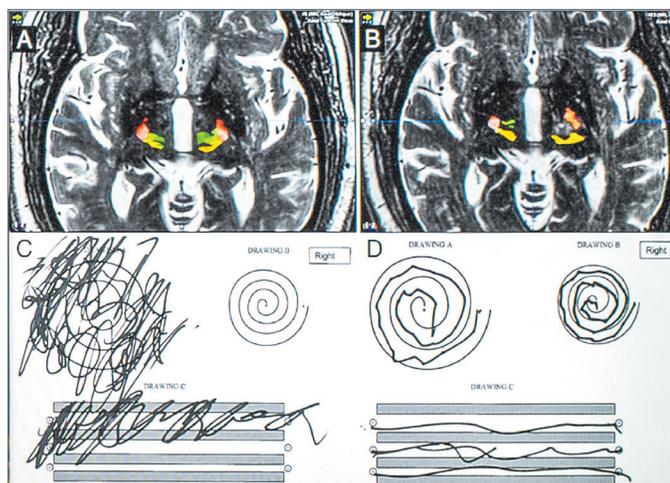
Dr. Michael G. Kaplitt and Dr. J. Levi Chazen

management is also dramatically reduced. In addition, HIFU exacts a permanent change in the brain, while DBS does not.”

The FDA has also approved the use of HIFU for treatment of tremor-dominated Parkinson’s disease. Weill Cornell is among 15 U.S. centers participating in a FDA clinical trial testing the safety and effectiveness of HIFU for tremor in Parkinson’s.

Dr. Kaplitt’s laboratory has also been investigating ways to use focused ultrasound to non-invasively deliver gene therapies to specific brain regions. The researchers are now studying a device in animal models that uses a lower level of ultrasound energy. This opens up the blood-brain barrier to allow gene therapy agents and other treatments to pass through. The researchers have been able to use a simple intravenous injection of the gene therapy agents and show that the area targeted with the ultrasound will take up these agents – all performed precisely and efficiently. Eventually, says Dr. Kaplitt, scientists could study the technique’s application to a variety of neurological disorders ranging from Alzheimer’s disease to addiction.

“With this low frequency ultrasound, we can deliver cavitation energy to a specific part of the brain, open up the blood-brain barrier for a 24-hour window, and potentially deliver a medication that might not normally get into the brain,” says Dr. Chazen. “In the case of Alzheimer’s, we target the hippocampus to enable the body’s systemic immune cells to access the brain and take away some of the beta amyloid and other damaging substances associated with Alzheimer’s.”



Pre-treatment (left) and post-treatment (right) MRI and patient drawings showing the immediate marked improvement in patient tremor when drawing a spiral and straight line.

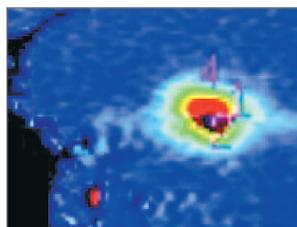
The Weill Cornell team has performed HIFU on some 50 patients with essential tremor with excellent results. “By not having hardware implanted, patients avoid such risks as infections or hemorrhage,” says Dr. Kaplitt. “Postoperative

# Epilepsy

## Emerging Advances in Seizure Control

**Guy M. McKhann II, MD**, Director, Epilepsy and Movement Disorder Surgery, and **Neil A. Feldstein, MD**, Director, Pediatric Neurological Surgery, NewYork-Presbyterian/Columbia University Irving Medical Center, are advancing methods for identifying more precise boundaries of seizure onset and minimally invasive treatment approaches for refractory epilepsy. “In the past, in order to narrow the site of the seizures we would open up the head and apply large arrays of electrodes onto the brain to record seizures,” says Dr. McKhann. “Stereo-electroencephalography [SEEG] has dramatically changed this approach. Using robotics, we can now put 2mm electrodes into the brain tissue through incisions that are just 3mm to capture data on the seizure as it occurs. This allows us to interrogate the brain in a much less invasive fashion. Once we know empirically through SEEG and advanced brain imaging where the seizures originate, we can determine if it makes sense to use a laser to ablate that area or perform an open surgery.”

