Neurology & Neurosurgery
2017 YEAR IN REVIEW

Advanced TECHNOLOGY FOR NEUROSURGICAL IMAGING

214 NEUROLOGY FACULTY

#10 IN U.S. NEWS & WORLD REPORT
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Dear Colleagues and Friends:

For the departments of Neurology and Neurosurgery at NYU Langone Health, 2017 was a year of continued advancement. Our record of excellence is reflected in our top 10 ranking among the nation’s most elite programs, a testament to our cross-specialty impact.

Whether refining surgical techniques, uncovering novel neurodegenerative disorder treatments, or investigating brain cancer’s biological underpinnings, our faculty have extended our leadership in every aspect of neurological medicine.

Fueling this leadership are cutting-edge diagnostic imaging techniques and applications, identified through interdisciplinary collaboration. Our Gamma Knife radiosurgery program has enabled noninvasive treatment of multiple brain tumors, and our Center for Neuromodulation is refining the latest generation of deep brain stimulation (DBS) devices for Parkinson’s disease. DBS is also under investigation for Tourette’s syndrome, as we explore the benefits of both DBS and Gamma Knife radiosurgery for obsessive-compulsive disorder. The complex cases highlighted in this report are a testament to how our neurosurgeons use these advances to achieve previously impossible feats.

Our faculty continue to pioneer and advance novel technology for both diagnosis and treatment. Our neuro-ophthalmologists are using optical coherence tomography to expand the diagnostic criteria for multiple sclerosis, and the Division of Neuro-Ophthalmology is analyzing eye movements to aid in the diagnosis of a variety of neurological disorders. At the Multiple Sclerosis Comprehensive Care Center, clinicians are demonstrating the efficacy of low-voltage transcranial direct current stimulation for MS-related fatigue. Collaboration between the Brain Tumor Center and NYU Langone pathologists has enabled the first U.S.-certified use of 450K methylation technology in tissue evaluations.

Interdisciplinary collaboration is central to advancing our clinical and research progress. Our close partnerships with Neuroradiology and other specialties have enabled such advances as MRI perfusion techniques to monitor brain tumor treatment response. At the Eye Movement Testing Lab, teamwork with our Concussion Center colleagues has evolved concussion diagnosis, and our stroke program—part of the integrated Center for Stroke and Neurovascular Diseases—benefits from close work with specialists across NYU Langone. Our cross-disciplinary expertise helps us unravel the most complex clinical puzzles, as demonstrated by recent insights revealed by our faculty in the Division of Headache Medicine.

Promising treatments emerging from clinical trials in the Center for Cognitive Neurology and our epilepsy, MS, and Parkinson’s programs are quickly put into practice for the benefit of our patients. Aided by one of the most extensive and complex tissue banks in the country, we are advancing the understanding of disease pathology and treatment response that expands our clinical options. Prominent new physician recruits at the growing Marlene and Paolo Fresco Institute for Parkinson’s and Movement Disorders bring enhanced research and clinical rigor to our programs.

With our dedicated clinicians’ and researchers’ unique blend of focused collaboration and innovation, we are ready to produce unprecedented change in our field. Together, we will continue to make promising discoveries that transform outcomes—and realize the great promise that neurological and neurosurgical advances hold for our patients.
# Neurology and Neurosurgery

## RESEARCH

- **70+** ongoing clinical trials in neurology and **30+** ongoing clinical trials in neurosurgery
- **20+** years of continuous NIH funding for a single R01 grant in neurosurgery
- **30+** ongoing research studies on the treatment and prevention of neurocognitive disorders
- **$11.75M** neurology grant funding awarded in 2017
- **18** resident presentations at the American Academy of Neurology 2017 annual meeting

## FACULTY

- **27** full-time neurosurgery faculty with more than 30 part-time and affiliated faculty
- **214** neurology faculty: 20 joined in 2017
- **91** residency positions: 75 in neurology, 16 in neurosurgery

## PATIENT CARE

- **5,100+** neurosurgical cases
- **560+** gamma knife cases
- **1,200+** spinal neurosurgery cases
- **77,000+** neurology outpatient visits
- **35** neurology faculty and residents involved in ongoing quality and safety projects

## ACCOLADES

- **#10** in the country for neurology and neurosurgery in U.S. News & World Report’s “Best Hospitals”
- **#1 in the Nation** for lowest mortality score in cranial neurosurgery as awarded by Vizient, Inc.
NYU Langone Health

NYU Langone Health is the only full-service hospital in New York State and one of 9 percent of hospitals nationwide to receive a five-star rating from the Centers for Medicare and Medicaid Services (CMS). The rating reflects overall safety, quality, and patient experience.

In the Nation

#19
IN THE NATION
and nationally ranked in 12 specialties:
Rehabilitation, Orthopedics,
Rheumatology, Neurology & Neurosurgery, Geriatrics, Urology,
Cardiology & Heart Surgery,
Gastroenterology & GI Surgery,
Diabetes & Endocrinology,
Pulmonology, Cancer, and Nephrology

#12
IN THE NATION
BEST MEDICAL SCHOOLS FOR RESEARCH
and a leader in innovation in medical education, including accelerated pathways to the MD degree

5 Star Rating
FROM CMS HOSPITAL COMPARE

Leader
IN QUALITY CARE AND PATIENT SAFETY
For the past four years, NYU Langone has received top rankings for overall patient safety and quality of care from Vizient, Inc., formerly the University HealthSystem Consortium. In 2017, NYU Langone received two significant awards from Vizient—the Bernard A. Birnbaum, MD, Quality Leadership Award and the Ambulatory Care Quality and Accountability Award for demonstrated excellence in delivering high-quality, patient-centered outpatient care.
Research and Innovation Transform Clinical Outcomes

Homing In on Cutting-Edge Headache Therapies

In the newly expanded Division of Headache Medicine, specialists are leading clinical trials aimed at delivering new treatment options for chronic or intractable headaches.

In one phase III clinical trial, investigators are testing an experimental drug that works by blocking calcitonin gene-related peptide (CGRP), a neurotransmitter thought to trigger migraines. Researchers are exploring whether eptinezumab, administered via injection once every 12 weeks, can prevent chronic and frequent episodic migraines. “The trials have been very promising, with minimal side effects,” says Lawrence C. Newman, MD, professor of neurology and director of the Division of Headache Medicine. “Results tend to be seen within a week or so—much faster than with other medications.”

BREAKING THE HEADACHE CYCLE

The new drug would add to the range of headache treatments currently available, including those offered at a new infusion center at NYU Langone, where patients are administered targeted treatments that often provide relief within the hour.

The division is also teaming with physicians at NYU Langone’s Concussion Center and vestibular rehabilitation program to increase our understanding of the mechanisms of headache associated with head trauma. “Each member of our collaborative team is interested in sharing their expertise to enhance the field,” notes Dr. Newman. Recently, headache faculty began offering an elective rotation in headache medicine, in which neurology residents are exposed to the full range of headache disorders.

“Although just a few drugs are currently FDA-approved for migraine prevention, our growing understanding of headache mechanisms continues to augment our armamentarium of treatments that provide relief,” adds Dr. Newman.

Advances in Epilepsy Target Seizure Activity and Severity

At the Comprehensive Epilepsy Center, recent research and clinical trials are shedding new light on ways to reduce the severity of seizures and provide better quality of life for patients with epilepsy and related disorders. Building on the center’s pioneering application of the cannabis-derived drug cannabidiol, investigators uncovered new signs of efficacy that could lead to FDA approval of the drug for seizures associated with Dravet syndrome and Lennox-Gastaut syndrome. On another drug front, a phase II trial of inhaled alprazolam is offering encouraging data demonstrating rapid absorption stems oncoming seizures, supporting use of the drug as a rescue medication. Researchers are also continuing their efforts to unravel the mystery of sudden unexpected death in epilepsy (SUDEP). Spurred by newly uncovered estimates of SUDEP prevalence indicating that earlier estimates were understated, the center is pursuing a new technology that would use heightened nervous system activity to warn family members of SUDEP onset—and potentially save lives.
Research Targets Triggers and Symptoms of Multiple Sclerosis

NYU Langone’s Multiple Sclerosis Comprehensive Care Center continues to uncover and pioneer novel approaches to multiple sclerosis (MS) symptom control, disease management, and treatment.

