

Neurology & Neurosurgery

#7

IN U.S. NEWS &
WORLD REPORT

14,000 +

NEUROSURGERY
PATIENT VISITS

194

FULL-TIME
NEUROLOGY FACULTY

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Dear Colleagues and Friends:



A handwritten signature in black ink that reads "Steve Galetta".

STEVEN L. GALETTA, MD

Phillip K. Moskowitz, MD Professor and Chair of
Neurology, Department of Neurology

Professor of Neurology and Ophthalmology



A handwritten signature in black ink that reads "John G. Golfinos".

JOHN G. GOLFINOS, MD

Chair, Department of Neurosurgery

Associate Professor of Neurosurgery
and Otolaryngology

NYU Langone Medical Center's Departments of Neurology and Neurosurgery rank among the nation's elite specialty programs—a point of pride that reflects our dedication to clinical, educational, and research advancements.

Yet none of our work would lead to meaningful improvements in patient care if not for the extensive interdisciplinary collaboration that influences everything we do. Indeed, our collaborative approach can be seen in virtually every aspect of our clinical and research activities. Our neurosurgeons have partnered with NYU Langone's neuroradiologists to pioneer new navigational techniques—from three-dimensional virtual imaging to diffusion tensor imaging, intraoperative CT scans, and ultra-rapid MRI scans—to make complex operations safer and more effective. Separately, neuro-ophthalmologists are partnering with NYU's Tandon School of Engineering to develop new biomarkers—and screening tools—for neurological conditions such as concussion, atypical Parkinson's, and multiple sclerosis.

This teamwork complements new initiatives that capitalize on technological innovation in the field. As “big data” envelops nearly every corner of medicine, our neurologists and neurosurgeons are using data collection in partnership with the Medical Center's IT Department, Clinical and Translational Science Institute, and the Population Health Biomedical Informatics program to detect meaningful trends in patient populations. The Multiple Sclerosis Comprehensive Care Center is now part of a major, multicenter project compiling data from adult and pediatric patients, while NYU Langone's Comprehensive Epilepsy Center participates in a national registry tracking sudden death related to epilepsy. In addition, the neurosurgery department's Center for Advanced Radiosurgery recently launched a comprehensive program to aggregate patient data in real time, with other divisions following close behind.

Our brain tumor researchers have spearheaded a unique collaboration with NYU Langone's neuropathologists to genetically test the tissues of every brain tumor patient we treat—an approach that allows clinicians to deliver customized therapeutic approaches based on the genetic profiles of patients' tumors. Meanwhile, a partnership between the Center for Cognitive Neurology and the Medical Center's Neuroscience Institute is yielding cutting-edge insights into brain degeneration, which are being translated into promising new treatments for people with memory disorders.

The payoff from each of these efforts has never been greater for our patients. In this report, you'll find complex cases highlighting the efficacious options enabled by interdepartmental surgical collaboration, including skull base tumor resections using nasal endoscopic approaches and hearing-restorative auditory brainstem implants for patients with prior brain tumors. In Parkinson's disease treatment and research, collaboration has fostered a new understanding of the brain circuits involved in motor disorders, while neurogenetics partnerships have elucidated a possible link between lysosomal storage impairment in Gaucher's disease and increased risk for Parkinson's disease.

As our expertise expands and our patient volume increases, our ultimate aim continues to be to enhance the quality of care we bring to patients. To achieve this, we monitor our patients' neurological status with state-of-the-art diagnostic techniques and work collaboratively to develop ever more effective therapies to manage their conditions. With our understanding of neurological illness advancing more rapidly than ever, we believe that even greater progress lies directly ahead.

Neurology & Neurosurgery

Volume

68,000 +

NEUROLOGY PATIENT VISITS

An 11% increase

14,000 +

NEUROSURGERY
PATIENT VISITS

500 +

GAMMA KNIFE CASES

NEUROSURGICAL
VOLUME HAS
**MORE THAN
DOUBLED**

in the last 5 years

Funding

> \$6.5M

IN NEUROLOGY GRANT
FUNDING AWARDED

> \$12.4M

IN NEUROSURGERY GRANT
FUNDING AWARDED IN THE LAST 2 YEARS

Accolades

#7

IN THE COUNTRY
FOR NEUROLOGY
AND NEUROSURGERY

in *U.S. News & World
Report's* "Best Hospitals"



Faculty & Residents

**194 FULL-TIME
NEUROLOGY
FACULTY**

19 JOINED IN 2016

**26 FULL-TIME
NEUROSURGERY
FACULTY**

3 JOINED IN 2016

90

RESIDENCY POSITIONS

18 IN NEUROSURGERY

72 IN NEUROLOGY

150

YEARS OF MODERN
NEUROLOGICAL CARE

Represents FY16 (Sept 2015–Aug 2016) unless otherwise noted



NYU Langone Medical Center



#10

**IN THE NATION
BEST HOSPITALS**

and nationally ranked in 12 specialties, including top 10 rankings in Orthopaedics, Geriatrics, Neurology & Neurosurgery, Rheumatology, Rehabilitation, Cardiology & Heart Surgery, and Urology. Nationally ranked in Cancer, Diabetes & Endocrinology, Ear, Nose & Throat, Gastroenterology & GI Surgery, and Pulmonology



#11

**IN THE NATION
BEST MEDICAL SCHOOLS
FOR RESEARCH**

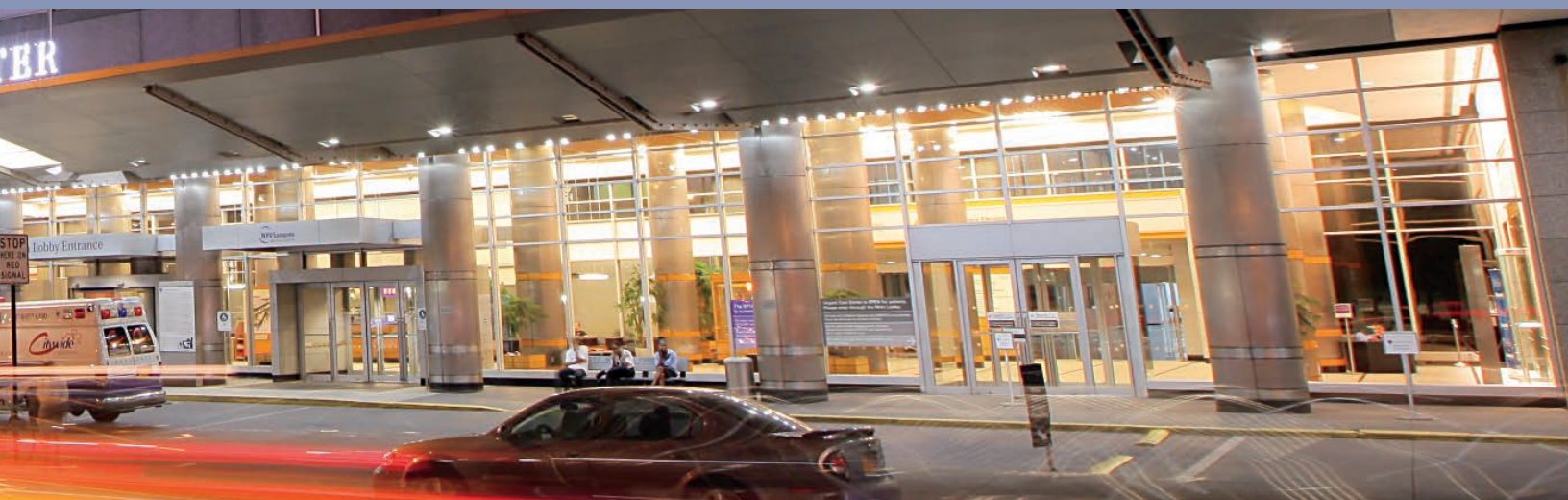
and a leader in innovation in medical education, including accelerated pathways to the MD degree



LEADER

**IN QUALITY CARE AND
PATIENT SAFETY**

and recognized for superior performance as measured by Vizient's nationwide 2016 Quality and Accountability Study



New Faculty, Research Inform New Modes of Care

Neurosurgery in Three Dimensions

NYU Langone's neurosurgeons made international news in November 2016, when the three-dimensional print model they used for a patient with a complex skull base deformity made the *Journal of Neurosurgery's* November cover. The publication highlighted just one of the many complex, cutting-edge skull base procedures the department has performed using patient-specific three-dimensional print models, which have also expanded the department's educational capabilities with challenging cases.

"We're working on a three-dimensional model that can be used to simulate

endoscopic endonasal skull base surgeries," says Donato R. Pacione, MD, assistant professor of neurosurgery. Dr. Pacione has teamed with Chandra Sen, MD, professor of neurosurgery, and Surgical Theater, the makers of Precision Virtual Reality™, a widely used software platform for translating virtual three-dimensional data into realistic three-dimensional print models of patients' skulls and nasal passages. This software has the potential to enable clinicians to realistically simulate surgeries to later be performed on patients' actual bone structure and tumors.

"It's a great teaching tool for residents, since they don't get to perform these procedures often, and it may also help practicing surgeons rehearse difficult cases," says Dr. Pacione. He and his colleagues are now studying which print materials will produce the most realistic physical models. "The ultimate goal," he adds, "is to create a drillable three-dimensional print model that lets us simulate open and endoscopic skull base surgeries."



↑ (from left) Anthony K. Frempong-Boadu, MD, Noel I. Perin, MD, and Thomas J. Errico, MD

NYU Langone and NYU Lutheran Receive The Joint Commission Stroke Care Designation

Following intensive two-day site visits, the acute-care stroke programs at NYU Langone and NYU Lutheran have received The Joint Commission's Comprehensive Stroke Center designation. "With the merger of the two hospitals, we've aligned the operations of both stroke programs," explains Koto Ishida, MD, assistant professor of neurology and medical director of the stroke service at NYU Langone. "By sharing the best practices of these two very high-quality divisions, we're refining our protocols and processes even further."

NYU Lutheran's stroke service, which has the second-highest volume in New York State, has also been awarded Target Stroke Elite status—meaning 75 percent or more of its acute stroke patients receive TPA within 45 minutes of arrival. NYU Langone's service, which had the lowest stroke mortality rate in the nation in 2014, has seen its own case volume increase steadily: some 1,300 stroke code patients were treated there in 2016, a nearly 40 percent increase from 2015, with an average door-to-needle time of 31 minutes.

Both institutions maintain teams of experienced neurointerventionalists, proactively coordinate their patients' post-discharge care, and offer comprehensive stroke rehabilitation programs. "We emphasize high quality across the stroke care continuum," says Dr. Ishida. "A lot of centers are strong in hyper-acute care, but we have all points of the stroke timeline covered in both boroughs."



↑ Koto Ishida, MD

ADVANCED STROKE CARE, BY THE NUMBERS

2

Comprehensive Stroke
Center Designations

40 %

increase in cases
since 2015

75 %

OR MORE

acute stroke patients receive TPA
within 45 minutes at NYU Lutheran

NYU Lutheran Rounds Out Clinical Team with Senior Neurosurgeons

NYU Lutheran Medical Center has added two highly experienced neurosurgeons to its clinical staff in Brooklyn. Erich G. Anderer, MD, clinical assistant professor of neurosurgery at NYU Langone since 2010, is NYU Lutheran's new chief of neurosurgery, and David S. Gordon, MD, assistant professor of neurosurgery at NYU Langone, joins the NYU Lutheran team as director of cranial, vascular, and skull base neurosurgery. In addition

to providing neurosurgical care, both physicians have published extensive clinical research highlighting a range of advances in neurosurgery practice.

Dr. Anderer has also been an attending physician in neurosurgery and orthopedics at Maimonides Medical Center in Brooklyn, and most recently he was director of the Maimonides neurotrauma program. Dr. Gordon served on the neurosurgical staff at Montefiore Medical Center in the Bronx

for 11 years, most recently as director of vascular neurosurgery.

"The appointments of Dr. Anderer and Dr. Gordon will not only give the people of Brooklyn access to the highest-quality neurosurgical care, but will also strengthen continuity and collaboration between NYU Lutheran and the team at NYU Langone," notes John G. Golfinos, MD, chair of NYU Langone's Department of Neurosurgery.