Coupled with the emergence of SEEG has been the development and refinement of thermal ablation therapies. “If the seizures are coming from a very focal area in the brain, then the patient is a potential candidate for laser ablation. This technique is particularly valuable for reaching seizures originating in the hippocampus,” adds Dr. McKhann, who has performed some 50 thermal ablation procedures.



Real-time MR thermography



Composite irreversible damage zone

“With the newest ablation technique – MR-guided laser interstitial thermal ablation – we can place a laser fiber through a very small opening in the skull into the hippocampus and using an MRI scanner we can see exactly what we’re doing in real time in terms of ablating the seizure focus,” continues Dr. McKhann. “The approach offers access to foci virtually anywhere in the brain with minimal disruption of the overlying cortex and white matter, resulting in fewer neurological side effects.”



Dr. Guy M. McKhann II and Dr. Alison M. Pack

As a member of Columbia’s Comprehensive Epilepsy Center, neurologist **Alison M. Pack, MD**, provides expertise in diagnosing, identifying the cause, and classifying the patient’s epilepsy. Dr. Pack also applies the latest technologies to localize seizure onset in order to optimize outcomes for patients who undergo a laser ablation or surgical resection. “Pre-surgical testing will involve neuroimaging, including a brain MRI and PET, as well as inpatient EEG monitoring,” says Dr. Pack. “With the availability of robot-assisted SEEG, the seizure-onset zone can often be localized to the mesial temporal lobe structures.”

In a recent study, Dr. McKhann, Dr. Pack, and their colleagues at Columbia looked at the effectiveness of laser ablation for temporal lobe epilepsy – with and without mesial temporal sclerosis (MTS) – if hippocampal seizure onsets are localized by SEEG. “We evaluated 30 patients who underwent MR-guided laser interstitial thermal ablation of the mesial temporal lobe,” says Dr. Pack. “Seizure freedom was achieved in 57 percent of patients overall, offering early evidence that by confirming mesial temporal onset with SEEG, patients without MTS can achieve rates of seizure freedom following laser ablation similar to those with MRI-diagnosed MTS.”

Dr. McKhann notes that because laser ablation is a focal therapy, surgical resection of the epileptogenic zone still offers the best chance of seizure freedom. “However, since the laser ablation is so much less invasive, most patients decide that they want to have laser ablation because some 60 percent will become seizure-free. And if not, they can always go on to have an open surgery.”

# Epilepsy

## Intractable Seizures: ECT as Salvage Therapy

A patient with refractory status epilepticus often faces weeks in an ICU requiring prolonged anesthesia with coma-inducing drugs to control the seizures. “Refractory status epilepticus is a condition that we face as neurointensivists, epileptologists, and neurologists,” says **Padmaja Kandula, MD**, Director of the Comprehensive Epilepsy Center at NewYork-Presbyterian/Weill Cornell Medical Center. “It is a continual seizure state that does not respond to any of our traditional, anticonvulsive medications, even when used back to back. In order to treat ongoing seizure burden and prevent further brain injury, and to some degree motor injury, we place the patient in a medically induced coma.”

General anesthetics are administered 24 hours a day in order to provide cerebral rest, however, all have long-term consequences affecting blood pressure and heart rate if used for prolonged periods. In some cases the seizure state recurs on the reduction or withdrawal of the anesthesia, a condition called super-refractory status epilepticus. “These patients have a very high mortality, depending on the cause of their seizure state,” says Dr. Kandula. “It can be caused by a structural problem, such as a stroke or a tumor, but sometimes we can never identify the cause, making this entity particularly challenging to treat.”

“The logic is that provoking a convulsion alters GABA, making it more difficult to have ongoing seizures by raising the seizure threshold.”