In a seminal 2018 publication in the Journal of Neurology, Neurosurgery & Psychiatry, center researchers identified an important potential environmental trigger for MS, showing that young MS patients with a lower intake of saturated fat had fewer relapses compared to those with a high intake. The new findings are part of an ongoing investigation of environmental factors that can exacerbate genetic predisposition to pediatric MS, with other potential risk factors including childhood obesity, pesticide exposure, secondhand smoke, and childhood trauma. “We’re making significant headway in identifying these environmental triggers,” notes center director Lauren B. Krupp, MD, the Nancy Glickenhaus Pier Professor of Pediatric Neuropsychiatry. “It’s my belief that what we’re finding in pediatric MS is also relevant to adults with MS and likely relevant to other autoimmune diseases as well.”

Separately, a randomized controlled study published in September 2017 in the Multiple Sclerosis Journal showed that 20 sessions of portable transcranial direct current stimulation (tDCS), using an NYU Langone–customized device that delivers low-voltage electric current to the scalp, significantly alleviated MS-related fatigue in adults. “This is a major advance, since we have no effective medication to treat the fatigue MS patients so commonly experience,” notes Leigh E. Charvet, PhD, associate professor of neurology, who led the research—the first-ever controlled study of tDCS benefits for MS patients. In a complementary controlled study, published in PLOS One in 2017, an in-home, computer-based cognitive remediation program was found to significantly improve subjects’ performance on various neuropsychological tests.

Researchers also continue to analyze and publish data collected through the center’s participation in the MS PATHS project—a multicenter effort in which iPads are used to collect detailed data from patients at each clinical visit. “So far, 5,000 people have been evaluated,” notes Dr. Krupp. “We’ll combine this information with MRI data on new lesions and, eventually, outcome measurements to significantly advance clinical MS research.”

Complex Case: Multidisciplinary Expertise and Precision Imaging Enable Resection of a Deep Thalamic Cavernous Malformation

Vascular lesions of the thalamus are rare, and information on their surgical removal is limited to a small series of case reports. Although excellent outcomes have been reported with a well-planned surgical approach, complications of surgery include devastating neurological injury. If the lesion is left untreated, however, mass effect, secondary compromise of the microcirculation, and irritation of the cortical and subcortical tissue by local deposition of hemosiderin from microhemorrhages can result in progressive neurological deficits and seizures.

A patient with a deep thalamic cavernous malformation turned to NYU Langone after being told by multiple surgeons that his lesion was inoperable. Leveraging cutting-edge research, advanced neuroimaging techniques, and cerebrovascular surgical expertise, the multidisciplinary neurovascular team at the Center for Stroke and Neurovascular Diseases planned and executed a successful resection of this patient’s thalamic cavernoma and enabled his swift recovery.
Commitment to Discovery Yields New Hope for Brain Cancer

At the Brain Tumor Center, recent research breakthroughs enabled by the center’s unique cross-disciplinary collaboration have brought investigators closer to major therapeutic and diagnostic discoveries.

In one such advance, a research team led by Dimitris G. Placantonakis, MD, PhD, assistant professor of neurosurgery, identified GPR133, a protein not normally found in the brain, on the cell surfaces of glioblastoma tissue—making it a promising target for novel therapies. “It turns out that the protein is found in all glioblastomas, and we’ve shown that when we knock it down, the tumor cells die,” says Dr. Placantonakis. The lab’s discovery, published in *Oncogenesis* in 2016 and *Clinical Neurosurgery* in September 2017, has led to a patent application and collaboration with a U.K. pharmaceutical firm and NYU Langone’s Office for Therapeutic Alliances to develop GPR133-inhibiting molecules.

In another breakthrough, published in the October 2017 issue of *Cell Reports*, researchers studied human neural stem cells engineered to express the IDH gene mutation that is found in the majority of low-grade gliomas. This mutation caused the neural progenitors to develop into low-grade astrocytoma-like cells. The lab discovered that the cells quickly stopped differentiating—an important first step in tumor creation—because transcription factor SOX2 was silenced. This effect was traced back to reduced binding of chromatin organizer CTCF to DNA, which led to the unraveling of the chromatin structure and the silencing of SOX2 by preventing SOX2’s promoter from interacting with nearby enhancer elements. “We’ve uncovered one of the first examples of chromatin restructuring acting as a mechanism in tumor formation—which ultimately could apply to many cancer types,” notes Dr. Placantonakis. “In addition, our low-grade glioma model can be used to screen drugs and test new therapies.”

**COLLABORATION LEADS TO DIAGNOSTIC PROGRESS**

The Brain Tumor Center, working closely with molecular pathologists and neuropathologists, will become the first U.S. program certified to use genomic DNA methylation technology in clinical evaluations of brain tumors. The technology, developed for research use at NYU Langone by Matija Snuderl, MD, assistant professor of pathology and director of Molecular Pathology, can determine a brain tumor’s genetic subtype by means of a single high-throughput, comprehensive DNA test on a small brain tissue sample.

“Our early adoption of this forward-thinking diagnostic...”
technology puts us in a strong position to move it from the lab to the clinical setting,” says Andrew S. Chi, MD, PhD, assistant professor of medicine, neurology, and neurosurgery, chief of neuro-oncology, and co-director of the Brain Tumor Center at Perlmutter Cancer Center.

Separately, Rajan Jain, MD, associate professor of radiology and neurosurgery, has discovered a novel structural biomarker known as a T2-FLAIR mismatch, which is 100 percent indicative of a molecular subtype of glioma that carries an IDH gene mutation and lacks codeletion of chromosomes 1p and 19q. This biomarker, reported in July 2017 in Clinical Cancer Research, can be easily detected using conventional clinical brain MRI scans, without specialized equipment or invasive protocols. “It’s what we’re all looking for— a way to diagnose a tumor’s molecular subtype without having to open the skull,” says Dr. Chi. In another project, Dr. Jain is pioneering the clinical use of MRI perfusion to better visualize how certain tumors respond to therapy.

“IT’s becoming clear that molecular subtyping is necessary for optimal management of brain tumors,” notes Dr. Chi, “since each subtype may respond differently to specific therapies.” Breakthroughs, then, will come not only from developing new classes of drugs and immune therapies, but also from identifying which molecular subtype is sensitive to a given therapy. “That’s why developing rapid, robust molecular subtyping diagnostics that can easily be applied to the clinical setting is so critical,” adds Dr. Chi.

Gamma Knife Radiosurgery Offers Versatility in Treating Brain Tumors and AVMs

Ongoing research continues to uncover and enhance the efficacy of Gamma Knife radiosurgery for an expanding array of conditions, including cancer and arteriovenous malformations (AVMs). Aided by enhanced surveillance, physicians at NYU Langone are tracking and targeting tumors more precisely and employing Gamma Knife’s versatility to treat conditions previously considered untreatable, improving options and outcomes for the most complex cases. The approach is illustrated by two recent, very different cases in which Gamma Knife radiosurgery’s precision proved invaluable: the successful treatment of a patient with more than 25 individual tumors and the highly delicate resolution of an otherwise unresectable AVM.

Novel Optical Assessments Provide New Windows into Neurological Conditions

As researchers and clinicians pursue new modes of treatment for complex neurological diseases, advancements in optical coherence tomography (OCT) — capable of delivering images at 1,000 times the resolution of MRI — and the expansion of OCT applications have enhanced clinicians’ capacity to diagnose and treat these conditions. OCT and other vision-based diagnostic tools have enabled the visualization of optic nerve lesions associated with multiple sclerosis, adding weight to efforts to incorporate these markers in diagnostic criteria for the disease. In traumatic brain injury, the new visualization techniques are being used to elucidate the mechanisms behind retinal loss associated with concussion and other neurological conditions.
Collaboration among Neuroradiologists and Neurosurgeons Enables Neuroimaging Firsts

The partnership between NYU Langone neurosurgeons and neuroradiologists contributes to continued advancements in the field of neurosurgical planning, pushing the limits of imaging technology and fundamentally shifting approaches to surgery. Among recent innovations: reduced field-of-view diffusion MRI; three-dimensional volumetric MRI; and advanced diffusion tractography, applied to spinal neurosurgery for the first time at NYU Langone. These technologies provide real-time maps of spinal cord tumor location and the relative positions of important spinal cord white matter tracts to improve safety and surgical outcomes.