Chief of Neurosurgery Appointed to Veterans Administration NY Harbor Health Care System

In October 2016, James L. Stone, MD, joined NYU Langone as chief of neurosurgery for the Veterans Administration (VA) NY Harbor Health System (formerly the Manhattan VA Medical Center), the primary neurosurgical referral center for more than 1 million veterans in Connecticut, Pennsylvania, New Jersey, and southern New York state. The division is staffed by attending physicians from NYU Langone's

Department of Neurosurgery and includes a 12-bed ICU shared by cardiac and general surgery, a 4-bed neurosurgery step-down unit, and 17 inpatient beds on a combined neurology and neurosurgery floor.

Board certified in neurosurgery, neurology, and neurophysiology, Dr. Stone has a particular interest in bringing automated neurological monitoring processes into the ICU setting. Before joining the

NYU Langone team, he worked for 30 years at Cook County Hospital in Chicago, where he served as chair of neurosurgery for 20 years and as professor and attending neurosurgeon at the University of Illinois. "Most of my career has been in public service," notes Dr. Stone, "and I look forward to continuing on this path at VA NY Harbor Health Care."

PEDIATRIC EPILEPSY SURGEON JOINS NEUROSURGERY DEPARTMENT

Amanda L. Yaun, assistant professor of neurosurgery and a specialist in pediatric epilepsy surgery, joined the Department of Neurosurgery in August 2016. Dr. Yaun comes to the Medical Center from the University of Oklahoma Health Sciences Center, where, as Chief of Pediatric Neurosurgery, she helped establish a pediatric epilepsy program.

At NYU Langone, Dr. Yaun is focusing her work on procedures to control children's seizures, as well as on improving the patient and family experience with surgery. Says Dr. Yaun, "These young patients often spend a week in the hospital prior to surgery with electrodes implanted under their skull to map their seizures; the more we can do to make that experience comfortable, the better." She adds, "It's not just about preventing seizures—it's about enabling these kids to live up to their full potential."



↑ Amanda L. Yaun, MD

NYU LANGONE MEDICAL CENTER AFFILIATION WITH WINTHROP-UNIVERSITY HOSPITAL BRINGS EXPANDED AND ENHANCED HEALTHCARE NETWORKS TO LONG ISLAND

NYU Langone Medical Center and Winthrop-University Hospital on Long Island have reached an agreement to affiliate the institutions' extensive healthcare networks. NYU Langone, with more than 150 ambulatory sites throughout the region, will complement Winthrop-University Hospital's main campus,

multiple ambulatory sites, and network of 66 faculty and community-based practices in more than 140 locations extending from eastern Long Island to Upper Manhattan. "This agreement publicly confirms our confidence that an affiliation will allow both of our institutions to collaborate and share

best practices to better meet the healthcare needs of the communities we serve," says Robert I. Grossman, MD, the Saul J. Farber Dean and CEO of NYU Langone. Pending regulatory approval, the institutions are aiming to complete their affiliation in spring 2017.

First Stem Cell Brain Transplant Holds Promise for Acute Brain Injury

NYU Langone's neurosurgeons, neurologists, and rehabilitation medicine specialists recently made a major advance in one of the most hopeful areas of clinical brain research: they introduced stem cells directly into the brain, where they can affect neurons, replacing dead or damaged brain cells. These multidisciplinary cell transplant studies, led by Douglas S. Kondziolka, MD, professor of neurosurgery and radiation oncology and vice chair of clinical research

in the Department of Neurosurgery, are expanding possibilities for patients with stroke or traumatic brain injury.

Dr. Kondziolka is co-author of a 2016 article published in the journal *Stroke*, highlighting a two-year study that evaluated safety and clinical outcomes after surgical transplantation of mesenchymal stem cells into the brains of stroke patients. The researchers concluded that the cell transplants were safe and associated with

significant improvement in measures of neurological function after 12 months. NYU Langone is now one of the key sites in a national, multicenter trial to further evaluate the approach.

"It's challenging research—cell transplantation is logistically difficult and costly," says Dr. Kondziolka, "but it's clearly an avenue that holds promise for patients."

Breakthrough Technique Lets Physicians Scan for a Hidden Gland

It is difficult to avoid bumping into what one cannot see—and a formidable challenge in skull base procedures to remove large pituitary tumors is created when the tumor pushes so hard against the pituitary gland that the gland gets flattened into virtual invisibility. This increases the risk that the surgeon might accidentally damage the gland while resecting the tumor—which could result in the patient's lifelong reliance on medications.

Recently, NYU Langone neuroradiologists devised a new solution to the problem, which

occurs when taking a series of ultrarapid MRI scans after injecting the patient with tumor-identifying dye. "The gland and the tumor pick up the contrast at the same rate, so with a larger tumor, it's difficult to distinguish tumor and gland on the scans," explains professor of neurosurgery and skull base surgeon Chandra Sen, MD. "But when you give the dye by IV, the gland picks up the contrast much faster than the tumor does."

Armed with this knowledge, the neuro-radiologists, led by Girish M. Fatterpekar, MD,

associate professor of radiology, reasoned that by giving the dye by IV and then performing a very rapid sequence of MRI scans and seeing which area lit up first, the location of the wafer-thin pituitary gland would be revealed. "They've been developing the process for close to a year, and it works quite well," says Dr. Sen. An article describing the process is expected to be published in the coming year.



↑ Lauren B. Krupp, MD (left) and Leigh E. Charvet, PhD (right)

Awards & Recognition

↓ Douglas S. Kondziolka, MD

→ **Orrin Devinsky, MD**, received the American Epilepsy Society J. Kiffin Penry Award and was recognized as the LouLou Foundation CDKL5 Investigator of the Year and the Danny Did Foundation Investigator of the Year.

→ **Jori E. Fleisher, MD, MSCE**, was one of two physician-researchers recognized by the inaugural Doris Duke Fund to Retain Clinical Scientists.

→ **David H. Harter, MD**, has been appointed as board secretary of the New York State Neurological Society.

→ **Horacio Kaufmann, MD**, was recognized as a Rare Disease Hero™ by the Rare Disease Report.

→ **Douglas S. Kondziolka, MD**, was the 2016 head of the American Board of Neurological Surgery's Oral Examination. Dr. Kondziolka is also the principal investigator of the stroke and traumatic brain injury stem cell therapy trials at NYU Langone.



→ **Lauren B. Krupp, MD**, was named chair of the United States Network of Pediatric Multiple Sclerosis Centers and the Nancy Glickenhauz Pier Professor of Pediatric Neuropsychiatry.

→ **Chris Morrison, PhD**, was recognized by the American Psychological Association with the Karl F. Heiser Presidential Award for Advocacy.

→ **Dimitris G. Placantonakis, MD, PhD**, was recognized for his research by the AANS/CNS Section on Tumors with a Preuss Research Award. He was also named to the executive committee of the AANS/CNS Section on Tumors.

→ **Hae-Ri Song, MD**, received a Childhood Brain Tumor Foundation Award.

Select Conference Highlights

→ **Allal Boutajangout, PhD**, was a selected keynote speaker and moderator at the 8th European Neurology Congress in Amsterdam, Netherlands.

→ **Eleanor Drummond, PhD**, served as session chair for “Beyond Amyloid—The Consequences of Exposure to Abeta and Other APP Metabolites” at the 2016 Alzheimer’s Association International Conference in Toronto, Canada.

→ **Horacio Kaufmann, MD**, served as conference chair and delivered presentations at the 5th International Congress on Multiple System Atrophy in Salerno, Italy.

→ **Martin Sadowski, MD, PhD**, was chosen as session chair for “Preclinical Therapeutics: Target Identification—Amyloid” at the 2016 Alzheimer’s Association International Conference in Toronto, Canada.

→ **The Fifth “Neurofibromatosis Type 2: State of the Art” Conference**, a biennial international meeting and the largest of its kind to date, was held at NYU Langone in March 2016. It attracted more than 120 researchers and clinicians devoted to advancing the care and improving the quality of life of children and adults affected by this rare genetic disorder.

→ **Michael H. Pourfar, MD**, served as a course instructor on “Deep Brain Stimulation Management” at the 2016 American Academy of Neurology Annual Meeting.



Expanding Possibilities, Transforming Outcomes

INNOVATIVE RESEARCH, NOVEL IMAGING TECHNIQUES, AND ENHANCED
CROSS-DISCIPLINARY COLLABORATION ARE EXPANDING CARE
AND YIELDING ADVANCED TREATMENT OPTIONS FOR EVEN
THE MOST COMPLEX NEUROLOGICAL CONDITIONS.

↑ John G. Golfinos, MD and Andrew S. Chi, MD, PhD

New Genetic Clues Unlock Targeted Treatment Options

The Brain Tumor Center's achievements in research and patient care are supported by cross-disciplinary collaboration, fostered by co-directors John G. Golfinos, MD, and Andrew S. Chi, MD, PhD, who work as one team—combining their expertise in neurosurgery and neuro-oncology—with colleagues from neuropathology, neuroradiology, radiation oncology, and other divisions to find new treatment approaches for patients.

GENETIC SEQUENCING MATCHES MUTATIONS WITH TUMOR TREATMENTS

Current research at the center is focused on the lack of effective drug therapies for malignant brain tumors. In a new initiative driven by Andrew S. Chi, MD, PhD, assistant professor of medicine, neurology, and neurosurgery, chief of neuro-oncology, and co-director of the center, each patient's up front treatment is being tailored to the genetic profile of their tumor tissue. "Every malignant brain tumor is defined by specific genetic mutations," explains Dr. Chi. "By identifying those mutations, we can select treatments that target those genetic subtypes."

Leveraging the sequencing expertise of NYU Langone's neuropathologists to analyze brain tissue samples, the Center conducts genetic testing on all of its brain tumor patients. This approach enables the center to cultivate two categories of novel treatments: experimental drugs and existing cancer drugs repurposed for brain tumors.

GENETICALLY TAILORED THERAPIES MOVE TO THE FRONT LINES

Although genetically tailored drug therapies are typically used in combination with standard chemotherapy and radiation treatments, or to treat tumor recurrences, the Center is also beginning to investigate their use as first-line monotherapy for selected brain cancers.

"Genetic testing has been a paradigm in cancer drug therapy; however, its adoption in the management of brain cancer patients has been slow," adds Dr. Chi.

"It's not a 'one drug fits all gliomas' world anymore.

In the future, it will be all about determining the specific genetic profile of each patient's tumor and matching the right treatment to that genetic subtype."

EXPLOITING METABOLIC VULNERABILITIES IN SPECIFIC GENETIC SUBTYPES

In December 2015, a research team co-led by Dr. Chi published a study in *Cancer Cell* on their efforts to exploit a metabolic abnormality in gliomas with mutations of the IDH1 gene. The team discovered that this mutation causes low cellular levels of the chemical nicotinamide adenine dinucleotide (NAD), which is critical for maintaining sufficient energy levels in the cell. When the researchers administered NAD-lowering nicotinamide phosphoribosyltransferase (NAMPT) inhibitors to mice implanted with IDH1-mutant glioma cells in their brains, they found the drugs extended the animals' lives with no significant side effects.

"These findings suggest that NAMPT inhibitors might be effective against IDH1-mutant gliomas, which are impervious to current anticancer drugs," notes Dr. Chi. The center is also preparing to launch and lead human trials testing two other gene-based therapies—a drug that targets IDH1-mutant glioma subtypes, and an immunotherapy treatment for late-stage IDH1/2 mutant gliomas.



↑ (from back to front) John G. Golfinos, MD, Andrew S. Chi, MD, PhD, and Rajan Jain, MD

TESTING ARRAYS OF SINGLE CANCER CELLS SIMULTANEOUSLY

Another step on the path toward individually tailored drug treatments involves the DEPAArray, an electrode grid device that can be used to isolate hundreds of single, fluorescent-labeled cancer cells in separate fluid wells. These single cells can then be individually exposed to various drugs and other agents to allow researchers to study the different interactions simultaneously.

“This technology lets us rapidly test each patient’s tumor against dozens of drugs,” says Dr. Chi. “We can then take the most potent drug against that person’s tumor and treat the patient up front.” With the DEPAArray, researchers can also conduct genetic testing in parallel to determine why a given drug is effective against that tumor subtype. “From there, we can do a trial to test how that drug works in other tumors with the same mutations.”