– Dr. Padmaja Kandula

Recently, a young woman in her 20s with new-onset refractory status epilepticus was transferred to the Neuro ICU. “We tried seven intravenous drugs – all anesthetics – as well as ketamine and an inhalational gas anesthetic, which is even one step further,” says Dr. Kandula. “She failed all of those. The patient was treated concurrently with immune therapy, but that targets the underlying cause, not necessarily the ongoing seizure state.”

After exhausting conventional therapies, Dr. Kandula and the ICU team in consultation with the patient’s family



Dr. Padmaja Kandula

discussed electroconvulsive therapy (ECT) as an alternative treatment. “The general guideline for ECT in status is loosely a ‘treatment consideration,’” says Dr. Kandula. “It is not an approved therapy for seizure states, but rather for refractory depression and difficult-to-control schizophrenia. Over the years, small case series have described the off-label use of ECT for super-refractory status epilepticus, but there have not been any large-scale studies. It’s considered a salvage therapy, but we believe worth trying in individuals who are so critically ill.”

In collaboration with **Darlene Mitera, MD**, Director of ECT, Department of Psychiatry at Weill Cornell, ECT was initiated with good results. “The mechanism is poorly understood, but the idea is that inducing an additional seizure with electrical stimulation alters neurotransmitter levels, in particular gamma-aminobutyric acid – GABA,” says Dr. Kandula. “The logic is that provoking a convulsion alters GABA, an inhibitory neurotransmitter, making it more difficult to have ongoing seizures by raising the seizure threshold.”

However, questions remain on the most effective ECT strategy, including stimulation parameters, spatial approach, and number of total sessions. “We took a bilateral approach since the seizures were multifocal,” says Dr. Kandula. “We have also tried ECT with a young man who is doing well. Certainly, this is an area of ongoing interest we are interested in pursuing. The idea of using ECT earlier in the status epilepsy treatment armamentarium, and not just as salvage therapy, remains an active area of exploration.”

# Och Spine Care

## A Playbook for an Integrated Approach



Dr. Evan Johnson and Dr. Paul C. McCormick

“Spinal conditions are extraordinarily heterogeneous in terms of causes, effect, natural history, and response to treatments,” says **Paul C. McCormick, MD, MPH**, Herbert and Linda Gallen Professor of Neurological Surgery, Columbia University Vagelos College of Physicians and Surgeons. “We offer the spine patient the collaboration of the best specialists in the world to identify, evaluate, and then define the most appropriate treatment. It’s like being on a football team: You’d like to be a Super Bowl champion, but you can’t do that by yourself. Each player has certain capabilities.”

The analogy is particularly apt for Dr. McCormick, who as an undergraduate captained the Columbia football team. “Playing on Coach Campbell’s team meant that you were going to wear the Columbia uniform, you were going to be part of something greater than yourself, greater than any individual accomplishment,” says Dr. McCormick. “Likewise, our program brings together individuals with different skill sets and perspectives – inside and outside the OR – working together to optimize the patient’s care.”

Dr. McCormick, and his neurosurgical colleagues, **Peter D. Angevine, MD**, and **Christopher E. Mandigo, MD**, work closely with the spine surgeons in Columbia’s Department of Orthopedic Surgery. Most recently, two new spine surgeons, **Patrick C. Reid, MD**, and **Simon Morr, MD**, with joint appointments in neurosurgery and orthopedic surgery have come on board. The neurosurgeons and orthopedic surgeons operate in the NewYork-Presbyterian Och Spine Hospital, which will soon have six dedicated ORs designed

explicitly for spinal procedures. In August 2018, an integrated neurosurgery and orthopedic spine fellowship program was established with rotations through both specialties.

**Evan Johnson, DPT**, Assistant Professor, Columbia University Vagelos College of Physicians and Surgeons, serves as administrator for the spine program and oversees physical therapy and research for the NewYork-Presbyterian Och Spine Hospital. “Because there are so many specialties involved in spine disorders, the most important communication is not between specialists in the same discipline, but with all the other practitioners involved in the patient’s care,” says Dr. Johnson. “So how do you put systems in place that facilitate the care process? That was our thinking as we developed our program.”

