Tomorrow’s Neurological Care.

Today.
Cleveland Clinic’s Neurological Institute is a multidisciplinary institute that combines all physicians and other healthcare providers in neurology, neurosurgery, neuroradiology, the behavioral sciences and nursing who treat adult and pediatric patients with neurological disorders. This structure allows for a disease-specific, patient-focused approach to care. Our unique, fully integrated model is beneficial to our current standard of care, allows us to measure quality and outcomes on a continual basis, and enhances our ability to conduct research.
DEAR COLLEAGUES

A newly arriving staff member mentioned to me that he thought cognition should be the fifth vital sign. Medical school has taught us to check for temperature, pulse, blood pressure and respiratory rate. But a key sign of a healthy brain is its ability to do its job: to think.

Today, cognitive disorders and their prevalence are a greater problem than anyone ever anticipated they could be. As we all live longer lives, we also encounter a greater magnitude of cognitive problems, on a personal, professional and societal level. At the same time, we also are at a unique age of discovery regarding these disorders. We’re learning that cognitive disorders can be identified at a stage earlier than previously believed and potentially be altered. We’re also learning that more precise identification of the problem and understanding of the mechanisms behind the damage can help us combat this high price of aging. We’re realizing that memory programs, physical and occupational therapy, even more precise identification of brain anomalies causing cognitive disorders can help us to better keep our mental capacities intact. We’ve also identified that the risk factors for dementia overlap with those relative to cardiovascular disease.

At a place like Cleveland Clinic, where we routinely incorporate multidisciplinary, disease-based care, within our Neurological Institute, we feel we have the perfect breeding ground for a cognitive disorders program. In 2007, we announced the creation of our new Center for Brain Health, which will bring together researchers, clinicians, therapists, surgeons, imaging specialists and a variety of other experts to continue to advance our understanding of cognitive disorders and to provide the optimum in care to patients who suffer from them.

The Center for Brain Health will share the unique attributes of our other centers and departments, promoting collaboration across all care providers, offering patients a complete continuum of care and infusing education and research into all that we do. In 2007, these centers and departments of the Neurological Institute continued to enhance their facilities, technologies and processes, which I am pleased to share with you here in our 2007 annual report.

Of particular note is our undertaking of the Knowledge Program, which is an institute-wide effort to standardize our data collection within each patient’s electronic medical record to better track outcomes and analyze data.

As we continue to evolve and enhance our institute, I look forward to sharing with you updates regarding our new Center for Brain Health, our Knowledge Program and other efforts to improve patient care.

Sincerely,

Michael T. Modic, MD, FACR
Chairman, Neurological Institute
The multidisciplinary Cleveland Clinic Neurological Institute (NI) includes more than 220 medical, surgical and research specialists dedicated to the treatment of adult and pediatric patients with neurological and psychiatric disorders. The institute offers a disease-specific, patient-focused approach to care. Our unique, fully integrated model strengthens our current standard of care, allows us to measure quality and outcomes on a continual basis, and enhances our ability to conduct research.

U.S. News & World Report’s “America’s Best Hospitals” survey consistently has ranked our neurology and neurosurgery programs among the top 10 in the nation. Our neurology, neurosurgery and psychiatry programs are also ranked best in Ohio.

The institute model allows our patients to better access the care they need through specialized, multidisciplinary, disease-specific centers that integrate the expertise of neurologists, neurosurgeons, psychiatrists, psychologists, neuroradiologists, and others, into the comprehensive care of a single disease:

- Center for Brain Health
- Brain Tumor and Neuro-Oncology Center
- Cerebrovascular Center
- Epilepsy Center
- Center for Headache and Pain
- Mellen Center for Multiple Sclerosis Treatment and Research
- Center for Neurological Restoration
- Neuromuscular Center
- Center for Pediatric Neurology and Neurosurgery
- Sleep Disorders Center
- Center for Spine Health

Additionally, our Center for Neuroimaging and Department of Psychiatry and Psychology provide care across all our disease-based centers.

We provide care across the spectrum of neurological disorders, including primary and metastatic tumors of the brain, spine and nerves; pediatric and adult epilepsy; headache, facial pain syndromes and associated disorders; movement disorders such as Parkinson’s disease, essential tremor and dystonia; cerebral palsy and spasticity; hydrocephalus; metabolic and mitochondrial disease; fetal and neonatal neurological problems; multiple sclerosis; stroke; cerebral aneurysms; brain and spinal vascular malformations; carotid stenosis; intracranial atherosclerosis; nerve and muscle diseases, including amyotrophic lateral sclerosis, peripheral neuropathy, myasthenia gravis and myopathies; sleep disorders; and mental/behavioral health disorders and chemical dependencies.

EXPERT, SPECIALIZED DIAGNOSIS

Our Neurological Institute physicians draw on advanced diagnostic capabilities and experience.

Our imaging services include structural and functional magnetic resonance imaging (MRI), computed tomography (CT), positron emission tomography (PET), myelography, diagnostic cerebral/spinal angiography, interventional neuroradiology, and carotid and transcranial Doppler ultrasound. Our neuroimaging staff subspecializes in specific
disease entities, such as epilepsy and cerebrovascular disease, ensuring accurate, in-depth interpretations.

Additional diagnostic tools are found in our epilepsy monitoring units, sleep laboratories, neuropsychological testing facilities, electromyography laboratory, autonomic laboratory and cutaneous nerve laboratory.

THE LATEST TREATMENT MODALITIES

Patients can receive leading-edge treatment options at the Neurological Institute, where we continue to advance such innovations as deep brain stimulation (brain pacemakers), epilepsy surgery, stereotactic spine radiosurgery, blood-brain barrier disruption, endovascular treatment of cerebral aneurysms and vascular malformations, and neuroendoscopy. Distinctive services such as our three-week outpatient program for sufferers of chronic headaches (IMATCH) and our Headache Infusion Suite provide intensive therapy when it is needed. The Brain Tumor and Neuro-Oncology Center's Translational Therapeutics Program is accelerating the process of bringing novel therapeutic agents from the laboratory to the patient, while maintaining the highest standards of efficacy and safety. Joint Commission certification as a Primary Stroke Center and accreditation by the American Academy of Sleep Medicine are just two examples of our commitment to providing the most advanced and highest quality of care to our patients.

RELEVANT RESEARCH

We strive to conduct research directly related to conditions experienced by our patients, including programs in translational research, clinical trials of drug and device interventions, neuroimaging research, epidemiology and health outcomes, behavioral and psychiatric research, and research into better diagnostic methods. More than 175 clinical research trials are under way at the Neurological Institute. In the area of basic science, a core of internationally recognized neuroscientists with external funding totaling $10 million annually conduct investigations at the Cleveland Clinic Lerner Research Institute.

CONVENIENT CARE IN THE COMMUNITY

We are committed to making access to world-class care convenient for all patients — whether coming to us from near or far. Our Neurological Institute Regional Centers are a system-wide effort to extend our services to regional hospitals and at Cleveland Clinic family health centers throughout the community. In addition, Cleveland Clinic neurologists oversee inpatient care at a number of Cleveland Clinic hospitals. Our Sleep Disorders Center has pioneered the idea of hotel-based sleep studies, offering overnight studies at multiple locations throughout the community for patients' convenience and comfort.

INTEGRATED NURSING SERVICES

Nursing in the institute integrates inpatient and ambulatory nursing, enhancing the continuum of patient care. This unique structure also lends itself to greater information sharing and process improvement opportunities. Through continuing education programs, we are able to broaden nursing educational opportunities from basic nursing instruction to subspecialization in neurological nursing, much like our physician colleagues.

At Cleveland Clinic’s Neurological Institute, we are dedicated to maximizing patient care outcomes and the patient experience, and to advancing medical education and research in all areas of neurology, neurosurgery and psychiatry.
E D U C A T I O N

The Neurological Institute is committed to providing quality medical education to physicians, nurses and other medical professionals within the institute, as well as regionally, across the country and all over the world. From continuing medical education to residencies and fellowships to our observer program, education is incorporated into all aspects of our institute.

C O N T I N U I N G  M E D I C A L  E D U C A T I O N

The Neurological Institute collaborates with Cleveland Clinic’s Center for Continuing Education to offer a variety of programs to physicians. The center is responsible for one of the largest and most diverse CME programs in the world. In 2007, there were more than 8,500 participants in 195 Neurological Institute-sponsored CME programs. The programs ranged from weekly grand rounds in neurosurgery, neurology, epilepsy and psychiatry to week-long symposia that provided in-depth updates about the latest treatment options or research results on a variety of neurological-based topics.

In its mission to provide a wide array of first-rate continuing medical education opportunities to medical professionals throughout the world, the center also offers neurology-based online CME credit. In 2007, 1,303 CME certificates were awarded for the completion of online neurological courses covering topics such as migraine headaches, depression and multiple sclerosis.

R E S I D E N C I E S  A N D  F E L L O W S H I P S

The Neurological Institute offers extensive opportunities in physician education and research. We take special pride in training future practitioners. The institute offers more than 30 training programs in neurology, neurosurgery, psychiatry and psychology. This includes core residency ACGME-accredited programs in adult neurology, child neurology, neurosurgery, adult psychiatry and child and adolescent psychiatry, as well as ACGME-accredited subspecialty fellowships and non-accredited fellowships. In 2007, 170 clinical and research fellows and residents were trained through our programs.

120 medical students matriculated in NI’s core and elective programs

170 clinical and research fellows and residents were trained

N I  R E S I D E N C I E S

Adult Neurology
Child and Adolescent Psychiatry
Child Neurology
Psychiatry
Neurosurgery

N I  F E L L O W S H I P S

Chronic Pain Rehabilitation
Clinical Neuroimmunology
Clinical Neurophysiology/EEG
Clinical Neurophysiology/EMG
Endovascular Neuroradiology
Epilepsy
Epilepsy Surgery
Functional and Restorative Neurosurgery
Headache
Health Psychology
Movement Disorders
Neurocritical Care
Neuromuscular Medicine
Neuropsychology
Neurosurgical Oncology
Pediatric Neurosurgery
Psychosomatic Medicine
Skull Base Surgery
Sleep Medicine
Spine Medicine
Spine Surgery
Vascular Neurology
Our training programs offer research opportunities for trainees who plan to pursue careers in academic neurology, neurosurgery, and psychiatry and psychology. We offer flexible programs that foster individual interests. Trainees are expected to participate in basic and clinical research projects and are encouraged to present their findings at national meetings.

CLEVELAND CLINIC LERNER COLLEGE OF MEDICINE

The Cleveland Clinic Lerner College of Medicine of Case Western Reserve University is a unique medical school established in 2002 that sets new standards for the training of physician investigators through innovative approaches to the integration of basic science, research and clinical medicine. Physicians within the Neurological Institute direct the basic neuroscience curriculum in years one and two of the school. This includes organization of the content and teaching of the topics in a problem-based learning format. In 2007, 76 Neurological Institute staff members taught courses at the medical school.

Additionally, physicians within the Neurological Institute direct the neurology, neurosurgery and psychiatry clinical curriculum, including basic rotations, acting internships and advanced electives. Cleveland Clinic’s basic rotations in neurosciences have been rated by the medical school students as the best in the city.
Research is a thread that runs throughout the entire five-year medical school curriculum. Neurological Institute physicians and scientists mentor a number of medical students with projects in the clinical and basic neurosciences. Medical students are invited to present their projects at the annual Neurological Institute Research Day, when poster and platform presentations are given, and medical students, residents and fellows compete for recognition awards.

**INTERNATIONAL PHYSICIAN OBSERVER PROGRAM**

International Physician Observers are foreign physicians selected to visit a designated medical department at Cleveland Clinic. The program exposes participants to the latest practices within a specialty area through clinical interactions, operating room observations and teaching conferences. In 2007, the Neurological Institute hosted 70 international observers to our centers of excellence.

**2007 EDUCATIONAL HIGHLIGHTS**

- The Brain Tumor and Neuro-Oncology Center held the first international symposium on Stereotactic Body Radiation Therapy and Stereotactic Radiosurgery in Orlando, Fla.
- The Center for Spine Health held its week-long spine review course in Cleveland and in Cairo, Egypt.
- The Epilepsy Center attracted nearly 650 attendees to its Epileptology Review course and the 17th International Epilepsy Symposium.
- Our Department of Neurosurgery held a neuro-endoscopic surgery course in Beijing, China, for more than 200 participants.
- The Department of Psychiatry and Psychology hosted the second annual Post Traumatic Stress Disorder Symposium for more than 230 mental healthcare professionals.
Conducting exceptional research has been an important part of the mission of Cleveland Clinic since its inception in 1921. At Cleveland Clinic, neurological research is conducted on three levels:

- Fundamental, laboratory-based biomedical research, conducted in the research institute
- Translational research that applies findings from the laboratories to our patients and clinical populations
- Patient-based clinical research aimed at developing new tests or treatments, or aimed at understanding disease and its impact

INNOVATIONS

In 2007, the NI founded the Neurological Institute Community of Collaborative Innovation (NICCI), a multidisciplinary group of physicians, scientists and bioethicists from the Neurological Institute, the Lerner Research Institute and the Department of Bioethics. The group’s mission is to create and maintain a culture of innovation within the institute, and to manage any associated conflicts of interest. NI staff were active innovators in 2007, registering 21 inventions with the Cleveland Clinic Innovations office and receiving three patents and four licenses for their discoveries. Three new spin-off companies were created in 2007 based on NI technology: Autonomic Technologies, CardioNomic and ReVasc Technologies.

GRANTS AND CONTRACTS

Neurological research conducted within the Neurological Institute, Lerner Research Institute and the Department of Neuroradiology received strong support in 2007. Grant and research dollars funding neurologic investigations totaled almost $14 million in 2007, including more than $9 million for laboratory-based research and nearly $5 million for patient-based research. Funding came from federal, state, local, corporate and private sources, including more than 50 grants from the National Institutes of Health.

**LERNER RESEARCH INSTITUTE**

The Lerner Research Institute is the basic science research arm of Cleveland Clinic, housing all of our laboratory-based and translational biomedical research. A hallmark of the institute is its focus on disease-oriented research, working to create new diagnostic tools, treatments and therapies, in collaboration with partners in the clinical institutes.

Thirty-six Lerner Research Institute scientists pursued neurologically based research projects in 2007, including 10 Neurological Institute clinicians who also conducted basic research in the Lerner Research Institute. This structure of bringing laboratory-based and clinical researchers together encourages translational research — taking the discoveries made in the laboratory to the patient’s bedside as quickly and safely as possible. The environment of collaboration between basic and clinical researchers has the more immediate effect of improving patient care today.

Neurological investigations within Lerner Research Institute are carried out in the departments of Biomedical Engineering, Cell Biology and Neurosciences.

**Department of Neurosciences**

The Department of Neurosciences, founded in 1994, is chaired by Bruce Trapp, PhD, and comprises a core of internationally recognized scientists. The department is divided into several core groups that focus on fundamental aspects of brain function and the pathogenesis of human disease. Strong basic science programs have resulted in the development of animal models of human diseases, which include rodents, zebrafish and primates. Departmental researchers directly investigate the pathogenesis of human central nervous system (CNS) diseases and have developed a unique rapid autopsy program for these studies. The overall goal of the department is to elucidate the cause of nervous system diseases and to develop therapeutics that stop or delay their progression. The interactions between faculty in the departments of neurosciences, neurology, neurological surgery, radiology and behavioral medicine provide a unique environment for reaching these goals.