The center is about to embark on its first research project with the new technology. The project, aimed at understanding the brain tumor microenvironment in pediatric brain tumors, will be led by Matija Snuderl, MD, assistant professor of neuropathology, and Dr. Golfinos. The researchers will use DEPAArray to conduct a molecular analysis of cancer and stromal cells, and to analyze the interactions between those two cell types.

GENETICS GIVE A GLIOMA PATIENT A LIFESAVING NEW OPTION

When a 28-year-old patient came to the Brain Tumor Center with a malignant glioma she had been told was inoperable and carried a poor prognosis, the team arranged for an urgent re-evaluation. The patient’s symptoms, combined with nuances revealed within the MRI, were consistent with a genetic subtype of glioma that carried a good prognosis with aggressive surgery. “Based on the tumor’s genetic subtype, we knew that by performing an aggressive resection, the patient’s prognosis would be excellent, even without any additional therapy after surgery,” recalls Dr. Chi. “After the procedure, we could simply monitor the area with the expectation that the patient would be fine for many years.”

The center has encountered multiple cases like this one, says Dr. Chi. “For a long time, we all thought there was one type of glioma and it was often presumed that everyone was going to do poor very quickly,” he notes. “But as we continue to compile these genetic analyses, we’re learning how gliomas behave and respond to treatment differently based on their mutations.”

The patient’s tumor was removed by NYU Langone’s neurosurgery team in the summer of 2016, and today her scans continue to show no signs of cancer recurrence.

Pushing the Therapeutic Envelope with Big Data and Innovation

At NYU Langone's Multiple Sclerosis Comprehensive Care Center, innovations, including practical applications informed by "big data," are pushing treatment toward new frontiers—leading to new therapeutic approaches both in the clinical setting and at home and ever-greater opportunities for patients living with multiple sclerosis.

TECHNOLOGY OFFERS A WINDOW TO CLINICAL INSIGHTS

One such innovation is an iPad app that measures patients' cognitive speed, visual discrimination, manual dexterity, walking speed, and other neurological benchmarks. Patients select shapes and the app calculates their scores, which are then delivered to a multi-site data collection bank, where they become part of an industry project aimed at deepening understanding of this debilitating autoimmune disorder.

"The iPad results will ultimately be merged with patients' other clinical data—their therapeutic regimens, how long they've had the disease, their MS subtype, MRI scans, and other parameters," explains the center's director, Lauren B. Krupp, MD, the Nancy Glickenhauz Pier Professor of Pediatric Neuropsychiatry and professor of neurology. "These records will then be combined with similar data from five other U.S. centers, giving us a very precise neurological record of thousands of MS patients over time."

The study, known as MS PATHS (Multiple Sclerosis Partners Advancing Technology and Health Solutions) is under way at NYU Langone, Cleveland Clinic, Johns Hopkins, and three other U.S. sites, and will eventually extend to other centers in the U.S. and Europe. "On the one hand, it's giving us real-time, research-quality data on our patients that can guide our clinical decision-making," notes Dr. Krupp. "Meanwhile, we're also compiling a massive amount of real-world data across a large cohort of patients, which we can analyze both cross-sectionally and longitudinally."

By elucidating trends and patterns that could otherwise go unnoted, the project will shed light on how different types of MS progress and respond to treatment—potentially pointing the way to new therapeutic approaches. "It's a tremendous example of how we're leveraging big data in medicine," says Dr. Krupp.

NOVEL DOSING REGIMEN MAY MAKE A POTENT MS DRUG SAFER

Center researchers recently presented evidence that extending the infusion schedule for the medication natalizumab from every four weeks (the FDA standard) to every eight weeks has the potential to dramatically lower risk of progressive multifocal leukoencephalopathy (PML)—a rare but potentially fatal side effect. Although natalizumab is one of the most efficacious drugs for relapsing remitting MS, its use has been limited because a sizable part of the MS population harbors the virus linked to PML. "The hope is that we can now safely administer this drug to a broader group of patients, and for a longer period of time," says the study's lead investigator, Lana Zhovtis Ryerson, MD, assistant professor of neurology.



↑ Leigh E. Charvet, PhD (right), demonstrating portable transcranial direct current stimulation equipment

PORTABLE tDCS EXTENDS REHABILITATION BENEFITS

The center is also investigating the in-home use of transcranial direct current stimulation (tDCS), in which a mild electric current is delivered to the brain through the scalp—an approach that appears to alleviate the debilitating fatigue and other symptoms frequently associated with MS and that could improve rehabilitation outcomes. After working with biomedical engineers at New York City College to design portable tDCS equipment for home use, the center is now conducting a controlled trial in which MS participants use the device regularly at home under the remote control and supervision of its trained study technicians.

“We believe tDCS has tremendous therapeutic potential,” says Dr. Charvet, who recently presented the center’s tDCS protocol at a National Institutes of Health workshop. “With this home-based approach, patients can undergo treatments far more often than if they had to visit the clinic each time, and we can accelerate the investigation of the technology by recruiting more study participants.”

BRINGING MS CARE HOME

The center is pioneering two cutting-edge therapies that patients can administer at home. One is a computer-based cognitive remediation program that the center has adapted specifically for individuals with MS. In a recent clinical trial, participants engaged in treatment sessions at home using study-provided computers, while trained study technicians monitored them remotely in real time. When compared to a control group that played ordinary computer games, the experimental group showed significant cognitive improvement.

“The more time patients spent on the therapy, the greater their cognitive benefits,” says clinical neuropsychologist Leigh E. Charvet, PhD, associate professor of neurology and director of the center’s research program. “This is the first evidence showing that computer-based training can combat MS-related cognitive impairment, so we’re very excited to know that it can be used effectively by patients at home.”

PEDIATRIC MS PROGRAM EXPANDS RESEARCH NATIONALLY

As a leading expert on childhood MS, Dr. Krupp is accustomed to wearing multiple hats. Since coming to NYU Langone less than two years ago, she has established its pediatric MS program as the premier clinical MS center in the New York metropolitan area. At the same time, as the founder of a national consortium of pediatric MS centers, Dr. Krupp is working with NYU Langone colleagues to extend the impact of the Medical Center's childhood MS research to the national arena.

"Clinically, the center's pediatric MS patient population has almost doubled over the last year," she says. "And we're spearheading a new nationally funded research program with 11 other U.S. centers to track the often-overlooked subtle changes in cognitive function experienced by children with MS, in comparison to both healthy peers and adults with MS." The project will soon add a sophisticated neuroimaging component, using conventional and functional MRI, diffusion tensor imaging, and other advanced techniques to measure atrophy of the brain's white and gray matter.

The center has also teamed with researchers at the University of California at San Francisco to study potential blood markers for pediatric MS. Notes Dr. Krupp, "We've found that low blood vitamin D levels, related to a child's genetic profile, play an important role in both the development and the severity of childhood MS."

The center also focuses intensively on psychosocial support for its young patients. It sponsors a sleepaway camp each summer for adolescents with MS, and is teaming with NYU Langone's Sala Institute for Child and Family Centered Care to explore other potential support systems for pediatric MS patients as they advance through school and prepare to live independent adult lives. "Our pediatric program is fortunate to have a wonderful group of social workers, nurses, and psychologists," says Dr. Krupp. "As we try to understand the disease's pathology, we must remember that, at the end of the day, what these kids really want is the opportunity to pursue their dreams."

NEUROMYELITIS OPTICA PROGRAM: ENHANCING AWARENESS OF A RARE—BUT TREATABLE—DISEASE

Neuromyelitis optica (NMO), known as Devic's disease, an inflammatory autoimmune disorder that affects the optic nerves and the spinal cord, is exceedingly rare, affecting only about 16,000 people the United States. Yet paradoxically, it is better understood than its more familiar counterpart, multiple sclerosis, which affects more than 400,000 Americans.

One reason behind the paradox is the 2005 discovery of antibody anti-aquaporin 4, an easily identified NMO marker. "The understanding of NMO's biology has yielded a number of effective treatments," says Ilya Kister, MD, associate professor of neurology and the director of NYU Langone's NMO Program, which was

launched in August 2016. Among the most exciting are the drugs rituximab, now the leading NMO therapy, and tocilizumab, an IL-6 antagonist, both previously approved for rheumatoid arthritis.

"If we treat NMO patients early enough, we can put them into remission most of the time," says Dr. Kister. His team is investigating additional therapeutic options, while also working to enhance physician awareness of the disease's signs—impaired vision, muscle weakness, and numbness—and highlighting the simple blood test that can detect it. "The key is to differentiate NMO from MS," he notes, "because some MS treatments can actually make NMO worse."

NYU Langone's NMO Program is now one of the nation's largest, with

> 100
PATIENTS

Multidisciplinary Surgical Team Enables New Options for Difficult Tumor Resections

Chandra Sen, MD, professor of neurosurgery, admits that he would not have tried a nasal endoscopy on a large skull base tumor 10 years ago—despite being one of the world’s preeminent skull base surgeons and one of the few with expertise in both open and endoscopic brain surgery.

Today, however, thanks to improved technology, Dr. Sen is readily using this technique, working with colleagues in the Department of Otolaryngology—Head and Neck Surgery to resect even some large skull base tumors. “In recent years, the instrumentation has gotten better, so we’re using this approach more and more,” notes Dr. Sen.

CASE PRESENTATION: BRAINSTEM CHORDOMA

In one recent case, a male patient in his forties presented with a walnut-sized tumor—a rare, slow-growing chordoma—that was compressing his brainstem. The patient struggled for breath whenever he lay down, and a respiratory consult at another center led to a brain scan, which revealed the tumor. At a subsequent consult with Dr. Sen, the patient was told the tumor would need to be removed surgically. “Eventually he would have become completely debilitated,” says Dr. Sen. “It had to come out.”

“The patient’s tumor was sitting in front of the brainstem, at the center of the head,” continues Dr. Sen. “I explained the two different ways we could remove it: we could cut open the skull and come at it from the side, which would mean going through many sensitive areas of the brain, or, since it was at the front of the brainstem, we could take it out endoscopically through the nose.”

Because the nasal approach offered a direct path to the tumor, it reduced the likelihood of collateral brain damage, which is why Dr. Sen ultimately recommended this approach to his patient. “Still, the operation had its risks,” he says. “He could end up unable to walk or talk properly, or with double vision. So, a very careful resection was required.”

