2015-2016 ANNUAL REPORT
NEUROLOGICAL SURGERY

Keck Medicine of USC
On behalf of the Department of Neurological Surgery at Keck Medicine of USC and LAC+USC Medical Center along with CHLA, we are pleased and proud to present our annual report. In the absence of previously published annual reports it is hard to know where to commence our current story. To begin, since 2004 when I became Chair of the Department, we have grown from eight full time neurological surgeons to 22 full time neurosurgical scientists. Along with our eight full time research scientists, nurses, and midlevel practitioners, and our very professional support and office staff; we are now among the largest neurological academic departments in the country. As a result, our subspecialty divisions take on new energy and vigor because of our ability to incorporate multiple experts in those disciplines. Because each of our surgeons brings his/her special areas of expertise to the overall group, this not only facilitates state of the art cutting edge neurosurgical care, but also allows us to investigate in the laboratory or by way of clinical trials some of the most vexing neurological medical problems that exist today.

Along with the expansion of our faculty, the residency training program has also grown in numbers and scope in the last few decades. A few years ago we were granted an increase in our residency training program by the Neurosurgical ACGME RRC to graduate three residents per year. This further establishes LAC+USC as one of the larger neurosurgical training programs in the country.

In our report you will learn about sophisticated, and in some instances, unique care delivery models for subspecialty neurosurgery. You will also understand how academic neurosurgeons can balance a busy subspecialty practice with resident and student teaching and sophisticated breakthroughs in the neurosurgical laboratory.

We do not function in a vacuum. For instance, we are particularly proud of our USC Spine Center which is an amalgamation of Keck Hospital of USC, the surgeons of the Department of Neurological Surgery and Orthopedics, and our support personnel that provide a unique patient centered experience. The entire University is enthused about our NeuroRestoration Center whose goal is to repair and regenerate damaged neurons and connections from traumatic injury, stroke, and degenerative neurological disorders. Our Center takes advantage of contributions from the USC Viterbi School of Engineering, Department of Neurology, and Neurological Surgery, scientists at the California Institute of Technology, and clinician scientists at Keck Medicine of USC, LAC+USC Medical Center, and Rancho Los Amigos National Rehabilitation Center.

You will read about some wonderful advances in the management of devastating neurological and neurosurgical disorders. This is a burden that the Department of Neurological Surgery cannot shoulder by itself. We are constantly in need of supportive partners to carry on our work. Those of you that are interested in knowing how you can help in the ultimate conquering of some of these disorders are encouraged to contact the Neurosciences Development Office or Mr. Chris Sickels.

Sincerely yours,

Steven L. Giannotta, MD
Professor and Chairman
Program Director
The quality of our program was recently acknowledged by the Neurosurgery Residency Review Committee, which allowed us to increase our enrollment to three residents per year. The factors governing such a decision include the quality of the faculty, the excellence of the care given, the success of the residents who graduate from our program, and the quality of the research efforts within the Department.

As a relatively large department (24 clinical and 7 research faculty) we not only provide excellence in subspecialty neurosurgical care but also provide an environment of cutting edge research. This attracts medical students from our most prestigious universities to apply to our training program. Over the past twenty years the top three medical schools providing residents in our training program were Columbia, Johns Hopkins, and USC. We are proud of the fact that a relatively high proportion (greater than 50%) of our residents seek full-time academic jobs upon completion of their training. Our resident graduates have assumed positions in such prestigious programs as Barrow Neurological Institute, Columbia, Yale, UCLA and USC. Currently four graduates of our training program are Chrmans of academic neurosurgical departments including University of Utah, Syracuse University, University of Arkansas, and University of Missouri. This past academic year alone our residents have authored, or co-authored, over 80 peer-reviewed publications and book chapters. Whether our graduates choose a career in academic medicine or private practice, they tend to ascend to leadership roles, whether it be locally at their hospitals, or nationally in organizations such as the Congress of Neurological Surgeons, the North American Spine Society or the Council of State Neurosurgical Societies.

PGY-5: Residents spend the entire PGY-5 year at Keck Hospital of USC with rotations focused on Complex Cranial Neurosurgery and Stereotactic Radiosurgery, as well as, acting as Chief Resident of the service.

PGY-4: During the PGY-4 year, residents focus on Spinal Neurosurgery at USC NeuroSurgery Center. This rotation focuses on basic clinical and spine care, as well as, acting as Chief Resident of the service.

PGY-3: During the PGY-3 year, the resident has several focused rotations:

- Pediatric Neurosurgery at the Children’s Hospital of Los Angeles: It is expected that the residents will become familiar with those disorders that occur with greatest frequency in the pediatric population and the surgical technique applied to their correction including removal of tumors and excisional craniotomies for hydrocephalus.

- Endovascular Neurosurgery at Keck Hospital of USC: This rotation focuses on the treatment of aneurysmal subarachnoid hemorrhage and other vascular lesions.

- Cranial Neurosurgery at Keck Hospital of USC: Residents learn the basics of complex cranial neurosurgery, as well as, acting as Chief Resident of the service.

PGY-2: The PGY-2 year is spent primarily on the service at the LAC+USC Medical Center focused on basic clinical neurosurgery and spine care.

PGY-1: The PGY-1 year includes neurosurgical, neuroradiology, and other surgical rotations.

PGY-6: The sixth year of residency is spent exclusively pursuing a focused area of interest either clinically or with research. This year provides the individual an opportunity to work towards the fulfillment of his academic goal that is centered around the generation of scientific knowledge.

PGY-7: As a PGY-7, the resident is promoted to a position of Resident Supervisor which entails the following:

- Assures primary responsibility of the day to day operation of one of the two services at LAC+USC Medical Center.

- All of the administrative needs of these services are provided by the resident supervisor, who has the authority to assign operative cases at all levels.

- This year provides a level opportunity to fully train in operative skills and prove oversight for the active management of the patient population on the service utilizing the consultation opportunities provided by the attending staff.

- Upon completion of this experience, it is anticipated that the individual will be able to manage the full spectrum of neurosurgical disease and is under the watchful eye of at least one attending surgeon.

- The individual will be fully prepared to assume total care of any patient with any neurological problem and to establish the foundation of a career in either academic or community based practice.
The USC Comprehensive Stroke and Cerebrovascular Center provides a wide range of services, using the latest medical, surgical, and interventional techniques, covering all aspects of stroke. The multi-disciplinary team meets the needs of patients with acute stroke and other serious neurological and neurosurgical conditions by providing immediate, advanced treatment and neurocritical care. More than 2600 stroke related visits occur per year in the Keck Hospital of USC and the Leslie P. Weiner Neurological Care and Research Center, with an even larger number occurring in the Los Angeles County system.