This fluorescence microscopy depicts cells being generated from neural stem cells, which can generate in vitro astrocytes, oligodendrocytes and neurons according to the stimuli they are under. These cells are prime candidates for stem cell transplantation therapies. Here, the green staining is for the astrocyte marker glial fibrillary acidic protein and the red is the oligodendrocyte precursor marker platelet-derived growth factor receptor-alpha. Oligodendrocyte precursors (red) migrate away from the core while astrocytes (green) proliferate without apparent migration.
A major strength of the department is developmental neurobiology. Most faculty members have a research program in brain development. These interests range from stem/progenitor cells to the function of disease-related genes including the amyloid precursor protein, chemokines, myelin proteins, neurotransmitter receptors, BACE1 and the reticulins.

The department is noted internationally for its program in glial development, recently discovering a primitive neural cell with stem-cell-like characteristics. These cells show a remarkable capacity to generate new myelin in a rodent model of human myelin disease. Other developments include mouse and zebrafish lines in which cells of the oligodendrocyte lineage express green fluorescence protein. The mice have become a common and valuable resource in the glial research community. A major project focuses on Akt signaling in oligodendrocytes, which induces hypermyelination. Another recent discovery is the identification of a role for chemokines in oligodendrocyte colonization of the developing rodent brain. Additional current research includes cerebellar development, especially migration of granule cells, and the use of both rodent and zebrafish models to study the function of the amyloid precursor protein during development.

The glial research program has close ties with physicians in the Neurological Institute’s Mellen Center for Multiple Sclerosis Treatment and Research. Studies conducted here on the function of myelin proteins in mice have demonstrated that long-term axonal survival depends upon trophic support from myelin. As an extension of these basic science studies, Cleveland Clinic researchers described axonal degeneration as a major cause of neurological disability in MS patients. A rapid autopsy program was developed for individuals with MS. A unique aspect of these autopsies is a post mortem MRI that has been instrumental in defining pathological correlates of MRI abnormalities.

Current research in the neurodegenerative disease program includes a strong focus on Alzheimer’s disease. This includes investigations of molecular mechanisms of neurodegeneration in Alzheimer’s disease, focusing on the role of β-secretase, its interacting proteins and modification of its activity in disease pathogenesis; the genetic, therapeutic and environmental factors modifying Alzheimer’s disease pathogenesis using transgenic mouse models of the disease; and the normal biological functions of the amyloid precursor protein in both zebrafish and mice and the implications these may have for neurodegenerative disease mechanisms underlying Alzheimer’s disease. Additional neurodegenerative research includes the mechanisms of neuronal degeneration in amyotrophic lateral sclerosis (ALS) and the pathogenesis of neurodegeneration in an animal model of
ALS. Neuroimaging research within the section examines the functional neuroimaging correlates of neurodegenerative disease pathogenesis, including Alzheimer’s disease, Parkinson’s disease and MS.

The Neuromodulation Research Center (NMRC) focuses on the functional and physical changes in patients with movement disorders, the mechanisms of deep brain stimulation (DBS), and the development of new applications for DBS. The center incorporates investigators from the institute’s departments of Neurosciences and Biomedical Engineering as well as faculty from the Neurological Institute and the Imaging Institute. The NMRC is unique in that it uses a multidisciplinary approach to understand how neurological diseases arise and progress within the CNS. The NMRC then works to translate these understandings into clinical therapeutic applications.

NMRC researchers were the first to describe the effect of stimulation in the subthalamic nucleus on the basal ganglia thalamic circuit. The NMRC also has modeled the effect of stimulation on neuronal tissue using finite element models of neural tissue based on anatomical and electrophysiological data from primates with Parkinsonism. Current research includes using quantitative kinematic measures to assess the effects of DBS on motor control and daily living experiences of Parkinson’s disease (PD) patients, including the interaction between cognitive and motor function and the effect of exercise on PD motor symptoms; studying the mechanisms of DBS using functional MRI to evaluate the network changes that take place during DBS in PD patients; studying mechanisms of DBS through imaging, modeling and quantitative kinematic studies in dystonia and PD; developing closed-loop systems for DBS programming; and using chronic recording from cortical neurons to develop prosthetic devices.

The Neuroinflammation Research Center (NIRC) conducts multidisciplinary translational research to address neuroinflammation in human disorders including MS, Alzheimer’s disease, Parkinson’s disease, amyotrophic lateral sclerosis (ALS) and stroke. The center includes an internationally recognized initiative in MS that provides

**DETECTING CHANGES IN BRAIN ACTIVATION PATTERNS IN EARLY ALZHEIMER’S DISEASE**

A team of investigators in the Neurological Institute is studying changes in brain activation of healthy older individuals (ages 65-85) who are genetically at risk for developing Alzheimer’s disease (AD) and individuals who have Mild Cognitive Impairment (MCI), a condition that typically precedes the diagnosis of AD. One goal of the study is to develop an imaging biomarker that can detect the earliest brain changes associated with AD. Nineteen MCI patients, 19 genetically at-risk but healthy older adults, and 19 healthy older adults not at-risk for AD (Control) were administered a memory task while undergoing functional magnetic resonance imaging (fMRI). Results indicate that fMRI is sensitive to detecting the earliest changes in AD, even before patients become symptomatic. The goal is to use this imaging technology to assess the efficacy of drugs designed to delay the onset of AD.

Studies supported by the NIH (NIA R01 AG022304).

Three groups of older participants, MCI patients, individuals at-risk for developing AD, and healthy not-at-risk control subjects were asked to discriminate names of famous individuals from those of unfamiliar persons. The difference in brain activation (Famous > Unfamiliar) is shown in blue. MCI and at-risk participants exhibited greater brain activity than controls. Results suggest that early AD-related changes require the brain to “work harder” to achieve similar levels of task performance. (Rao SM, et al. Submitted.)
EVALUATING DEEP BRAIN STIMULATION WITH fMRI

Investigators from the Neurological Institute and the Imaging Institute have collaborated to study the effect of deep brain stimulation (DBS) in patients with Parkinson’s disease using functional MRI. The investigators are determining how the brain is activated during DBS for Parkinson’s disease. Early results demonstrated a consistent pattern of brain activation produced by stimulation within the ipsilateral thalamus and globus pallidus. These studies will lead to a better understanding of the relationship between brain activation and DBS in Parkinson’s disease, and will provide the necessary information to maximize therapeutic benefits of this treatment.

Studies Supported by the NIH (NINDS R01 NS052566-01A1).


The overall goal of the department is to elucidate the cause of nervous system diseases and to develop therapeutics that stop or delay their progression.

The interactions between faculty in the departments of neurosciences, neurology, neurological surgery, radiology and behavioral medicine provide a unique environment for reaching these goals.

a template for program development and exemplifies bench-to-bedside evolution. Our current focus includes neuroimmunology, leukocyte trafficking, blood-brain barrier function, cytokine action and signaling, and innate immune mechanisms (including Toll-like receptors) in furtherance of the mission to understand how the CNS interacts with the hematogenous compartment and the peripheral nervous system. The center recently established a program of study in a viral model of MS and received grant support from the National Institute of Allergy and Infectious Diseases/NIH for this research. In 2007, the center developed a new mouse model of cerebral vasospasm to study how inflammatory cells in the cerebrospinal fluid precipitate ischemic stroke in patients who have suffered subarachnoid bleeding. Other current projects include the study of a novel mouse model of microglial activation in Alzheimer’s disease, and a new and more clinically relevant model of Duchenne muscular dystrophy, which will be used to define how inflamed and dystrophic muscle becomes fibrotic.

Biomedical Engineering

Lerner Research Institute’s Biomedical Engineering Department provides a forum in which engineers, basic scientists and physicians can interact, seeking together to apply engineering principles to solve biomedical problems. Active research programs include biological microelectromechanical systems (BioMEMS) and the design and utilization of micro-computed tomography (micro-CT), quantifying images of the brain in multiple sclerosis, and recording and modeling the brain’s electrical activity.

Biomedical imaging staff researchers work on a variety of research projects that include clinical, microscopic and small animal imaging applications. The primary goal of these investigators is to develop novel imaging and image post-processing techniques to detect, diagnose and monitor the progression of disease and to evaluate different treatment therapies. Research and development within this group includes tissue characterization using high-frequency intravascular ultrasound, 3D real-time ultrasound and multimodality imaging, quantitative analysis of tissue damage due to multiple sclerosis in MR images of the brain, and 3D quantitative phenotyping in micro-CT images of mice.
INVESTIGATING BRAIN PATHOLOGY IN MULTIPLE SCLEROSIS

A team of investigators in the Neurological Institute and Lerner Research Institute is studying changes in the brains and spinal cords of patients with multiple sclerosis. One goal of the study is to develop more informative imaging tools that can be used to monitor and treat MS patients. In this study, regions of brain were selected from postmortem MRIs of 10 multiple sclerosis patients, and classified into MRI-defined categories. One of the categories identified swollen axons and axonal loss, pathologies that are associated with neurological disability in MS. Studies to characterize cellular and molecular changes in brain tissue are continuing. We expect to gain improved understanding of mechanisms leading to brain damage in MS patients, and improve methods to monitor treatments for individual patients using noninvasive MRI methods.

Studies Supported by the NIH (NINDS PO1 NS38667).

Axonal Measurements By MRI Region Type

Plot of percentage axonal area, axonal count and swelling index in each magnetic resonance imaging group (gray bars denote T2-weighted imaging only; black bars denote T2-weighted, T1-weighted and magnetization transfer ratio abnormal [T2T1MTR]) relative to the means for normal-appearing white matter (NAWM; hatched bars) regions. Sd - standard deviation. Fisher E, et al. Ann Neurol. 2007;62:219-228.

Nanotechnologists use microelectronics, microfabrication and micromachining technologies to improve medical diagnostics and therapies by reducing device size and cost. Their collaborative studies involve engineering micro-/nanometer-sized features for tissue engineering, protein analyses, assays and cell interrogation. Among the applications being developed are miniaturized versions of drug delivery systems, transducers for ultrasound images and in situ telemetrically monitored pressure/temperature sensors for minimally invasive surgery/follow-up.

The neural control group performs basic science and clinical research related to neural control of movement. The program focuses mainly at system level of the central nervous system (CNS) as well as the muscular system. Research interests include understanding CNS plasticity/reorganization as a result of disease and medical intervention, and its relation with functional recovery. Current projects include evaluating effects of deep brain stimulation on lessening symptoms in Parkinson’s disease and the underlying mechanisms using neural-network simulation, and understanding CNS reorganization in stroke and other neurological disorders using neuroimaging and electrophysiological techniques.

Cell Biology

The Department of Cell Biology investigates the roles of specific cell types in health and disease, researching cell and molecular biology and inflammation. Neurological-
based research currently being conducted includes investigations of the blood-brain barrier, multiple drug resistance, stroke and cerebrovascular damage, peripheral markers of CNS damage, and molecular and proteomic analysis of neurological disorders.

PATIENT-BASED RESEARCH

The Neurological Institute conducts research on conditions experienced by our patients. Clinical research protocols include programs in bench-to-bedside translational research, trials of drugs and devices, neuroimaging research, epidemiology and health outcomes, behavioral and psychiatric research, and investigations into better diagnostic methods. More than 175 clinical research protocols were active within the Neurological Institute in 2007, including 44 newly opened studies. Patient-based clinical research within the institute is conducted by multidisciplinary research teams combining expertise and clinical knowledge of investigators focusing on research computing and informatics, clinical trial methods, outcomes assessment and neuroimaging. Multidisciplinary teams that comprise of staff physicians, clinical investigators of various professional disciplines, clinical fellows, full-time research fellows, residents, nurses and certified research coordinators are supported by shared enabling resources to coordinate study startup and conduct, and to assist with study design, data capture and analysis. Through a multidisciplinary, team approach that uses central resources, we are able to generate new knowledge that will create better treatment options for our patients.

More than 1,600 patients were enrolled in clinical trials at the Neurological Institute in 2007, including almost 700 newly enrolled patients, with more than 60 of our staff members leading these trials. Research studies covered the range of neurological conditions we treat, including Alzheimer’s disease and dementia, spine disease, brain tumors, epilepsy, headache and pain, multiple sclerosis, Parkinson’s disease and other movement disorders, depression and affective disorders, nerve and muscle disease, neuropediatrics and congenital disorders, sleep disorders, stroke and neurocritical care.

2007 NI CLINICAL TRIAL HIGHLIGHTS

- Assessing the entry of chemotherapeutic agents into brain metastases in women with breast cancer
- Evaluating selective, 5-lipoxygenase inhibition by Boswellia serrata herbal medicine approach as an adjuvant therapy in newly diagnosed and recurrent high grade gliomas
- CONFIRM: comparing fumarate with Copaxone® in patients with relapsing-remitting multiple sclerosis
- CARE-MS II: comparing two doses of alemtuzimab (CAMPATH-1h) with Rebif® in patients with relapsing-remitting multiple sclerosis
- Deep brain stimulation for obsessive-compulsive disorder
- Deep brain stimulation for the minimally conscious state
- Predictors of bipolar disorder recurrence in pregnancy and the postpartum period
- Sensitivity of fMRI in identifying cognitive and functional brain changes in preclinical Huntington’s disease
- Evaluating Duragen® plus adhesion barrier matrix to minimize adhesions following lumbar discectomy
- Assessing changes in quality of life following surgery versus medical management in persons with medically intractable epilepsy
- IRIS: determining if pioglitazone is effective in lowering the risk of stroke or myocardial infarction among non-diabetic men and women with a recent ischemic stroke and insulin resistance

2007 NI CLINICAL RESEARCH TRIALS AT A GLANCE

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At the core of the Knowledge Program is a redesign of the way the Neurological Institute organizes the immense amount of clinical information it has. “The project is an institute-wide effort to change the way we collect data so that it can be harvested and used,” explains neurologist Irene Katzan, MD, who is directing the Knowledge Program. “Our goal is to be able to look at data on both an individual and group level to evaluate clinical treatment over time and provide better care.”

One of the first obstacles to be overcome was how to make patient information that traditionally is gathered by the nurse or physician during the clinical encounters more readily available for future use. The Knowledge Program is tackling this by utilizing a standardized format for entering information during patient visits. During the patient’s appointment, all clinical information will be collected and entered into the patient’s electronic medical record in a standardized way, beginning with the evaluation of incoming patients’ current health status. Obtaining information on patients’ health using validated scales provides means to determine how patients are doing and to better judge responses to treatment.

“This is an electronic system in which patients complete a self-administered questionnaire when they come in for their appointment, prior to seeing the physician,” Dr. Katzan explains. The health status measures will include generic measures, such as the European Quality of Life scale, as well as well-established disease-specific scales such as the Headache Impact Test 6. “Establishing a quantitative baseline will allow us to then look at trends over time,” Dr. Katzan notes. Part of the process, too, is ensuring that all physicians know how to access the information to use it during each patient encounter. The electronic patient questionnaires, which interface with EPIC, Cleveland Clinic’s electronic medical record software, are being rolled out center by center within the Neurological Institute. By the end of 2008, they will be in use institute-wide.

In addition, the Knowledge Program is in the process of implementing a computer-adaptive testing system to assess patients’ health status, in collaboration with a National Institutes of Health initiative called the Patient-Reported Outcomes Measurement Information System (PROMIS). With this method, a computerized algorithm determines the next best question in the series, based upon prior responses from the patient. Dr. Katzan describes this tool as “the future of patient-reported outcomes assessment,” adding that it “creates a more precise picture of what’s going on with the patient, using fewer questions.”