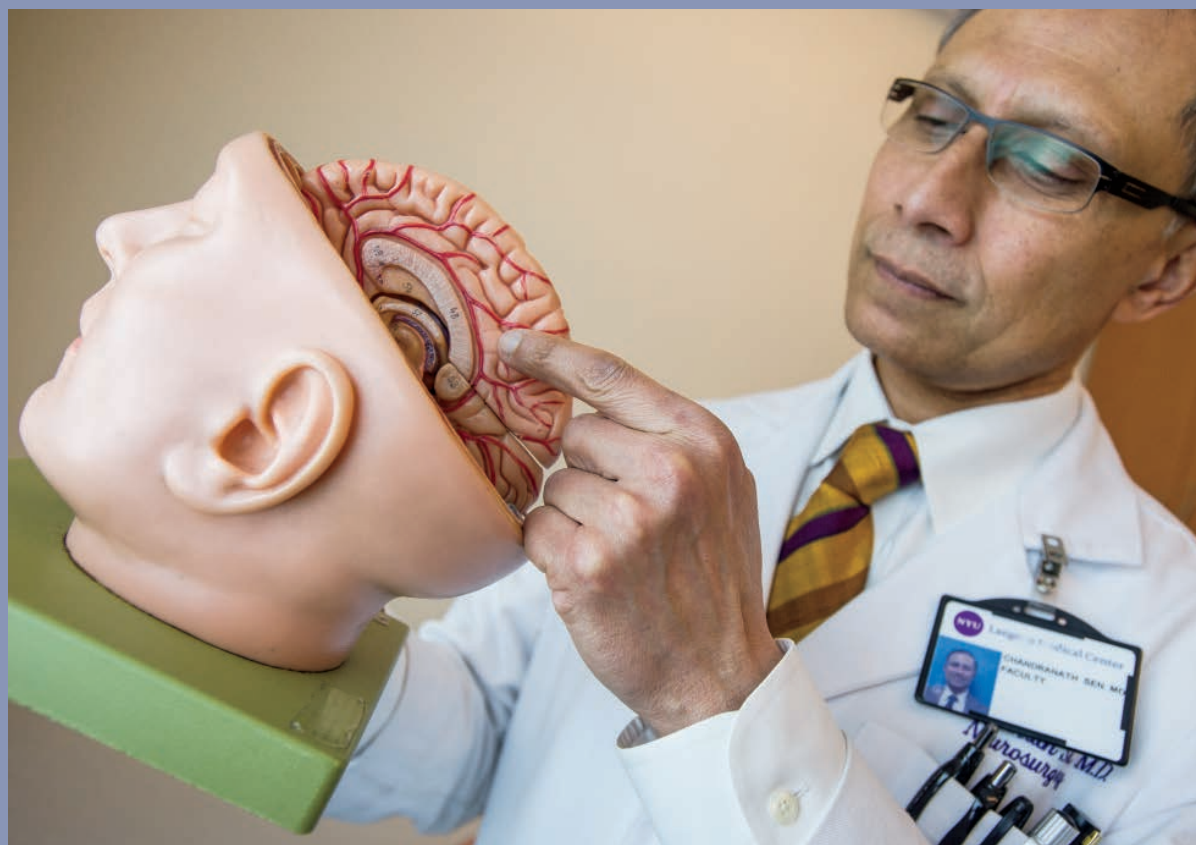
A SYNCHRONIZED SURGICAL APPROACH

When the eight-hour operation began, Dr. Sen stood side by side with Richard A. Lebowitz, MD, associate professor of otolaryngology. An expert nasal surgeon, Dr. Lebowitz regularly partners with NYU Langone’s neurosurgeons to perform endoscopic brain tumor resections.

“I’m responsible for the surgical approach,” says Dr. Lebowitz. “My job is to create space so Dr. Sen can reach the tumor, which involves moving—and in some areas removing—various nasal structures.” After the surgical team inserted a drain to divert the skull’s cerebrospinal fluid during the procedure, Dr. Lebowitz got to work. Elevating the nasal flaps and preserving them for reconstructive use, he took down the back of the septum and cut an opening in the front wall of the sphenoid sinus to provide access to the bone at the back of the sinus.

At that point, Dr. Sen took the lead. With stereotactic navigational guidance, he drilled a silver-dollar-sized hole through the sinus wall into the skull and removed the tumor piecemeal. Keeping an eye on the patient’s motor-evoked potentials, Dr. Sen progressed slowly to reach the spot where the tumor pressed into the brainstem.

“Once the central portion of the tumor was debulked,” says Dr. Sen, “I established a plane around the tumor against the brainstem.” Careful to avoid nearby blood vessels to the brainstem, he exposed the sixth cranial nerve and dissected the tumor away from it until he had removed the entire tumor. Dr. Lebowitz then took the lead again and patched the hole in the back of the sinus with abdominal fat, then rotated the nasal flaps to cover the patch. In a surgery as finely tuned as this one, the surgeons say they come to be so closely in sync that they operate simultaneously as four hands directed by two sets of eyes.



↑ Chandra Sen, MD

CASE OUTCOME: FUNCTION PRESERVED, RECOVERY EXPEDITED

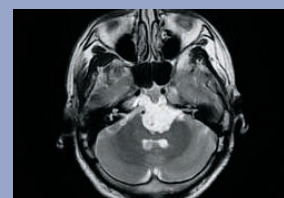
With the tumor fully resected, the patient's brainstem quickly resumed its normal position and his symptoms subsided. Some ongoing leakage of cerebrospinal fluid into the nose—a common occurrence—required a minor second procedure, and the patient needed regular visits to have scabs removed from his nasal passages. “The nasal resection is less traumatic than the alternative approach, but it’s still a big operation,” says Dr. Lebowitz.

The patient was able to resume his normal activities within six weeks after his operation—a significantly faster recovery than would have been likely with a craniotomy. “He basically returned to his life and work without impairment,” says Dr. Sen.

By offering a direct approach to the tumor with reduced risk of functional impairment and complications, the endoscopic procedure was clearly the right option for this patient. “If the tumor had been located more laterally, though, I would have been very ready to do a craniotomy instead,” notes Dr. Sen.

“What makes NYU Langone’s skull base practice unique is that we offer the full spectrum of surgical options to meet every patient’s needs, so we can choose the option best suited to the situation. This was an especially tough case to do endoscopically—but it was the best option, and in the end, we were able to have a very good impact on the patient’s life.”

→ Preoperative axial MRI, showing the tumor pushing into the brainstem



→ After surgery, the brainstem has recovered its normal shape



Expanding Surgical Possibilities with Advanced Spinal Imaging

Studying the MRI scans of a patient with a spinal cord tumor neurosurgeons Anthony K. Frempong-Boadu, MD, and Donato R. Pacione, MD, initially thought they would have to perform a laminectomy to remove the tumor—creating a sizable opening in the bone that would then require a spinal fusion procedure to repair.



↑ Anthony K. Frempong-Boadu, MD

“These new imaging capabilities are letting us do things more precisely, with more confidence. We’re now able to perform very aggressive resections and even operate on tumors we previously couldn’t resect.”

—Anthony K. Frempong-Boadu, MD

Instead, they did something that was not possible a year ago: Using techniques developed and refined by NYU Langone’s neuroradiologists, they fed the patient’s spinal MRI images into the Surgical Theater software platform, Precision Virtual Reality™, which turned the series of two-dimensional images into a three-dimensional landscape.

Now able to examine the patient’s spine in three dimensions—manipulating the image and visually peeling away tissue layers at will—the surgeons spotted a potential corridor to the tumor through the spinal column. To confirm their observation, they each put on an Oculus™, specialized goggles that create a virtual reality of the patient’s magnified tissues.

“With the Oculus we clearly saw there was plenty of room to maneuver,” says Dr. Frempong-Boadu, associate professor of neurosurgery and director of the Division of Spinal Surgery. “We brought the images into the OR as a navigation guide, and we achieved a great outcome with no need for a fusion—saving the patient three extra months of recovery. And the most amazing thing is, we planned the whole procedure right here in my office.”

NYU Langone’s spinal neurosurgeons were the first in the world to adapt the Surgical Theater technology for spinal procedures. “We’re using it primarily for procedures in the spinal column, including spinal cord tumors and intradural cysts,” says Dr. Frempong-Boadu. “We’re also applying it to complex fractures, and we’re teaming up with our orthopedic colleagues at the NYU Langone Spine Center to explore its use for deformity surgery.”



↑ Donato R. Pacione, MD

MAPPING THE SPINE WITH NERVE FIBER TRACKING AND INTRAOPERATIVE CT

In addition to using the Surgical Theater platform, the spinal neurosurgery group has employed a series of novel intraoperative imaging tools in the operating room over the past year. One is diffusion tensor imaging (DTI)—also known as fiber tracking—an imaging sequence that pinpoints the functional neural pathways in the spinal cord. DTI has been available for some time, but until recently the bony mass of the spinal column has prevented its use in spinal cord procedures. NYU Langone's neuroradiologists, led by Timothy M. Shepherd, MD, PhD, assistant professor of radiology, developed the appropriate algorithm to overcome this limitation, allowing surgeons to visualize and map the spinal nerve tracts despite the presence of bone and tumor. With this development, NYU Langone became one of the first to employ DTI in real time during spinal surgeries. "We import these fiber tracking images into our navigational guidance software during procedures, and use them to determine the safest approach to spinal tumors," says Dr. Frempong-Boadu.

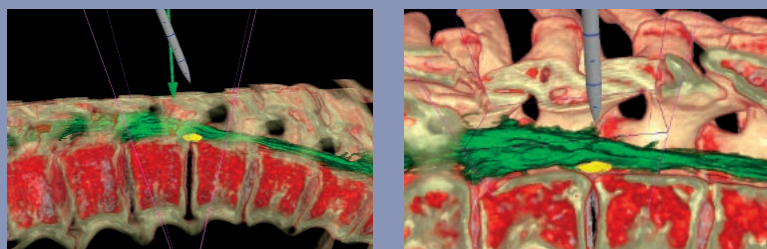
Mobile intraoperative CT scanning is another leading-edge technology being used in the spinal neurosurgery OR. The device, the Brainlab Airo, lets surgeons acquire real-time CT scan images during an operation. The images can then be integrated with both Surgical Theater and the microscopic image of the actual surgical site.

"Together, these new imaging capabilities are letting us do things more precisely, with more confidence," says Dr. Frempong-Boadu. "We're now able to perform very aggressive resections and even operate on tumors we previously couldn't resect, like astrocytomas in the spinal cord. The great thing about this new technology is that it has tremendous practical impact—it allows for more complete resections, with less neurological deficit, which translates to a faster recovery and improved long-term outcomes for our patients."

NEW SPINE CENTER TAKES INTERDISCIPLINARY APPROACH TO HEALING BACK CONDITIONS

NYU Langone's Spine Center, a collaboration of the Medical Center's nationally ranked departments of Neurosurgery, Orthopedic Surgery, and Rehabilitation Medicine, offers state-of-the-art treatment for the full spectrum of spinal conditions, including degenerative conditions, spinal deformities, fractures, spinal tumors, herniated discs, and congenital conditions such as spinal bifida.

The Spine Center emphasizes conservative treatment as a first-line option, but when surgery is needed, the collaborative structure of the center ensures comprehensive, expert care. Says Dr. Frempong-Boadu, "For especially complex cases, a neurosurgeon and an orthopedic surgeon may consult on the diagnosis and, if necessary, perform the surgery together to ensure the best outcome for the patient."



↑ Three-dimensional imaging of an intradural cyst

Pioneering New Seizure-Control Medications and Easing Pregnancy Concerns

Building on its reputation for groundbreaking translational research, the NYU Langone Comprehensive Epilepsy Center spearheaded several studies in 2016, including clinical trials of two promising new seizure-control therapies.

As part of the first-ever double-blind study of cannabidiol (CBD)—a nonpsychoactive ingredient of cannabis, or marijuana, a center physician was the lead investigator for a phase III trial testing the efficacy of a purified liquid CBD extract in children with Dravet syndrome. The international, multisite study found that the drug, Epidiolex, reduced convulsive seizures by 39 percent on average. “Cannabis has probably been used by humans for 3,000 years to treat epilepsy,” says Orrin Devinsky, MD, director of the Comprehensive Epilepsy Center and professor of neurology, neurosurgery, and psychiatry. “Now, for the first time, we have solid evidence that a cannabis-based product actually works.”

BLOCKING A KEY SEIZURE-RELATED PATHWAY

Another center physician was the lead investigator for a phase III clinical trial assessing the use of the immunosuppressant drug everolimus for seizure prevention in highly resistant epilepsy related to

tuberous sclerosis (TSC). The results, presented at the annual meeting of the American Academy of Neurology and scheduled for publication in *The Lancet* in early 2017, show that a form of everolimus already used to treat tumors and other TSC symptoms also substantially reduces seizures in this population.

“More than half of TSC patients suffer seizures that can’t be controlled with existing medications,” says Jacqueline French, MD, professor of neurology and director of Translational Research and Clinical Trials. “To date, this form of everolimus is the only drug to demonstrate benefits for this treatment-resistant group.”

The fact that the drug works by blocking hyperactivity in the mTOR signaling pathway, which is considered to be the underlying cause of TSC, makes the study especially meaningful, notes Dr. French. “This is the first drug used for epilepsy that targets what’s actually causing TSC, so it could potentially be used to treat the entire range of TSC symptoms,” she says. “Encouragingly, we think disruption in this same pathway may also underlie

CENTER ADVANCES: GENE-BASED THERAPY AND AN INNOVATIVE BRAIN WRAP

→ **A clinical trial of ataluren as a treatment for Dravet’s syndrome and CDKL5 disorder was launched in fall 2015.** The drug, already approved in Europe for Duchenne muscular dystrophy, helps the body’s RNA overcome genetic mutations that impair production of key proteins. The NYU Langone-led trial is the first-ever attempt to treat epilepsy using a genetic therapy.