“Imaging science experts have developed newer techniques for the conventional diffusion tractography already used by our neuroradiologists, giving us unprecedented visualization of brain and spinal cord structures,” explains Timothy M. Shepherd, MD, PhD, assistant professor of radiology. Dr. Shepherd’s team is working on a novel protocol that will enable surgeons to visualize important eloquent white matter pathways, such as the arcuate fasciculus, even in the presence of edema. “Edema or mass effect from tumors can impair our ability to visualize these pathways with conventional tractography for operative planning and is a major imaging challenge in neurosurgery,” says Dr. Shepherd. “By seeing through edema effectively, we can enhance the accuracy of the brain maps we provide for neurosurgical navigation—and thus reduce patient risk.”

PROGRESS IN IMAGING ENABLES PRECISION

Neuroradiologists are also preparing to publish their novel use of simultaneous multi-slice diffusion and track density imaging to directly visualize key anatomical targets in the brain for functional neurosurgery applications. “The sequence has been around for a few years, but it’s never been altered in this way to make it practical for use in patients. Our collaboration with colleagues in imaging physics, neurology, and neurosurgery helped us realize its value for functional neurosurgery,” explains Dr. Shepherd. With this sequence, the modified images show the structures and interconnections in the thalamus, subthalamus, and basal ganglia regions in more detail than was previously possible, an advance that will help surgeons to more clearly visualize where deep brain stimulation electrodes are being placed.

“This is another example of how enhanced imaging is moving us away from indirect targeting based on anatomical atlases,” adds Dr. Shepherd. “The methods our work uncovers could have a profound impact on functional neurosurgery—ultimately improving outcomes and decreasing risk.”

Complex Case: Cutting-Edge Neuroimaging Adapted to Safely Resect a Challenging Spinal Tumor

The use of newer imaging technologies such as advanced diffusion tensor imaging (DTI) has enabled safe resection of once-inoperable spinal cord tumors. Initially pioneered for brain surgery, the technology was used in the spine for the first time by Anthony K. Frempong-Boadu, MD, associate professor of neurosurgery and director of the Division of Spinal Surgery. This was two years before a 29-year-old patient presented with a risky intramedullary cavernoma whose removal carried the risk of permanent morbidity. These rare tumors—only a small fraction of all the central nervous system lesions that are seen—are so complex that few centers are equipped to treat them. For this patient, Dr. Frempong-Boadu teamed with neuroradiologists to apply the leading-edge DTI approach, creating visual touchpoints for the surgery that enabled resection of the tumor while leaving the patient’s neurological function—and quality of life—intact.

Read more on PAGE 20
Novel Drugs and Biological Discoveries Accelerate Hunt for an Alzheimer’s Cure

With 12 ongoing clinical trials, NYU Langone’s Center for Cognitive Neurology is one of the world’s most active centers for research on Alzheimer’s disease and other neurocognitive disorders. The center’s more than 70 researchers are working across a range of disciplines to unravel the root causes of these conditions. Research into immunotherapies for Alzheimer’s and related dementias is one of the pathways offering promise—and the recently published groundbreaking studies are paving the way for human trials. At the same time, investigations into the biological mechanisms behind these conditions—including several studies funded by the National Institutes of Health—are yielding new insights into the proteomic and genetic markers of Alzheimer’s that could eventually lead to a preventive treatment.

Read more on PAGE 22

Innovative Neuromodulation Approaches for Movement Disorders

At the Center for Neuromodulation, new and expanded applications of deep brain stimulation (DBS) and related innovations are targeting symptoms and enhancing quality of life for patients with Parkinson’s disease, tremor, and other disorders.

The center has been involved in clinical trials of newer DBS technologies and devices, giving clinicians a unique view of their efficacy in delivering electrical stimulation to targeted brain regions to reduce motor symptoms of Parkinson’s, essential tremor, and dystonia. The DBS technologies provide additional options—and new therapeutic targets—for personalizing treatment of Parkinson’s symptoms while limiting side effects and also offer new hope as an off-label treatment for the debilitating symptoms of severe Tourette’s syndrome. The expanding field of neuromodulation also includes MRI-guided focused ultrasound, which targets areas of the brain linked to tremor and other symptoms, eliminating the need for surgery while potentially mitigating symptoms.

Read more on PAGE 24

New Leadership Renews Commitment to Translational Research in Movement Disorder Treatment

With newly appointed leadership, the Division of Parkinson’s and Movement Disorders at NYU Langone is increasing its focus on translational research. Steven J. Frucht, MD, professor and associate chair of neurology and director of NYU Langone’s Division of Parkinson’s and Movement Disorders, and Andrew S. Feigin, MD, professor and associate chair of neurology and executive director of the Marlene and Paolo Fresco Institute for Parkinson’s and Movement Disorders, bring a mix of experience that will help the division cultivate new pathways for transforming its research discoveries into new therapies.

Both Dr. Frucht and Dr. Feigin have launched clinical trials testing novel vaccines and antibody drugs designed to block toxic brain proteins, including alpha-synuclein and tau proteins, thought to contribute to movement disorders. In addition, institute researchers will investigate novel methods of administering symptom-relieving medications such as subcutaneous infusion of levodopa and dopamine agonists, and new imaging techniques that may yield movement disorder biomarkers.

Clinicians and researchers will also work closely with colleagues across NYU Langone to develop a new biological understanding of movement disorders and refine leading-edge diagnostic and treatment approaches—including deep brain stimulation for Parkinson’s symptoms and eye movement tracking technology for diagnosis—to improve quality of life for patients with these disorders.

“We have a unique opportunity to establish the institute as a leading center for clinical and translational research for movement disorders,” says Dr. Frucht, who has been involved in many Parkinson’s studies as well as pilot studies of refractory movement disorders. “Together, we will provide multidisciplinary care while simultaneously advancing clinical research,” adds Dr. Feigin.
2017 IN DEPTH

Pushing Treatment Boundaries through Collaboration and Discovery

John G. Golfinos, MD, and Andrew S. Chi, MD, PhD
Epilepsy Studies Uncover New Options for Shortening Seizures—and Extending Lives

A growing body of knowledge, informed by recent investigations and clinical trials at the Comprehensive Epilepsy Center, could equip physicians and family members with new tools for stemming seizures and preventing sudden death in patients with epilepsy and related disorders.

SUCCESSFUL CANNABIDIOL TRIAL HERALDS FIRST TREATMENT FOR DRAVET-RELATED SEIZURES

Epileptologists have uncovered a potential new treatment option in the cannabis-derived drug cannabidiol (Epidiolex), shown to significantly reduce convulsive seizures related to Dravet syndrome, a rare pediatric-onset disorder for which there are currently no U.S.-approved medications.

The Dravet trial, published in May 2017 in *The New England Journal of Medicine*, found that cannabidiol in liquid form reduced seizures in children and young adults with Dravet syndrome by 39 percent on average. Two other soon-to-be-published studies found that the drug also reduced the frequency of drop seizures in individuals with Lennox-Gastaut syndrome, another form of epilepsy that often resists drug treatment.

On the basis of these studies, cannabidiol will soon be formally submitted for FDA approval as a treatment for both Dravet and Lennox-Gastaut syndromes, according to lead author Orrin Devinsky, MD, professor of neurology, neurosurgery, and psychiatry and director of the Comprehensive Epilepsy Center. “The FDA could approve it as soon as mid-2018, which would be a huge milestone,” says Dr. Devinsky. NYU Langone Health has been involved in cannabidiol’s pharmaceutical development from the very beginning, having hosted the first meeting with the drug’s manufacturer to discuss these trials five years ago.
INHALED ALPRAZOLAM SHOWS PROMISE AS A PRE-SEIZURE RESCUE MEDICATION

Separately, NYU Langone researchers are spearheading a phase II clinical trial testing an inhaled form of the benzodiazepine alprazolam (Xanax) as a rescue medication for incipient seizures. “Oral benzodiazepines are already used to shorten the duration of seizure clusters, but they don’t work fast enough to actually abort a seizure when a person feels it coming on,” explains Jacqueline A. French, MD, professor of neurology and director of Translational Research and Clinical Trials at the Comprehensive Epilepsy Center. “This approach uses a device that vaporizes the medication so the lungs absorb it at a rapid rate, nearly equivalent to an intravenous dose.”

A preliminary study with individuals susceptible to light-induced seizures showed that inhaled alprazolam produced an anti-seizure effect within two minutes. Through a connection made via the NYU Langone–affiliated nonprofit FACES (Finding a Cure for Epilepsy and Seizures), researchers are now collaborating with a start-up enterprise to support the yearlong efficacy trial.