At the other end of the patient care process, the Neurological Institute needed a method to consistently track outcomes of interventions, an essential element in creating a meaningful database. Unfortunately, some Neurological Institute patients are lost to follow-up due to geographic distance or other reasons, Dr. Katzan says. To
As part of the Knowledge Program, all Neurological Institute patients input their answers to standardized health questions prior to their appointments.

capture data on these patients, the Neurological Institute plans to implement a simple but consistent and organized telephone follow-up system. “This will make our patient follow-up more systematic and ensure that the outcomes information we capture is as accurate as possible.” Dr. Katzan says.

By virtue of its complexity and scope, the Knowledge Program is undoubtedly a bold concept, but Dr. Katzan notes that the Neurological Institute is uniquely positioned to make it a success due to its large patient population, technological capabilities and organizational structure. “We are one of the few institutions with all of the necessary elements to implement such an ambitious database, and we are leading the way,” she says. “Once we have all of the pieces in place and operational, it is a matter of using the database for improving the quality and outcomes of care.”
BRAIN TUMOR AND NEURO-ONCOLOGY CENTER
Neuro-oncologists, medical oncologists, neurosurgical oncologists, radiation oncologists, neuropathologists, neuroradiologists and nurses in the Brain Tumor and Neuro-Oncology Center (BTNC) collaborated in the treatment of more than 4,600 children and adults with brain tumors and other related conditions in 2007.

Innovative and experimental nonsurgical treatments for life-threatening tumors, state-of-the-art surgical techniques and targeted radiation neuro-oncology technologies applied in combination with molecular and chromosomal testing have positioned the Brain Tumor and Neuro-Oncology Center at the forefront of individualized care for patients with brain tumors.

Clinical programs in the center include medical therapeutics, radiation therapy and neurosurgical treatment, as well as alternative methods for patients with a variety of benign and malignant CNS conditions. The team at the BTNC cares for patients with gliomas, metastases, pituitary and neuro-endocrine tumors, skull base tumors (meningiomas and schwannomas), neurofibromatosis and other phakomatoses, and primary central nervous system lymphoma.

**NEURO-ONCOLOGY**

BTNC neuro-oncology team members are experts in the use of medical therapeutics for the treatment of brain tumors, including:

- Chemotherapy/growth modifiers — traditional anti-tumor drugs as well as new agents targeted at specific tumor modalities
- Immunotherapy — stimulating the patient’s immune system against tumor cells
- Intra-arterial chemotherapy with or without blood-brain barrier disruption — a procedure in which chemotherapeutic agents are delivered to the brain through the bloodstream with or without opening the normal barriers that may prevent those drugs from entering the brain
- Alternative and complementary treatments — including dietary interventions and yoga

**NEUROSURGICAL ONCOLOGY AND RADIATION NEURO-ONCOLOGY**

BTNC surgeons, who pioneered computer-assisted stereotactic techniques for brain surgery in the 1980s, have extended the scope of operable brain tumors through the use of leading-edge technology, including:

- Stereotactic neurosurgery — computer-guided surgery that serves as a GPS system for the brain, often using ‘fiber tracking’ and functional MRI that allows the surgeon to see the function and ‘wiring’ of the brain
- Minimally invasive as well as endoscopic and endoscopic-assisted surgical procedures
- Intraoperative magnetic resonance imaging (iMRI) — navigational guidance and monitoring during tumor resection
- Convection-enhanced delivery — the slow, continuous infusion of drugs through the brain to enhance drug delivery to brain tumors
- Intraoperative radiation therapy — uses the INTRABEAM®, a 50 kVp device placed in the resection cavity of metastatic brain tumors to deliver a high local dose of radiation at the time of surgery to prevent or delay the need for whole brain irradiation
- Fractionated radiotherapy — widespread exposure of the brain and tumor to repeated low doses of radiation
Brachytherapy — direct implantation of a radiation source within a tumor site

Cranial radiosurgery — the delivery of high-intensity, focused radiation directly to multiple sites within the tumor using the Gamma Knife® or Novalis®. Gamma Knife® is used for single treatments of small tumors; Novalis® is used for larger tumors.

Spinal radiosurgery — the delivery of high-intensity, focused radiation directly to spinal metastases employing the Novalis® shaped-beam platform.

FELLOWSHIPS

The BTNC offers several non-ACGME-accredited fellowships. These include two two-year fellowships in neurosurgical oncology and a one-year fellowship in skull base surgery.

A fundamental goal of this combined clinical and research fellowship program is exposure to the design and operation of clinical trials, as well as contribution to the neuro-oncology literature. Fellows are expected to participate in the design, IRB application process and management of new clinical trials and to produce clinical trials and reports.

CLINICAL RESEARCH

In 2007, 374 patients were enrolled in clinical trials related to their diagnosis. In addition to its own phase I-II trials, the BTNC participates in several national and international consortia, including New Approaches to Brain Tumor Therapy (NABTT) sponsored by the National Cancer Institute, Radiation Therapy Oncology Group (RTOG), American College of Surgeons Oncology Group (ACoSOG) and Children’s Oncology Group (COG).

BTNC physicians have developed a reputation for national and international leadership in neuro-oncology clinical trials. BTNC physicians serve as national and international principal investigators on multiple RTOG and pharmaceutical industry trials.

Open adult clinical trials include studies of medications, radiation therapies, stereotactic radiosurgery, chemotherapies, gene therapies, hormone therapies, blood-brain barrier disruption, devices, intraoperative optical spectroscopy, dietary and herbal complementary and alternative medicine and stress reduction for astrocytomas, glioblastomas, lymphomas, metastases and oligodendrogliomas.

Open child and adolescent protocols include studies of medications, chemotherapies, chemoradiation therapies, radiotherapies and second-look surgeries for malignant brain tumors, CNS AT/RT, CNS embryonal tumors, ependymoma, NGGCT, gliomas, CNS germinomas, medulloblastomas, neurofibromatosis type 1, astrocytomas and solid tumors.

The Brain Tumor and Neuro-Oncology Center’s new Gamma Knife® Perfexion equipment is the most technologically advanced model available, allowing for treatment in a wider range of anatomical structures, enhanced planning, use of all imaging modalities and reduced treatment time.

The Brain Tumor and Neuro-Oncology Center initiated a collaboration with industry to develop laser interstitial thermal therapy for brain tumors — moving initial research from the preclinical phase to a first-in-man trial.
The BTNC has two primary laboratories under the direction of Drs. Michael Vogelbaum and Robert Weil. Current research focuses on molecular genetics, apoptosis, engineering, immunology, progenitor cells and genomics/proteomics. In addition to basic research in these areas, BTNC researchers in the Translational Therapeutics Program, directed by Michael Vogelbaum, MD, PhD, perform preclinical testing of novel agents for treating brain tumors with the aim of bringing these agents to clinical trials. The BTNC laboratories collaborate closely on basic research projects with the Cancer Biology and Immunology departments in the Lerner Research Institute.

Basic research projects in progress include:

- Mechanisms for sensitizing glioma cells to chemotherapy
- The role of STAT3 in the biology of gliomas
- Genetic alterations and biological characterization of primary cell cultures derived from malignant gliomas
- Genetic alterations in GBMs (loss or gain of 19q, 1p and other novel alterations) and their correlations with patient survival
- Development of a clinical assay for detection of deletions in CDKN2A, ARF, PTEN and p53 genes in gliomas
- 7,5-lipoxygenase inhibition as an adjuvant glioma therapy
- Molecular biology of brain tumors
- Blood-brain barrier, tumor markers and human gliomas project
- Molecular pathology of gliomas: “glioma genotyping”
- Transcription factors and brain tumors
- Molecular genetic investigation of pituitary tumors
- Genetic polymorphism analyses of brain tumors
### Outcomes Highlights

#### Supratentorial Craniotomy: Inpatient Mortality and Length of Stay

<table>
<thead>
<tr>
<th>Days</th>
<th>Number of Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>2003</td>
<td>100</td>
</tr>
<tr>
<td>2004</td>
<td>90</td>
</tr>
<tr>
<td>2005</td>
<td>80</td>
</tr>
<tr>
<td>2006</td>
<td>70</td>
</tr>
<tr>
<td>2007</td>
<td>60</td>
</tr>
</tbody>
</table>

- Target LOS
- Mean LOS
- Actual Mortality
- Expected Mortality

Expected deaths are based on APR-DRGs, which adjust for the severity of the patient population.

#### Infratentorial Craniotomy: Survival

<table>
<thead>
<tr>
<th>Percent Survival</th>
<th>Number of Surgeries</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-Day Survival</td>
<td># of Surgeries</td>
</tr>
<tr>
<td>180-Day Survival</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Thirty and 180-day survival remained robust in 2007 for infratentorial craniotomies at 100 and 96.2 percent.

#### Pituitary Surgery: Inpatient Mortality

<table>
<thead>
<tr>
<th>Days</th>
<th>Number of Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>2003</td>
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</tr>
<tr>
<td>2004</td>
<td>0.8</td>
</tr>
<tr>
<td>2005</td>
<td>0.6</td>
</tr>
<tr>
<td>2006</td>
<td>0.4</td>
</tr>
<tr>
<td>2007</td>
<td>0.2</td>
</tr>
</tbody>
</table>

- Mean LOS
- Target LOS
- Actual Mortality
- Expected Mortality

There have been no inpatient deaths following pituitary surgery in the past five years. Target length of stay (LOS) is calculated based on APR-DRGs, which adjust for the severity of the patient population.
Dizziness wasn’t enough to slow down Joe Case, a busy business owner who had not seen a doctor in years. As hearing and visual disturbances set in, however, Mr. Case knew it was time to seek help. CT and MR imaging confirmed a tumor, but surgery at a local hospital failed to remove it entirely. He made the commitment to get the best care he possibly could, and found people to drive him more than an hour to Cleveland Clinic every day for six weeks for radiation therapy. Afterward, he joined a trial of Tarceva®, a lung cancer chemotherapy drug being studied in glioblastoma. Three years later, the tumor hasn’t grown. Case, who is married and has a 1½-year-old son, stays more active than ever, and just participated in the American Brain Tumor Association’s annual 5K race.

“Next to my wife and family, Cleveland Clinic has been my godsend. I tell anyone who has any cancer problems not to waste their time anywhere else. I don’t have the words to praise Cleveland Clinic enough for the fact that I am still here. My doctors and nurses are like family to me now.”
**OUTCOMES HIGHLIGHTS**

Stereotactic Radiosurgery: Survival

<table>
<thead>
<tr>
<th>Year</th>
<th>30-Day Survival</th>
<th>180-Day Survival</th>
<th># of Procedures</th>
</tr>
</thead>
<tbody>
<tr>
<td>2003</td>
<td>100</td>
<td>100</td>
<td>20</td>
</tr>
<tr>
<td>2004</td>
<td>80</td>
<td>80</td>
<td>20</td>
</tr>
<tr>
<td>2005</td>
<td>60</td>
<td>60</td>
<td>20</td>
</tr>
<tr>
<td>2006</td>
<td>40</td>
<td>40</td>
<td>20</td>
</tr>
<tr>
<td>2007</td>
<td>20</td>
<td>20</td>
<td>20</td>
</tr>
</tbody>
</table>

The number of Gamma Knife® cases peaked in 2007 despite a six-week hiatus for upgrading to the Gamma Knife® Perfexion™. Thirty and 180-day survival for Gamma Knife® were 97.6 and 91.3 percent respectively with the highest 180-day survival in the last five years.

**PUBLICATION HIGHLIGHTS**


**EDUCATION**

More than 300 physicians and physicists have been trained on Gamma Knife® technology through the Brain Tumor and Neuro-Oncology Center.
CLINICAL PROGRAMS

Cleveland Clinic’s Cerebrovascular Center offers a unique mix of physician subspecialties delivering endovascular therapy and cutting-edge care of the highest quality with proven successful outcomes. The quality stroke care that we deliver places an emphasis on aggressive acute stroke intervention and multi-modality therapy of brain aneurysms and AVMs. In addition, there is strength in stroke prevention through our vascular neurology team, with leverage on outcomes research.

Endovascular approaches are standard of care, and our advanced imaging capabilities will guide treatment decisions. Patients also receive comprehensive care in our 16-bed neurointensive care unit staffed by neurointensivists, inpatient nursing and dedicated mid-level practitioners. Our Cerebrovascular Center received re-certification as a Primary Stroke Center in 2007.

We provide patients efficient, high-quality care for acute stroke, coupled with excellent patient outcomes and shorter lengths of stay. With a case severity index in the top 2.2 percent in the United States, the Cerebrovascular Center performed better than national comparisons for inpatient mortality, length of stay and hospital costs in 2007.

Long-term, risk-factor modification programs are available through the Cerebrovascular Center in conjunction with physical medicine and rehabilitation services.

Cerebrovascular disease states we treat include:

**Carotid Occlusive Disease (Stenosis)**

Cleveland Clinic specialists are leaders in carotid endarterectomy and carotid angioplasty for this disease with outcomes that surpass national averages.

**Cerebral Aneurysms**

Treatment of ruptured and unruptured brain aneurysms and arteriovenous malformations (AVMs) continues to outnumber all other cerebrovascular surgical procedures. In addition to microsurgical clipping, endovascular neurosurgeons also use detachable coils, intracranial self-expanding stents and new embolic agents to treat aneurysms and AVMs.
Arteriovenous Malformations (AVMs)

The center provides multidisciplinary consultation and treatment for these disorders, including microsurgical resection, embolization and Gamma Knife® stereotactic radiosurgery.

2007 Cerebrovascular Center highlights:

° In collaboration with hospitals across the Cleveland area, we are working to increase the number of Joint Commission-certified stroke sites and provide coverage where needed
° We developed the Temporary Endovascular Bypass technology for stroke treatment
° We completed the world’s largest-ever study of intracranial atherosclerotic disease

FELLOWSHIPS

Neurointensive Care

Four two-year fellowships are available in neurointensive care. The fellowship provides comprehensive training in neurointensive care, medical and surgical intensive care and vascular neurology. There is an active clinical research program including therapeutic hypothermia and neuromonitoring. This fellowship is the only UCNS-approved Neurological Intensive Care Unit fellowship in the region, and is one of the first nine programs in the country to receive this certification.

Vascular Neurology

Two ACGME-accredited one-year fellowships in vascular neurology are offered for those who desire further subspecialty training in this area.

Endovascular Neuroradiology

The Cerebrovascular Center offers two ACGME-accredited two-year fellowships in endovascular neuroradiology. The fellowships provide trainees an organized, comprehensive, supervised, full-time educational experience in neuro-endovascular surgery/interventional neuroradiology (NES/INR). This experience includes the management of patients with neurological disease,
the performance of NES/INR procedures, and the integration of NES/INR therapy into the clinical management of patients.