The Keck Medical Center of USC offers a highly specialized level of care and treatment for stroke and other cerebrovascular disorders that is unavailable in many community hospitals. Frequently, community hospitals and primary stroke centers will offer immediate, brain-saving treatment in the emergency department and then transfer the patient to a specialty center for a higher level of care. The Keck Hospital of USC provides community hospitals with a tertiary/quaternary transfer option via our Rapid Transport Program for patients presenting with acute stroke. Upon arrival at our hospital, the patient is rapidly admitted to our neurocritical care unit dedicated to patients with severe brain or spine injuries where they can receive cutting edge multi-disciplinary care, specialized procedures and surgeries as needed. The collaboration between stroke neurologists, neurointensivists, neurosurgeons, interventional radiologists, neuroradiologists and vascular surgeons, allows us to offer unique treatment options to our patients, including: endovascular procedures to open a blocked artery, surgery to repair a source of bleeding or to bypass a blockage, and exceptional neurocritical care to prevent and manage life-threatening complications.
The Cerebrovascular Center, headed by Steven Giannotta, MD, leads the nation in experience with operative management of aneurysms and arteriovenous malformations. Our team of endovascularly trained neurosurgeons and interventional neuroradiologists also treats cavernous malformations, hemorrhagic spasm, stroke/transient ischemic attack and trigeminal neuralgia.

The cerebrovascular team at USC is comprised of neurosurgeons, neurologists and radiologists. They have worked closely with the Stroke and Neurocritical care team to develop a robust transfer program for emergent and complex neurovascular care. The endovascular team performs procedures at Keck Hospital, LA County Hospital, Good Samaritan Hospital, and Arcadia Methodist Hospital.  Open cerebrovascular procedures are performed at Keck Medical Center and LA County Hospital.

From July 2014–June 2015 more than 200 diagnostic angiograms and more than 250 therapeutic endovascular procedures were performed. More than 160 open vascular cases were performed including aneurysm clipping/trapping, arteriovenous malformation resections, carotid endarterectomies, carotid revascularization, and carotid endarterectomy for stroke.

Dr. Arun Amar is the Director of Endovascular Neurosurgery at USC and also serves as the Stroke Director and Associate Chief of Neurosurgery at the LAC+USC Medical Center. LAC+USC is on track to achieve Primary Stroke Center (PSC) Certification in 2016, becoming the first PSC in the Los Angeles Department of Health Services and one of the rare PSCs at a government-funded facility.

Dr. William Mack was elected to the Board of Directors of the Society of Neurointerventional Surgery (SNIS) and is the Membership Chair of the American Association of Neurological Surgeons (AANS)/Congress of Neurological Surgeons (CNS) Cerebrovascular Section. He is an Associate Editor of Journal of Neurointerventional Surgery and a member of the editorial board of World Neurosurgery. Dr. Mack Co-chaired the 2015 Cerebrovascular Section/SNIS meeting and has been named the Co-Chair of the 2016 SNIS national meeting. He is a member of the scientific program committee for the International Stroke Conference and serves as a peer reviewer for the American Heart Association Brain Clinical Research study section. Dr. Mack received a 2014 Keck School of Medicine Outstanding Mentor Award for promoting excellence in medical student research.

Dr. Matthew Tenser has been active in establishing both stroke and neurointerventional programs at several surrounding hospitals in the community. He serves as the Medical Director of the stroke program at Glendale Memorial Hospital and at Good Samaritan Hospital, both of which were recently awarded certification as a Primary Stroke Center by the Joint Commission on Accreditation of Healthcare Organizations (JCAHO). Along with the endovascular team, he has developed neurointerventional programs at Good Samaritan Hospital and Arcadia Methodist Hospital, performing embolization of ruptured and unruptured aneurysms, tumor embolization, and mechanical thrombectomy for acute stroke, in addition to diagnostic angiography.

Dr. Tenser has been active in our outreach program and has given CME lectures for physicians regarding the medical and endovascular care of patients with cerebrovascular disease. He is also active in community education and frequently gives lectures for non-physicians regarding treatment of acute stroke and stroke prevention. Dr. Tenser has been active in professional societies, serving as a moderator for the International Stroke Conference and SNIS meeting and as an instructor for the SNIS/Cerebrovascular Section Fellow’s Course.

Dr. Jonathan Russin joined the USC Cerebrovascular team in July of 2015 and has a primary interest in extracranial-to-intracranial (EC-IC) bypass. He performed over 100 open cerebrovascular procedures during his first year at Keck Hospital with greater than one third involving complex EC-IC bypass techniques. Dr. Russin has ongoing grant funded research through the Brain Aneurysm Foundation, is an active member in the joint AANS/SNIS Cerebrovascular Section and serves as an Associate Director of the USC Neurointerventional Center.

The annual USC Cerebrovascular Symposium, directed by Dr. Arun Amar, was held on October 3, 2015. The conference was a great success with 17 USC and guest faculty speakers and more than 150 participants in attendance. Topics covered included mechanical thrombectomy, the continuum of stroke care, management of complex aneurysms and intracerebral/interventricular hemorrhage. Novel management and treatment paradigms were discussed from a stroke neurology, neurocritical care, and surgical/endovascular perspective. Drs. William Mack and Matthew Tenser participated as invited faculty at the Glendale Memorial Stroke Symposium. They gave lectures on management of intracerebral hemorrhage and acute stroke. Dr. Tenser lectured at the Stroke Symposium at Good Samaritan Hospital.

Dr. Tenser has lectured at the Stroke Symposium at Good Samaritan Hospital.
Dr. William Mack is an Associate Professor of Neurosurgery (Clinical Scholar), a faculty member of the Neuroscience Graduate Program, and the Director of the Cerebrovascular Laboratory at the Zilkha Neurogenetic Institute. Dr. Mack’s laboratory is focused on translational efforts to treat stroke and cerebrovascular disease. The group employs experimental models of stroke and chronic cerebral hypoperfusion (decreased blood flow to the brain) to assess environmental exposures and evaluate novel therapeutic agents. Current studies are focused on the impact of nanoparticle matter from vehicular exhaust (air pollution), a potent source of inflammation and oxidative stress. Dr. Mack employs a refined model of carotid stenosis to demonstrate the impact of air pollution on white matter ischemic injury and neurocognitive decline in the setting of underlying cerebrovascular disease. Dr. Mack was awarded an R01 through the NIH/NIEHS OINES (Outstanding New Environmental Scientist) The proposed research program seeks to determine the impact of particulate matter (PM) exposure on white matter injury and neurocognitive decline. These associations are further examined in the setting of underlying cerebrovascular disease (chronic cerebral hypoperfusion).

Dr. Mack is a co-investigator on a team of scientists supported by an NIH U01 grant to study cellular heterogeneity using patchclamp and RNA-Seq of single cells to examine transcriptome variability among ostensibly identical cells in order to validate newest generation RNA-Seq platforms.