→ **The center has expanded use of genetic testing to identify specific mutations such as *SCN1A*,** a gene that can give rise to different types of epilepsy phenotypes. Genetic testing helps center physicians better understand and manage individual cases of epilepsy, while educating

and preparing patients and families for medical events that may occur across generations.

→ **A three-year, \$2.95 million grant was awarded by the National Institute of Neurological Disorders and Stroke (NINDS)** to investigate different uses of the Neuro-Grid—an innovative, ultrathin electrode-containing material developed by an NYU Langone postdoctoral fellow. The material, which conforms to the brain’s contours to detect electrical activity on and below the brain’s surface, has been recognized by NINDS as a key technology that can help researchers understand how the brain works.



many other kinds of epilepsy—so this may be a step toward finding an underlying treatment for these other epilepsy subtypes as well.” Already, she adds, center researchers are exploring the drug’s effects on the brain tissue of patients with one subtype, treatment-resistant cortical dysplasia.

EXPLORING THE EPILEPSY-PREGNANCY CONNECTION

Another recently completed center-led study observed pregnancy outcomes over five years in women with epilepsy between the ages of 18 and 41. “Earlier research suggested this group has higher infertility rates and increased risk of a difficult pregnancy,” notes Dr. French. Though 24,000 babies are born to women with epilepsy each year, this prospective, multisite study was the first to actually compare women with epilepsy to a control group of healthy women to observe pregnancy rates and outcomes.

The investigation found no statistical difference between the two groups in their likelihood of achieving pregnancy, time taken to become pregnant, or adverse pregnancy outcomes, such as miscarriage.

“We hope that women with epilepsy who are thinking of becoming pregnant will be reassured by these findings,” says Dr. French.

INVESTIGATING SUDDEN DEATH IN EPILEPSY

With data demonstrating a 27-fold greater risk of sudden unexpected death in epilepsy (SUDEP), the center continues to play a leading role in uncovering the risks and mechanisms behind this phenomenon. Current work includes studies to identify autonomic and neuroimaging biomarkers and neuropathological changes associated with SUDEP, as part of the National Institutes of Health’s national Center for SUDEP Research.

In 2016, center researchers had numerous SUDEP-related publications, including an overview of SUDEP epidemiology and prevention in *Lancet*, and a case-control study exploring the link between SUDEP and isodicentric chromosome 15 syndrome in *Epilepsy & Behavior*. In addition, a case series from the center published in *Epilepsia* confirmed the existence of an uncommon occurrence known as nonseizure SUDEP, in which death occurs without the onset of a seizure.

Innovative Visual Analysis Tools Enhance Neurological Diagnoses

With the evidence of sports-related concussions' many symptoms and long-term health risks continuing to mount, NYU Langone's Division of Neuro-Ophthalmology has extended its leadership in concussion testing by introducing innovative concussion screening and symptom tracking tools.

NEW SYSTEM REFINES SIDELINE DIAGNOSIS

A sideline screening tool, called MULES (Mobile Universal Lexicon Evaluation System), was developed by Laura J. Balcer, MD, MSCE, professor of neurology, population health, and ophthalmology, and vice chair of the Department of Neurology, and Steven L. Galetta, MD, the Philip K. Moskowitz, MD Chair of Neurology, and professor of neurology and ophthalmology. Unlike the rapid number naming King-Devick test currently used to detect concussion, the MULES test requires an individual to identify objects in a series of photos as quickly as possible. Within their current working framework, investigators suspect concussion if athletes take even one additional second to complete the series compared with their pre-season baseline performance.

"We moved toward image naming with this tool because it engages significantly more neural pathways than number identification," explains Dr. Galetta. "At the same time, like the King-Devick test, the MULES test can be quickly administered on the sideline by any adult."

NYU Langone has applied for a copyright for the MULES test, and Dr. Balcer and colleagues recently published a description of MULES testing in adult research volunteers in the *Journal of the Neurological Sciences*. They have further investigated applications of the MULES test through a field trial with local youth leagues, college athletes, and professional women's hockey players. "Once it's validated, we plan to make this powerful test available online, so a greater number of people will be able to detect concussion," says Dr. Balcer.



↑ Laura J. Balcer, MD, MSCE

TRACKING EYE MOVEMENT TO DETECT ABNORMALITIES

A digital version of the MULES test is also being used in the Department of Neurology Vision Research Eye Movement Testing Lab, which was established two years ago under the leadership of Janet C. Rucker, MD, the Bernard A. and Charlotte Marden Professor of Neurology and director of the Division of Neuro-Ophthalmology, and John Ross Rizzo, MD, assistant professor of rehabilitation medicine and neurology. In the lab, Todd E. Hudson, PhD, research assistant professor of rehabilitation medicine, and signal processing experts Ivan W. Selesnick, PhD, professor

of electrical and computer engineering, and WeiWei Dai, PhD candidate at the NYU Tandon School of Engineering, use state-of-the-art Eye Link high-resolution video cameras with infrared illuminators to track subtle eye movements related to neurological function. In 2016, the lab published research showing that people with slower scores on the King-Devick test—indicating a concussion—display longer intervals between saccades, the fast movements that eyes make when shifting focus from one number or object to another.

“Vision involves nearly half the brain, so any brain injury is likely to have a visual component,” notes Dr. Rucker. By analyzing eye movements as patients perform various tasks, she and her colleagues can help further characterize impairments in concussion, MS, Parkinson’s disease, and other neurological disorders that have a visual component.

In another significant advance, lab researchers recently teamed with engineers at the Tandon School of Engineering to develop tools and software that track the way the eyes move in three dimensions as they converge on an approaching object. “Convergence is

often the eye movement primarily affected by concussion,” says Dr. Rucker, “so this new three-dimensional capability may help us to both diagnose concussion and measure patients’ recovery.”



↑ Janet C. Rucker, MD, and John Ross Rizzo, MD, using eye-tracking technology to study concussion

NIH-FUNDED STUDY INVESTIGATES POTENTIAL CTE BIOMARKERS IN FORMER FOOTBALL PLAYERS

In fall 2016, NYU Langone began enrolling subjects in a national, four-site study funded by the National Institutes of Health (NIH) designed to identify biomarkers and clinical diagnostic criteria for chronic traumatic encephalopathy (CTE)—a degenerative brain disease that has been linked to repeated head trauma. The seven-year study will follow middle-aged former college and NFL football players, along with a control group of men without a history of head trauma.

“The study will administer PET and MRI scans, blood tests, and cognitive measures,” says Laura J. Balcer, MD, MSCE,

professor of neurology, population health, and ophthalmology, and vice chair of the Department of Neurology. “We will also invite study participants to undergo structural and functional testing of their visual pathways as additional potential markers that could indicate CTE.” In addition to developing benchmarks that may help clinicians diagnose and track the disease course, researchers also hope to learn more about how CTE develops, what mechanisms are involved, and, eventually, how to treat and prevent it.

One Tumor, Many Pathways: Acoustic Neuroma Management Takes a Patient-Specific Approach

New treatment pathways, leveraging novel surgical approaches and expanded device applications, have increased the options for hearing-restorative treatment for patients with NF2 tumors, including acoustic neuromas.

REAL-TIME SURGICAL FINDINGS POINT TO AUDITORY BRAINSTEM IMPLANT FOR NF2 HEARING LOSS

When a 27-year-old male with NF2 presented with an acoustic neuroma that had robbed his right ear of hearing, he was already a veteran of surgery performed at other institutions, including a left-side tumor resection a decade earlier.

An auditory brainstem implant (ABI) placed at that time proved ineffective and left him with no hearing in his left ear. More recently, a right-side middle fossa decompression procedure to relieve pressure on his auditory nerve from the new tumor had failed to stem his hearing loss. Now almost completely deaf, the patient sought a second opinion at NYU Langone, where he consulted with a multidisciplinary team highly experienced in treating the most complex acoustic neuroma cases, including those of prior treatment failure.

TEAM CONSENSUS: TUMOR RESECTION, IMPLANT PLACEMENT

The team was in agreement: the tumor had to come out. The patient also wished to enroll in an NYU Langone clinical trial for axitinib, a multikinase inhibitor that had the potential to prevent NF2 tumor growth by inhibiting the cell proliferation pathway at several points. Taking these factors into account, the team recommended a new surgical plan, involving a cranial nerve-sparing translabyrinthine approach plus right-side installation of either a cochlear implant or an ABI, depending on findings during the tumor resection.

CAREFUL ABI PLACEMENT SIGNIFICANTLY IMPROVES HEARING

Over the course of many acoustic neuroma operations, John G. Golfinos, MD, associate professor of neurosurgery and otolaryngology and chair of the Department of Neurosurgery,

and J. Thomas Roland Jr., MD, the Mendik Foundation Professor of Otolaryngology, professor of neurosurgery, and chair of the Department of Otolaryngology–Head and Neck Surgery, have implanted scores of ABIs. These high-tech devices, FDA approved for NF2 patients, restore some hearing after electrodes are placed in the brainstem’s auditory region; these electrodes turn sound into brain signals to simulate hearing.

In the current case, once the surgeons accessed the tumor, the team determined that there was not enough residual auditory function to warrant a cochlear implant, leaving the ABI the option of choice. After the tumor was resected, Dr. Roland drilled spaces in the skull to seat the implant and the electrode. Dr. Golfinos, working under high magnification, then opened the foramen to the fourth ventricle and carefully advanced the ABI’s electrode paddle into position on the cochlear nuclei inside the brainstem. Final placement of the ABI was fine-tuned on the basis of evoked auditory brainstem response readings, and the electrode paddle was fixed in place using Teflon felt and Gelfoam.

SURGICAL OUTCOME: FUNCTION INTACT, HEARING ENHANCED

Several weeks later, the patient met with the Medical Center’s audiologists, who programmed the ABI. The patient’s outcome has been excellent; he has 20 active electrode channels and significantly improved hearing. His cranial nerve function remains intact, and he is proceeding with the drug trial as planned.

“We take a multifaceted approach, matching each patient’s tumors with the therapeutic and surgical options in our arsenal,” says Dr. Golfinos. “Our ability to fine-tune treatment, even in the midst of surgery, means we’re ready to take on the most complex patients—including those who have not responded to prior treatment.”

IN ACOUSTIC NEUROMA RESECTION, EXPERIENCE IS A STEADY HAND

The patient, a retiree in his early seventies, first noticed hearing loss on his right side, but wrote it off to a lifetime of working with heavy equipment. But after his right ear went completely deaf, he reluctantly agreed to an MRI scan. A few days later, he found himself in the office of Dr. Golfinos, reviewing an image of a walnut-sized vestibular schwannoma, also known as an acoustic neuroma, pressed against his brainstem.

The scan showed the tumor extending into the patient's auditory canal and compressing his trigeminal and other cranial nerves. In addition to his hearing, it had begun to affect his balance and facial sensation—symptoms that Dr. Golfinos advised would only worsen over time. “I explained to him that watchful waiting was no longer a viable option,” says Dr. Golfinos.

With the patient's right-ear deafness now permanent, preserving the facial nerve became the top priority. The surgeons chose a translabarynthine transmastoid approach, because it offered the best sightlines for identifying the nerves. Working with an operating microscope, Dr. Roland created access by performing a mastoidectomy and then drilling out the labyrinth, removing bone from the internal auditory canal, and incising two flaps in the dura to expose the tumor. Using a Cavitron Ultrasonic Surgical Aspirator (CUSA), he carefully debulked the center of the tumor, then opened the dura of the internal auditory canal to follow the tumor into the canal. There, he identified the facial nerve and followed it out to the porus, where the nerve became involved with the thicker portion of the tumor.

SEPARATING TUMOR FROM NERVE WITH PRECISION DISSECTION

Dissecting the tumor from the cerebellum down to the brainstem, Dr. Golfinos used the CUSA to open all the tumor's cysts. The tumor was now just a thin shell along the brainstem. While the eighth cranial nerve was still hidden from sight—“likely played through and over the back of the tumor cysts,” notes Dr. Golfinos—he identified the seventh cranial nerve and the trigeminal nerve and dissected them away from the thin tumor remnant.