The spine care team has developed standardized safety practices, including preoperative protocols to lower risk for complications and postoperative guidelines for mobilization and medication.

Importantly, the NewYork-Presbyterian Och Spine Hospital provides the infrastructure to facilitate integrated spine care – one location where all disciplines practice and interact, uniting the expertise of neurosurgeons, neurologists, orthopedic surgeons, physiatrists, pain management specialists, physical therapists, and specialized nursing staff. “We have implemented very clear-cut strategies to enhance this integration,” notes Dr. McCormick. “We have case conferences every week as well as indication conferences where upcoming operations are shared. And we have quality assurance rounds. When we have a suboptimal outcome, we analyze it, learn from it, and improve care overall.”

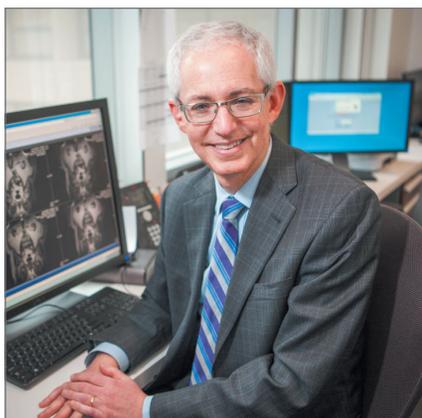
“In addition, it’s very important to distinguish care of the individual who has an acute or subacute condition from the individual who has a chronic disease process,” adds Dr. Johnson. “We knew that we had to differentiate the pathway of each patient group for maximum efficiency.” The solution: A call center that operates across multiple departments and a registered nurse navigator who triages patients and schedules appointments.

# Spine

## Minimally Invasive Surgery Offers More with Less

At the Center for Comprehensive Spine Care at NewYork-Presbyterian/Weill Cornell Medical Center, neurosurgeons **Eric H. Elowitz, MD**, and **Michael S. Virk, MD, PhD**, are taking advantage of the many techniques and technologies now available in minimally invasive spine surgery. “I have been performing minimally invasive spine surgery for the last 15 years and achieving the same goals or even better than with conventional open surgeries,” says Dr. Elowitz. “The area in which we’re seeing explosive growth is endoscopic surgery. This approach allows us to do spinal decompressions, as well as discectomies, with 7mm incisions via tissue and muscle-sparing corridors through natural openings into the spinal canal. The endoscope is not much bigger than a No. 2 pencil and offers excellent visualization. Micro instruments enable us to remove herniated disks and bone spurs in an extremely minimally invasive way.”

As Dr. Elowitz notes, indications for endoscopic spinal surgery are expanding, primarily in the lumbar region. “There are some instances where I can perform an endoscopic procedure as opposed to doing a fusion, which is a much bigger operation,” he says. “There is a select group of patients with a particular type of nerve pain that can be relieved with endoscopic surgery, thereby avoiding or delaying fusion surgery. I can also foresee in the not too distant future performing endoscopic spinal fusions with patients being able to go home the same day.”



Dr. Eric H. Elowitz



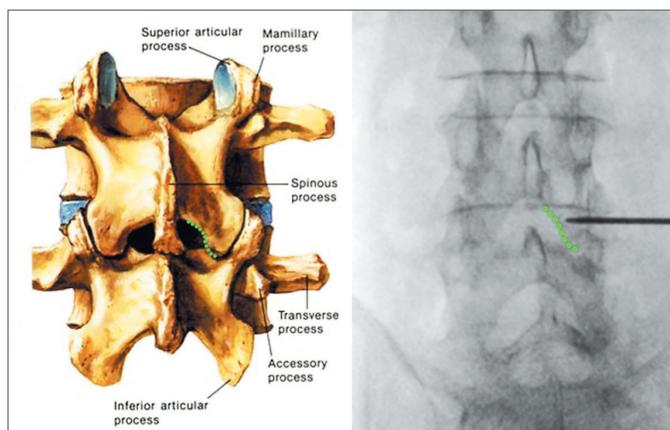
Dr. Michael S. Virk

“Certain revision cases or cases that are technically complex may require an open procedure, but my first approach is to accomplish our goals in a minimally invasive fashion,” says Dr. Virk.