UNRAVELING THE MYSTERY OF EPILEPSY-RELATED SUDDEN DEATH

Ongoing research continues to unravel the prevalence and biology of SUDEP. One finding, published in August 2017 in Neurology, suggests that the annual number of deaths from SUDEP in the United States could actually be far higher than the reported and widely accepted number of 3,000. The recalculation was based on an examination of data for all sudden cardiac deaths in the San Francisco area over a three-year period. Researchers reviewed autopsy and medical records of any decedents with a history of seizures or epilepsy, and concluded that the number of definite or possible SUDEP cases was three times greater than the number reported by the medical examiner.

“Combine this new estimate with the number of deaths of people with epileptic seizures that result in drowning, car accidents, or falls,” says Dr. Devinsky, “and it becomes clear that epilepsy-related death is an underestimated and under-addressed public health problem.”

To address this issue, researchers are studying a wrist sensor that monitors sympathetic nervous system activity via the skin. The goal is twofold: to examine the link between heightened electrodermal activity and the onset of seizures and to explore the device’s usefulness in warning family members of a potential SUDEP-causing seizure.

“Our continued research has revealed one more clue we can pursue to unravel the mystery of SUDEP,” notes Dr. Devinsky. “In time, with further resources devoted to understanding how these deaths occur, we hope to prevent them.”

HUMAN EPILEPSY PROJECT: HUNTING FOR BIOMARKERS TO OVERCOME TREATMENT RESISTANCE

In an effort to find biomarkers enabling early identification of treatment-resistant epilepsy, the Human Epilepsy Project recently enrolled 500 newly diagnosed focal-seizure epilepsy patients in a multisite study co-led by NYU Langone. For three years, researchers will follow patients in the United States, Europe, and Australia, gathering biological information including DNA and blood samples, urinalyses, EEG readings, and a special MRI evaluation while also tracking participants’ response to epilepsy medications.

This information is being logged in a data bank, where it can be mined by collaborating scientists. “We know that a third of people with epilepsy won’t respond well to any medication, but currently there’s no way to determine at the onset of treatment who they are,” says Dr. French. “This is an effort to understand the biological drivers behind that resistance.”

Three proposals from scientific groups seeking to examine specific biomarkers have been green-lit, she adds. Two will explore autoimmune factors, believed to trigger epilepsy in some cases. A third group is looking at a blood biomarker involved in inflammation, which is hypothesized to exacerbate seizures.

The project has already yielded one unexpected discovery: Many study subjects were found to have experienced subtle seizures for months or years before their epilepsy diagnosis. “People can experience numerous safety issues if their diagnosis is delayed,” notes Dr. French. “This finding indicates that we need to better help the public and the medical community to identify seizures.”
Complex Case: Progressive Symptoms Point to the Resection of a Deep Thalamic Cavernous Malformation

Previously advised against surgery because of the risky location of his thalamic lesion, a patient found new hope in NYU Langone Health’s Center for Stroke and Neurovascular Diseases and an advanced approach carefully coordinated by a multidisciplinary team.

In the 16 years since a right thalamic cavernous malformation was identified on MRI imaging, the patient had had multiple hemorrhages, a relatively common complication of thalamic cavernous malformations. In addition to expansion of the lesion, the patient had also experienced progressive hemisensory loss and dysesthetic pain syndrome, making treatment imperative. “The patient had been told by other surgical teams that the cavernous malformation was inoperable, because there was increasing concern about progressive functional damage,” says Howard A. Riina, MD, professor of neurosurgery, neurology, and radiology. “It was critical to find a surgical approach that could help mitigate potential risks, including left hemiplegia and venous infarction of the thalamus.”

PREOPERATIVE PLANNING AND TARGETED MAPPING SET TRAJECTORY FOR SUCCESS

The optimal resection approach for a thalamic cavernous malformation depends on the location of the malformation in the thalamus. This patient’s malformation was in the lateral posteroinferior region, bordered anteriorly by the medial and lateral thalamus, so that a parieto-occipital transventricular approach through the superior parietal lobe could be used to bypass the optic radiations and the somatosensory region.

“We decided that the best way to access the malformation safely was to perform the procedure through a small tube, a minimally invasive approach typically used for brain tumors,” explains Dr. Riina, who handled the
The cerebrovascular aspects of the surgery. “Rather than cut into the thalamus, we found a very simple trajectory through the ventricle, from which I could extend into the thalamus to gain access to the lesion.”

Advanced imaging was imperative to guide the surgeons’ precision approach. Using Surgical Theater’s surgical planning software to combine MRI, MR angiography, and diffusion tensor imaging, the team selected a target point. The combination of the data sets into a three-dimensional surgical planning model allowed the surgeons to map multiple trajectories and choose the best one: through the posterior medial parietal lobe, superior to the optic radiations and posterior to the somatosensory cortex, to the lesion. The borders of the cavernous malformation were simultaneously drawn in the Brainlab image guidance system to create a lesion volume around the target. This combined approach, using surgical planning software and image guidance, provided surgical access that transversed the least amount of brain tissue, significantly reducing the risk of complications and permanent injury.

**INTRAOPERATIVE PROJECTIONS IMPROVE SURGICAL PRECISION**

With planning in place, Dr. Riina was joined in the operating room by John G. Golfinos, MD, associate professor of neurosurgery and otolaryngology and chair of the Department of Neurosurgery, and Jeffrey H. Wisoff, MD, professor of neurosurgery and pediatrics. Continuous stereotactic guidance and tractography supported the procedure’s navigation, while Surgical Theater and Brainlab projections oriented the surgeons to the limits of the tumor, confirmed the approach vector, and guided the placement of the tubular retractor. The surgeons worked as a team throughout the procedure, with each surgeon rotating in at critical junctures to lend his specific expertise.

After performing a circular craniotomy, the dura was opened in cruciate fashion. The operating microscope was introduced through a prominent sulcus selected as the entry point. To displace delicate tissues and folds of the brain—and limit intraoperative damage—a tubular retractor was advanced along the chosen trajectory into the atrium of the lateral ventricle, entering the thalamus at a point identified by the microscope and pointer as superior and lateral to the choroid plexus. Precise navigation for microdissection was enabled by visual tracking.

Immediately after making a small corticectomy, the surgeons encountered hemosiderin staining within the tissue. A large developmental venous anomaly was identified medially and preserved intact. “The lesion was only a few millimeters deep to the surface, just as we had seen in presurgical imaging,” Dr. Riina recalls. “We worked in turns to resect the cavernous malformation and evacuate old hemorrhage products so that we could ensure that we reached the borders in all planes.”

The thorough excision of the malformation was enabled by comprehensive, imaging-aided preplanning that allowed the surgical team to choreograph the removal without leaving a trace—and set the patient on a swift path to recovery. “Two days after the operation, the patient went home,” reports Dr. Golfinos. “This is a remarkable outcome given the lesion’s treacherous location and the precision approach it demanded.”

**MULTIDISCIPLINARY COLLABORATION AND CONCENTRATED RESOURCES ENHANCE NEUROVASCULAR CARE**

This achievement, notes Dr. Riina, is a credit to the collaboration and teamwork fostered by experts in the Center for Stroke and Neurovascular Diseases. “These lesions would be extraordinarily difficult for surgeons to treat without the concentration of advanced neuroimaging, protocols, and neurosurgical expertise available at NYU Langone,” he adds. “Our center is unique in that respect, giving patients with unique and complex cases options for successful surgical treatment that are simply unavailable elsewhere.”
Launched in 2017, the NYU Langone Center for Stroke and Neurovascular Diseases has established a multidisciplinary clinical and research hub for its preeminent stroke and neurovascular capabilities.

“We seized the opportunity to create a highly specialized center that integrates the latest research, educational, and clinical advances for patients with stroke and neurovascular disease,” says the center’s director, Howard A. Riina, MD, professor of neurosurgery, neurology, and radiology.

The center comprises the institution’s renowned Comprehensive Stroke Center and its cerebrovascular neurosurgery program, as well as its neurocritical care, stroke neuroradiology, and interventional neuroradiology divisions.

By providing a shared framework, the center will ensure that the latest advances in neurovascular diagnoses, treatments, and patient care are readily shared across these programs, while facilitating collaboration among clinical and basic science investigators in these areas.

In addition, the new center will support ongoing training and education initiatives in neurovascular medicine, with fellowships planned in stroke neurology, interventional neuroradiology, and vascular interventional neurosurgery.