“All that remained then was a small amount of tumor, just along the distal trigeminal nerve and along the facial nerve as it went into the internal auditory canal,” Dr. Golfinos recalls. With more than 85 percent of the tumor removed and reassuring motor-evoked potential readings of the relevant nerves, the surgeons determined that any additional resection would jeopardize the facial nerve and the brainstem. They closed the surgical site, coagulating any remaining suspicious tissue along the way, and used an abdominal fat graft to patch the dura. With the tumor largely gone and adjoining nerves still intact, an exceptionally difficult surgery was complete. The patient did very well postoperatively, with a complete resolution of his headaches, imbalance, and trigeminal symptoms.

“Our ability to fine-tune treatment, even in the midst of surgery, means we’re ready to take on the most complex patients—including those who have not responded to prior treatment.”

—John G. Golfinos, MD

Radiosurgery is among the options typically employed to treat acoustic neuromas at the Medical Center. “For this tumor, however, because of its size and degree of brainstem compression, microsurgical resection was the only reasonable treatment,” says Dr. Golfinos. “And although it’s very difficult to remove these types of tumors entirely, in this case, given the patient’s age, we didn’t need a total resection.”

EXPERIENCE, FACIAL FUNCTION GUIDE SURGICAL APPROACH

Safely detaching an acoustic neuroma from the nerve fibers adhering to it is a demanding operation, and the size and location of this particular tumor heightened the risk of possible nerve damage. Fortunately, the patient found himself with Dr. Golfinos and Dr. Roland, who have performed more than 1,800 acoustic neuroma resections—a record few surgical teams can match.

Extending the Benefits of Deep Brain Stimulation

Although deep brain stimulation (DBS) has been used for more than 20 years to control symptoms of Parkinson's disease and other neurological conditions, the treatment—which involves sending electrical current into the brain through surgically implanted electrodes—continues to evolve. As one of the most active DBS programs in the nation, the Center for Neuromodulation plays a key role in this evolution.

TRACT DENSITY IMAGING TARGETS ELECTRODE PLACEMENT

To better understand how stimulation of different brain locations influences movement and other functions, the Center for Neuromodulation has been collaborating with NYU Langone's neuroradiologists on a diffusion MRI technique called tract density imaging, which provides a functional map of the brain. This map enables center clinicians to place and orient the electrodes more precisely.

"One aspect we're very focused on is refining the placement of DBS electrodes, since even a tiny shift in placement can affect both benefits and side effects," says Alon Mogilner, MD, PhD, associate professor of

neurosurgery and anesthesiology and co-director of the center.

In a recent article published in *Neuromodulation*, Dr. Mogilner and fellow co-director, Michael H. Pourfar, MD, assistant professor of neurology and neurosurgery, described how advanced imaging led them to tweak the angle of an electrode lead they had implanted in the subthalamic nucleus of a Parkinson's patient. The subtle change was enough to significantly reduce unwanted side effects of dysarthria and dystonia, while still producing the desired effect of reducing Parkinson's-related tremors. "The introduction of high-resolution functional imaging for DBS is taking us to the next level," says Dr. Mogilner.

↓ Michael H. Pourfar, MD



NEUROSURGERY TEAM REVIVES TIME-TESTED PAIN RELIEF PROCEDURE

One of the most effective surgical pain management techniques is also one of the oldest. The cordotomy, in which pain-conducting nerves in the spinal cord are selectively destroyed, has been used since the early 1900s to relieve intractable pain. Improvements to other pain management approaches caused cordotomies to fall out of favor, but NYU Langone recently revived the technique for end-stage cancer patients, and is currently the only medical center in New York City performing them.

During the procedure, which is performed in the CT scan suite under CT guidance, surgeons place a needle through the skin and through the dura and then inject contrast to outline the spinal cord in great detail.

Subsequently, a lesioning probe placed through the needle into the spinal cord provides electrical stimulation to lesion sensory pathways.

The procedure is performed by Alon Y. Mogilner, MD, PhD, associate professor of neurosurgery and anesthesiology and co-director of the Center for Neuromodulation, and Timothy M. Shepherd, MD, PhD, assistant professor of radiology, who explain what led them to revive it in a forthcoming issue of the *American Journal of Neuroradiology*. “It’s an excellent option for cancer patients who otherwise would be bedridden on pain medication,” says Dr. Mogilner. “The patients we treat become able to function and spend precious time with their families.”

A NEW GENERATION OF DBS DEVICES

The center is also one of several U.S. sites investigating a next-generation DBS device manufactured by Boston Scientific. In addition to doubling the number of individual electrodes in each implanted array from four to eight, the device can distribute its electrical output among its electrodes in any configuration the clinicians choose.

“Traditionally, we have selected the one electrode in an array that works best and then used that electrode to stimulate the surrounding tissue in a spherical fashion,” explains Dr. Pourfar. “With this new technology, we can distribute electrical stimulation in a much more refined way, which should help us avoid stimulating areas we don’t want to activate—such as those associated with worsening of speech or balance.”

Although the outcomes of the multisite trial involving these next-generation devices will not be known for some time, early anecdotal results are promising, says Dr. Pourfar. Additional developments on the near horizon include subdivided electrodes that can more selectively direct stimulation, and another technology that uses self-modulating stimulation to deliver electrical current only as needed based on signals from the brain.

DBS AND TOURETTE’S—THE NEXT FRONTIER

The Center for Neuromodulation has also led the extension of DBS to treat conditions other than Parkinson’s disease and essential tremor. The center was involved with early studies that looked at DBS for severe depression, an indication still under investigation. The center has also helped pioneer the potential role of DBS as an off-label treatment for medication-resistant Tourette’s syndrome. It has treated 15 Tourette’s patients to date, one of the largest such series in the United States, with outcomes data scheduled for publication in the *Journal of Neurosurgery* in early 2017.

“Our results with Tourette’s patients have been very compelling,” says Dr. Pourfar. “To take a young person who was literally housebound and enable them to attend college—it’s a special thing to be a part of.”

Fresco Institute Accelerates Groundbreaking Movement Disorders Research

At the Fresco Institute for Parkinson's and Movement Disorders, cross-disciplinary research exploring the root causes of Parkinson's disease is leading investigators toward new, more effective ways of targeting the condition and alleviating its symptoms.



↑ Alessandro Di Rocco, MD

NEUROLOGY-NEUROSCIENCE COLLABORATION SPEEDS HUNT FOR ELUSIVE PARKINSON'S CURE

Although medications can relieve symptoms of Parkinson's disease, the quest continues for a drug that arrests the underlying brain disorder. Supported by a \$25 million grant from The Paolo and Marlene Fresco Foundation, NYU Langone's Fresco Institute for Parkinson's and Movement Disorders—a collaboration between the Medical Center's internationally known movement disorders clinic and its innovative neuroscience program—is leading the hunt for a cure.

"The collaboration has already produced several promising investigations," says Alessandro Di Rocco, MD, Founders Professor of Neurology, executive

director of the institute, and Director of the Division of Movement Disorders. One group is studying exercise—known to slow Parkinson's-related decline—to identify its beneficial mechanisms. A possible explanation is that ketones produced during exercise trigger release of growth factors, which then modify brain connectivity and plasticity.

To explore this idea, institute clinicians are monitoring exercising patients for growth factor expression, and institute neuroscientists are studying this growth factor response in animals in a complementary study that is also putting transcranial magnetic stimulation into the research mix. "The two groups doing parallel studies greatly increases the power and the speed of the research," notes Dr. Di Rocco.

PROBING THE BIOLOGY OF PARKINSON'S DISEASE

In other groundbreaking research, Nicolas Tritsch, PhD, associate professor of neuroscience and physiology, is studying brain circuits that control movement. Dr. Tritsch's research has shown that the dopamine-producing cells that die off in Parkinson's disease also produce other brain chemicals—suggesting dopamine loss is not the sole driver of the disease and opening the way to a new understanding of how to combat it.

A separate collaboration with the Division of Neurogenetics, which specializes in lysosomal storage disorders (LSD), has yielded an intriguing clue to Parkinson's pathophysiology. "We've determined that Gaucher's disease, an inherited LSD, significantly increases risk of Parkinson's," says Dr. Di Rocco, "indicating that impaired lysosomal disposal may contribute to the disease."

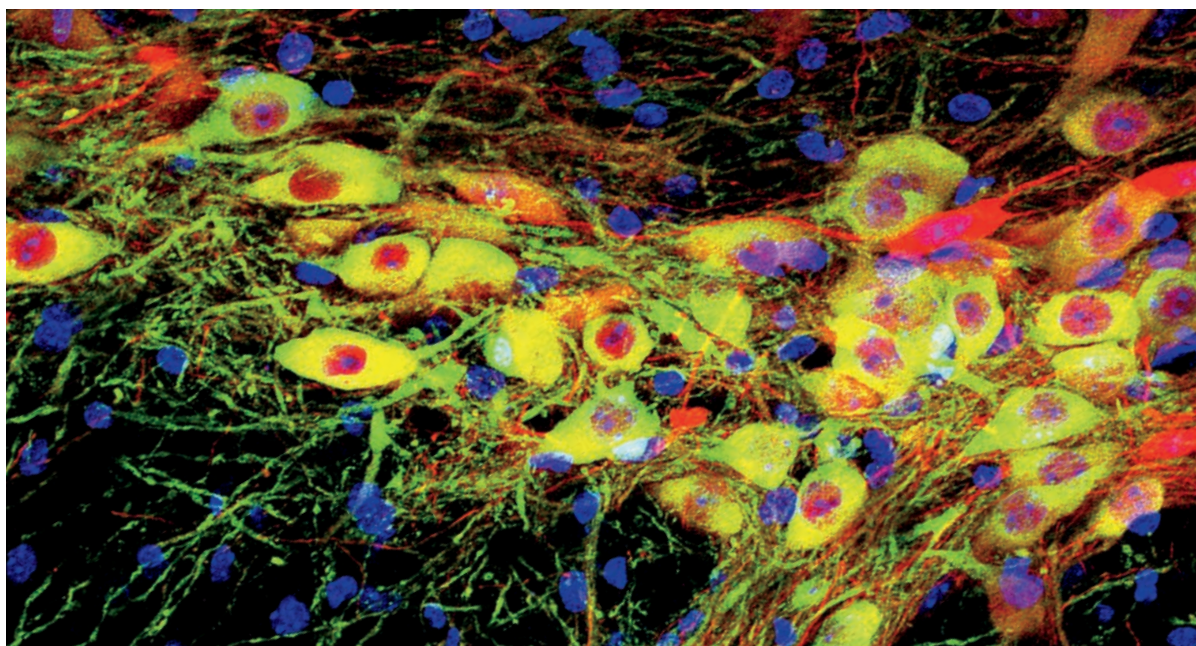
The institute recently joined a multisite project studying whether enzyme-based LSD treatments, modified to cross the blood-brain barrier, hold promise for Parkinson's. "Scientists are working on

THE FRESCO INSTITUTE'S GLOBAL REACH

A portion of the Fresco Institute's funding is being used to forge a strong connection with Parkinson's programs in Italy. In 2016, five Italian academic centers were selected to form a Network of Excellence, with each center receiving annual grants from the institute to support Parkinson's research in Italy. The Fresco Institute will also select several network researchers each year for fellowships at the institute's headquarters in New York.

"We're hosting four fellows now, and they're all tremendous," says Dr. Di Rocco. "The collaboration is a wonderful opportunity to exchange ideas and expand Parkinson's knowledge in both countries."

proof of concept now. If they're successful, we'll start testing the drugs outright on Parkinson's patients," says Dr. Di Rocco.



↑ Midbrain dopaminergic neurons in the substantia nigra pars compacta, stained green to mark tyrosine hydroxylase, an enzyme that helps make dopamine in neurons, and red to mark a cellular reporter

Rare Lysosomal Storage Disorders Spur Demand for Novel Treatments

NYU Langone's expertise in lysosomal storage disorders and trials of cutting-edge experimental therapies draw patients from around the world.

For Heather A. Lau, MD, assistant professor of neurology and director of the Lysosomal Storage Disorders (LSD) Program in the Division of Neurogenetics, complexity is commonplace. LSDs, rare conditions that block cells' ability to make key enzymes that metabolize toxins, vary in both their symptom profile and their average age of onset, but they all attack multiple organs, often with disabling—or even deadly—effects.