Weill Cornell spine surgeons often take a circumferential approach to the spine. “We are pushing the envelope of performing extended applications for complex pathologies through smaller corridors,” he says. “Using an anterior approach, we can access the retroperitoneal space through an abdominal incision, or use a thoracic approach into the lateral corridor, going through the flank or between the ribs, and then performing percutaneous posterior instrumentation. Circumferential approaches generally involve multiple small incisions versus one extended incision in the back and this often translates into less global tissue disruption.”

Some of the approaches call on established collaborations with other surgical specialists. “For extended anterior approaches to the cervical spine, I have an ENT partner, **Dr. Babak Sadoughi**,” says Dr. Virk. “These cases may address complex deformity, tumors, or revisions and may require larger openings with more tissue mobilization, and his skills in this region help facilitate these cases.”

For anterior retroperitoneal lumbar approaches, Dr. Virk enlists the expertise of a Weill Cornell vascular surgeon, **Dr. Sharif Ellozy**. “He can mobilize the aorta or vena cava to provide access to the front of the spine,” he says. “Once a narrow corridor is established, we come in and do what we have to do.”



Target site – inferomedial edge of the lamina – is identified with fluoroscopy imaging.



# NIH Clinical Trials

## Advancing Progress through Nationwide Networks

### NeuroNEXT

#### NN107, FX-LEARN: A Study of AFQ056 in Fragile X Syndrome

Fragile X syndrome is a single-gene disorder and the most commonly inherited cause of intellectual disability. Effects range from learning disabilities to severe intellectual impairment. This study will examine if drug therapy with AFQ056 can improve communication and learning in children with Fragile X syndrome. The study will also determine the most effective dosing to improve neural plasticity. Participants between the ages of 32 months and six years of age will be randomized to either receive the drug therapy or a placebo for the initial period of about one year. All participants will be evaluated by speech language therapists. In the study's extension phase, all participants

will be treated with the active drug for a period of about 8 months. The study is the first of its kind to evaluate whether a treatment aimed at improving a core deficit of brain connectivity can change the ability to learn in young children with Fragile X syndrome.

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### StrokeNet

#### ARCADIA: Atrial Cardiopathy and Antithrombotic Drugs In Prevention After Cryptogenic Stroke

ARCADIA is a multicenter phase 3 clinical trial of apixaban versus aspirin in patients who have evidence of atrial cardiopathy and a recent stroke of unknown cause. This trial seeks to advance the understanding of stroke pathophysiology by assessing whether atrial cardiopathy is a valid therapeutic target, which may set the stage for a primary prevention trial, and also to advance understanding of optimal secondary stroke prevention therapy. ARCADIA will recruit 1,100 subjects over 2.5 years at 120 sites in the NINDS StrokeNet consortium. Subjects will be followed for a minimum of 1.5 years and a maximum of 4 years for the primary efficacy outcome of recurrent stroke and the primary safety outcomes of symptomatic intracranial hemorrhage and major hemorrhage other than intracranial hemorrhage.

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#### CREST-H: Carotid Revascularization and Medical Management for Asymptomatic Carotid Stenosis

As an ancillary study to the CREST-2 clinical trial, CREST-H will assess cognitive outcomes in CREST-2 patients with cerebral hypoperfusion and mild cognitive impairment, comparing those who get revascularized versus those who get intensive medical management alone. The main hypothesis is that patients with hemodynamic impairment due to the carotid stenosis have a reversible factor contributing to their mild cognitive impairment, and thus, compared with those who have no hemodynamic impairment, will benefit cognitively from reversing the hemodynamic impairment. 500 patients will be enrolled from 75 CREST-2 sites. The primary outcome measure is change in cognition at 1 year.