Dr. Mack was supported by a grant through the American Heart Association to study a novel delivery mechanism for the rescue of threatened brain tissue that can be administered rapidly following acute stroke. Through distal endovascular access (catheters advanced through the blocked arteries and to the region of brain tissue damage), the team has devised a technique that allows rapid measurement and delivery of neuroprotective agents to brain tissue affected by a stroke. Dr. Russin and Mack were supported by a grant from the Brain Aneurysm Foundation to utilize data obtained from advanced MR perfusion imaging sequences to assess for an association between an inflammatory mediator, Matrix Metalloproteinase (MMP-9), and breakdown of the blood brain barrier following aneurysm rupture. The study examines the relationship between compromised blood brain barrier integrity and the occurrence of stroke. A positive correlation would suggest a potential role for MMP as an early diagnostic biomarker and blood brain barrier permeability as a therapeutic target in the management of stroke following rupture of brain aneurysms.

Dr. Tenser in the site interventional PI on the Defuse 3 Endovascular Therapy following Imaging Evaluation for Ischemic Stroke Trial.

Dr. Mack is the site PI on the Coast (Coiling of aneurysms smaller than 5mm with hypersoft) registry. Members of our cerebrovascular team have been on the steering committees of multiple landmark clinical trials resulting in the approval of stroke devices for mechanical thrombectomy. Dr. Amari has served as chairman or co-chair of the Clinical Events Committee for several multicenter cerebrovascular trials, including SWIFT PRIME, PREMIER, APOLLO, PLEX, and STRATIS. He is also site PI on the Intraventricular Nimodipine for preventing cerebral vasospasm following subarachnoid hemorrhage trial.


In February 14, 2016, a former patient at the USC Comprehensive Stroke and Cerebrovascular Center ran the Los Angeles Marathon, accompanied by the treatment team that saved her life. Prior to her stroke, 41-year-old Kathy Nguyen had nine marathons under her belt. In March 2015, Nguyen collapsed at a family brunch and was taken via ambulance to a local emergency room. Her doctors determined she had serious bleeding in her brain, but could not determine the source of the bleed.

“The bleed was so severe that the neurosurgeon told my family I would be lucky to wake up," recalled Nguyen, a part-time realtor and former cardio kickboxing instructor. Nguyen was transferred to Keck Medical Center of USC for evaluation by their comprehensive cerebrovascular stroke team. A CAT scan helped William Mack, MD, Associate Professor of Neurological Surgery, find the aneurysm causing the bleed. He quickly recognized the complexity of the problem.

“There was a ruptured aneurysm that involved the entire left vertebral artery, including the posterior inferior cerebellar artery (PICA), which provides blood to part of the patient’s brainstem,” said Jonathan Russin, MD, Associate Surgical Director at the USC Neurorestoration Center. “Cutting off the blood supply to the artery would also cut off blood to the brainstem, causing brain damage or even death.”

Dr. Russin performed a PICA-PICA bypass, which involves suturing the right and left PICAs together to ensure proper blood flow to the brainstem while preventing additional bleeding from the aneurysm. The USC Stroke Center is one of a handful in the country that can perform this rare procedure. Immediately following the bypass, Dr. Mack and his team blocked the vertebral artery and the aneurysm through endovascular coiling.

On Friday, March 13, Nguyen woke up. “Friday the 13th has always been my lucky day,” she said. “My twins were born on that day.”

Nguyen made a remarkable recovery with strong support from her treatment team.

“Kathy’s motivation and commitment to physical fitness enabled her to engage in high-intensity activities soon after her surgery,” said Cherise Lathan, physical therapist at Keck Medical Center. “There are not many patients that I can push to do circuit training after a stroke. But her spirit inspired me to push myself and join her for her comeback race.”

Nguyen recruited Lathan, Russin, Joseph Hendrix (physician assistant at the neurosciences clinic), administrative assistant Valerie Sanchez and Senior Director of Development Chris Sickels to run by her side. It was the first marathon for all of them.

Nguyen also raised more than $4,800 for the USC Stroke Center.

“In addition to raising awareness for brain aneurysm research, I wanted to thank my treatment team, especially all the nurses at 7 South ICU. I wouldn’t be here if it weren’t for them.”
For many patients with Parkinson’s disease, essential tremor, dystonia or other movement disorders, otherwise useful medications cannot prevent troublesome or even disabling symptoms. For these patients, surgical intervention with deep brain stimulation (DBS) is an option.

Deep brain stimulation is a surgical technique in which an electrical current is applied through a wire placed in a very specific location in the brain, depending on the targeted disease. DBS is approved by the Food and Drug Administration for the treatment of Parkinson’s disease, essential tremor, dystonia and obsessive compulsive disorder (under a Human Device Exemption). The technique is believed to alter abnormal electrical signals in the brain that are caused by these illnesses, although the exact mechanism is not fully understood.

The USC Deep Brain Stimulation Center at Keck Medicine of USC in Los Angeles offers Southern California’s most comprehensive care for patients requiring deep brain stimulation. The Center’s team of experienced health-care professionals provides the highest quality care to patients considering DBS. It also conducts advanced research in these and other disorders and is a National Parkinson Foundation Center of Excellence, one of only 39 such centers nationwide (and the only designated center in Southern California).
DEEP BRAIN STIMULATION

The USC Deep Brain Stimulation Center at Keck Medicine of USC is an interdisciplinary program that draws from adult and pediatric neurologists, neurosurgeons, psychiatrists, nurse practitioners, clinical psychologists, neuropsychologists and social workers. It also collaborates with the Parkinson’s Disease and Movement Disorders Center, Intraoperative Neurophysiological Monitoring Program, and the Viterbi School of Engineering.

As part of a renowned university-based medical center, members of the center conduct research in other projects exploring such areas as: behavioral side effects of deep brain stimulation (DBS) and medication for Parkinson’s disease; the effect of exercise in Parkinson’s disease; treatment of dyskinesias in Parkinson’s disease; novel DBS electrode coating metallurgy; optimization of electrode placement for complex pediatric dystonia population; and outcomes of DBS in patients with Parkinson’s disease essential tremor, dystonia and obsessive compulsive disorder.

The USC Parkinson’s Disease and Movement Disorder Center at Keck Medicine of USC is the most comprehensive center in Southern California for Parkinson’s disease and other movement disorders. Our team is a unique collaboration of health-care professionals who deliver the highest quality care to ensure the most successful outcomes in our patients. We also are a National Parkinson Foundation Center of Excellence and home to the largest clinical trials program in Southern California for Parkinson’s disease and dystonia. Our commitment to providing compassionate, comprehensive and customized care is reflected in the care we provide to our patients. Following are conditions we commonly see at our center:

- Parkinson’s disease and other parkinsonian syndromes
- Dystonia
- Essential tremor
- Tourette’s syndrome and other tic disorders
- Ataxia
- Huntington’s disease
- Myoclonus and other disorders of movement

The USC Parkinson’s Disease and Movement Disorder Center takes a multidisciplinary approach to treatment. Patients receive a wide range of medical care from our neurologists, neurosurgeons, and nurse practitioners, but also can receive sub-specialized services from clinical psychologists, social workers, speech therapists, occupational and physical therapists. As part of a major university-affiliated medical center, patients can also participate in clinical trials that lead to new developments in treatments. We also offer deep brain stimulation, in collaboration with the USC Deep Brain Stimulation Center, for those patients who are appropriate candidates having failed optimized pharmacotherapy. As a National Parkinson Foundation Center of Excellence – a designation bestowed on only 39 medical centers nationwide – we are recognized by peer institutions for our leadership in research, comprehensive care delivery, professional education, and patient outreach services. The Center is the only Center of Excellence in Southern California.