LIMITED OPTIONS LEAD TO EXPERIMENTAL ENZYME THERAPY FOR MPS VII

Enzyme-replacement therapies—including several drugs that Dr. Lau helped shepherd to approval—are available for certain LSDs, but currently there's no FDA-approved treatment for mucopolysaccharidosis VII (MPS VII, or Sly syndrome). The condition affects the brain, heart, lungs, and skeletal system, and children who develop it at birth often survive only into their teens.

Recently, a newborn presented with MPS VII who seemed unlikely to have even that survival horizon. Beset with respiratory and heart issues, the infant had to be resuscitated repeatedly after episodes of hypoxia and bradycardia. Fortunately, a new experimental enzyme therapy—recombinant human beta-glucuronidase (rhGUS)—was being tested on MPS VII in older children and adults, with promising early results.

With the baby's health deteriorating, Dr. Lau acted swiftly. "I got emergency IRB and FDA approval, and began infusing the baby with the drug," she recalls. After four weeks of treatment, urine levels of the targeted storage material had dropped by 75 percent. At 18 weeks the dosage was doubled, and by 48 weeks the child was showing significant symptomatic improvement. Dr. Lau presented a poster on the case at the Lysosomal Disease Network's 2016 *WORLD Symposium*. "We're now conducting a phase II trial of the drug in children with MPS VII," she adds. "I have three patients in the trial, and two of these patients' families have moved so their child could be part of it."

The Division of Neurogenetics has become accustomed to patients relocating from around the world to take advantage of the division's expertise with approved LSD treatments and gain access to cutting-edge experimental therapies offered at NYU Langone.

ADDITIONAL CLINICAL TRIALS

- **A phase III trial** of extended-release aceneuramic acid (sialic acid) for GNE myopathy—a condition for which there is currently no approved therapy—and a phase II trial of the same treatment for severely affected patients
- **A study on long-term effects** of velaglucerase alfa on bone pathology in type 1 Gaucher's disease
- **An extension trial** of intrathecal idursulfase for mucopolysaccharidosis II (MPS II, or Hunter Syndrome)
- **An observational study** of the natural history of Canavan disease
- **A recently-launched trial** of an experimental treatment for Fabry disease

↓ (at left) Heather A. Lau, MD



EXPANDING RESEARCH SHEDS LIGHT ON GAUCHER'S

Dr. Lau is also an expert in treating Gaucher's disease—which results from a glucocerebrosidase deficiency, and this has played a large role in making the Medical Center's Gaucher's practice one of the most robust in the nation. In addition, in 2015, Dr. Lau published research reviewing pregnancy outcomes associated with Gaucher's, and presented on a collaboration with Howard G. Liang, MD, assistant professor of surgery, that involved a Gaucher's patient with a rare case of migrating spleen.

The division's expertise in Gaucher's disease is augmented by its frequent collaboration with David H. Harter, MD, assistant professor of neurosurgery and a pediatric neurosurgeon with expertise in spinal decompressions for children with LSD-related skeletal deformities. The division's clinical practice recently added a genetic counselor, and the practice consults regularly with adult and pediatric specialists across the Medical Center as well.

"It takes a range of specialists to treat our patients," explains Dr. Lau. "NYU Langone's multidisciplinary expertise is a big reason why our program is so effective."

Peripheral Autonomic Disorder May Trigger Parkinson's, Other Neurodegenerative Conditions

New research from NYU Langone's Dysautonomia Center indicates that Parkinson's and other Lewy body diseases may, in some cases, start in the peripheral nervous system before crossing through the blood-brain barrier into the central nervous system.

This ongoing investigation is part of a National Institutes of Health-funded longitudinal study of patients with pure autonomic failure, a disease that affects the peripheral nervous system. Analyzing data from biannual patient exams conducted at centers around the world, the researchers found that within four years, 38 percent of these patients developed Parkinson's, multiple system atrophy, or Lewy body dementia.

"While pure autonomic failure causes bothersome symptoms like fainting from orthostatic hypotension, as well as bladder, sweating, and erectile issues, it was considered to be largely benign until now," explains Horacio Kaufmann, MD, the Felicia B. Axelrod Professor of Dysautonomia Research in the Department of Neurology, professor of medicine and pediatrics, and director of the Dysautonomia Center and of the Division of Autonomic Disorders. "However, the frequent progression from pure autonomic failure to these other, more serious conditions suggests it may actually be a precursor—which could help us identify people at risk for Parkinson's and other synucleinopathies and potentially allow us to intervene to prevent these diseases."

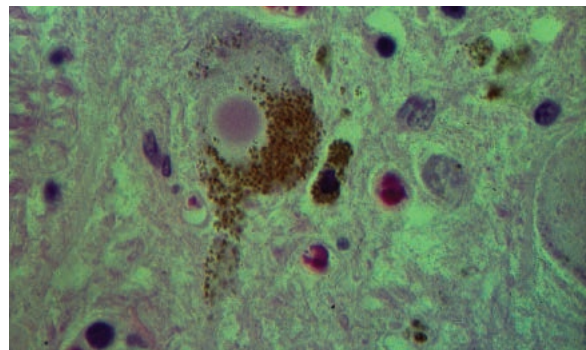
DISEASES LINKED BY A MISFOLDED PROTEIN

Years earlier, Dr. Kaufmann was the first to identify misfolded alpha-synuclein proteins in the peripheral nerves innervating the heart, the blood vessels, and the bladder of a patient with pure autonomic failure. These misfolded proteins are the core component of Lewy bodies, which also accumulate in the central nervous system of people with Parkinson's disease, Lewy body dementia, and multiple system atrophy. On the basis of other prior research, investigators at the center are now conducting a prospective study using optical coherence tomography to evaluate individuals with

Parkinson's disease and related disorders for progressive retinal nerve thinning, another potential biomarker for these conditions.

NEW AUTONOMIC DRUG TRIALS

The center continues to pioneer new drugs for autonomic disorders with funding from the FDA's orphan drug program. Clinical trials of new agents are under way to treat abnormally low blood pressure, and to target the gene defect linked to familial dysautonomia (FD), a rare inherited disease for which the Dysautonomia Center is the only international treatment site. The center is also conducting a phase II trial of the enzyme inhibitor carbidopa to control FD-related blood pressure surges, as well as a trial of dronabinol as a treatment for FD-related nausea. "With ongoing support from the Familial Dysautonomia Foundation, we offer the approximately 400 FD patients worldwide a level of expertise that is not available anywhere else," notes Dr. Kaufmann.



↑ Intraneuronal Lewy body with a characteristic surrounding halo, formed by the abnormal aggregation of the protein alpha-synuclein

Headache Division Expands, Targets Novel Treatments

NYU Langone's Headache Division continues to expand, with additional specialists joining to meet rising demand.

The Division's growing team includes Lawrence Newman, MD, who joined as director at the end of 2016. Dr. Newman was the founding director of the Headache Institute at Mount Sinai West, which was designated a National Institutes of Health Center of Excellence under his leadership, and has served as president of the American Headache Society from 2014 to 2016. His colleague Adelene E. Jann, MD, will also be joining the division as clinical assistant professor of neurology.

REFINING PROTOCOLS FOR THE FULL SPECTRUM OF PATIENTS

The team sees a wide spectrum of patients, including many "who are very refractory," says Mia Minen, MD, assistant professor of neurology. "These patients often come here for a second opinion after visiting other centers, and stay for treatment."

With scores of headache medications available, Dr. Minen has been working with other leaders in the field to refine treatment protocols. In 2016, she was part of an American Headache Society expert panel that set new emergency department guidelines for acute migraine therapy. The panel, whose recommendations were published in *Headache* in 2016, examined trials of 28 injectable drugs and determined that intravenous metoclopramide and prochlorperazine and subcutaneous sumatriptan were the only acute treatments that showed consistent positive results and that dexamethasone was the option proven to prevent headache recurrence.

CLINICAL RESEARCH EXPANDS THERAPEUTIC OPTIONS

The division's rising patient volume has also spurred the activity of its clinical research program. In 2016, faculty presented several studies at the American Headache Society conference, including one that examined the link between migraine and insomnia, and another that highlighted how patients with post-traumatic headache scored on concussion screens typically used during

sideline testing. Division investigators are now studying how self-efficacy beliefs influence patient adherence to proven behavioral headache treatments, such as progressive muscle relaxation (PMR), cognitive behavioral therapy, and biofeedback.

In a separate study, notes Dr. Minen, researchers are working with a smartphone app that lets people track headache triggers and plays recorded PMR instructions. Dr. Minen also published a review article on migraines and psychiatric comorbidities, and she led a course on the subject at the 2016 Academy of American Neurology Annual Meeting. The division may also participate in upcoming phase III trials of CGRP antagonists, a promising new class of migraine drugs. As Dr. Minen notes, "We are expanding the division's breadth of work, so we can better match the right headache therapies to the right patients."

GENERAL NEUROLOGY: A HUB FOR TREATMENT, AN ENTRY POINT FOR COMPLEX CARE

General neurology is typically the first stop for patients when their primary care doctors suspect a neurological problem. With their broad training, NYU Langone's general neurologists can treat the vast majority of conditions they see, from back pain and headache to neurodegenerative disease and dementia. And when the complexities of a patient's condition demand more finely tuned care, the general neurologists refer patients to the Medical Center's neurological subspecialists and specialty centers, directing them to the physician, team, or center with the specific type of expertise that they need.

"Between our general expertise and their specialized knowledge, we can be certain our patients are getting the best possible care," says Harold J. Weinberg, MD, PhD, clinical professor of neurology and director of the Division of General Neurology.

Dementia Treatment Augments Comprehensive Care with Cutting-Edge Clinical Trials

Fueled by state and national grants, and a host of translational research studies and clinical trials, researchers are rapidly homing in on the root causes of Alzheimer's disease and related dementias in their search for treatments—and, eventually, cures.

GRANTS CATALYZE TRANSLATIONAL RESEARCH, NEW MODES OF CARE

At the Center for Cognitive Neurology, hope for patients with Alzheimer's disease (AD) and related dementias comes in the form of a pioneering translational research program—now in the second year of a five-year, \$10 million National Institute of Aging grant engaged in a wide range of cutting-edge AD drug trials. “We’re currently enrolling subjects in 12 clinical trials,” says Thomas Wisniewski, MD, the Lulu P. and David J. Levidow Professor of Neurology, professor of pathology and psychiatry, and director of the Center. The studies include a phase III trial of Biogen's aducanumab—an especially promising passive immunization therapy that acts on amyloid-beta, one of the toxic proteins associated with AD.

The research program complements a busy clinical practice backed by two 2016 grants from New York State: a \$2.2 million Center for Excellence for Alzheimer's Disease grant supporting state-of-the-art care for New York City residents, and a \$7.5 million grant to help provide free, personalized support services for caregivers of those with AD and related dementias.

NOVEL ALZHEIMER'S VACCINES MOVE AHEAD

Center investigators have developed two immunological AD therapies in house that elicited positive responses in animal studies and should soon begin human trials. Type B CpG ODN—CpG, for short—stimulates Toll-like receptor 9 (TLR9) to activate microglia and other innate immune cells, which then work to clear the brain of AD-related toxins. Following successful mouse studies, results of a two-year trial in elderly squirrel monkeys are being analyzed and appear very promising.

2016 GRANTS

\$2.2 million

grant to establish a Center for Excellence
for Alzheimer's Disease

\$7.5 million

grant to provide caregivers of individuals with
Alzheimer's disease and related dementias with access
to state-of-the-art support programs and services

Says Dr. Wisniewski, “So far, we have found that subcutaneous CpG injections reduced AD pathology and also produced cognitive benefits in the monkeys without toxic side effects. The fact that we achieved this in non-human primates with a natural model of AD is particularly encouraging.”

The center has also patented a conformational monoclonal antibody that is the only known agent to attack both amyloid-beta and tau proteins concurrently—a capability that increases its therapeutic potential. “We hope to start phase I human trials soon,” says Dr. Wisniewski. Intriguingly, he adds, the conformational molecules also target the toxic oligomers associated with Parkinson's disease, prion diseases, and other neurodegenerative conditions.