**CLINICAL RESEARCH**

Current clinical trials offered through Cleveland Clinic’s Cerebrovascular Center include:

- Phase III, randomized, multicenter, open label clinical trial to examine whether a combined intravenous (IV) and intra-arterial (IA) approach to recanalization is superior to standard IV rt-PA (Activase®) alone when initiated within three hours of acute ischemic stroke onset
- NeuroThera® Effectiveness and Safety Trial (NEST-2), a phase III, randomized, multicenter, double-blind, controlled study to assess safety and effectiveness of the treatment of ischemic stroke with the NeuroThera® Laser system within 24 hours from stroke onset
- Carotid occlusion surgery study (COSS) for symptomatic carotid occlusion
- IRIS trial to determine if pioglitazone, compared with placebo, is effective in lowering the risk for stroke or myocardial infarction among non-diabetic men and women with a recent ischemic stroke and insulin resistance
- Long-term cardiac complications of subarachnoid hemorrhage
- Percutaneous mechanical hematoma evacuation of spontaneous intracranial hemorrhage
- Matrix and Platinum Science (MAPS) trial for cerebral aneurysm embolization comparing two FDA-approved embolic coil types for safety and efficacy
- Trial for patients who have had a stroke or TIA possibly related to a patent foramen ovale (CLOSURE-I)
- Warfarin vs. Aspirin (WARCEF) in reduced cardiac ejection fraction
- Use of rimonabant vs. placebo in patients with multiple cardiovascular risk factors and abdominal obesity to show reduction of cerebrovascular events (CRESCENDO)

In 2007, the Cerebrovascular Center completed the 160-patient, five-center U.S. Multicenter Wingspan Registry.
OUTCOMES HIGHLIGHTS

Treatment of Unruptured Aneurysms

Number of Procedures

Treatment of Ruptured Aneurysms

Number of Procedures

Discharge Status

<table>
<thead>
<tr>
<th>2007 Discharge Status</th>
<th>Unruptured Aneurysms</th>
<th>Ruptured Aneurysms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Home</td>
<td>80%</td>
<td>37%</td>
</tr>
<tr>
<td>Home Health</td>
<td>5%</td>
<td>5%</td>
</tr>
<tr>
<td>Acute Rehab</td>
<td>3%</td>
<td>14%</td>
</tr>
<tr>
<td>Skilled Nursing Facility</td>
<td>1%</td>
<td>19%</td>
</tr>
<tr>
<td>Expired</td>
<td>1%</td>
<td>19%</td>
</tr>
<tr>
<td>Other</td>
<td>5%</td>
<td>18%</td>
</tr>
</tbody>
</table>

The Cerebrovascular Center offers four different fellowships for training in advanced cerebrovascular care.
Teresa Martens was having a series of mini-strokes, but she was busy with school and planning her wedding, so she ignored them. When she finally went to see a local neurologist, he wanted to do a brain biopsy, which would have required her to shave her head. As a bride to be, she was quite hesitant. Meanwhile, her insurance company noticed all the tests she was having and called to suggest she travel to Cleveland Clinic to see Peter Rasmussen, MD. She agreed, and was diagnosed, treated and ready to go home within 10 days of arriving in Cleveland. Today, she feels great and is back to her busy life.

“This was such a scary thing to go through. I really needed answers and hope. Since my treatment, I have talked with a few people who know someone who is suffering from similar mini-stroke-like episodes, and I always refer them to Cleveland Clinic. I even carry the phone number to Cleveland Clinic in my cell phone to have ready to hand out! Without Cleveland Clinic, I really could have suffered irreversible brain damage.”
PUBLICATION HIGHLIGHTS


CLINICAL PROGRAMS

Adult and Pediatric Epilepsy

Cleveland Clinic’s Epilepsy Center is one of the leading epilepsy programs in the world. In 2007 our team again saw one of the largest patient volumes in the world in outpatient clinics and evaluated nearly 1,000 adult and pediatric patients in two dedicated, state-of-the-art epilepsy monitoring units equipped with digital video-EEG technology.

Specialized neuroimaging services include advanced high-resolution magnetic resonance imaging (MRI using specialized imaging techniques), functional magnetic resonance imaging (fMRI), magnetic resonance spectroscopy (MRS), ictal single-photon-emission computed tomography (SPECT) and positron emission tomography (PET). Cleveland Clinic’s Epilepsy Center recently opened the first clinical magnetoencephalography (MEG) program in northeastern Ohio to further assist in the diagnosis and workup of patients with epilepsy. With advanced MEG equipment and world-renowned research scientists in the field of clinical and applied neurophysiology, we are introducing state-of-the-art noninvasive diagnostic abilities that will enable our physicians and staff to manage the most complex and challenging epilepsy cases.

Our Pediatric Epilepsy Program is one of the world’s premier programs for children and adolescents who are affected with epilepsy. Combining a multidisciplinary approach towards the most advanced monitoring and treatment with compassion and caring, Cleveland Clinic’s program achieves excellent patient outcomes. Pediatric patients are evaluated in the newly expanded Pediatric Epilepsy Monitoring Unit and in the Pediatric and Neonatal ICUs.
Epilepsy Surgery

Our Epilepsy Surgery Program for adults and children with medication-resistant epilepsy is one of the foremost programs of its kind in the world. Cleveland Clinic was one of the first institutions in the world to perform brain mapping for pre-surgical evaluation in epilepsy. Performing more than 200 surgeries annually, including nearly 90 pediatric epilepsy procedures, our surgeons have expertise in the leading treatments for surgical epilepsy, including extra-temporal surgery, hemispherectomy, lesionectomy, temporal lobectomy and vagal nerve stimulation. In addition, Cleveland Clinic Epilepsy Center is the only program in the state of Ohio to offer a new investigational technique of computer-assisted responsive neurostimulation (RNS, NeuroPace®) for select patients with focal epilepsy who failed various antiepileptic medications and are not resective surgery candidates.

Cognitive Behavioral Program

This multidisciplinary, comprehensive cognitive and behavioral program provides psychosocial assistance to patients with seizures at various stages of the patient’s evaluation and treatment. By bringing together epileptologists, psychiatrists, neuropsychologists, social workers and rehabilitation specialists, the program seeks to care for the full spectrum of physical, mental, emotional, social and practical needs and issues that affect the lives of our epilepsy patients.

FELLOWSHIPS

The Epilepsy Center’s education programs offer in-depth exposure to our comprehensive approach to the diagnosis and management of adults and children with epilepsy, including surgical and investigational treatments. The aim of our program is the most comprehensive training of future academic epileptologists and epilepsy surgeons. Our graduates have played and will continue to play an integral role in treatment and innovation in epilepsy.

Currently, our approved educational/training programs consist of the following:

- Five one-year fellowships in clinical neurophysiology/EEG, which provide an intensive experience in EEG and evoked potentials in the diagnosis and management of epilepsy
- Five one-year non-ACGME epilepsy fellowships
- A one-year surgical epilepsy fellowship

The Epilepsy Center installed the first clinical MEG (magnetoencephalogram) system in Ohio. The MEG will improve noninvasive localization of the seizure focus in patients who suffer from intractable epilepsies.

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- A one-year surgical epilepsy fellowship

The Pediatric Epilepsy Support Group is led by a pediatric epileptologist and provides families of children with epilepsy a venue for education, discussion and camaraderie.
CLINICAL RESEARCH

The many facets of epilepsy are reflected in the scope of the Epilepsy Center’s clinical research. Some of the areas currently being studied through clinical trials include:

- The genetics of epilepsy
- Hormone therapy for women with seizures
- Development of novel treatment techniques
- Responsive neurostimulation (RNS) with the NeuroPace® trial
- Clinical drug trials
- Physiologic markers and characterization of depressive subtypes in treatment-refractory epilepsy

LABORATORY RESEARCH

Cleveland Clinic Lerner Research Institute and Epilepsy Center scientists are pursuing basic and translational research that aids in the understanding of the neurological basis for epilepsy and potential molecular-level interventions for the disease. Some of our current areas of research include:

- Molecular genetics and cellular mechanisms of epilepsy
- Molecular and cellular mechanisms of resistance to antiepileptic medications
- Application of deep brain stimulation in epilepsy

In 2007, 411 patients were enrolled in clinical trials through the Epilepsy Center.

The Epilepsy Center’s monitoring units use digital video-EEG technology to accurately locate seizure origin.
OUTCOMES HIGHLIGHTS

Long-Term Seizure Freedom Following Frontal Lobe Surgery for Epilepsy (n=119 surgeries from 1997-2007)

Seizure Freedom Following Hemispherectomy for Epilepsy (n=65 surgeries from 2004-2006)

Seizure Freedom Following Temporal Lobectomy for Epilepsy (n=474 surgeries from 1997-2007)

Seizure Freedom Following Posterior Quadrant Resections for Epilepsy (n=60 surgeries from 1997-2007)
Russell began having seizures at 2 weeks old. A trip to the local emergency room and a stay in a Columbus hospital didn’t yield any answers. The seizures returned about six months later, along with pneumonia. A doctor in Columbus advised Russell’s parents to take their worsening child to Cleveland Clinic, where he was taken to the ICU immediately due to complications with his breathing. William Bingaman, MD, and colleagues removed Russell’s right hemisphere over the course of two surgeries. Russell has been completely seizure-free ever since and undergoes therapy to improve his left-side motor skills.

“If we hadn’t gone to Cleveland Clinic, Russell wouldn’t be here today,” says Russell’s mother. “They saved my son’s life. It was so scary, but they explained everything so well and made us feel like they were going to fix it. And they did.”
**PUBLICATION HIGHLIGHTS**


The Epilepsy Center hosted its 17th International Epilepsy Symposium in June 2007.
CENTER FOR
HEADACHE AND PAIN
The Center for Headache and Pain offers a unique, interdisciplinary approach to headache management involving specialists in adult neurology, pediatric neurology, internal medicine, psychology, nursing, physical therapy and nutrition. Effective preventive and abortive treatment for migraine, tension headache and cluster headache frequently involves a combination of pharmacologic agents, behavioral therapy, psychotherapy, nutrition, physical therapy and other modalities.

The infusion program is devoted to intravenous infusions specific for headaches and provides urgent, inpatient-type care to patients who would otherwise have visited an emergency room. In 2007, infusion patient volume continued to increase. This allowed for the successful outpatient treatment of many otherwise stable headache patients who suffered episodes of acute exacerbations of pain as well as the initiation of treatment for the many patients with chronic headache disorders. The infusion program also provided an accessible site for initiation of analgesic research studies and analgesic treatment, including detoxification from medications that perpetuate headaches.

The Cleveland Clinic Center for Headache and Pain also has pioneered home care infusion nursing, which has allowed patients to remain in the comfort of familiar surroundings while receiving aggressive medical therapy.

Additionally, Cleveland Clinic has been one of the early adopters of botulinum type A therapy for headache, and this service has attained steady growth since the headache program was created in 2004. Patient referrals for this treatment continued to expand in 2007.

In 2007, the Center for Headache and Pain initiated the IMATCH Program (Interdisciplinary Method for the Assessment and Treatment of Chronic Headache). This three-week program was designed to provide a multidisciplinary approach to the diagnosis and intensive treatment of longstanding, functionally disabling headache disorders. It incorporates the fusion and coordination of a number of invaluable services for this impaired patient population, including behavioral management, intensive physical therapy, medical management (including the infusion room) and education, and has treated nearly 100 patients to date. Treatment focuses on enabling patients to regain normal functioning that has been lost due to pain. While pain may not be eliminated completely, patients are taught how to manage the pain so that it does not consume their lives.
Pain Outcome Following IMATCH (n=36)

**Pain Ratings** (0=no pain; 10=worst possible pain)

- Admission
- Discharge

Measure of pain scores (mean + s.d.) decrease following the IMATCH (Interdisciplinary Method for the Assessment and Treatment of Chronic Headache) Program. N=36 patients completing the three-week program in 2007.

Stress, Anxiety and Depression Following IMATCH (n=36)

**Emotional functioning scores**

- Admission
- Discharge

Measures of stress, anxiety, and depression all decrease following IMATCH, indicating improvement. Mean DASS-42 (Depression, Stress and Anxiety Scale) subscale scores are plotted with their standard deviations.

Functional Status Following IMATCH (n=36)

**Disability scores**

- Admission
- Discharge

Disability scores improve (higher scores indicate greater levels of disability) following completion of the IMATCH program.
Ms. Newhouse started having chronic migraines when she was 13 years old. They continued as she went to college, and she even had to take one semester off when her headaches caused her to miss classes too frequently. She saw 15 neurologists in Pennsylvania over the years searching for relief. When she read about Cleveland Clinic’s IMATCH program on the Internet, she went to Cleveland right away. She experienced significant relief within one week of beginning the program and, importantly, is now able to function through the rare headaches that she does get. She recently graduated from college after making the Dean’s List two semesters in a row and is going to graduate school soon.

“This program absolutely put my life back on track. I am a functioning adult now. I was taking 29 pills a day; now I take only six. I recently went eight months without a headache. I had one this winter but I didn’t end up in the hospital, which is a big improvement for me. Cleveland Clinic changed my life.”
FELLOWSHIPS

Two one-year clinical/research fellowships in headache are available, one in adult headache and another in pediatric headache medicine. This training program provides significant experience in the diagnosis and management of adult and pediatric headache disorders, inpatient headache management, ancillary treatment techniques such as biofeedback and stress management, and the design and execution of headache research protocols. This is a non-ACGME position, but has been accredited by the UCNS and AAN and AHS. After one year the applicant may sit for the UCNS-accredited board examination.

CLINICAL RESEARCH

For headache sufferers, access to clinical trials of the newest, potentially effective pharmacologic agents is an important attribute of the Cleveland Clinic Center for Headache and Pain.

Some of the current trials include:

- Comparison of an investigational oral drug with placebo for the treatment of moderate or severe headache
- Neurogenetic studies of migraine headache
- Comparison of an investigational oral drug with placebo for the treatment of early migraine headache
- Comparison of an investigational oral drug with placebo for the treatment of an acute menstrual migraine
- Measurement of psychophysical markers in patients with a variety of headaches

PUBLICATION HIGHLIGHTS


The Center for Headache and Pain had 37 patients enrolled in clinical trials in 2007.

More than 600 participants received CME credit for Cleveland Clinic’s online “Update on Migraine Headache” course.

Pain Reduction with Infusion Therapy (n=198)

![Graph showing pain reduction with infusion therapy](chart.jpg)
MELLEN CENTER FOR
MULTIPLE SCLEROSIS
TREATMENT AND RESEARCH
As one of the leading centers in the world for the diagnosis and management of multiple sclerosis (MS), the Mellen Center includes a comprehensive array of clinical programs related to its core mission.

Medical Programs

The core team includes neurologists, advanced practice nurses and physician assistants. The Infusion Center, in its recently expanded 15-chair setting, has seen a 30 percent increase in volume with the reintroduction of natalizumab (Tysabri®), a monthly infusion therapy for relapsing forms of MS. The medical program also has been enhanced by the addition of Dr. Alexander Rae-Grant to the staff.

Imaging Program

Two large grants were awarded by the National Multiple Sclerosis Society: one is to study the clinical and imaging characteristics of damage to the hippocampus, which is a commonly injured brain region supporting memory; the other is to further study functional connectivity in white matter, which is known to be impaired in MS patients and may lead to reduced cognitive and memory function. Methodological development work was published observing a correlation between white matter disease burden and functional connectivity, as well as a novel method to determine fiber direction within diseased white matter.

Comprehensive Care Program

We are refocusing our comprehensive care program using the Chronic Care Model developed by Edward Wagner at the MacColl Institute. To that end we are enhancing the educational opportunities on our website, offering programs for patients who are newly diagnosed and conducting the “Mellen Center Learning Series” that is intended to help participants improve their overall wellness and self-management strategies for living with MS.
Rehabilitation Program

The clinical activity of the rehabilitation and spasticity clinic continues to expand. Additional equipment has been added to the therapy program to assess patient balance and the effectiveness of wheelchair seating and selection. We continue to improve and validate the Mellen Center Gait Test to improve sensitivity to change and safety of the patient.

FELLOWSHIPS

The Mellen Center offers four non-ACGME-approved fellowships in clinical neuroimmunology. Fellows have the option of focusing clinical work/rehabilitation in a one-year program or on clinical trials, MRI or clinical research in a two-to-three year program.