The Surgical Neurophysiology Program at Keck Medicine of USC is unlike any surgical monitoring program in the country; it provides all aspects of surgical neurophysiology to greatly reduce the risk of damaging key nervous system areas during surgery. The program consists of three parts:

- Intraoperative monitoring
- Brain mapping
- Brain implants

Intra-operative monitoring reduces risk and improves outcomes during brain, spine, head and neck surgery or other surgeries where any part of the nervous system is at risk. By monitoring the electrical signals of nerve cells in the brain and spinal cord during surgery, the program at Keck Medicine of USC can help prevent injuries like stroke or paralysis during the operation.

Brain mapping localizes important functions of the brain, such as language, motor function, vision, and sensation - brain areas that can vary a great deal between individuals. As a consequence, surgeons will know which key areas to bypass when performing operations, sparing vital structures in the brain.

Brain implants: We offer deep brain stimulation for the treatment of conditions like Parkinson’s disease, essential tremor, dystonia, and obsessive-compulsive disorder, among others. By navigating electrodes deep into the brain using a computer generated trajectory, we are able to locate the group of neurons which, when stimulated with an electrical current, ameliorate some of the patient’s major symptoms. These devices are first activated in the operating room to determine the potential for adverse effects and to confirm the correct location for surgical implant leading to improvement in symptoms.

Program physicians use a number of methods to measure nervous system activity in the brain and spinal cord, and that of individual nerves during surgery, using a variety of techniques including evoked potentials, electroencephalograms, electrocorticography, and microelectrode recording.

Program physicians work with a wide variety of surgeons, including neurosurgeons, orthopedic surgeons, otolaryngologists (ear, nose and throat specialists), movement disorder specialists, interventional neuroradiologists, and vascular surgeons. The program monitors and assists surgeons at Los Angeles County+USC Medical Center, as well as, the hospitals at the Keck Medical Center of USC.

As part of a large university-based medical center, program physicians are involved in research projects aimed at improving monitoring, deep brain stimulation and mapping capabilities, as well as testing new surgical techniques to treat a variety of conditions including aneurysms, brain and spinal cord tumors, complex spine conditions, head and neck tumors among others. Physicians at the program also have authored several chapters in the most widely used textbooks on neurophysiological monitoring.

Learn more at http://keck.usc.edu/services/deep-brain-stimulation-center/
In addition to Togasaki and Esnaashari, Shea’s team includes neurosurgeon Mark Liker, MD, assistant clinical professor of neurosurgery at USC. Neuroscientists of Keck Medicine of USC, who says this collaborative effort between specialists is important to the patient experience. “We want good outcomes,” says Liker, who has 15 years experience performing DBS surgery at Keck Medicine. “We don’t want a lot of patients who are implanted to not receive benefit from the procedure. I can say almost universally every patient that’s cleared for surgery has a dramatic benefit from the DBS.”

Part of the reason for this collaborative effort is the nature of Parkinson’s. “It’s a boutique disease,” Shea says. “Everyone is affected differently.”

Many patients experience “freezing,” where their lower body refuses to move from a tile floor to a carpeted floor, for example. Some patients experience rigidity and/or slowness. Some experience dystonia, painful muscle contractions in various body parts, such as the foot and ankle. Others experience tremors, fatigue, decline in fine motor skills, more general gait issues, balance problems and falls, a loss of sense of smell, trouble sleeping, difficulty speaking, or loss of ability to use facial expressions. The symptoms and consequences are so varied, the disease can be difficult to diagnose. Even with a proper diagnosis, some patients are not aware that they may be eligible for the DBS procedure.

“Fifty percent of the people who can benefit from DBS never consider the opportunity,” says Esnaashari. Lack of access or fear of brain surgery could contribute to this low number. However, the doctors who perform this surgery consider it minimally invasive, and most patients who undergo the procedures recover quickly afterwards. Before surgery, patients are cautioned that DBS is not a cure, and it should not be expected to relieve all physical symptoms. However, many patients who receive this treatment report improvement in so many areas that they may feel as though they have a new lease on life.

The benefits of this thoughtful and dedicated process are not lost on patients like Shea. “I can’t speak highly enough of Dr. Togasaki, Nasrin and the specialists of Keck Medicine of USC,” she says. “As far as being cutting-edge, taking time with patients, explaining things to you, giving you hope for the future, they really take the time to prepare you for the procedure in every way.”

In 2015-2016, 50 patients expressed interest in being considered for the program, and 10 to 15 of those were treated each year. Of the 10 to 15 treated patients, the program has been successful in improving 90% of them. Shea is one of the few people who has benefited from the treatment.

The process continues to be comprehensive after the surgery. Some institutions program the DBS implants while the patient is under anesthesia for implantation of the battery pack, but this leaves the patient unable to respond to stimuli. At Keck Medicine, each DBS patient’s implants are programmed post-surgery, enabling the patient to be active and reactive to the changes. The programming is based on the patient’s clinical symptoms and its therapeutic effects occur when the contacts located in the brain are stimulated.

Shea was diagnosed with Parkinson’s disease in 2006, after noticing a tremor in her left index finger when it rested on the steering wheel of her car. Her neurologist at the time told her not to worry about it, but she did worry. Eventually, she sought out a movement disorder specialist. Enter Dr. Togasaki, who diagnosed her with both Parkinson’s disease and essential tremor in 2009.

Shea was educated about DBS while she was awake, then mildly sedated. Once the electrodes are positioned in the correct locations of the brain for the patient, wires are attached and coiled under the scalp for the second part of the operation, which typically occurs within the next one to two weeks. In the second procedure, the wires coiled under the scalp are unwound and channeled internally behind the ears, down to the neck to the battery pack implanted in this same operation in the upper chest. The battery pack, somewhat similar to a pacemaker, sends electrical impulses that stimulate specific areas of the brain, blocking abnormal electrical signals from targeted areas.

In 2009, Shea was diagnosed with essential tremor, a secondary movement disorder not related to PD. “Subliminally, it’s always with you,” she says. “You might be at the happiest occasion, but always thinking about how your hands will work, what symptoms will be noticeable to others, and when your next dosage is due. Even when people know it, it is uncomfortable being on display in this way.”

With the SkyCap’s help, she finally retrieved the license, but after the experience, she was more convinced than ever that she needed to take additional steps to improve her daily functioning and her life. It was time to pursue deep brain stimulation (DBS) with her neurologist, Daniel Togasaki, MD, PhD, associate professor of neurology at USC. Neuroscientists of Keck Medicine of USC. DBS is a procedure that can decrease the tremors, dyskinesia (tics), and other movement issues that commonly come with Parkinson’s and ET and can often out the amount of medication required. The majority of patients undergoing DBS have either PD or ET, meaning they will have only one area of the brain stimulated, typically on both sides. In Shea’s case, she had a double diagnosis of PD and ET resulting in two different areas of the brain requiring stimulation on both sides.