MULTIPLE ADVANCES CHART A HOPEFUL PATH

The center's more than 70 researchers received support for a range of other research initiatives in 2016, including two patents for additional vaccine approaches, and investigations by the lab of Martin Sadowski, MD, PhD, associate professor of neurology, psychiatry, and biochemistry and molecular pharmacology, to elucidate the link between Alzheimer's and apolipoprotein E, and uncover potential therapeutics for Alzheimer's and prion diseases. In addition, the lab of Arjun V. Masurkar, MD, PhD, assistant professor of neurology and neuroscience and physiology, has been actively studying links between olfactory dysfunction and Alzheimer's.

Center researchers have also made progress in their development of a novel methodology for identifying proteins associated with AD lesions in formalin-fixed, paraffin-embedded human tissue so they can plumb their extensive patient tissue bank. "We're using this methodology to examine various subtypes of AD, including a rapidly progressing form of AD that we've

submitted a paper on for review," notes Dr. Wisniewski. "As we gain a better understanding of these disease pathologies, we're also identifying more and more pathways that we can target with novel interventions."

The center is also working to develop tau tracers—irradiated dyes that light up tau proteins so they can be detected on scans—and continues to field test the prion vaccine it created to combat elk wasting disease. Particularly intriguing is a study, published in 2016 in *Current Alzheimer's Research*, that reports AD pathology reductions and associated cognitive benefits after human umbilical stem cells were injected into the carotid arteries of mice.

"Previous experimental stem cell approaches required injecting the cells directly into a subject's brain," says Dr. Wisniewski. "This shows that stem cells can be injected peripherally, cross the blood-brain barrier, and survive in enough numbers to generate new brain cells. It's one more sign that we're moving in the right direction."



↑ Thomas Wisniewski, MD

Novel Brain Cooling Technique Uncovers Brain Regions That Control Speech Production

Efforts to understand where and how the brain encodes and produces speech could lead researchers and clinicians to novel therapies and better-targeted rehabilitation methods.

INNOVATIVE PROBE HIGHLIGHTS NUANCED NEURAL FUNCTION

A novel electronic probe that mildly cools down quarter-sized patches of brain cells has helped to clarify the function of two key brain circuits that underlie human speech. The probe, which cools the nerve cells by about seven degrees Celsius, was invented by Michael A. Long, PhD, assistant professor of otolaryngology and neuroscience and physiology. Building on similar findings from their study of the brain regions contributing to song production in the zebra finch, Dr. Long and his research team used the probe on 22 neurosurgical patient volunteers who were undergoing neurosurgery to address epilepsy or to remove brain tumors. These individuals were awake prior to brain surgery in order to supplement perioperative brain mapping, which identifies speech-oriented brain regions so that these areas can be protected during the procedure.

The study, published in *Neuron*, was conducted in collaboration with Mario A. Svirsky, MD, the Noel L. Cohen Professor of Hearing Science and

professor of neuroscience and physiology, and colleagues at the University of Iowa. Its aim was to learn more about key speech centers and show that the cooling probe could be a safe, effective alternative to standard methods used for brain function mapping—typically, the administration of electrical current, which carries the risk of triggering seizures.

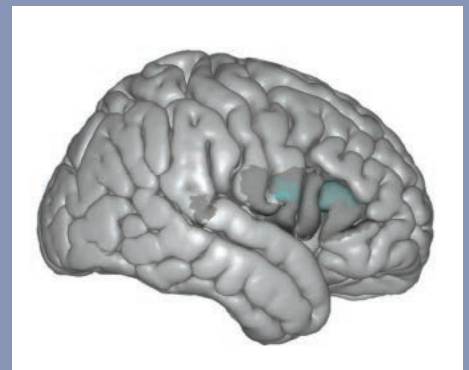
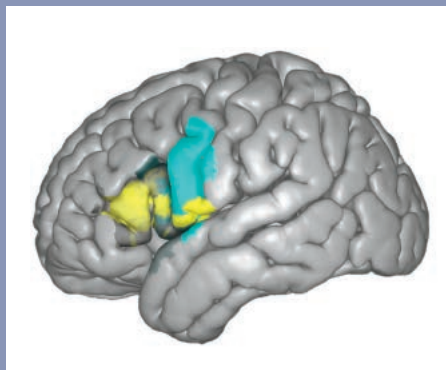
“Unlike traditional mapping with electrical stimulation, which completely—though temporarily—knocks out speech, our probe causes more nuanced changes to neural function in the areas where it is placed,” explains Dr. Long. “We found that when we cooled Broca’s region and had patients perform simple speech tasks, it changed the timing of their speech, slowing it down. When we cooled the speech motor cortex, on the other hand, speech quality was affected, with speech becoming slurred.”

The researchers next plan to use recording methods, including the NeuroGrid (also an NYU Langone invention), to study electrical activity in these speech regions in greater detail.

A FUNCTIONAL MAP OF SPEECH PRODUCTION BASED ON DATA FROM 16 PATIENT VOLUNTEERS

→ Left and right hemispheres of the brain. Focal cooling resulted in changes in articulation (shown in blue) and timing (yellow) that were located primarily on the left hemisphere in distinct cortical regions

Images: Long et al., 2016



Advancing Precision Medicine with Big Data

Across the Medical Center's neurological specialties, comprehensive data gathered every day, from every patient at the point of care, are fed into databanks that, in turn, provide clinicians with real-time, up-to-date, nuanced insights that inform and shape care decisions.

WORLD'S FIRST RADIOSURGERY DATABANK ANSWERS KEY QUESTIONS

At the NYU Langone brain radiosurgery practice, one of the nation's busiest, such a databank is "the first of its kind in the world," says Douglas S. Kondziolka, MD, professor of neurosurgery and radiation oncology, vice chair of Clinical Research in the Department of Neurosurgery, and director of NYU Langone's Gamma Knife program. "We now have patient information and follow-up from almost 2,000 procedures for which complete data is available serially. These data are giving us a deeper understanding of our results and outcomes."

The databank is part of a system-wide effort to employ big data for the benefit of patients and clinical outcomes. "The rise of big data analytics, harnessing sophisticated algorithms and tremendous computing power, now allows researchers and clinicians to answer critical questions that have the potential to drive optimal outcomes for every patient," writes Dr. Kondziolka in a 2016 essay for *Practical Neurology*.

DATA-DRIVEN INITIATIVES UNCOVER NEUROLOGICAL INSIGHTS

Similar efforts to collect and analyze patient data on a population health scale are under way across NYU Langone's neurological specialties.

At the Multiple Sclerosis Comprehensive Care Center, detailed data, including the results of iterative tests of neurological function, are collected on iPads at each patient visit and then combined with results from other collaborating centers.

NYU Langone's epilepsy program is part of a national registry that compiles data on sudden unexplained epilepsy-related deaths.

The Concussion Center is collating results of patients concussion screens with eye-tracking measurements and other biomarkers.

At the Center for Cognitive Neurology, data aggregated on the disease progression of dementia patients is cross-referenced with histological analyses of their brain tissue.

NYU Langone neurologists are coordinating an international database containing brain scans of patients with autism, and NYU Langone neurosurgeons are collating genetic profiles with cancer outcomes to determine optimal treatments for patients with different gene mutations.

These efforts are supported by initiatives like Datacore, a collaboration among the Medical Center's IT Department, Clinical and Translational Science Institute, and Population Health Biomedical Informatics program that provides data collection and extraction support to clinicians and researchers. The insights gleaned from these wide-scale analytic efforts are expected to accelerate as collection and analytic techniques steadily improve. "The application of big data approaches to key questions in clinical neuroscience is just beginning," says Dr. Kondziolka.



Learning Reaches New Heights

NEW FELLOWSHIPS AND AN INNOVATIVE THREE-YEAR PROGRAM
AUGMENT LEARNING OPPORTUNITIES FOR THOSE TRAINING
IN NEUROLOGY AND NEUROSURGERY.

↑ (from left to right) Ericka Wong, MD, Ariane K. Lewis, MD, and Aaron S. Lord, MD

Expanded Learning Options Enhance Training

FRESCO INSTITUTE WELCOMES INITIAL GROUP OF FRESCO FELLOWS FROM ITALY. In keeping with its mission, NYU Langone's Marlene and Paolo Fresco Institute for Parkinson's and Movement Disorders is sponsoring a cohort of new clinical fellows to enable them to pursue translational research at the institute. The newly appointed participants include:

Clinical fellow Alberto Cucca, MD, who completed his neurology residency at the University of Udine-Trieste in June 2016. At NYU Langone, he sees patients and is working on a research project as the first recipient of the Marlene and Paolo Fresco Clinical Fellowship for Italian Neurologists and Related Specialists.

Research fellow Marta Maltese, PhD, who received her doctorate from the University of Rome in 2016. At NYU Langone, she received one of the inaugural Marlene and Paolo Fresco Institute Research Fellowships for Italian Researchers and is studying synaptic mechanisms that drive movement under the mentorship of researcher Nicolas Tritsch, PhD.

Research fellow Maria Mancini, PhD, who recently served as a visiting scholar at the IRCCS in Rome. At NYU Langone, she also received one of the inaugural Marlene and Paolo Fresco Institute Research Fellowships for Italian Researchers, and is working in the lab of Margaret Rice, PhD, professor of neurosurgery and neuroscience and physiology, on research involving the regulation of dopamine release.

During their two-year fellowships, the early-career physician-scientists and researchers from the Fresco Institute's affiliated academic centers in Italy train under the guidance of institute physicians and researchers. The expanding visiting fellows program, which will welcome a fourth fellow in early 2017, is strengthening NYU Langone's partnerships with Italian institutions while drawing talented researchers poised to contribute to cutting-edge movement disorders investigations.

WFNS FELLOWSHIP ENHANCES NEUROSURGERY TRAINING FOR GLOBAL PARTICIPANTS. In 2016, NYU Langone's Neurosurgery Department hosted its latest cohort of World Federation of Neurosurgical Societies (WFNS) fellows. For the past 10 years, the department has awarded these three-month fellowships to neurosurgeons in training from across the globe. Recent participants have included neurosurgeons from Mexico, Brazil, Peru, China, India, Egypt, Thailand, and Iraq. During their time at the Medical Center, the WFNS Fellows, who are in their last year of residency or one or two years post-residency, observe the full range of neurosurgical procedures that department faculty perform, as well as participate in clinical research.

"We seek to invite physicians from countries whose neurosurgery programs aren't yet well developed, and to expose them to the latest techniques and methods," explains Jafar J. Jafar, MD, professor of neurosurgery, who oversees the program at NYU Langone. "Many of these neurosurgeons go on to very successful careers in their own countries. Past fellows that I see at international conferences, they are always quick to express their appreciation for the experience they gained here."

RESIDENCY PROGRAMS WELCOME FIRST NYU SCHOOL OF MEDICINE THREE-YEAR GRADUATES. In 2016, the residency programs of the departments of Neurology and Neurosurgery welcomed their first graduates of the NYU School of Medicine's Three-Year MD Pathway. The recently launched track lets students complete virtually the same core curriculum as the traditional four-year pathway in an abbreviated timeframe. Through the Main Residency Match, Three-Year MD students choose their specialty area at the start of medical school, and are offered acceptance into the NYU Langone residency program in their chosen department immediately upon graduation.

The accelerated track offers a continuum of training between undergraduate medical school and graduate residency training, while reducing the debt burden that often accompanies medical education. It is ideal for highly motivated students, including career-changers like Jenna Conway, MD, one of two new neurology residents from the program. Previously employed as an investment banker, Dr. Conway discovered a faster transition to her chosen career in neuroscience through the three-year pathway. Along with Dr. Conway, Jina Park, MD, joins the Department of Neurology as a resident from the Three-Year MD Pathway program.

In the Department of Neurosurgery, Travis Hill, MD, also joins as a resident from the accelerated program. Dr. Hill earned his PhD in neuroscience from the University of California, Davis, where he pursued a clinical career while he completed his dissertation research in synapse formation. He then completed the three-year pathway at NYU School of Medicine and is now poised to undertake his training side by side with NYU Langone's renowned neurosurgery faculty.

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