As one of the premier centers in the world for treatment and research related to multiple sclerosis, the Mellen Center provides fellows with an unparalleled opportunity to experience a comprehensive clinical multiple sclerosis program and participate in a world-class research program.

CLINICAL RESEARCH

The Mellen Center staff and the individuals who come here for care maintain a strong partnership in MS research. Research is aimed at unraveling the complexities of MS. The staff is dedicated to understanding the effects and causes of the disease, improving its management and working toward a cure. Researchers investigate more effective supportive care, better rehabilitation techniques and more effective medical therapies.

Current studies of new MS therapies include: fingolimod (FTY-720) in both relapsing-remitting and primary progressive MS, fumarate (BG-12), fampridine (4-aminopyridine), double-dose glatiramer acetate (Copaxone), alemtuzumab (CAMPATH-1h), ocrelizumab, glatiramer acetate (Copaxone) combined with interferon beta-1a (Avonex), laquinimod, atacicept and atorvastatin (Lipitor), each of which may provide new treatment options for MS patients. Mellen Center physicians occupy leadership positions in all of these multinational trials.

Physical therapists at the Mellen Center develop personalized treatments to help MS patients improve their strength, gait and overall function.

The Mellen Center utilized Diffusion Tensor Imaging as a noninvasive MRI-based technique to measure remyelination.
Some of our ongoing non-treatment studies include:

- A clinical trial of a web-based self-monitoring program, which aims to develop the Internet for use in patient self-management
- Diffusion tensor MR imaging studies of natalizumab (Tysabri®) and corticosteroids (Solu-Medrol®), which will develop new imaging markers of degeneration
- A biomarker study of interferon beta-1a (Avonex) therapy, which hopes to predict who will respond to therapy
- A functional MRI study of hand movements in MS, which aims to understand how the brain re-organizes after injury from MS
- Studies of optical coherence tomography, which seek to develop a new approach to monitor neural degeneration
- A 15-year follow-up of patients in the pivotal trial of interferon beta-1a (Avonex®) in relapsing-remitting MS

LABORATORY RESEARCH

Neurologists at the Mellen Center collaborate with researchers at major medical centers, universities and the NIH in sophisticated laboratory research. The dual focus of this research is to contribute to the understanding of the underlying disease process in MS and to advance our knowledge of currently available treatments. Significant grants to the Mellen Center from agencies such as the NIH and the National Multiple Sclerosis Society reflect the Mellen Center’s exemplary standing as a nationally recognized center for laboratory research.

Current areas under study include:

- mechanisms responsible for myelin and nerve cell destruction in MS patients
- cellular and molecular biology of inflammation, myelin formation and regeneration
- investigation of laboratory models of MS

In 2007, the Mellen Center received $1,296,884 for research through grants and contracts.

EDUCATION

The Mellen Center offers a monthly lunch-and-learn series for newly diagnosed patients and their families that reviews the disease, its symptoms and treatment options.

The center’s 1.5 Tesla MR scanner provides images of MS lesions in the brain and spinal cord to track disease state and responsiveness to treatment.
**Modified Ashworth Scale Following Intrathecal Baclofen Therapy (n=17)**

Spasticity Score

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<thead>
<tr>
<th>Spasticity Score</th>
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<td>4</td>
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Spasticity scores on the Modified Ashworth Scale (0 = no increase in tone, 4 = severe increase in tone) at baseline and after ITB therapy. There was a statistically significant (p<0.001, paired t-test) reduction in spasticity after treatment. Average follow-up for the 17 patients was 167 days.

**Spasm Frequency Following Intrathecal Baclofen Therapy (n=17)**

Spasm Frequency Score

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Spasm Frequency Scale scores (0 = no spasms, 4 = more than 10 spasms/hour) at baseline and at most recent follow-up visit. There was a statistically significant (p<0.001, paired t-test) reduction in spasm frequency after treatment. Average follow-up for the 17 patients was 167 days.

**Botox® Treatment Effectiveness (n=47)**

Percent Patients Reporting Treatment Effectiveness

Percent of patients reporting treatment effectiveness following Botox® therapy for focal spasticity. Patients were assessed at first follow-up visit (three months after initial treatment) and subsequently every three months. Average last follow-up was six months, with a range up to 12 months. The average follow-up period for the 47 patients who continued treatment is 170 days. The average dose injected at the most recent session was 360 units of botulinum toxin A. Most patients reported benefit with treatment both on symptoms and function, and the results were stable over time.
PATRICIA SUBSTELNY

Age: 39
Hometown: Cleveland Heights, Ohio
Diagnosis: Multiple Sclerosis
Treatment: Monthly natalizumab (Tysabri®) infusions for MS and botulinum toxin injections for leg spasticity and tightness every three months.

Patricia Substelny was a busy Human Resources professional by day and an aerobics instructor by night 11 years ago when she started to have problems with her eyes and weakness in her legs. The diagnosis of MS came one month before her wedding in the fall of 1997. Although today she is no longer able to be employed, she is active as a volunteer with the MS Society and other local charities, which she actually finds to be more fulfilling.

“It is a true partnership at the Mellen Center. I am the patient and I am responsible for taking my medication and doing my exercises, but I really feel like I am on a team with the doctors and nurses. We are all working toward the same goal. They are just as happy as I am when I am doing well and just as concerned when I am not.”
PUBLICATION HIGHLIGHTS


CENTER FOR
NEUROIMAGING
The Center for Neuroimaging includes specialists in structural and functional imaging of the central nervous system for the diagnosis of neurological lesions, injury or metabolic disease. Subspecialization in specific disease entities (e.g., epilepsy and cerebrovascular disease) ensures accurate, in-depth, relevant interpretations. Across the Cleveland Clinic health system, the Center for Neuroimaging supervises and interprets more than 60,000 CT scans and more than 50,000 MR scans each year. The normal turn-around time for reports is two to three hours, with daily quality checks performed according to American College of Radiology guidelines.

Neuroimaging also functions in cooperation with the Cerebrovascular Center to provide cerebrovascular ultrasound, angiography and interventional neuroradiology services. The latter includes more than 3,000 cerebral angiograms per year, as well as state-of-the-art management of acute stroke, internal/external carotid artery embolizations, Guglielmi detachable coil occlusion of intracranial aneurysms, treatment of vasospasm and atherosclerotic occlusive disease, and carotid artery stenting.

**FELLOWSHIPS**

Two ACGME-accredited fellowships are available: endovascular surgical neuroradiology and diagnostic neuroradiology. The endovascular fellowship provides trainees an organized, comprehensive, supervised, full-time educational experience and is available to candidates with appropriate prior training in neurosurgery, neuroradiology and stroke neurology. The diagnostic neuroradiology program is open to suitable radiology candidates and provides a broad experience with state-of-the-art imaging equipment across all modalities for the evaluation of adult and pediatric disorders of the brain and spine.

**PUBLICATION HIGHLIGHTS**


CEREBROVASCULAR CENTER | 61
CLEVELANDCLINIC.ORG/NEUROSCIENCE | 866.588.2264

**DALE WESSELL**

**Age:** 67  
**Hometown:** Fort Walton Beach, Fla.  
**Diagnosis:** Stroke due to carotid dissection  
**Treatment:** Emergency carotid artery stenting

Dale Wessell and his wife were up from Florida visiting family for the holidays. On Christmas Eve, while driving from Oberlin to Elyria to go shopping, his vision suddenly became blurred. He pulled over to let his wife, Debbie, drive, and was near crawling just to get to the passenger seat. A former nurse, Debbie recognized the symptoms of stroke and rushed to a nearby Oberlin hospital. Doctors there confirmed an evolving stroke, initiated treatment and, recognizing an impending catastrophe, summoned an emergency helicopter. Upon arrival at Cleveland Clinic, Mr. Wessell was unable to speak and paralyzed on the right side; his family was told he might not survive. He was rushed to the operating room for emergency treatment, where he was found to have a carotid dissection, a spontaneous injury to the inner wall of the artery to the left side of the brain. With the consent of his wife and emergent approval from the institutional review board, an experimental flexible stent was used to re-open the artery before significant permanent damage to the brain. Several hours later, he was able to speak and move his entire body again. Today, he is completely recovered.

"Thank the Lord I was near Cleveland when this happened. They did an awesome job and saved my life. Afterward, the doctors answered all my questions and never made me feel like they had another patient in the world. They gave me as much time as I needed. I can't say enough about my care. It was miraculous."
CLINICAL PROGRAMS

Movement Disorders

A team of experts including renowned neurologists, neurosurgeons, researchers and a host of support personnel offers the latest proven treatments for people with movement disorders, including Parkinson’s disease, essential tremor and dystonia. Our surgical team is world-renowned for performing deep brain stimulation (DBS) surgeries and has experience with more than 1,200 DBS implants. This group also has expertise in the surgical management of spasticity. Various medication clinical trials as well as gene therapy surgical trial programs are under way.

Psychiatric Disorders

The Center for Neurological Restoration (CNR) team of neurosurgeons, psychiatrists and psychologists has been involved in studies using DBS for treating obsessive-compulsive disorder and major depression for the past seven years with promising outcomes. Patients with disabling OCD and depression are being actively enrolled in these studies. The center also performs vagal nerve stimulation for medically refractory depression.

Chronic Pain

For more than a decade, our neurosurgical surgeons have provided surgical management of chronic pain conditions including failed back surgery syndrome, RSD, CRPS, facial pain, stroke pain and other chronic pain disorders. Various surgical procedures including lesioning and the implantation of intrathecal infusion pumps, spinal cord stimulators, peripheral nerve stimulators, cranial nerve stimulators and brain stimulators are performed for patients.

FELLOWSHIPS

Surgical Fellowship: Deep brain stimulation surgery is an area of specialty training available with a one-year and two-year fellowship in functional and restorative neurosurgery. One fellow is accepted for intensive training in surgery for the management of movement disorders such as Parkinson’s disease, dystonia and spasticity; chronic pain; psychiatric disorders; and other central nervous system disease states. In addition, fellows gain experience in peripheral and central neurostimulation, intra-axial medication delivery and ablative procedures for pain and movement disorders.

Medical Fellowship: For those interested in the medical management of movement disorders, a one-year and two-year fellowship in movement disorders is offered. Two fellows are accepted for this intensive program, which includes exposure to all of the movement disorders seen in our clinics. The depth and breadth of our program provides fellows with an unparalleled experience in the diagnosis and management of all aspects of these complex disorders.

CLINICAL RESEARCH

Clinical research interests in the center are focused on refining the use of DBS in movement disorders and expanding its application to other problems. Current clinical trials available relate to:

- Application of deep brain stimulation to psychiatric disorders, including depression and obsessive-compulsive disorder

2007 STATS

Initial outpatient visits 326
Total outpatient visits 6,499
Admissions 333
Inpatient Days 1,475
Surgical Cases 489
Evaluation of functional MRI in patients with implanted neurostimulators
Development of frameless techniques for deep brain stimulator placement
Development of cortical interfaces for neural prostheses
Multidisciplinary assessment of severe brain injury and application of deep brain stimulation to treat cognitive disorders following severe brain injury
Deep brain stimulation for pain

LABORATORY RESEARCH

Scientists at Cleveland Clinic’s Lerner Research Institute are involved in several major projects related to deep brain stimulation and neurological restoration:

- Cerebellar stimulation for recovery of motor function following cortical strokes
- Corpus callosum stimulation for recovery of functions following subcortical strokes
- Effects of chronic electrical stimulation of the subthalamic nucleus on tissue integrity
- The effectiveness of deep brain stimulation of intralaminar nuclei of thalamus in a model of focal cortical seizures induced by intracortical penicillin and generalized seizures induced by intraperitoneal PTZ (pentylenetetrazole) in adult rats
- Efficacy of subthalamic nucleus stimulation using variable wave-form external pulse generator (VWEPG) in ameliorating Parkinsonism in 6-hydroxydopamine-lesioned hemiparkinsonian rats

PUBLICATION HIGHLIGHTS


RESEARCH

The Center for Neurological Restoration, in collaboration with the Center for Headache and Pain, investigated stimulation of the sphenopalatine ganglia for treatment of severe cluster and migraine headaches.

EDUCATION

The Center for Neurological Restoration held a one-day symposium on movement disorders in 2007 for physicians and nurse practitioners, addressing restless legs syndrome, pharmacological management of Parkinson’s disease, and surgical therapies for advanced Parkinson’s disease, dystonia and essential tremor.
Diane Hire struggled with unrelenting depression for 20 years. Every morning, her first thought was that she would be able to go back to bed in 16 hours. She tried a variety of treatments, but none provided sustained relief. One day, a therapist she was seeing heard a lecture by Donald Malone, M.D., about deep brain stimulation at Cleveland Clinic and sent Ms. Hire’s records to him. She had surgery with Ali Rezai, M.D., in November 2006; the device was activated in January 2007. Today, Ms. Hire is excited to wake up and enjoys talking to people, reading, working around the yard and house, and just being active — things she hadn’t done in decades.

“Before, I was just a walking dead person. Only my body was alive. I didn’t know if I even knew how to be well anymore. But I couldn’t ask for kinder, gentler people than Dr. Malone and Dr. Rezai. They were so responsive and always had my best interest at heart. Because of them, I am now 180 degrees away from where I was. My life is changed completely.”
OUTCOMES HIGHLIGHTS

Deep Brain Stimulation (DBS) procedures

Improvement in Motor Scores with DBS

UPDRS Motor Scores

Percent Improvement in Motor Function Following DBS for Parkinson’s Disease

Improvement in motor functioning in Parkinson’s disease with deep brain stimulation. Motor functioning is measured with the Unified Parkinson’s Disease Rating Scale, Part III (Motor Subscale). Motor scores are shown with the stimulator in the on and off states.

Percent improvement on Unified Parkinson’s Disease Rating Scale (UPDRS), Part III (Motor Subscale) following deep brain stimulation treatment for Parkinson’s Disease.
NEUROMUSCULAR CENTER
CLINICAL PROGRAM

Treating neuromuscular diseases such as amyotrophic lateral sclerosis (ALS), peripheral nerve injury, myasthenia gravis and myopathies requires a unique combination of medical expertise and compassion. Specialists in the Neuromuscular Center successfully achieve this blend and strive to apply the latest technology to help patients optimize their quality of life and minimize their disability. To assist in the accurate diagnosis of these disorders, our specialists rely on diagnostic modalities such as electrodiagnosis (e.g., EMG); autonomic testing; and muscle, nerve and skin biopsies to supplement the history and physical examination.

FELLOWSHIPS

A one-year, ACGME-accredited fellowship is available in neuromuscular medicine, and a one-year ACGME-approved fellowship is offered in clinical neurophysiology/EMG. Fellows have the opportunity to gain experience in the range of neuromuscular diseases, as well as training in the EMG laboratory, the autonomic disorders laboratory (tilt table, valsalva and pupillometry testing), the quantitative sensory testing laboratory (QST, QSART and thermoregulatory sweat testing), the quantitative muscle testing laboratory, and the histopathology laboratory for epidermal nerve fiber analysis in skin.