In September 2017, the high-volume stroke units at NYU Langone’s Tisch Hospital in Manhattan and NYU Langone Hospital–Brooklyn were, for the first time, certified as a single Comprehensive Stroke Center by the Joint Commission. In its assessment, the commission praised the rapid, seamless integration of the two campuses, and the center’s emphasis on the entire stroke care continuum, enabled by the center’s excellent rehabilitation facilities and innovative research initiatives. The joint certification underscores NYU Langone’s commitment to providing cutting-edge neurovascular care for a large—and expanding—patient population.

“These approaches represent the new standards of post-stroke care at work in our center,” notes Koto Ishida, MD, assistant professor of neurology and director of NYU Langone’s Stroke Service. “Our certification was a chance to look back at our growth and accomplishments over the last few years and redouble our research efforts—with our newly integrated team—to offer new hope for stroke patients.”

Over 1,100 VASCULAR PROCEDURES PERFORMED IN THE PAST YEAR

55% Reduction IN MEDIAN TIME TO tPA IN THE PAST 7 YEARS

In one avenue of research at the center, investigators are pursuing strategies to help restore function after a stroke, such as improving hand and arm function by promoting connections between the two sides of the brain. Additional center protocols showing promise for stroke patients include the use of music to create enriched environments, tailored treatment to facilitate movement and reduce muscle stiffness, and the creation of personalized rehabilitation protocols based on data feedback from interactive devices.
Gamma Knife Radiosurgery Delivers Precision Treatment for Brain Tumors and AVMs

Two recent, very different, very complex cases highlight the utility and efficacy of Gamma Knife radiosurgery for brain tumors and arteriovenous malformations.

**Precision Radiosurgery Combines with Genetically Tailored Drugs to Control Cancer**

For cancer patients with brain metastases, conventional whole-brain radiation treatment can result in a host of side effects, including memory impairment, fatigue, hair loss, and reduced independence. With the use of Gamma Knife radiosurgery, a more targeted effective alternative, notes Douglas S. Kondziolka, MD, the Gray Family Professor of Neurosurgery, professor of radiation oncology, vice chair of Clinical Research in the Department of Neurosurgery, and director of NYU Langone’s Gamma Knife program, patients can be spared these side effects.

Paradoxically, as systemic treatments improve for various cancers, the incidence of metastases in the brain—less affected by systemic therapies—is increasing, making their targeted treatment more important than ever. In 2017, Dr. Kondziolka and colleagues at NYU Langone published a study in the *Journal of Neurosurgery* demonstrating tumor control rates near 100 percent for brain tumors less than a centimeter in diameter that had been targeted early. “As the evidence continues to mount and prove the Gamma Knife’s efficacy, more oncologists are surveilling patients and finding brain tumors earlier—enabling us to be more proactive and to avoid neurological symptoms,” says Dr. Kondziolka.

A recent patient provides a case in point. Referred to Dr. Kondziolka for consultation, the patient had been previously diagnosed with, and treated for, lung cancer, which involved a mutation that made it susceptible to a targeted drug treatment. In addition to the lung cancer, the patient was found to have 15 small tumors in his brain. “We used precisely targeted Gamma Knife radiosurgery to destroy all 15 tumors, and the patient responded beautifully,” notes Dr. Kondziolka.

During the next year, the patient’s lung cancer improved with drug treatment, and quarterly brain scans showed he was clear of brain tumors. A year after the initial Gamma Knife treatment, however, 13 new brain tumors appeared. “With quarterly surveillance, we spotted them early, when they were still small,” says Dr. Kondziolka, “and at that size, we expected these new tumors to respond very well again.”

As before, Dr. Kondziolka’s team treated the 13 tumors with the Gamma Knife and the patient continued on drug therapy. A year later—two years after the patient’s first brain cancer diagnosis—he remains active and without symptoms, which Dr. Kondziolka attributes in part to the effective genetically targeted lung cancer treatment and in part to the early detection and successful radiosurgery of the brain tumors that did occur. Although tumors could recur, notes Dr. Kondziolka, that has not happened, and the patient maintains perfect neurological function. “Patients like these are breaking the ‘rules’ of cancer,” he adds.

**Gamma Knife Registry Enables Research, Enhances Care**

Having registered several thousand patients, NYU Langone physicians are the leading contributors to the American Association of Neurological Surgeons/ASTRO national radiosurgery registry, which maintains detailed information on patient conditions, histories, and outcomes. The information is available on demand to NYU Langone physicians, and to physicians across the country, to inform care and improve patient diagnosis and treatment.

The greatest value of the registry is that the outcome data are always available: a physician studying the effectiveness of radiosurgery for a specific condition can retrieve those cases quickly. “Keeping the registry current involves significant time and effort, with information required prospectively on each patient, every day—with the payoff being complete data access,” notes Dr. Kondziolka. As the registry continues to evolve, its applications are expected to expand, guiding surgeons toward enhanced outcomes as part of a data-driven approach to patient care.
GAMMA KNIFE SURGERY FOR AN “UNRESECTABLE” AVM

Treatment of arteriovenous malformations (AVMs) in the brainstem always presents a clinical challenge because of the region’s many critical neurologic functions, but in many cases the Gamma Knife has proved to be a critical tool in their treatment. In 2017, the NYU Langone radiosurgery team co-authored a series of publications—two that appeared in the journal Neurosurgery and a third in World Neurosurgery—highlighting multicenter studies of Gamma Knife surgery outcomes for AVMs in the brain, all affirming the surgery’s efficacy for patients less suitable for resection or curative embolization.

For some patients with highly complex AVMs, the Gamma Knife provides a surgical option when traditional resection is ruled out. One such patient presented to Dr. Kondziolka more than five years ago with a congenital brainstem AVM so complex, it was thought to be untreatable. The whole brainstem looked like a massive collection of blood vessels, requiring a very thoughtful treatment approach. “At that time, nobody knew what to do—you could never have cut it out,” notes Dr. Kondziolka. “Because of its complexity, we decided not to touch this AVM.”

Several years later, that plan became untenable, when the AVM hemorrhaged and caused a stroke. “At this point, we had to do something,” continues Dr. Kondziolka. “I talked to colleagues around the country, and we decided to attempt a very careful treatment approach using the Gamma Knife.”

In collaboration with NYU Langone’s neuroradiologists, the team employed diffusion tensor imaging during the procedure to visualize the brainstem nerve fiber tracts. Then, to avoid injuring the nerve fibers, they used a small amount of Gamma Knife energy to target the AVM. “It was a very precise use of the technology,” notes Dr. Kondziolka.

A year later, the patient is doing well. “The AVM looks like it’s closing off, the patient’s motor tracts are fine, and he is an active young man,” says Dr. Kondziolka. “This patient experienced an excellent outcome for what was thought to be an unresectable condition,” he says. “We’re seeing more and more cases where Gamma Knife changes the trajectory of treatment, ultimately delivering a positive outcome.”

Presurgical diffusion tractography of the left corticospinal tract in the brainstem, showing a large AVM centered in the mid and rostral pons.

Six months after treatment, the vascular mass has reduced in size and the tract remains intact and in stable position within the central pons.
Expanded applications of optical coherence tomography (OCT)—delivering 1,000 times the resolution of MRI—and other vision-based diagnostic tools are elucidating the markers and mechanisms behind complex neurological conditions.

**OCT SCANS OF RETINAL NERVE FIBER LAYER SHOW PROMISE FOR EARLY DIAGNOSIS OF MS-RELATED EYE DAMAGE**

Although the optic nerve is involved in the manifestation of multiple sclerosis (MS) for most patients—in a quarter of them, acute optic neuritis is its initial manifestation—the optic nerve remains absent from the condition’s diagnostic criteria. Bolstered by new NYU Langone Health–led research with an international reach, clinicians can now turn to OCT scans of the retinal nerve fiber layer to identify how the optic nerve can add to MS diagnostic criteria.

A high-resolution, noninvasive ocular imaging method, OCT allows clinicians to spot microscopic changes in nerve fiber layer thickness that MRIs can’t detect. “With OCT scans, we have an effective structural measure for this important dimension of MS,” notes Laura J. Balcer, MD, professor of neurology, ophthalmology, and population health and vice chair of the Department of Neurology. Furthermore, Dr. Balcer notes, OCT can identify even very subtle optic nerve damage that occurs before there is any subjective change in vision. This can be useful for early diagnosis for the large cohort of MS patients whose condition begins with acute optic neuritis.