DBS is a series of two procedures in which electrodes are implanted in the brain while the patient is awake, though mildly sedated. Once the electrodes are positioned in the correct locations of the brain for the patient, wires are attached and coiled under the scalp for the second part of the operation, which typically occurs within the next one to two weeks. In the second procedure, the wires coiled under the scalp are unwound and channeled internally behind the ears, down to the neck to the battery pack implanted in this same operation in the upper chest. The battery pack, somewhat similar to a pacemaker, sends electrical impulses that stimulate specific areas of the brain, blocking abnormal electrical signals from targeted areas.

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The USC Comprehensive Epilepsy Program is a multi-institutional effort to provide accessible, customized, multi-disciplinary care using the most innovative therapies and research protocols in the quest to cure epilepsy. Our program serves Keck Hospital of USC, Children’s Hospital of Los Angeles (CHLA), LAC+USC Medical Center, and Rancho Los Amigos National Rehabilitation Center.

Additionally, this past year we have begun an exciting collaboration with Hoag Hospital Newport Beach. Together with Dr. David Millett, the epilepsy program director at Hoag hospital, we have begun to expand the treatments offered at Hoag for the management of medically resistant epilepsy. Continued programmatic expansion is underway in order to provide patients access to our experienced specialists and committed support staff.

The integration of Children’s Hospital of Los Angeles into our program provides our patients with a lifetime of continuous care. Transitioning from pediatric to adult specialists can be stressful and potentially disruptive to the treatment plans and goals of individual patients. At the USC Comprehensive Epilepsy Program our patients can be seamlessly transitioned to adult services without losing the continuity of care that optimizes patient’s experiences.
Epilepsy Surgery

The USC Comprehensive Epilepsy Center at Keck Medicine of USC combines the resources of the Keck Medical Center of USC in Los Angeles, the Los Angeles County + USC Medical Center and Rancho Los Amigos National Rehabilitation Center. The center is designated by the National Association of Epilepsy Centers as a Level 4 epilepsy specialist center, the highest designation which indicates the center can provide care for the most complex cases.

Providing world-class medical and surgical care for epilepsy across the cultural and socioeconomic spectrum of Los Angeles and beyond, the program also incorporates research and education as key components of its goal to improve knowledge of and find a cure for epilepsy.

The center was established more than 20 years ago. Our physicians are voted among the best in patient polls, and in 2011, our center received a Productivity and Quality Special Merit Award from the Los Angeles Board of Supervisors. Many of our doctors have received the Top Doctors Award from Pasadena Magazine. Our goal is to provide accessible, multi-disciplinary care, tailoring treatments to the specific needs of each patient.

As a Level 4 accredited epilepsy center we can offer a full range of epilepsy treatments. New treatments are:

- Responsive Neuro-Stimulation. This technology, approved by the FDA in 2013, greatly expands the horizon for patients with medically intractable epilepsy localized in brain regions not amenable to surgical resection.

- Stereotactically placed electrodes to perform thermoablation of epileptogenic tissue.

- In 2012, the capability to perform Ictal-Spect was added as a routine option for the pre-surgical workup of the most complex patients. In this nuclear medicine study, a highly coordinated effort is required to obtain the imaging study after a radiotracer is injected during a seizure. This represents a very important new tool for the care of our patients.

- A young man with a hypothalamic hamartoma causing intractable epilepsy and behavioral disturbances was treated with the VISUALASE Stereotactic Laser Thermal Ablation method. This method allowed the patient to be treated in a minimally invasive way, avoiding a high-risk open surgical procedure and a long hospitalization and rehabilitation course, with significant cost savings. The surgery represents the first such case treated in the Los Angeles area.

Publications

Selected epilepsy papers from 2015-2016 publications.


ttp://epilepsy.kemedicine.org/
On December 18, 2013, Keck Medicine of USC became the world’s first medical center to surgically implant a responsive brain device newly approved by the U.S. Food and Drug Administration (FDA) to treat epilepsy, with the potential to help millions of people worldwide.

The device, manufactured by NeuroPace Inc., detects and then directly responds to abnormal brain activity to prevent seizures before they occur. In a three-hour surgery, USC faculty physicians implanted the device in a 28-year-old Lakewood, California, woman who was diagnosed with epilepsy in 2004.

Kathleen Rivas, an aspiring journalist who sought care from the university’s student health center in 2009 while earning her master’s degree elected to have the implant because medication had not fully controlled her seizures. Over the next few months, her doctors will program the device to detect specific brain activity indicative of a seizure’s onset.

“I’m just so lucky to be here at USC,” said Rivas. “Without faith and trust in my neurologist and neurosurgeon, I don’t know where I’d be. My life is in their hands.”

Epilepsy affects approximately 65 million people worldwide, including nearly 3 million in the United States. Those who can tolerate medication and whose seizures are completely controlled usually lead a normal life, but the disease can be devastating for the up to 40 percent who experience uncontrolled seizures.

The device is the world’s only responsive neurostimulation (RNS) system approved for clinical use. USC physicians have been studying the technology since 2006 and are among the first authorized to prescribe its use since FDA approval on November 14, 2013.

“This has the potential to be a game-changer for patients with epilepsy,” said Christianne Heck, MD, MM, Associate Professor of Neurology at the Keck School of Medicine of USC, Medical Director of the USC Comprehensive Epilepsy Program and principal investigator of the device’s clinical study at USC. “Unlike other neurostimulators on the market, this system looks for just the right circumstances to stop a person’s seizure from happening.”

Most people with epilepsy gain complete or partial control of their seizures through medicine or surgery. USC’s surgical epilepsy program has had an 80 percent cure rate among patients who do not respond to anti-seizure medications. RNS may help the remaining 20 percent.

“We have become very good at surgically removing the areas of the brain where these seizures start, but we have limited options when a person’s seizures begin in critical zones, such as those that affect speech or movement,” said Charles Liu, MD, PhD, Professor of Neurosurgery and Neurology at the Keck School, Surgical Director of the USC Comprehensive Epilepsy Program and co-director of the new USC Center for Neurorestoration with Heck.

“Devices like this provide an option for patients who live with uncontrollable seizures because no available treatment works for them.”

FDA approval of the RNS device came after a randomized clinical trial of 191 patients with drug-resistant epilepsy across 32 clinical sites. The study showed that, by three months after the device was turned on, patients experienced a nearly 38 percent reduction in monthly seizures, compared to a roughly 17 percent reduction among patients who had the implant turned off. Two years post implant, 55 percent of patients experienced a 50 percent or greater reduction in seizures.
About half of all pediatric neurosurgical operations in Los Angeles County are performed by neurosurgeons from Children’s Hospital Los Angeles (CHLA) Division of Neurosurgery. This high volume of cases leads to high success rates in treatment with our experts routinely performing surgeries for complex neurological conditions.