CLINICAL RESEARCH

Physicians in the Neuromuscular Center are engaged in a number of clinical and translational research projects focused on improving the treatment of this cluster of diseases. Our patients have the opportunity to participate in new drug trials sponsored by pharmaceutical companies and the National Institutes of Health (NIH). Some of the current protocols include:

- Recombinant methionyl human brain-derived neurotrophic factor (r-metHuBDNF) in patients with ALS
- SR 57746A in patients with ALS
- Topiramate in ALS
- Celebrex® in patients with ALS
- The ALS Care Program: a database resource for measuring and improving ALS outcomes
- AVP-923 (dextromethorphan/quinidine) in the treatment of patients with pseudobulbar affect
- High-dose CoQ10 in ALS
- Arimoclomol in a single patient with ALS
- IGIV chromatography (IGIV-C) 10 percent treatment in subjects with chronic inflammatory demyelinating polyneuropathy

LABORATORY RESEARCH

Researchers in the Department of Neurosciences in Cleveland Clinic’s Lerner Research Institute are dedicated to advancing the understanding of the genetic basis of neuromuscular diseases. Examples of basic research related to neuromuscular diseases include:

- Genetic therapy utilizing genes for neural growth factors and anti-apoptotic intracellular proteins for treatment of neuromuscular disorders
- Identification of molecular pathways leading to degeneration of motor neurons in ALS
- Incorporation of the WLDS mutation to delay axonal degeneration
- Exploration of mechanisms and potential therapies for treating muscle inflammation and fibrosis associated with Duchenne muscular dystrophy
Cleveland Clinic is one of a few medical centers with a cutaneous nerve laboratory to facilitate evaluation of small fiber sensory neuropathy (SFSN). In 2007, we performed skin biopsies with intraepidermal nerve fiber density evaluation for 233 patients. One hundred and seventy eight patients (76 percent) were diagnosed with SFSN based on the biopsy results. In 79 patients (44 percent) the diagnosis was made exclusively by skin biopsy. Our data are consistent with reports by other medical centers that skin biopsy is a valuable diagnostic tool and is more sensitive than electrophysiological studies for diagnosing SFSN.

Of 42 patients with painful peripheral polyneuropathy followed for up to one year, 60 percent showed improvement in visual-analog pain scores (VAS) with various treatment modalities.

Patients showed an average improvement (reduction in pain scores) of 25 percent. This compares to an average improvement of 12 to 42 percent in published studies of treatment of neuropathic pain.
Cathleen Wagner began having weakness in her neck and arms, drooping eyelids and difficulty speaking. Her primary care doctor accurately diagnosed myasthenia gravis and sent her to a local neurologist, who ordered a CT scan. This revealed a coexisting thymoma, and Ms. Wagner’s neurologist then referred her to Cleveland Clinic neurologist Kerry Levin, MD. Because Ms. Wagner had a history of cardiac arrhythmia, surgery was riskier. Cleveland Clinic thoracic surgeons, however, were able to successfully remove the thymoma and Dr. Levin began a treatment regime to treat her myasthenia gravis. Today her condition is managed with immunosuppression — and she is back at her rigorous job as a kindergarten teacher.

“Dr. Levin takes such a personal interest. He really listens and wants to know what is going on. He always takes in account the fact that I spend all day with little kids when we are making decisions about my care and is never willing to settle for ‘good enough.’ When I told him I was having trouble smiling, he didn’t dismiss that as something I would just have to live with. He insisted we could get me back to 100 percent. He has never given up.”
Neuromuscular Center research is exploring mechanisms and potential therapies for treating muscle inflammation and fibrosis associated with Duchenne muscular dystrophy.

The Neuromuscular Center has trained three fellows per year in EMG and neuromuscular disease for the last 20 years, and has continuously trained residents, fellows and observers in our EMG lab since 1975.

**PUBLICATION HIGHLIGHTS**


CENTER FOR

PEDIATRIC NEUROLOGY
AND NEUROSURGERY
CLINICAL PROGRAMS

Child neurologists and neurosurgeons at Cleveland Clinic provide family-integrated, comprehensive, advanced care in the diagnosis and treatment of children with a wide array of neurological disorders. U.S. News & World Report recently ranked Cleveland Clinic’s pediatric neurology and neurosurgery services among the top four programs in the country.

PEDIATRIC NEUROLOGY

Our staff members — all board-certified in both pediatrics and neurology — are committed to providing the highest quality clinical care, research, teaching and training in the pediatric neurosciences. This is achieved through collaboration with Cleveland Clinic pediatric subspecialists in every medical and surgical field to offer the most advanced care and individualized treatment for a wide range of pediatric neurological conditions. The center includes dedicated disease-based clinical programs:

The Pediatric Neuromuscular Disease Program diagnoses and treats such conditions as muscular dystrophy, spinal muscular atrophy, congenital myopathies and myasthenia gravis, hereditary neuropathies and other polyneuropathies using advanced techniques including specialized DNA tests, pediatric EMG and neuropathological examination of nerve and muscle biopsies. Affected children have access to the latest therapies, including drug trials, plasmapheresis and immunoglobulin infusion when indicated.

The Pediatric Movement Disorders and Spasticity Program offers traditional medical and innovative therapies, including botulinum toxin injections guided by electromyography, deep brain stimulation, physical therapy, orthopaedic interventions, intrathecal baclofen infusion and selective dorsal rhizotomy. Conditions treated include Tourette syndrome, ataxia, spasticity, cerebral palsy and myelomeningocele.

The Pediatric/Adolescent Headache Program offers state-of-the-art patient care, education and innovative research. The program provides expert evaluation and treatment of those affected by both acute and chronic headaches, especially those with refractory headaches who have failed previous attempts at therapy. In addition, a three-week inpatient rehabilitation program is offered to those whose headaches have resulted in excessive school absences and overuse of medication. Collaboration with other specialties including psychology and rehabilitation ensures positive outcomes. An infusion suite is available on an urgent/emergency basis for those experiencing headache crises.

The Pediatric Neurometabolic and Genetic Disorders Program provides diagnosis and treatment for the complex genetic and metabolic disorders that are the underlying basis of many pediatric neurological and developmental issues. Areas of particular focus include central nervous system white matter disorders, underlying genetic and metabolic disorders in the setting of mental retardation and epilepsy, disturbances of mitochondrial oxidative phosphorylation and fatty acid oxidation, disorders of amino and organic acid metabolism, and lysosomal storage diseases.

The Pediatric Cerebrovascular Disorders Program offers advanced imaging, including brain MRI, MRA, cerebral angiogram and CT angiogram, as well as other comprehensive diagnostic and therapeutic interventions for all forms of neonatal and childhood stroke. Children with acute stroke are cared for in a pediatric intensive care unit staffed full-time by experienced

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2007 STATS

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2007 ANNUAL REPORT
pediatric intensivists in conjunction with our pediatric neurologists. Special areas of stroke interest include children with central nervous system vasculitis, stroke associated with cardiac disease or interventions, neonatal stroke and the vasculopathy of neurofibromatosis.

The Pediatric Neurocardiology Program offers care for children with a wide variety of congenital and acquired heart diseases, including the management of associated neurological conditions and complications of these disorders, as well as a comprehensive neuromuscular and neurometabolic evaluation for children with unexplained cardiomyopathy or children undergoing heart transplantation.

The Neonatal and Fetal Neurology Program offers prenatal consultation for a wide range of neurological disorders detected in utero by fetal ultrasound, magnetic resonance imaging or amniocentesis. Consultation and treatment also is provided for a variety of newborn conditions including hypoxic-ischemic encephalopathy, neonatal seizures, stroke, CNS malformations, brachial plexopathies and other newborn problems.

The Pediatric Neuro-Oncology Program specializes in the treatment of brain and spinal cord cancer and offers sophisticated radiotherapies, including Gamma Knife® for brain tumors; computer-assisted imaging for precise surgical planning, navigation and tumor resection; and the most advanced chemotherapy as part of national study protocols.

The Neurocutaneous Disorders Program provides multidisciplinary care for a large population of children with neurocutaneous disorders such as neurofibromatosis, tuberous sclerosis and Sturge-Weber syndrome. Cleveland Clinic received designation from the Children’s Tumor Foundation as one of only 33 affiliate neurofibromatosis clinics nationally.

INNOVATION

The Center for Pediatric Neurology and Neurosurgery developed the first Pediatric Multiple Sclerosis and White Matter Disorders Clinic in Ohio in collaboration with the Mellen Center.

U.S. News & World Report recently ranked Cleveland Clinic’s pediatric neurology and neurosurgery services among the top four programs in the country.
The Pediatric White Matter Disorders and Multiple Sclerosis Program offers advanced diagnosis and treatment of multiple sclerosis and white matter disease in children. Distinction between the many genetic, metabolic and acquired forms of pediatric white matter disease is facilitated by collaboration with Pediatric Neurology team members who are world-renowned specialists in the clinical and laboratory diagnosis of this group of disorders.

The Cyclic Vomiting Program provides expert evaluation and treatment for those individuals with episodic unexplained vomiting. This program is one of only three in the country and the only one in Northeast Ohio. The consultation includes evaluation by a neurometabolic specialist and metabolic gastroenterologist. Experts in pediatric headache, psychology and psychiatry are an integral part of the team.

The Pediatric Epilepsy and Sleep Disorders Program provides comprehensive care for children with epilepsy, often in the setting of complex neurological diseases. Sophisticated diagnosis of pediatric seizure disorders and their underlying causes is available. Children with sleep disorders receive state-of-the-art consultation and testing by pediatric sleep specialists.

Through the Community Pediatric Neurology Program, Cleveland Clinic pediatric neurologists deliver clinical services in community settings including Hillcrest Hospital, Fairview Hospital and Cleveland Clinic Wooster. These practices provide convenient access for patients and their families in a community setting.
PEDIATRIC AND CONGENITAL NEUROSURGERY

Cleveland Clinic’s pediatric and congenital neurosurgery services were one of the first in the country to emphasize the continuity of treatment of pediatric problems into adulthood, treating congenital problems regardless of age. A variety of subspecialty programs are offered.

The center has broad experience in the treatment of brain and spinal cord malformations, including Chiari malformation in children and adults. Surgical intervention for these congenital abnormalities uses an innovative minimally invasive approach. Brain and spinal cord tumors are biopsied and surgically resected in coordination with Pediatric Oncology and the Brain Tumor and Neuro-Oncology Center using the latest localizing and minimally invasive techniques.

The latest technology, such as an adjustable antibiotic system, is offered for the treatment of hydrocephalus in children and adults, resulting in an infection rate lower than national norms. A $1 million study of outcomes for shunting in hydrocephalus is ongoing.

Our neuroendoscopy program has extensive experience in ventricular and extra ventricular minimally invasive procedures. Advances include a combination of endoscopy with navigation systems for complex procedures and resection of tumor masses. In 2007, the neuroendoscopic program directed a neurosurgical course in Beijing, China, in a unique collaboration with Peking Union Medical Center.

Cerebral palsy patients are seen in a unique multidisciplinary clinic for assessment, surgical evaluation, follow-up and ongoing care. Combined neurosurgical and orthopaedic procedures are performed to treat spasticity quickly and effectively. The section directs a course in the treatment of spasticity and its regional therapies in children.

Center neurosurgeons and plastic surgeons collaborate in the treatment of craniofacial disorders. Cleveland Clinic designed a pneumatic molding helmet that is utilized for more control and flexible head reshaping.

In our Aging Brain Clinic, specialists from multiple disciplines evaluate patients from around the country with regard to dementia and normal pressure hydrocephalus.

FELLOWSHIPS

Pediatric neurosurgery offers a one-year, non-ACGME accredited fellowship in pediatric neurosurgery under the auspices of the Department of Neurosurgery. In the pediatric neurosurgery fellowship, the focus is on learning the most advanced surgical treatments for hydrocephalus and congenital abnormalities in children and adults. Minimally invasive techniques using endoscopy are emphasized.

In addition to its certified residency training program in Pediatric Neurology, Cleveland Clinic also offers certified subspecialty pediatric fellowships in Headache, Neuromuscular Disease, Sleep Medicine and Epilepsy. These fellowships benefit from collaboration with specialists in other centers throughout Cleveland Clinic, and are among only a few in the country that offer in-depth subspecialty training in the diagnosis and treatment of children and adolescents with these disorders.

CLINICAL RESEARCH

The Center for Pediatric Neurology and Neurosurgery participates in a range of clinical trials aimed at improving management of a number of specific pediatric neurologic and neurosurgical disorders.
Current clinical research includes:

**Pediatric Neurology**
- Ongoing coordination of the Ohio Pediatric Stroke Registry, the only pediatric state-based registry in the country
- Ongoing participation in the International Pediatric Stroke Study (IPSS) collaborative
- Drug treatments in Duchenne muscular dystrophy and spinal muscular atrophy

**Pediatric and Congenital Neurosurgery**
- Treatment of children with spasticity: differences in intrathecal baclofen delivery
- Evaluation of new molding helmet in cranial abnormality
- Third ventriculostomy: outcome-related to CSF flow
- Neuroendoscopic-assisted chiari surgery compared with conventional standard surgical approach
- Evaluating cognitive and neuropsychological effects of a study drug in children with partial seizures
- Accelerator quantitation of imbalance in normal pressure hydrocephalus
- Treatment of children with chronic hydrocephalus
- Gait and balance in normal pressure hydrocephalus using the Medtronic Strata® Adjustable Valve and the Codman® Hakim™ Programmable Valve
- CSF content in normal pressure hydrocephalus
- Developmental venous anomaly indices for patients undergoing lumbar drainage of CSF for normal pressure hydrocephalus

**Laboratory Research**

Basic research at Cleveland Clinic’s Lerner Research Institute that investigates the cellular and molecular biology of brain development and neuronal and glial function contributes significantly to advances in clinical care in pediatric neurology and neurosurgery.

Current basic research projects include:
- Oxygen delivery in hydrocephalus after surgical treatment
- Cerebrovascular and blood flow changes in chronic hydrocephalus
- CSF metabolite/cytokine expression in hydrocephalic CSF
Pediatric Neurosurgery (<18 years)

Procedures

Mean LOS

Pediatric Neurosurgery Procedures
Mean LOS

2003 2004 2005 2006 2007

Peds MIDAS Headache

Frequency

Rescue Doses

School Days Missed

Pediatric Headache (n=18)

Visit 1
Visit 2

Pediatric patients treated for headache showed an improvement in PedsMIDAS (Migraine Disability Assessment Score), headache frequency, and number of rescue medications needed. The number of school days missed is one of the questions included in the PedsMIDAS interview. N=18 pediatric patients with two PedsMIDAS scores an average of three months apart.

Neurometabolic Clinic Diagnostic Yield

Number of Patients

New patient consults
Diagnosis established via muscle, genetic or CSF

In 2007 our Neurometabolic Clinic evaluated more than 300 patients presenting with unexplained neurologic and/or developmental symptoms, and we were able to establish a diagnosis in 125 patients, or 40 percent.
AIDAN VON GUNTEN

Age: 4
Hometown: Amherst, Ohio
Diagnosis: Left-side hemiparesis, due to presumed perinatal ischemic stroke
Treatment: Physical and occupational therapy and adaptive aquatics

When Aidan was about 3 months old, his mother, who works in early childhood intervention, noticed that he was only reaching with his right hand. She watched him for about a month before taking him to his Cleveland Clinic pediatrician. Aidan was referred to Cleveland Clinic pediatric neurologist Neil Friedman, MB, ChB, who quickly began a comprehensive series of diagnostic tests. An MRI demonstrated that a stroke had occurred, most likely before birth. Aidan has been going for therapy to improve his balance and left-side strength for about three years and today is a very social and active little boy. He plays soccer and many people who interact with him are surprised to learn he has any limitations at all.