Dr. Balcer and a team of investigators conducted an extensive analysis of OCT scan data from MS patients and from individuals without MS and determined that a five-micron reduction in the thickness of the retinal nerve fiber layer is enough to indicate MS-related nerve damage. In conjunction with the International Multiple Sclerosis Visual System Consortium (IMSVISUAL), researchers are now using these results, published in late 2017, to lead the effort to expand studies of OCT-visualized optic nerve lesions as a potential diagnostic marker for MS. Dr. Balcer, a co-director of IMSVISUAL, and Steven L. Galetta, MD, the Philip K. Moskowitz, MD Professor and Chair of Neurology and professor of neurology and ophthalmology, co-wrote an editorial published in 2017 in *Multiple Sclerosis Journal*, advocating for the inclusion of the optic nerve in the international MS diagnosis criteria.

OCT imaging technology affects the MS field beyond its use in measuring acute optic nerve damage from MS, adds Dr. Balcer. Since optic nerve thinning has been found to reflect the overall impact of MS on the central nervous system, she speculates that OCT retinal scans could one day be used as one of several measures to track overall progression of the disease, including therapeutic response.
ASSESSING CONCUSSION-RELATED BRAIN DAMAGE WITH VISUAL SCREENS

Researchers are also investigating the use of OCT and other vision-based testing to measure function in the setting of concussion and related neurological damage. The Division of Neuro-Ophthalmology plays a leadership role in NYU Langone’s Concussion Center, where research on the use of a rapid number-naming test and laboratory-based eye tracking is aiding in the sideline diagnosis and assessment of sports-related concussion.

The division is spearheading a study of OCT in active and retired contact-sport athletes. At the same time, NYU Langone is an enrolling site for a Boston University-led, National Institutes of Health-funded study of potential markers for chronic traumatic encephalopathy among retired football players and individuals with little or no contact sport exposure.

In a separate study, published in 2017 in the Journal of Neuro-Ophthalmology, division researchers and colleagues from the Illinois College of Optometry found that average retinal nerve thickness among collision-sport athletes was reduced relative to controls. The difference was especially pronounced among the study’s subgroup of boxers, who had an average nerve thickness reduction of almost 11 microns compared with the control group. “This study suggests that OCT may identify athletes who have had significant repetitive traumatic brain injury,” notes Dr. Galetta. A test of the same subjects’ low-contrast letter acuity also found significant differences between the athletes and controls, with boxers again showing the greatest disparity.

Further investigations are under way to better determine the relationship between retinal nerve fiber loss and traumatic brain injury.

“We were fortunate to be early adopters of OCT and low-contrast visual tests in MS, over a decade ago,” says Dr. Galetta. “Now we’re taking the paradigms we learned in MS and applying them to traumatic brain injury, studying visual tests and OCT as outcome measures in other neurological conditions.”

EXPANDING THE USE OF RAPID EYE MOVEMENTS AS A CLUE TO NEUROLOGICAL ILLNESS

With the help of the EyeLink high-speed camera, investigators in the Eye Movement Testing Lab are seeking a new understanding of the eye movement abnormalities associated with a variety of neurological disorders—insights that could lead to enhanced diagnostic and treatment approaches.

NYU Langone researchers have made important connections between eye movements and concussion over the past several years, finding that concussion produces an increased intersaccadic interval—the time it takes the eye to prepare for rapid jumps from one focal point to another—explaining slower performance on rapid number-reading tests. “Two factors that may play a role in this increased intersaccadic interval in concussion are prolongation of the latency period—the time that the brain needs to prepare to make fine eye movements—and neurocognitive dysfunction,” says Janet C. Rucker, MD, the Bernard A. and Charlotte Marden Professor of Neurology, professor of ophthalmology, and Chief of the Division of Neuro-Ophthalmology.

Dr. Rucker leads the Eye Movement Testing Lab in partnership with two physicians at NYU Langone’s Rusk Rehabilitation: John-Ross Rizzo, MD, assistant professor of rehabilitation medicine and neurology, and Todd E. Hudson, PhD, research assistant professor of rehabilitation medicine. Together, these investigators are evaluating how attention and cognition affect the scores of concussed patients. “Once we understand concussion’s activity in the brain, we hope to find ways to predict recovery and develop therapies,” Dr. Rucker says.

Separately, investigators are working on EyeLink applications to enhance diagnosis and therapeutic intervention in multiple sclerosis (MS) and Parkinson’s disease. The information gained from detailed analysis of nystagmus and internuclear ophthalmoplegia may help investigators to advance therapeutic options for MS, and rapid number-reading and picture-naming tests are being studied as quick screening tools for vision problems in MS. In Parkinson’s, eye movement analysis is being used to confirm diagnosis of atypical Parkinson’s disorders such as progressive supranuclear palsy and multiple system atrophy.

“It’s hard to name a neurological disease that doesn’t have the capacity to affect eye movements in some way,” notes Dr. Rucker. “Eye movement recording technology can help us establish a more accurate diagnosis and evaluate potentially more efficacious treatments.”
Complex Case: Intramedullary Cavernoma Calls for Intervention—but Carries Risks

For a 29-year-old patient presenting with a rare and risky intramedullary cavernoma, the use of advanced diffusion tensor imaging (DTI), pioneered at NYU Langone for spinal surgery, proved essential to a successful resection—and restored quality of life.

When Anthony K. Frempong-Boadu, MD, associate professor of neurosurgery and director of the Division of Spinal Surgery, evaluated the patient’s symptoms and progressing condition, he quickly saw the dilemma: Resection of such a complex tumor required the use of a leading-edge, highly precise imaging technique that had only a limited track record—but postponing the surgery was not an option. The debilitating effects of the intradural intramedullary cavernoma had become increasingly apparent in the year since it was first diagnosed, and they would only worsen as the tumor grew. “It was clear that this tumor needed to be managed surgically,” says Dr. Frempong-Boadu.

However, such a resection carried formidable risks. Intramedullary tumors, which account for just 2 to 4 percent of all intrinsic central nervous system tumors, often permeate the surrounding tissues after arising from the cells of the spinal cord. Resection of this tumor would require a myelotomy—dissection of the spinal cord at the midline—to achieve access, a surgery with a high risk of permanent morbidity, damage to paraspinal structures, cerebrospinal fluid leak, central nervous system infection, and significant neurological injury, including paraplegia. The tumor was densely adhered to surrounding nerve tissue, increasing the likelihood of surgical complications. Other leading tertiary centers had been reluctant to perform the operation.

ADVANCED NEURAL IMAGES PROVIDE A ROAD MAP FOR RESECTION

With Dr. Frempong-Boadu’s successful DTI application two years earlier, NYU Langone had become the nation’s only center to use real-time intraoperative functional data during spinal surgery. In this case, use of this approach—which employs multiple high-information MRI scans of the water diffusion rates across nerve membranes to map the exact location of a patient’s nerve tracts—was critical to keeping the patient neurologically intact as the tumor was resected.

“With DTI, combined with Surgical Theater’s three-dimensional virtual imagery of the surgical site, we could visualize exactly where the motor tracts of the patient’s spinal cord and all other relevant structures were at all times, so we could go in and confidently remove the tumor,” says Dr. Frempong-Boadu.
A MULTIDISCIPLINARY TEAM EFFORT AUGMENTS ADVANCED IMAGING

With the full array of spinal imaging techniques at work in the operating room, the surgical team began with a decompressive osteoplastic laminectomy of the third and fourth thoracic vertebrae. They then located the tumor via ultrasound and confirmed the location using an intraoperative CT scan, intraoperative navigation, and Surgical Theater’s virtual imagery of the site. The dura was opened and retracted, the arachnoid layer was dissected free and opened, and the dorsal root entry zone was identified using intraoperative navigation. The surgeons performed a myelotomy and isolated the tumor, carefully dissecting it free from the underlying neural tissue, utilizing both microscope-integrated stereotactic navigation and three-dimensional visualization. After removal of the tumor, the dura was closed and the vertebrae were reconstructed.

“The imaging precisely outlined the tumor in three dimensions, so I knew when I needed to back off and when I could press ahead right to its margin,” explains Dr. Frempong-Boadu. “In these procedures, our goal is to get the greatest amount of resection possible with the least amount of functional decline.”

BEYOND TUMORS: EXTENDING THE NEURAL MAPS’ REACH

Although neurophysiological monitoring indicated some reduction in left leg sensory and motor signals during this patient’s operation, says Dr. Frempong-Boadu, the procedure concluded with the intramedullary cavernoma completely resected and no motor impairment beyond a very slight limp. “A half year later, the patient is doing really well—an incredible outcome given the complexity of his tumor,” he adds.