Our patients range in age from newborns to young adults. Armed with the latest technologies, the Division provides advanced surgical solutions, with outcome statistics that match or exceed other programs across the nation and beyond. These therapies significantly improve outcomes for children suffering from a wide range of conditions such as brain and spinal cord tumors, deafness, hydrocephalus and medically intractable epilepsy.

Because our hospital operates the only Level I Trauma Center in Los Angeles solely for children, our neurosurgeons are well-versed in caring for severely injured children and have pioneered new therapies that are improving surgical outcomes.
This past year has been an exciting time for the Division of Neurosurgery, and we are proud to share the following highlights:

Leo underwent lifesaving surgery even more enhanced treatments for this devastating disease. Leo does not have any brain damage and is now a healthy 7-month-old who only needs routine checkups at CHLA.

The Division has extensive expertise treating hydrocephalus, which occurs in nearly 1 in 1,000 births. Earlier this year, J. Gordon McComb, MD, received grants from the Los Angeles Kings’ Kings Care Foundation and the Garry D. Browne Trust to propel his research on this condition. His work will focus on gaining a deeper understanding of its pathology with the ultimate goal to develop even more advanced treatments for this devastating disease.

Edie Kiehna, MD, one of the neurosurgeons for the hospital’s comprehensive Epilepsy Surgery Program, collaborated with CHLA neurologists on a revolutionary procedure—the first on the West Coast—to help 18-year-old Johny Escalero manage the nearly 250 seizures he had been suffering each day. The team implanted a special device in his chest to detect and respond to heart rate increases associated with seizures. With nearly 60 percent of sudden, unexplained epilepsy deaths occurring during sleep, the device is a game-changer, providing a crucial layer of security and support for patients like Johny.

As another step in its dedication to educating the next generation of pediatric specialists, the Division is pleased to welcome new attending R. Aaron Robison, MD, and fellow Albert D. Tu, MD. Dr. Robison comes to CHLA from Seattle Children’s Hospital where he completed a fellowship in pediatric neurological surgery.

Prior to that, he was a neurological surgery resident at Los Angeles County + USC Medical Center. He received his medical degree from Washington University School of Medicine in St. Louis, Missouri. Dr. Tu joins the Division from the University of British Columbia in Vancouver, Canada, where he completed medical school and a residency in neurosurgery. As a fellow, he will train in all areas of pediatric neurosurgery under the mentorship of the Division’s faculty during a one-year program.

Our pediatric neurosurgery program is among the nation’s busiest with 700 surgical procedures and 4,000 outpatients this year, while continuing to conduct leading-edge research. It can take a very special team of people to provide the very best care for children who need neurosurgery. Families who choose care from our specialists benefit from having access to all of the specialists below under one roof, including:

- Neurologists
- Neurosurgeons
- Pediatric neuroradiologists
- Neuro-ophthalmologists
- Neuropsychologists
- Physical therapists
- Clinical nurse specialists
- Neuropsychologists
- Neuro-ophthalmologists
- Rehabilitation therapists
- Neuro-oncologists
- Medical Genetics
- Orthopedics
- Neuro-oncologists
- Otolaryngology
- Physical Therapy

The Neuro-oncology Program at Children’s Hospital Los Angeles treats children with brain tumors and spinal cord tumors, which are the second most common types of tumors in children. We are one of the largest pediatric neuro-oncology programs in the country with more than 150 new referrals per year from Southern California, nationally and internationally. Our program offers patients access to the latest treatment options being tested in clinical trials through participation in national and international research consortia.

Every patient receives comprehensive care from a multi-disciplinary team of physicians and nurses that include neuro-oncologists, neurosurgeons, neurologists, neuroradiologists, radiation oncologists, neuropathologists, neuro-endocrinologists, rehabilitation medicine specialists, neuropsychologists, and advanced practice nurses, who are national leaders in their respective fields.

Functional Neurosurgery Program

Using auditory brain stem implants to give deaf children a chance to hear is just one innovative technique of the Division’s Functional Neurosurgery Program. The program also works to restore function for patients with previously untreatable conditions such as seizures, movement disorders and other neurological conditions through the following therapies:

- Epilepsy surgery: For patients whose seizures can’t be controlled with medication, surgery is the best chance at leading a seizure-free life. Using a high-tech system of measuring brain waves, called “brain mapping,” to pinpoint the area where seizures originate, the Division partners with CHLA neurologists and epileptologists to remove the troubled area and eliminate seizures for good.

- Deep brain stimulation: For patients suffering from conditions such as essential tremor and dystonia, deep brain stimulation provides highly customized treatment to target and improve symptoms. A pacemaker-like device connects to electrodes implanted within certain areas of the brain to produce electrical stimulation that regulates abnormal impulses.

CHLA is the largest freestanding pediatric hospital in the West performing functional neurosurgery. This means that for thousands of children, we are the only institution providing the care they need to enjoy a life free from the physical and psychological burdens of their neurological conditions.

Neuro-Endoscopy Program

The Neuro-endoscopy Program at Children’s Hospital Los Angeles treats children with brain tumors and innovative treatment strategies for patients with Central Nervous System (CNS) germ cell tumors. We also conduct research for patients with neurofibromatosis, low grade gliomas, and diffuse intrinsic pontine gliomas (DIPGs). We study molecularly targeted therapies and the role of inflammation in embryonal brain tumors including medulloblastoma and atypical teratoid/rhabdoid tumor (ATRT) to improve outcomes for these patients.

The Radiation Oncology Program at CHLA is an internationally recognized leader in pediatric radiation oncology and one of only two radiation oncology programs in the nation focused exclusively on children.

The Neuropathology Program at CHLA includes three distinguished pediatric neuropathologists. Within the Department of Pathology and Laboratory Medicine also resides the Center for Personalized Medicine, whose mission is to discover the human genome’s potential to guide preventive medicine, targeted therapies and personalized health care for the benefit of generations to come.
Our research team has developed a pump which allows automated continuous or time-interruptible intrathecal delivery of chemotherapy. Our program recently developed a novel transgenic murine medulloblastoma model, which develops leptomeningeal dissemination, and will be used to select candidate drugs for delivery via this device. This device has recently received FDA designation by the FDA, which would permit a first-in-human testing clinical trial. A pilot protocol for a first-in-human testing of this device, in children with leptomeningeal dissemination of CNS tumors, is currently in development.

Clinical Trials

Children’s Hospital Los Angeles participates in the latest clinical trials for movement disorders. Currently, the following trials are open for enrollment for eligible children:

- Translational Direct Current Stimulation (tDCS) for treatment of dystonia.
- Repetitive Transcranial Magnetic Stimulation (rTMS) for treatment of dystonia.
- Portable Wearable Biofeedback for Treatment of Weakness, Sensory Neglect, or Dystonia.
- New Assessment Tool for Evaluation of Dyspraxia in Children with Autism, Cerebral Palsy, and Other Disorders.
- Improving Assistive Communication Devices and Computer Interfaces for Children with Motor Disorders.
- Measurement of Accuracy Using a New Muscle Electrical Interface for Prosthetic or Computer Control.
- Compensation Strategies for Increased Movement Variability and Inaccuracy.