"The systematic approach of helping us right away gave us such a positive impression of Cleveland Clinic," says Aidan’s mom. "If our pediatrician hadn't been so open to referring us to Dr. Friedman right away and if we hadn't gotten in to see such an excellent neurologist so quickly, Aidan might not have gotten the help he needed so fast. Dr. Friedman is very thorough and very comforting. He takes my concerns seriously and has always treated me like a partner in Aidan’s care."
- Dural substitutes
- Telemetric intracranial pressure measurement
- CSF circulation and solute clearance
- Intracranial pulse pressure changes in chronic hydrocephalus
- Study of the brain’s adaptation to chronic hypoxia hydrocephalus through stimulation of VEGF and angiogenesis
- Study of cerebral hydro- and hemodynamic interaction to increase cerebral blood flow at time of ischemic risks

**Publication Highlights**


Cleveland Clinic psychiatrists and psychologists participate in the team-based care of patients across the various Neurological Institute centers and Cleveland Clinic institutes, incorporating mental and behavioral health services into the continuum of patient care.

2007 STATS

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<td>Total outpatient visits</td>
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<td>Admissions</td>
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<td>Inpatient Days</td>
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</tbody>
</table>

CLINICAL PROGRAMS

The Department of Psychiatry and Psychology provides comprehensive adult, child and adolescent mental health and chemical dependency services.

Adult Psychiatry

Inpatient and outpatient services are provided for the full range of adult psychiatric disorders. The chief inpatient diagnoses are psychoses, alcohol and/or drug abuse, personality disorders and mood disorders. The most common outpatient diagnoses treated are mood, anxiety and somatoform disorders. Adult psychiatry also includes the Center for Psychiatric Neuromodulation and the growing Mood Disorders Research Program.

Child and Adolescent Psychiatry

The department’s very active program in child and adolescent psychiatry offers outpatient and crisis-oriented inpatient treatment. In the under 18 population, the leading inpatient diagnoses in 2007 were psychoses, personality disorders, depression, anxiety disorders and DSM-IV “childhood mental disorders,” including disruptive behavior disorders, pervasive developmental disorders, eating disorders and tic disorders. The top three diagnoses in 2007 among the pediatric outpatient population were Attention Deficit-Hyperactivity Disorder, mood disorders and anxiety, and dissociative or somatoform disorders.

Section of Pain Medicine

The Section of Pain Medicine provides diagnosis and treatment of chronic pain and related problems. It operates the Chronic Pain Rehabilitation Program, which is an interdisciplinary, biopsychosocial rehabilitation program for patients with serious pain-related functional impair-
ment or psychological distress. This all-day program provides inpatient care as well when needed.

**Psychosomatic Medicine**

This section is staffed by psychiatrists, residents, a fellow in psychosomatic medicine and a team of psychiatric occupational therapists who provide psychiatric consultation to hospitalized patients and their caregivers on medical and surgical units for psychiatric and neuropsychiatric disorders that occur during hospital admission. It is among the most active and highly valued teaching services. The most common problems encountered include postoperative delirium, mood disorders, adjustment disorders and assessment for either safety or capacity, or both. Section staff also participate in the Epilepsy, Preventive Cardiology, Transplant and Women’s Health centers and the Taussig Cancer Institute, as well as the Bakken Heart-Brain Institute.

**General and Health Psychology**

Health psychologists provide behavioral assessment and treatment including biofeedback and cognitive-behavioral, supportive and other types of psychotherapy on an outpatient basis. Section members also serve important roles in Executive Health, the Center for Headache and Pain, Bariatric Surgery and Women’s Health.

**Neuropsychology**

Specialists in this area work closely with physicians in other disciplines to provide neuropsychological testing for patients with cognitive disturbance related to epilepsy, multiple sclerosis, movement disorders, dementia, hydrocephalus, head injury and cardiothoracic surgery.

**Alcohol and Drug Recovery Center**

Our specialists in this area provide high-quality, multidisciplinary care and treatment for all age groups with alcohol and drug abuse or addiction. Treatment is individualized to include inpatient care, partial hospitalization and intensive or routine outpatient care or a combination of these as needed to evaluate, detoxify and treat patients.

**Psychiatric Neuromodulation Center**

The Psychiatric Neuromodulation Center is a unique and distinctive feature of the department’s collaboration with the Center for Neurological Restoration. It provides conventional and innovative treatments to patients with psychiatric disorders refractory to common treatment modalities. Patients with treatment-resistant depression or obsessive compulsive disorder in particular can benefit from evaluation and consultation with center physicians.

**Fellowships**

Two comprehensive chronic pain rehabilitation fellowships are available through the Section of Pain Medicine. Each fellow participates in the Chronic Pain Rehabilitation Program doing biofeedback-assisted psychotherapy. Research primarily involves using our IRB-approved data registry. Fellows also participate in couples and groups sessions, including a psychodynamic group and CBT-based groups, as well as monthly aftercare.

The psychosomatic fellowship is a one-year training program, and involves rotations in cardiology, oncology, transplantation and Women’s Health. In addition, the fellow may

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**INNOVATION**

The Department of Psychiatry and Psychology developed and implemented an SBAR modified for psychiatry. The SBAR (Situation, Background, Assessment and Recommendation) is a tool that is used to report to the next shift, improving communication between providers.
participate in research related to a topic of interest in consultation-liaison psychiatry. The fellow also teaches residents and medical students, and provides supervision in the Emergency Department. The fellow may also see patients for longitudinal follow-up in the Psychosomatic Clinic with supervision from faculty.

The neuropsychology fellowship through the Association of Postdoctoral Programs in Clinical Neuropsychology is a two-year program and is designed to provide specialty training in pediatric or adult neuropsychology at the post-doctoral level.

**CLINICAL RESEARCH**

The department participates in multicenter clinical trials supported by the National Institutes of Health (NIH), corporations and private foundations, as well as in-house trials conducted exclusively at Cleveland Clinic. The primary focus of clinical trials is the development and investigation of new pharmacological and other treatments for psychiatric disorders.

The Cleveland Clinic Mood Disorders Research Center is nearing the completion of the largest double-blind, placebo-controlled trial of divalproex sodium to date in the acute treatment of bipolar depression. The trial is being completed in collaboration with partners at Case Western Reserve University.

Current child and adolescent psychiatry clinical trials include:

- First psychotic episode in children and adolescents, a four-year retrospective review
- S-100 B as a serum marker for early detection of inflammation in psychotic children
- Cytokines in psychotic children
- Depression and epilepsy in childhood
- Inflammatory markers in depression and epilepsy
- MRI findings in temporal lobe epilepsy and depression
- A retrospective review of cognitive impact on epileptic children post-frontal lobectomy

Current psychology research includes:

- Cancer fatigue
- Facial allograft research and clinical protocol
- Palliative care and quality of life for those in long-term care
- Evaluation and treatment of tinnitus
- Strategies for managing patients with tinnitus
- Psychophysiological remodeling of the failing human heart
- Heart-rate variability biofeedback in the treatment of early heart failure
- The health effects of spiritually focused meditation for people with acute leukemia

Current neuropsychology research includes:

- The role of cortisol dysregulation in depression and hippocampal dysfunction associated with temporal lobe epilepsy
- An fMRI study of attention networks in multiple sclerosis
- Evaluating the risks and benefits associated with the application of deep brain stimulation in the treatment of a variety of disorders such as Parkinson disease, tremor, dystonia, pain, obsessive compulsive disorder, depression and neurocognitive disorders as a result of brain injury
Mean pain scores decrease following enrollment in the Chronic Pain Rehabilitation Program. Two hundred fifty-nine patients were admitted to the program in 2006 and 233 in 2007. Approximately 80 percent of patients completed the program. Typical treatment duration is 3.5 weeks.

The patient average on the BES showed a significant reduction following group treatment (p < .001). The average number of binge eating episodes also showed a significant reduction following group treatment (p < .001). Average patient satisfaction was 4.52 (Very Satisfied to Extremely Satisfied) on a scale of 1 (Extremely Dissatisfied) to 5 (Extremely Satisfied).
This husband and wife spent years addicted to prescription drugs and alcohol. They tried many times to stop, but nothing lasted. Mr. Ragozine finally went to see Gregory Collins, MD, who put him on Suboxone®, which often is used as initial therapy, but less often offered as long-term maintenance. Several months later, Mrs. Ragozine also sought help from Dr. Collins. Today they are both clean and attend 12-step meetings with sponsors several times a week. They continue to take Suboxone® daily.

“I was a slave to my addiction,” says Mr. Ragozine. “It took our money and our pride. Dr. Collins really understands how hopeless narcotic addiction is and he’s been a miracle man for us. His approach of combining the medication with intensive therapy is what saved us.”

“I was slowly dying and would be dead today if it weren’t for Dr. Collins’ help. My heart is not heavy anymore. I don’t know what I would do without this treatment,” says Mrs. Ragozine.
PUBLICATION HIGHLIGHTS


The Sleep Disorders Center is accredited by the American Academy of Sleep Medicine. Our clinical program continues to expand, reflecting the widespread incidence of these disorders in the population. To date, the center has performed more than 47,000 sleep studies. The introduction of hotel-based sleep laboratories in 2005 strategically situated in the Greater Cleveland region contributed significantly to the center’s expansion throughout 2006 and 2007. Jyoti Krishna, MD, joined the center in 2007 as head of the pediatric sleep program. Construction is under way for a new pediatric sleep clinic at our Fairhill location.

**FELLOWSHIPS**

Five one-year, ACGME-accredited fellowships are available with the center. Designed to develop a range of competencies in sleep medicine, the fellowship provides trainees with eligibility for the American Board of Sleep Medicine. Trainees are provided with a broad exposure to sleep medicine including polysomnographic technology and the treatment of adult and pediatric patients with sleep disorders, with a strong emphasis on clinical neurophysiology.
Sleep Apnea: Improvement in Sleepiness (n=60)

ESS Score

Sleepiness as measured with the Epworth Sleepiness Scale (ESS) in sleep apnea patients seen from June to December 2007, before and after PAP (positive airway pressure) treatment. Higher scores indicate more severe daytime sleepiness; PAP treatment reduced sleepiness into the normal range (<10). Average duration of treatment was 86 days.

Sleep Apnea: Improvement in Depressive Symptoms (n=60)

PHQ-9 Score

Depressive symptoms as measured with the Patient Health Questionnaire (PHQ-9), in sleep apnea patients seen from June to December 2007 also improved after PAP treatment. PHQ-9 scores of 5-9 suggest mild depression, <5 suggests minimal depression.

Insomnia Sleep Skills Group

Number of Patients

The Sleep Skills Group is a novel treatment for insomnia started in 2007, one of the first of its kind in Northeast Ohio. After a five-week session, 69 percent of participants had a significant improvement in insomnia, and 22 percent of participants no longer had insomnia, as measured with the Insomnia Severity Index.
Edwina Polk was helping countless people to find the source of their sleeping problems working as a polysomnography technologist at Cleveland Clinic’s Sleep Disorders Center. Yet it took her a while to consider that her excessive tiredness could be due to a sleep disorder of her own. She considered the difficulty concentrating and remembering information to be a way of life. Finally, when even adding extra sleep to her routine didn’t help, she decided to undergo some of the tests she had administered so frequently to others. After going through basic sleep tests and positional sleep therapy, her doctor found that a CPAP was just what she needed. Now Ms. Polk enjoys having much more energy during the day and getting things done.

“Cleveland Clinic solved my problems — I’m not tired during the daytime and I’m able to concentrate. Now I’m able to get up and do all the things I need to do.”

**EDWINA POLK**

**Age:** 39  
**Hometown:** Cleveland, Ohio  
**Diagnosis:** Obstructive sleep apnea  
**Treatment:** Continuous positive airway pressure (CPAP)
Clinical Research

Clinical studies in the Sleep Disorders Center include research into the causes of sleep disorders, evaluation of innovative treatments and understanding co-morbidities and sleep disorders. Current areas of research include:

- Major depressive disorder in sleep disorder patients
- Effects and prevalence of sleep apnea in bariatric surgery patients
- Finding the gene for restless legs syndrome
- Sleep disorders complicating epilepsy
- Use of wireless polysomnography in hospitalized patients
- Comparison of ambulatory and laboratory polysomnography for the diagnosis of obstructive sleep apnea

Publication Highlights


Research

The Sleep Disorders Center collaborated with Cleveland Clinic’s Cardiovascular Surgery Department to study the perioperative morbidity of sleep apnea.

Education

Since 1995, when the accredited clinical sleep medicine fellowship began, the Sleep Disorders Center has trained 54 clinical fellows who currently practice sleep medicine around the world, including Korea, Singapore, Saudi Arabia, Greece, Thailand and Lebanon.
Specialists in neurosurgery, orthopaedic surgery and medical spine provide state-of-the-art medical and surgical management for the full scope of back and spine problems.

The following highlights some of the subspecialty programs in the Center for Spine Health that have achieved a national reputation:

**Scoliosis and Kyphosis:** Non-operative treatment typically involves bracing to temporarily halt the worsening of the curve during a growth spurt. For spinal deformities approaching or greater than 45 degrees associated with pain, functional impairment or severe cosmetic deformity, spine stabilization surgery is performed. Surgeons employ spinal fusion in combination with bone grafts and pedicle screws to stabilize the spine and correct the deformity. Whenever possible, the procedure is performed in part or completely minimally invasively.

**Spondylolisthesis:** Nonsurgical treatment includes muscle relaxants, acetaminophen or anti-inflammatory agents in combination with physical therapy, non-aerobic exercise and stretching to improve flexibility of the trunk muscles. Spinal fusion and spinal instrumentation are recommended in cases in which the spondylolisthesis causes neuropathy or incontinence.

**Spinal Stenosis:** Medical treatment options for spinal stenosis include nonsteroidal anti-inflammatory drugs (NSAIDs), intrathecal cortisone injections, exercise and physical therapy. We also offer gabapentin and related drugs, the first group of medications to provide an effective nonsurgical treatment option for symptomatic lumbar stenosis with neurogenic claudication. Surgical intervention is recommended when these measures are ineffective and pain interferes with quality of life. Surgical treatment to permanently decompress the spinal canal includes laminectomy with or without fusion, foraminotomy and spinal fusion with or without instrumentation.

**Primary and Metastatic Spinal Tumors:** Depending on the pathology and location of the tumor, treatment options include analgesics and steroids to manage pain and inflammation, bracing to increase spinal stability, chemotherapy, radiation therapy, and/or surgical resection in

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**2007 Stats**

<table>
<thead>
<tr>
<th>Category</th>
<th>Number</th>
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</thead>
<tbody>
<tr>
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<td>Inpatient Days</td>
<td>8,409</td>
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<td>Surgical Cases</td>
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</table>

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Center for Spine Health surgeons offer spine stabilization surgery for both adult and pediatric cases of scoliosis, performing the procedure using minimally invasive techniques whenever possible.
combination with spinal fusion. Embolization is performed as an adjunct to surgery for very vascular tumors.

**Mature Spine:** The focus of the program is on conservative treatment for patients over age 60 experiencing chronic back pain. Options include pharmacologic and non-pharmacologic treatments such as medications and supplements, physical, occupational and aquatic therapy, and bracing.

**Degenerative Spine:** Conservative treatment is emphasized, including bed rest for acute pain, stretching, low-impact exercise, pharmacologic therapy, spinal manipulation, heat and acupuncture. When pain is refractory to conservative treatments, surgical options may be used and include laminectomy, spinal fusion or discectomy.

**Cervical Fractures:** Minor fractures frequently are treated with a cervical collar. Surgery is recommended for cases that involve neurological injury and the removal of a portion of bone to relieve pressure on the spinal cord. More severe fractures may require manipulation or surgery to restore the normal skeletal conformation. This may involve traction or surgery with bone grafting and instrumentation.