Since assembly of the neural maps is itself a highly complex process, use of the maps is currently limited to the most complex, high-acuity spine tumor cases. The neurosurgery and neuroradiology groups are working on new automation processes to streamline image acquisition and nerve map construction, to potentially extend the technology’s application to cervical spondylosis, myelopathy, and other spinal conditions. “The applicability of this mapping to spinal disease extends well beyond its current use,” says Dr. Frempong-Boadu. “If we can accomplish that, it will be another huge step forward.”
The Pursuit of New Alzheimer’s Pathways, Fueled by Promising Research

The Center for Cognitive Neurology is working to unravel the mechanisms behind Alzheimer’s disease and other neurocognitive disorders, while forging new pathways toward transformative treatment and prevention modalities.

PROMISING IMMUNOTHERAPIES MOVE CLOSER TO HUMAN TESTING

In 2017, the Center for Cognitive Neurology conducted several groundbreaking studies that could give rise to novel Alzheimer’s disease immunotherapies. “We now know that Alzheimer’s is driven by many pathways, which can vary from patient to patient,” notes Thomas M. Wisniewski, MD, the Gerald J. and Dorothy R. Friedman Professor of Neurology, professor of pathology and psychiatry, and director of the center. “As our understanding of Alzheimer’s improves, we’re testing many promising therapeutic interventions.”

One such intervention involves conformational monoclonal antibodies, the only agents known to target neurotoxic oligomers—clusters of misfolded proteins associated with both amyloid-beta and tau, and with neurodegenerative diseases including Parkinson’s. In an article in *Scientific Reports* in 2017, NYU Langone Health investigators described how a protein fragment derived from the rare disease British amyloidosis can be used to prime antibodies to attack the beta-sheet structure common across various oligomers. In the near future, center researchers hope to move this unified treatment approach, successful in animal studies, to human trials.

In another 2017 animal study, published in *The Journal of Neuroscience*, Allal Boutajangout, PhD, and Thomas M. Wisniewski, MD
center investigators demonstrated the efficacy of the NYU Langone–developed immunotherapy drug Class B CpG ODN in reducing cerebral amyloid angiopathy, another key element of Alzheimer’s pathology, with accompanying short-term memory improvements. This drug, previously found to enhance clearance of amyloid-beta and tau in animals, boosts activity of microglia—the primary immune cells in the brain—by stimulating Toll-like receptor 9. The center hopes to commence phase I human trials within the next two years.

Another 2017 study published in Scientific Reports extended NYU Langone’s groundbreaking investigations of interaction between amyloid-beta and apolipoprotein E (apoE)—the brain’s main lipid-carrying protein, which can accelerate accumulation of amyloid-beta in the brain. In the study, a novel peptoid developed by NYU Langone researchers was highly effective at preventing amyloid-beta from binding with apoE, including apoE4, the most neurotoxic apoE variant.

In a fourth study, published in early 2017 in Current Alzheimer Research, center researchers showed that human umbilical cord stem cells injected into the carotid arteries of transgenic mice can cross the blood–brain barrier and reduce Alzheimer’s-related pathology, offering another possible dementia-prevention approach. Meanwhile, the center continues its phase III clinical trials of the monoclonal antibody aducanumab, which appears to clear amyloid plaque from the brains of individuals with early Alzheimer’s.

**UNRAVELING THE BIOLOGY OF ALZHEIMER’S DISEASE**

As new therapies are pursued, the center continues to probe the biology underlying Alzheimer’s. In a seminal 2017 study published in Acta Neuropathologica, researchers applied proteomics to analyze amyloid plaques associated with rapidly progressive Alzheimer’s disease. The researchers found that the plaques contained significantly higher levels of neuronal proteins and lower levels of astrocytic proteins compared with standard Alzheimer’s, opening a new research pathway. The center will pursue the pathway with support from a five-year, $3.9 million R01 grant awarded by the National Institutes of Health (NIH) in 2017. “This study was critically dependent on the proteomic core that we have here at NYU Langone, one of the best in the world,” says Dr. Wisniewski.

Another animal study, led by Martin Sadowski, MD, PhD, associate professor of neurology, psychiatry, and biochemistry and molecular pharmacology, adds a key piece to the apoE puzzle. The 2017 study, published in Molecular Degeneration, found that transgenic mice with the apoE4 gene variant—the greatest genetic risk factor for late-onset Alzheimer’s—showed the most robust stimulation of microglia and the greatest reduction in amyloid plaques when injected with the experimental anti-amyloid-beta antibody 10D5. “This offers hope that Alzheimer’s vaccines may work better in human apoE4 carriers, even though they tend to get Alzheimer’s at a younger age and have more amyloid buildup than people without the variant,” says Dr. Sadowski. He and his team are engaged in further study of this phenomenon through two NIH grants.
Patients with Movement Disorder Symptoms Find New Relief in Neuromodulation

Clinical trials under way at NYU Langone Health’s Center for Neuromodulation are expanding the availability and applications of deep brain stimulation (DBS) techniques, MRI-guided ultrasound approaches, and other innovations—bringing benefits to a broad range of patients.

NYU Langone Charts New Territory with Second-Generation DBS Devices

Medtronic’s DBS device has been the only FDA-approved DBS technology for more than 20 years, but the field is now expanding with the recent approval of Abbott’s DBS system, as well as an ongoing clinical trial utilizing a DBS system manufactured by Boston Scientific. Both new devices offer more nuanced distribution of electrical stimulation, which may prove advantageous in some cases, says Michael H. Pourfar, MD, assistant professor of neurosurgery and neurology and co-director of NYU Langone’s Center for Neuromodulation—the only facility in New York with extensive experience with all three devices.

All three technologies have their strengths, says the center’s other co-director, Alon Y. Mogilner, MD, PhD, associate professor of neurosurgery and anesthesiology. “At the moment, the Medtronic device is the only MRI-compatible system, which can benefit certain patients,” he notes. “In other instances, the alternate approaches broaden the therapeutic window by letting us more effectively troubleshoot side effects, such as impaired speech or balance.”

Clinicians used to grapple with simply whether someone was a candidate for DBS. Now, observes Dr. Mogilner, “we’re having increasingly sophisticated conversations about which DBS system to use and which targets to select within that system.”

Adding to the Neuromodulation Arsenal: Focused Ultrasound

The center is investigating other neuromodulation treatment modalities, including MRI-guided focused ultrasound, which noninvasively targets precise areas of brain tissue to alleviate tremor. Under MRI guidance, the ultrasound device first heats mapped tissue, producing a temporary effect so clinicians can confirm that ablating the targeted area will improve symptoms without problematic side effects. Then the ultrasound beam is intensified to destroy the selected brain cells associated with the tremor.
“Since this nonsurgical approach requires little or no anesthesia, it can benefit patients who are too elderly or ill for DBS,” notes Dr. Pourfar. “Unlike with DBS, there’s no implanted hardware and no need for repeated visits to adjust the programming.” Although focused ultrasound is currently used only for tremors, the center’s clinicians are working with NYU Langone neuroradiologists to identify possible ablation targets for symptoms such as stiffness or slowed movement. The system will be fully operational in early 2018, and clinicians are hoping to begin clinical trials soon after.

NEW FRONTIERS IN DBS FOR TOURETTE’S AND REFRACTORY PARKINSON’S

DBS can also offer hope for those with treatment-resistant Tourette’s syndrome. The center’s clinicians continue to pioneer this off-label application with groundbreaking research, including a recent study of 13 NYU Langone patients who underwent thalamic DBS for severe Tourette’s, the largest such series in the United States. Led by Dr. Mogilner and Dr. Pourfar and published in April 2017 in the Journal of Neurosurgery, the study found that after the DBS procedure, the patients’ tic severity decreased by 50 percent, on average, by the time of their last postsurgery follow-up.

“While results can vary, DBS has been life-changing for some Tourette’s patients,” says Dr. Mogilner. “We’re all working to gain a better understanding of this therapeutic approach, leading, we hope, to FDA approval of DBS as a Tourette’s treatment.”

Center researchers continue to mine their own data in combination with the national Tourette’s database at the University of Florida in order to refine the target brain regions and stimulation parameters used to treat the condition. Clinicians have also been refining their use of rescue leads—additional electrode clusters implanted in Parkinson’s patients who continue to experience significant tremors or dyskinesia after initial bilateral DBS lead implantation. “We’ve found that adding the third electrode provides benefit to a number of patients,” says Dr. Mogilner, who is leading the preparation of an article on the center’s rescue lead patient series. “This is an area where the field will continue to improve,” he notes.