Grants

- National Science Foundation EFRI-1332384: EFRI/BioFlex: Hybrid polymer-based multi-sensor implants for continuous remote monitoring (Krieger, McComb), 2014-15, $2,000,000.
- Los Angeles Kings Care Foundation: Hydrocephalus research (McComb), 2015-2010, $1,000,000.
- Gerry D. Brownson Trust: Quantification of Ventricular CSF (McComb), 2015-2016, $1,000,000.
- Rudi Schulte Research Institute: MRI Visualization of CSF (McComb), 2015-2020, $50,000.


The Pituitary Disorders Center is a unique clinical and academic program dedicated to the treatment and evaluation of patients with disorders affecting the hypothalamus and pituitary gland. The center provides a cutting-edge, multidisciplinary approach to patient care under the leadership of neurosurgeon Gabriel Zada, MD, and neuroendocrinologist John D. Carmichael, MD. It is staffed by a team of experts in neurosurgery, neuroendocrinology, neuroradiology, neuropathology, neuro-ophthalmology, radiation oncology and interventional endovascular neurosurgery, who provide high-quality clinical care and conduct research in genetic analysis, precision treatment and comprehensive management of pituitary tumors and related disorders. Patients with refractory or complex pituitary conditions may also participate in the center’s clinical trials.

The Skull Base Surgery Center is a collaboration of the Department of Neurological Surgery, the Caruso Department of Otolaryngology – Head and Neck Surgery, and the Department of Surgery’s plastic and reconstructive surgery program. By merging the expertise of these distinct disciplines, the center maximizes the effectiveness of surgeries to resect lesions of the skull base.
Endoscopic neurosurgery is a rapidly evolving subspecialty that takes tumors and other conditions using minimally invasive approaches. In technology as well as surgical instrumentation to treat a variety of brain endoscopic neurosurgery, small incisions and natural openings in the skull are used to safely and adequately perform a given operation. Using natural pathways and smaller incisions to approach various brain regions results in decreased injury to the brain, reduced risks of cerebrospinal fluid leakage, and may minimize pain, risk of infection and the length of hospital stays. Integration of advanced technology, including high quality endoscopy systems and high definition viewing monitors, into many of these approaches on a daily basis.

Neuro-endoscopic surgical approaches are generally classified into the following categories based on how the endoscope is used during the procedure:

1. **Endoscopic endonasal skull base surgery**
   These minimally-invasive procedures are used to treat a variety of tumors and cysts arising at the base of the skull and in the paranasal sinuses. These operations are typically performed through small incisions in the eyebrow or behind the hairline, which typically cannot be seen once healed. Depending on the location in the brain, a keyhole approach can be performed for several types of tumors and cysts. It is generally believed that the smaller bony openings used in these approaches result in decreased incidence of infections and complications such as cerebrospinal fluid (CSF) leakage.

2. **Endoscopic-assisted “keyhole” operations**
   This subset of endoscopic neurosurgery is a rapidly evolving subspecialty that takes full advantage of the most recent advancements in optical and video technology as well as surgical instrumentation to treat a variety of brain tumors and other conditions using minimally invasive approaches. In endoscopic neurosurgery, small incisions and natural openings in the skull are used to safely and adequately perform a given operation. Using natural pathways and smaller incisions to approach various brain regions results in decreased injury to the brain, reduced risks of cerebrospinal fluid leakage, and may minimize pain, risk of infection and the length of hospital stays. Integration of advanced technology, including high quality endoscopy systems and high definition viewing monitors, into many of these approaches on a daily basis.

3. **Neuro-endoscopic intraventricular operations**
   The cerebral ventricles are a network of chambers deep in the brain that produce and circulate CSF throughout the nervous system. At times, the normal pathways of CSF circulation can become blocked by tumors, cysts, or other conditions, resulting in a buildup of fluid and raised intraventricular pressure known as hydrocephalus. Because the ventricles are anatomically deeper structures, they can be a challenge to operate within using more traditional approaches. Neuro-endoscopic approaches to intraventricular conditions have become the preferred way to treat many conditions arising within the ventricular system, including colloid cysts, arachnoid cysts, some intraventricular tumors and some of hydrocephalus. Typically, a small incision is made behind the hairline in the frontal area, and a dime-sized hole is created for insertion of the endoscope into the ventricle. Sometimes, a procedure called an endoscopic third ventriculostomy (ETV) can be performed to treat hydrocephalus and may eliminate the need for implanting a permanent CSF shunt.

4. **Exoscopic channel neurosurgery**
   The NICO BrainPath® is an innovative tool that allows our neurosurgeons to provide treatment in cases where it may not have been safe to do so before. This minimally invasive surgery uses a 6 Pillar Approach Brain imaging, neuro-navigation, access, optics, tissue resection and regenerative medicine that allows neurosurgeons to safely resect brain tumors and intracerebral hematomas that may have previously been deemed inoperable due to location or size.

The procedure requires an opening less than the size of a dime and uses brain mapping, neuronavigation and the BrainPath channel to safely move through the natural folds and delicate fibers of the brain. The tool allows neurosurgeons to gently displace and reposition healthy brain tissue while locating a tumor, instead of cutting it, thereby lowering the risk of complications. The BrainPath® also uses neuronavigation to lock on a target lesion and creates a clear passageway for surgeons to maintain access to the tumor for removal while protecting the surrounding brain tissue.

**Publications**

2015-2016 select publications from a total of 30 neuro-endoscopy papers.


Brain and Spine Tumor Center provides exemplary patient care and develops novel therapies in a multidisciplinary fashion. Brain and spinal tumors come in a great variety of types, each requiring a different approach to treatment that may require medical, surgical or radiation-based intervention. As a result, an effective neuro-oncology program requires close collaboration and expertise in all of these therapeutic modalities. This expertise is available at the Neuro-Oncology Program at Keck Medicine of USC.

The USC Neuro-Oncology Program offers a comprehensive approach to caring for patients with brain and spinal tumors, bringing together medical neuro-oncologists, radiation oncologists, radiologists and neurosurgeons to provide patients with a broad range of treatment options. Such an approach can be of great benefit to patients, not only during the initial diagnosis but at any point during treatment. Our patients benefit from having physicians that collaborate as a team, which introduces best-practice medical decisions and streamlines patient care.

Brain tumors
Gliomas account for more than half of primary brain tumors treated by the USC Brain and Spine Tumor Center. The most malignant type of glioma, the glioblastoma multiforme, constitutes more than 60 percent of all gliomas.