**Minimally Invasive Spinal Surgery:** In certain cases of degenerative disease of the spine, scoliosis, kyphosis, spinal column tumors, infection, fractures and herniated discs, minimally invasive techniques may be used to speed recovery from surgery, minimize postoperative pain and improve the final outcome. The spine surgeons at Cleveland Clinic are leaders in the field and have been instrumental in advancing these techniques, including: spinal fusion, deformity corrections (such as for scoliosis), repair of herniated discs, decompression of spinal tumors and repair and stabilization of vertebral compression fractures.

**Degenerative Diseases of the Spine:** Degenerative diseases of the spine affect all regions of the spine. Physicians at Cleveland Clinic provide state-of-the-art care that ranges from the least invasive to complex surgical procedures to decompress neurological compression and/or stereotactic spine radiosurgery can deliver a very precisely targeted, high dose of radiation that can effectively control pain or tumors in as little as a single session.
spinal instability or deformity. All treatments are individualized and may be multi-staged. The most effective and least risky approaches are chosen on a case-specific basis.

FELLOWSHIPS

The Center for Spine Health offers a one-year fellowship in spine surgery that provides expertise in diagnosing and treating all aspects of spinal disease, with emphasis on degenerative disorders, adult deformity, complex reconstruction and revision techniques, and emerging technologies. Surgical decision-making is emphasized as the fellow rotates through both orthopaedic and neurosurgical spine services. Laparoscopic and thoracoscopic minimally invasive techniques, kyphoplasty and artificial disc techniques are taught. The fellow develops expertise in applying both anterior and posterior spinal instrumentation systems. Fellows participate in basic science and/or clinical research, and are expected to complete two research projects over the course of the year.

The Center for Spine Health also offers a fellowship in spine medicine, training broadly competent specialists in this emerging specialty, focused on the evaluation and management of the full spectrum of spine disorders. Fellows have the opportunity to develop outstanding clinical skills grounded in an evidence-based framework. Fellows are exposed to a wide range of diagnostic and therapeutic modalities including electrodiagnostics, acupuncture, manipulation, physical

Center for Spine Health physicians perform 1,600 interventional spine procedures with center fellows as part of the spine medicine fellowship.
therapy, pain management and lumbar interventional spine procedures. Scholarly activity is encouraged and expected. Fellows are active participants in clinical research and writing.

**CLINICAL RESEARCH**

Physicians in the Center for Spine Health participate in numerous clinical trials related to pain management, advanced surgical techniques and new technology.

Current protocols include:

- Prospective outcomes evaluation of decompression with or without instrumented fusion for lumbar stenosis with degenerative grade I spondylolisthesis (SLIP)
- Lumbar spine instability study: the role of flexion/extension radiographs
- A prospective, randomized clinical investigation of the Cervitech, Inc. porous-coated motion artificial disc for stabilization of the cervical spine
- A chart review comparing surgical to conservative management in the treatment of type II odontoid fractures among the elderly
- A retrospective, randomized controlled trial of duragen plus adhesion barrier matrix to minimize adhesions following lumbar discectomy
- Cost savings in the operative room, standard radiographs vs. fluoroscopy for localization
- A prospective, multicenter, randomized controlled study to compare the spinal sealant system as an adjunct to sutured dural repair with standard of care methods during spinal surgery
- A multicenter, prospective, randomized, controlled clinical trial comparing the safety and effectiveness of the Mobi-C prosthesis with conventional anterior cervical discectomy and fusion in the treatment of symptomatic degenerative disc disease in the cervical spine
- The effectiveness of physical therapy for patients with lumbar spinal stenosis
- An assessment of P-15 bone putty in anterior cervical fusion with instrumentation investigational plan
- Determining the optimal surgical approach (ventral versus dorsal) for patients with multi-level cervical spondylotic myelopathy
The research focus of the Spine Research Laboratory (SRL) is largely “translational” in its emphasis on moving discoveries in basic science research to applications at the clinical level. The close involvement of clinicians from Cleveland Clinic’s Center for Spine Health is a key ingredient in maintaining this translational focus. The current “research portfolio” of the SRL mirrors the interests of Center for Spine Health clinicians, and therefore incorporates the views of surgical spine specialists (neurosurgical and orthopaedic) and medical spine specialists (trained in physical medicine and rehabilitation, and osteopathic medicine).

The SRL has a number of ongoing, long-term research endeavors conducted under the auspices of five unique research pillars:

**SpinalMEMS.** Development of wireless, miniature pressure sensors that can be implanted within an intervertebral disc and transmit real-time data for extended periods of time — providing clinicians with information as to the load-bearing, hydration and overall health of the disc in response to different treatments and rehabilitation strategies.

**Spine Biomechanics.** Use of robotics technology to simulate changes in spinal neuromuscular control strategies in response to pain.

**Bone Bioengineering.** Computational simulation of spinal bone remodeling and adaptive processes in response to aging, trauma and disease.

**Tissue Engineering.** Development of animal models of intervertebral disc degeneration for establishing causal links between disc degeneration, neoinnervation and pain.

**Spinal Cord Injury.** Development of biologic approaches to spinal cord regeneration following traumatic injury.

Additionally, customized research projects are developed by medical students, residents and fellows involved with the SRL.
Selected Spinal Procedures

Type of Procedure

- Tumor
- Correction
- Deformity
- Decompressive
- Biopsy
- Arthrodesis

Number of Procedures

Mean Length of Stay (LOS) in Spinal Disorders

Days

Spinal decompression remains the most frequently performed procedure for spine disease.

Target LOS is calculated based on APR-DRGs, which adjust for the severity of the patient population.
Mrs. Steinhurst had injured her spine about 50 years ago when she was chasing her four-year-old son and fell down the stairs. Years of physical therapy weren't enough to ward off the pain and she was forced to wear a leather and metal brace frequently to ease the pain. Recently, she discovered medical acupuncture with Daniel Mazanec, MD, at Cleveland Clinic's Center for Spine Health and had immediate results. She now takes only over-the-counter arthritis pills for her spinal injury because of the success of acupuncture.

"Nothing did for me what the first go at acupuncture did. My back has not been as comfortable for most of my adult life as it is now. And, I have a physician doing it, which adds a feeling of security. I go back every six to eight weeks for a 'tune-up.' The only regret I have is that I waited until I was 84 to do this."
PUBLICATION HIGHLIGHTS


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Cleveland Clinic’s Neurological Institute is a multidisciplinary team of specialists offering innovative technology for diagnosis and treatment of all neurological conditions affecting adult and pediatric patients. Because of our clinical expertise, academic achievement and innovative research, the Neurological Institute has earned an international reputation for excellence.

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Jerrold Vitek, MD, PhD
Riqiang Yan, PhD

LERNER RESEARCH INSTITUTE
BIOMEDICAL ENGINEERING
Jay Alberts, PhD
Elizabeth Fisher, PhD
Aaron Fleischman, PhD
Cameron McIntyre, PhD
Shuvo Roy, PhD

LERNER RESEARCH INSTITUTE
CELL BIOLOGY
Damir Janigro, PhD

PATHOLOGY AND LABORATORY MEDICINE INSTITUTE
ANATOMIC PATHOLOGY
Richard Prayson, MD

NEWLY ARRIVING STAFF
Ferdinand Hui, MD
Bushra Malik, MD

LERNER RESEARCH INSTITUTE
DEPARTMENT OF NEUROSCIENCES
Bruce Trapp, PhD
Chairman, Department of Neurosciences,
Lerner Research Institute
Cornelia Bergmann, PhD
Hitoshi Komuro, PhD
Bruce Lamb, PhD
All physicians are cordially invited to attend the following Cleveland Clinic Neurological Institute CME symposia and ongoing programs:

**September 26-27, 2008**
Optimizing Function through Spasticity Management: Midwest Spasticity Conference 2008
COURSE DIRECTORS: Francois Bethoux, MD, and Mark Luciano, MD, PhD
Bertram Inn and Conference Center
Aurora, Ohio

**October 20-22, 2008**
Gamma Knife Perfexion — Update Training
COURSE DIRECTOR: Gene Barnett, MD
Cleveland Clinic Gamma Knife Center
Cleveland, Ohio

**October 30-31, 2008**
Neuroimaging in Traumatic Brain Injury
COURSE DIRECTORS: Stephen Rao, MD, and Harvey Lenin, PhD
InterContinental Hotel and Bank of America Conference Center
Cleveland, Ohio

**November 6-8, 2008**
Neuro-Oncology: Current Concepts in conjunction with Mexican Neurosurgery, Neuro-Oncology, and Radiosurgery Societies
COURSE DIRECTOR: Gene Barnett, MD
Fiesta Americana Grand Los Cabos
Los Cabos, Mexico

**November 21, 2008**
3rd Annual Post Traumatic Stress Disorder Symposium
COURSE DIRECTORS: Joseph Janesz, PhD, and Bridget Dwyer, MA, PC
InterContinental Hotel and Bank of America Conference Center
Cleveland, Ohio

**December 1-5, 2008**
Gamma Knife Perfexion Training
COURSE DIRECTOR: Gene Barnett, MD
Cleveland Clinic Gamma Knife Center
Cleveland, Ohio

**December 4-7, 2008**
North American Neuromodulation Society 12th Annual Meeting
SCIENTIFIC PROGRAM DIRECTOR: Ali R. Rezaei, MD
Mandalay Bay Resort and Casino
Las Vegas, Nev.

**February 9-11, 2009**
Case Studies in Epilepsy Surgery
COURSE DIRECTORS: William Bingaman, MD, and Imad Najm, MD
The Silvertree Hotel
Snowmass Village, Colo.

**February 20-22, 2009**
3rd Annual International Symposium on Stereotactic Body Radiation Therapy and Stereotactic Radiosurgery
COURSE DIRECTORS: Lilyana Angelov, MD, Gene Barnett, MD, Edward Benzel, MD, Sam Chao, MD, and John Suh, MD
The Grand Floridian Resort and Spa
Lake Buena Vista, Fla.

**June 19-21, 2009**
Epileptology: Comprehensive Review and Practical Exercises
COURSE DIRECTORS: Andreas Alexopoulos, MD, Deepak Lachhwani, MD, and Imad Najm, MD
InterContinental Hotel and Bank of America Conference Center
Cleveland, Ohio

**June 22-24, 2009**
18th International Cleveland Clinic Epilepsy Symposium: Epilepsy Surgery — Improving Outcomes
COURSE DIRECTORS: Imad Najm, MD and William Bingaman, MD
InterContinental Hotel and Bank of America Conference Center
Cleveland, Ohio

For more information, please visit clevelandclinic.org/neuroscience/CME.
CONTACT INFORMATION AND LOCATIONS

General Patient Referral
24/7 hospital transfers
or physician consults
800.553.5056

Neurological Institute
Appointments/Referrals Toll-free
866.588.2264

On the Web at
[clevelandclinic.org/neuroscience]

The Neurological Institute is a
Cleveland Clinic-wide endeavor to
provide world-class diagnosis and
treatment to all patients — whether
coming to us from near or far.
Institute physicians see patients
at Cleveland Clinic’s main campus,
six Neurological Institute Regional
Centers and nine Cleveland Clinic
family health centers.

Please inquire about availability
of specific services at each location
when calling.

Main Campus
9500 Euclid Ave.
Cleveland, Ohio 44195
866.588.2264

Neurological Institute Regional Centers
Euclid Hospital
18901 Lake Shore Blvd.
Euclid, Ohio 44119
216.531.9000
Fairview Hospital
18101 Lorain Ave.
Cleveland, Ohio 44111
216.476.7000
Hillcrest Hospital
6780 Mayfield Road
Mayfield Heights, Ohio 44124
440.312.4500

Huron Hospital
13951 Terrace Road
East Cleveland, Ohio 44112
216.761.3300

Lakewood Hospital
14519 Detroit Ave.
Lakewood, Ohio 44107
216.521.4200

Lutheran Hospital
1730 West 25th St.
Cleveland, Ohio 44113
216.696.4300

Cleveland Clinic Family Health Centers
Beachwood Family Health and
Surgery Center
26900 Cedar Road
Beachwood, Ohio 44122
216.839.3000

Chagrin Falls Family Health Center
551 E. Washington St.
Chagrin Falls, Ohio 44022
440.893.9393

Independence Family Health Center
5001 Rockside Road
Crown Center II
Independence, Ohio 44131
216.986.4000

Lorain Family Health and Surgery Center
5700 Cooper Foster Park Road
Lorain, Ohio 44053
440.204.7400

Solon Family Health Center
29800 Bainbridge Road
Solon, Ohio 44139
440.519.6800

Strongsville Family Health and
Surgery Center
16761 SouthPark Center
Strongsville, Ohio 44136
440.878.2500

Westlake Family Health Center
30033 Clemens Road
Westlake, Ohio 44145
440.899.5555

Willoughby Hills Family Health Center
2570 SOM Center Rd.
Willoughby Hills, Ohio 44094
440.943.2500

Cleveland Clinic Wooster
1739 Cleveland Road
Wooster, Ohio 44691
330.287.4500
OUTCOMES DATA AVAILABLE

The latest outcomes data from Cleveland Clinic’s Neurological Institute are now available. Charts, graphs and tables illustrate the scope and volume of procedures performed in our institute each year. To view the outcomes books for the Neurological Institute and many other Cleveland Clinic institutes, visit clevelandclinic.org/quality/outcomes.

Cleveland Clinic’s neurology and neurosurgery programs are ranked sixth in the nation and our pediatric neurology and neurosurgery services are ranked fourth by U.S.News & World Report.

INTRODUCING
THE FUTURE OF HEALTHCARE

Innovative new buildings improve patient access, experience.

This fall, Cleveland Clinic is introducing the future of healthcare with the opening of the Sydell and Arnold Miller Family Pavilion and the Glickman Tower.

These buildings, which represent the largest construction and philanthropy project in Cleveland Clinic history, embody the pioneering spirit and commitment to quality that define Cleveland Clinic. These structures are a tangible expression of institutes, our new model of care that organizes patient services by organ and disease.

At 1 million square feet, the Miller Family Pavillon is the country’s largest single-use facility for heart and vascular care. The 12-story Glickman Tower, new home to the Glickman Urological & Kidney Institute, is the tallest building on Cleveland Clinic’s main campus. Both will help us improve patient experience by increasing our capacity and by consolidating services, so patients can stay in one location for their care.

With 278 private patient rooms, more than 90 ICU beds and a combined total of nearly 200 exam rooms and more than 90 procedure rooms, patients will have faster access to Cleveland Clinic cardiac and urological services.

For details, including a virtual tour, please visit meetthebuildings.com.
The Neurological Institute is one of 26 institutes at Cleveland Clinic that group multiple specialties together to provide collaborative, patient-centered care. The institute is a leader in treating the most complex neurological disorders, advancing innovations such as deep brain stimulation, epilepsy surgery, stereotactic spine radiosurgery and blood-brain barrier disruption. Annually, our staff of more than 200 specialists serves 140,000 patients and performs 6,000 surgeries. Cleveland Clinic is a nonprofit multispecialty academic medical center, consistently ranked among the top hospitals in America by U.S. News & World Report. Founded in 1921, it is dedicated to providing quality specialized care and includes an outpatient clinic, a hospital with more than 1,000 staffed beds, an education institute and a research institute.
Our neurology and neurosurgery services are ranked sixth in the nation and our pediatric neurology and neurosurgery services are ranked fourth by U.S. News & World Report.