PIONEERING GAMMA KNIFE SURGERY AS TREATMENT FOR OBSESSIVE-COMPULSIVE DISORDER

Gamma Knife radiosurgery has emerged alongside FDA-approved DBS as a novel treatment for obsessive-compulsive disorder (OCD). The approach uses radiation to create a pinpoint lesion in well-identified bilateral targets in the anterior limb of the internal capsule of the brain, between the thalamus and the frontal lobe, known to be involved in OCD.

“We are one of the few institutions in the world offering Gamma Knife radiosurgery as an OCD treatment modality,” says Douglas S. Kondziolka, MD, the Gray Family Professor of Neurosurgery, professor of radiation oncology, vice chair for Clinical Research in the Department of Neurosurgery, and director of NYU Langone’s Gamma Knife program.

Dr. Kondziolka’s team is conducting a national study on Gamma Knife OCD outcomes; though investigators are seeing positive anecdotal results, the brain requires time to rewire itself, so it can take years to produce the full treatment benefit.

“This approach can moderate symptoms for the most debilitated OCD patients,” notes Dr. Kondziolka.

“Following treatment, patients score better on measures of thought resistance and behavior avoidance; the goal is to reduce the intrusive thoughts and compulsive rituals that so dominate their lives,” Dr. Kondziolka adds.

Joshua S. Silverman, MD, PhD, and Douglas S. Kondziolka, MD
Horacio Kaufmann, MD, was a selected keynote speaker at the 28th International Symposium on the Autonomic Nervous System in Clearwater, Florida.


Chandranath Sen, MD, served as a program moderator at the 27th Annual Meeting of the North American Skull Base Society in New Orleans, Louisiana, and at the annual Association of Neurological Surgeons meeting in Los Angeles, California.

AWARDS & RECOGNITION: NEUROLOGY & NEUROSURGERY

Erich G. Anderer, MD, was recognized by the Medical Society of the County of Kings with the 2017 Award of Excellence.

Orrin Devinsky, MD, received the J. Kiffin Penny Excellence in Epilepsy Care Award from the American Epilepsy Society.

David H. Harter, MD, was appointed president elect of the New York State Neurosurgical Society.

Douglas S. Kondziolka, MD, was appointed treasurer of the American Academy of Neurological Surgery.

Lauren B. Krupp, MD, was appointed chair of the International Multiple Sclerosis Cognition Society steering committee.

Mia T. Minen, MD, MPH, was appointed chair of the Emergency Medicine, Inpatient and Refractory Section of the American Headache Society.

James L. Stone, MD, was chosen as a consultant for the National Aeronautics and Space Administration.

Blanca Vazquez, MD, was appointed chair of the Professional Advisory Board of the Epilepsy Foundation of Metropolitan New York.

Thomas M. Wisniewski, MD, was appointed to the board of directors of the New York City chapter of the Alzheimer’s Association.


Academic Activities


Academic Activities


Academic Activities

SELECT PUBLICATIONS: NEUROSURGERY


Sheehan JP. Early versus late gamma knife radiosurgery


Leadership

**NEUROSURGERY**

John G. Golfinos, MD  
Associate Professor of Neurosurgery  
and Otolaryngology  
Chair of the Department of Neurosurgery  
Co-Director, Brain Tumor Center  
Investigator, Neuroscience Institute

Erich G. Anderer, MD  
Assistant Professor of Neurosurgery  
Chief of Neurosurgery, NYU Langone Hospital—Brooklyn

Mitchell Chesler, MD, PhD  
Professor of Neurosurgery and Neuroscience and Physiology  
Vice Chair of Research  
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Anthony K. Frempong-Boadu, MD  
Associate Professor of Neurosurgery and Orthopedic Surgery  
Director, Division of Spinal Neurosurgery  
Co-Director, Spine Center

David H. Harter, MD  
Associate Professor of Neurosurgery  
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Paul Huang, MD  
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Alon Mogilner, MD, PhD  
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Director, Center for Neuromodulation

Noel I. Perin, MD  
Associate Professor of Neurosurgery  
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Howard A. Riina, MD  
Professor of Neurosurgery, Neurology, and Radiology  
Vice Chair of the Department of Neurosurgery  
Director, Endovascular Surgery  
Associate Director, Neurosurgery Residency Training Program  
Director, Advanced Stroke Center

Chandranath Sen, MD  
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Vice Chair for Education  
Director, Skull Base Surgery

James L. Stone, MD  
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Chair of Service, VA NY Harbor Health Care System

Lee E. Tessler, MD  
Associate Professor of Neurosurgery  
Chief of Neurosurgery, NYU Winthrop Hospital

Jeffrey H. Wisoff, MD  
Professor of Neurosurgery and Pediatrics  
Director, Division of Pediatric Neurosurgery

**NEUROLOGY**

Steven L. Galetta, MD  
Philip K. Moskowitz, MD Professor and Chair of Neurology  
Professor of Neurology and Ophthalmology  
Chair of the Department of Neurology

Laura J. Balcer, MD  
Professor of Neurology, Ophthalmology, and Population Health  
Vice Chair of the Department of Neurology

William B. Barr, PhD  
Associate Professor of Neurology and Psychiatry  
Director, Neuropsychology Program

Aleksandar Beric, MD  
Professor of Neurology, Neurosurgery, Orthopedic Surgery, and Rehabilitation Medicine  
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Catherine Cho, MD  
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Professor of Neurology, Neurosurgery, and Psychiatry  
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Albert S. Favate, MD  
Associate Professor of Neurology  
Director, Division of Vascular Neurology

Andrew S. Feigin, MD  
Professor of Neurology  
Associate Chair of Neurology, Clinical Research  
Executive Director, Marlene and Paolo Fresco Institute for Parkinson’s and Movement Disorders

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Chief of Neurology, NYU Langone Hospital—Brooklyn  
Vice Chair of Neurology, NYU Langone Hospital—Brooklyn

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Professor of Neurology  
Associate Chair of Neurology, Clinical Practices  
Director, Division of Parkinson’s and Movement Disorders

Richard M. Hanson, MD  
Clinical Associate Professor of Neurology  
Chief of Service, VA NY Harbor Health Care System

Horacio Kaufmann, MD  
Felicia B. Axelrod Professor of Dysautonomia Research  
Professor of Medicine and Pediatrics  
Director, Division of Autonomic Disorders

Lauren B. Krupp, MD  
Nancy Glickenhaus Pier Professor of Pediatric Neurology  
Director, Division of Multiple Sclerosis

Aaron S. Lord, MD  
Assistant Professor of Neurology and Neurosurgery  
Director, Division of Neurocritical Care

Lawrence C. Newman, MD  
Professor of Neurology  
Director, Division of Headache Medicine

Janet C. Rucker, MD  
Bernard A. and Charlotte Marden Professor of Neurology  
Professor of Ophthalmology  
Chief, Division of Neuro-Ophthalmology  
Director, Neuro-Ophthalmology Fellowship Program

Howard W. Sander, MD  
Professor of Neurology, Psychiatry, and Anesthesiology, Perioperative Care, and Pain Medicine  
Associate Chair, Education  
Director, Division of Neuromuscular Medicine

Heidi Schambra, MD  
Assistant Professor of Neurology and Rehabilitation Medicine  
Director, Division of Neuropsychiatry

Anuradha Singh, MD  
Professor of Neurology  
Director, Neurology Service, NYCH+Hospitals/Bellevue

Harold J. Weinberg, MD, PhD  
Clinical Professor of Neurology  
Associate Chair, Clinical Affairs  
Director, Division of General Neurology  
Chief, Neurology Service

John T. Wells, MD  
Clinical Professor of Neurology  
Director, Division of Child Neurology

Thomas M. Wisniewski, MD  
Gerald J. and Dorothy B. Friedman Professor of Neurology  
Professor of Pathology and Psychiatry  
Associate Chair, Research  
Director, Division of Cognitive Neurology

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1,519 Beds
98 Operating Rooms
172,072 Emergency Room Visits
68,884 Patient Discharges
4,500,000 Outpatient Faculty Practice Visits
9,654 Births

3,633 Physicians
5,104 Nurses
516 MD Candidates
85 MD/PhD Candidates
263 PhD Candidates
418 Postdoctoral Fellows
1,327 Residents and Fellows

5,087 Original Research Papers
549,707 Square Feet of Research Space
$359M NIH Funding
$364M Total Grant Revenue

*Numbers represent FY17 (Sept 2016–Aug 2017) and include NYU Langone Hospital—Brooklyn