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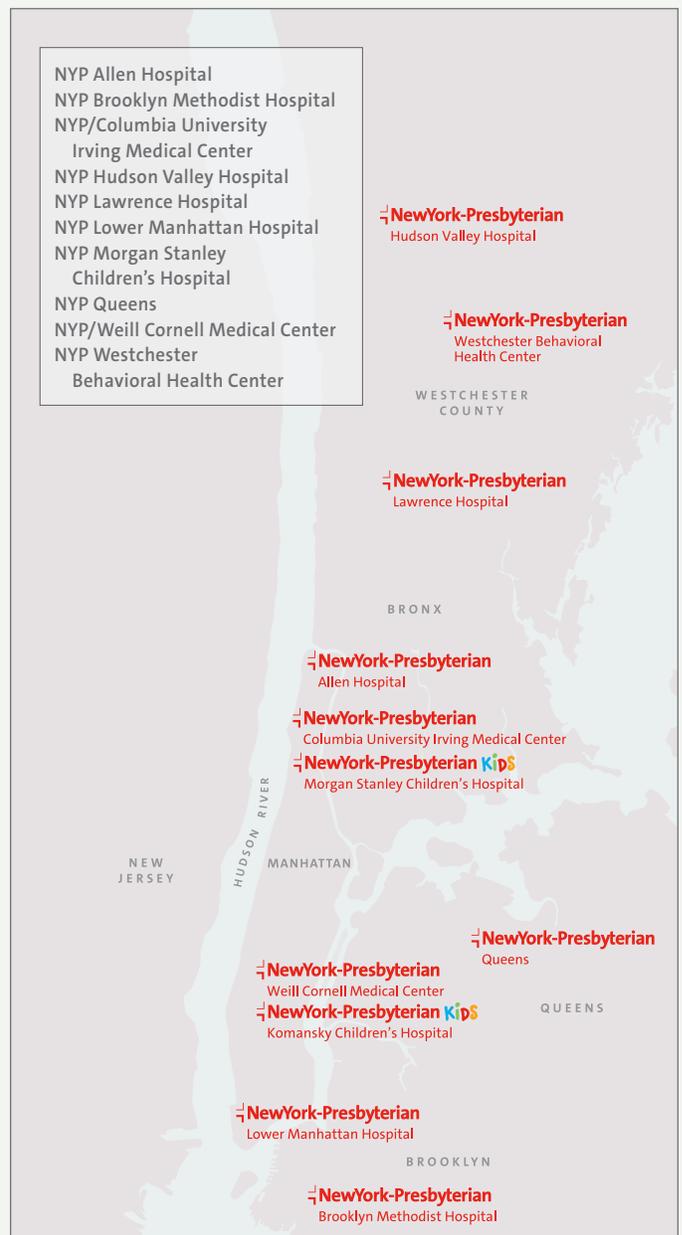
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NewYork-Presbyterian is one of the nation's most comprehensive, integrated academic healthcare systems, encompassing 10 hospital campuses across the Greater New York area, more than 200 primary and specialty care clinics and medical groups, and an array of telemedicine services.

A leader in medical education, NewYork-Presbyterian Hospital is the only academic medical center in the nation affiliated with two world-class medical schools, Weill Cornell Medicine and Columbia University Vagelos College of Physicians and Surgeons. This collaboration means patients have access to the country's leading physicians, the full range of medical specialties, latest innovations in care, and research that is developing cures and saving lives. Ranked the #5 hospital in the nation and #1 in New York in *U.S. News & World Report's* "Best Hospitals" survey, NewYork-Presbyterian Hospital is also recognized as among the best in the nation in every pediatric specialty evaluated in the *U.S. News* "Best Children's Hospitals" survey. Founded nearly 250 years ago, NewYork-Presbyterian Hospital has a long legacy of medical breakthroughs and innovation, from the invention of the Pap test to the first successful pediatric heart transplant, to pioneering the groundbreaking heart valve replacement procedure called TAVR.

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