Brain tumors treated include:
- Acoustic neuroma – a benign, slow-growing tumor that grows on the nerve connected the inner ear and the brain.
- Central Nervous System Lymphoma – a cancer in which malignant cells form in the lymph tissue in the brain.
- Epidermoid tumors – tumors that arise in the cells that line the ventricles of the brain, or the center of the spinal cord.
- Glioblastoma – cancers, usually highly malignant, that form in the “astrocytes,” cells that form supportive tissues in the brain.
- Low Grade Glioma – any slow-growing cancer that forms in the brain’s “astrocytes” or supportive tissue cells.
- Oligodendroglomas arise from the myelin-producing oligodendrocytes in the white matter region of the central nervous system.
- Craniopharyngiomas – cancers, usually benign, that arise in groups of cells making up the “stalk” of the pituitary gland.
- Meningioma – a tumor that arises in tissues that surround and protect the surfaces of the brain and spinal cord.
- Metastatic brain tumors – tumors that originated from another part of the body and have spread into the brain tissue.
- Pituitary Tumor – cancer in the pituitary gland, which controls the body’s growth.

Keck Medical Center of USC is one of six facilities in California to offer an advanced Gamma Knife® and only one of two in Los Angeles to feature its latest version, Perfexion™.

In addition, USC is one of three centers in California offering CyberKnife® stereotactic radiotherapy. Providing surgeons with non-invasive methods of treating inoperable brain tumors, the goal of Gamma Knife® or CyberKnife® treatment is to reduce risk to the patient while maximizing the therapy’s effectiveness.
As an integral component in the continuum of care for patients who were diagnosed with neurogenetic conditions as children, our program extends care to patients as they move into adulthood. We also provide care to patients who have been diagnosed as adults. Patients who have these conditions can be symptom free, but can also be susceptible to a variety of malignant or benign tumors, including neurofibromas, astrocytomas, papillomas, acoustic neuromas, meningiomas.

Surgery is the preferred method of treatment for tumors arising from these conditions. If a tumor does occur, it is important that diagnosis and treatment occur quickly. Therefore, our team follows each patient on an ongoing basis. We work in concert with members of the Adolescent and Young Adult Cancer Program at USC, which offers a unique breadth and scope of multidisciplinary treatment and care for adolescents and young adults. In cases where a tumor is in a location in the body that makes surgery impossible or inadvisable, we are able to provide radiation therapy as alternate treatment. We are the only academic medical center in Southern California to offer all three of the most advanced technologies in radiosurgery – CyberKnife®, Gamma Knife® and TrueBeam™. These methods deliver a high dose of radiation to only the unhealthy tissue, avoiding the healthy tissue that surrounds it.

Our patients benefit from a multi-disciplinary network of neuro-oncology professionals, including experts in medical oncology, neurosurgery, radiation oncology, neuropathology and neuroradiology.

As chordoma is a very rare disease, most physicians may see only one or two cases in their career. Our physicians regularly see patients who have chordoma, giving us the knowledge and experience needed to design and implement a proper treatment plan. Our oncologists are renowned experts in chordoma and sarcoma, and we offer ongoing clinical trials and protocols for treatment.

We are among only a few institutions in the United States to offer treatment for chordoma and the only center in the greater southwest region to offer an endoscopic sacrectomy and spinal tumor resection that has been shown to improve long-term survival and provide the best chance for cure.

Chordomas are typically slow growing but can become aggressive in some cases. There are three subtypes of chordoma:
- Chondroid
- Conventional (classic)
- Dedifferentiated

Dedifferentiated chordomas are the most aggressive, fastest growing of the three subtypes and are the most likely to metastasize to another area of the body. Chondroid chordomas are typically the least aggressive.

Surgical treatments
- **En bloc sacrectomy.** The USC Chordoma Center is the only facility in the greater southwest region of the United States to perform this procedure, in which a portion of the sacrum (base of the spine) is resected to allow full access for removal of the tumor.
- **Spinal tumor resection.** In this procedure, soft tissue and lamina (a posterior bony structure that covers the spinal canal) are removed, so that the tumor can then be separated from healthy tissue and removed.
- **Endoscopic skull base tumor resection.** In this minimally-invasive procedure the endoscope (device providing lighting and visualization) and other instruments are inserted through the nose, eliminating the need for an incision and the resulting scar. This approach allows access to the base of the skull from the bottom rather than the top as is the case with traditional craniotomy, and thus avoids potential damage to other important anatomical structures, such as the brain.
- **Epilepsy surgery** – for patients with epilepsy who have tuberous sclerosis who are having seizures, epilepsy surgery may be considered.
- **Laminctomy** – removal of a portion of the lamina (the vertebral bone) allows surgeons to reach and resect a spinal tumor.
- **Lumpectomy** – removal of a portion of the lamina (the vertebral bone) allows surgeons to reach and resect a spinal tumor.
- **Neurofibromatosis 1** – an inherited disorder in which nerve tissue tumors form in the skin, bottom layer of skin, or cranial or spinal root nerves.
- **Neurofibromatosis 2** – a genetic disorder in which tumors form on the nerves of the brain and spine, or the central nervous system.
- **Von Hippel-Lindau syndrome** – an inherited disorder characterized by tumors and cysts forming in different areas of the body.
- **Li-Fraumeni syndrome** – a rare, hereditary disorder that increases cancer risk in patients.
- **Tuberous sclerosis** – a group of two genetic disorders affecting multiple organs that causes tumors to grow.

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ORTHOPEDIC SURGERY, the Director of the Program

Josh Nem an, PhD, Assistant Professor of Neurological Surgery, current research investigates the biology and tumor microenvironment of medulloblastoma (the most lethal pediatric brain tumor and breast to brain metastatic tumors. Dr. Nem an’s expertise and strengths in Developmental and Neurobiology have allowed him to develop novel molecular, cellular, and systems approach to study the interaction between the brain and cancer cells—a biologically interesting field to understand. His recent studies have established that the physiological microenvironment of the brain must become a tumor favorable microenvironment for successful tumor colonization. Dr. Nem an’s overall research goals are: 1) innovatively enhance and exploit the tumor-brain interactions; 2) investigate the cellular roots of treatment failure; 3) test agents to selectively attack the resistant cells, in order to better treat patients with brain tumors.

Since arriving at Keck School of Medicine in July 2014, Dr. Nem an has been the recipient of grants from USC/ American Cancer Society, and American Brain Tumor Association. He is particularly interested in the advancing minimally invasive surgical treatments for spine tumors. Most recently, he was able to collaborate with USC urologists to be one of the first in the country to successfully excise several spine tumors using the Da Vinci robot.
Radu Minea, MD
Dr. Minea received his MD from Carol Davila University in Romania and did postdoctoral studies in Immunology at UCLA, and Biochemistry and Molecular Biology at USC where he developed a number of recombinant polypeptides with anti-metastatic properties. Although his primary scientific training is in molecular biology and the recombinant production of protein biologics, Dr. Minea’s current research interests focus on the development of assays and in vivo models to better understand the contribution of integrins and extracellular matrix to the process of metastatic colonization of the brain and leptomeninges. Dr. Minea is an expert in integrin biology, integrin-targeted polypeptides, and engineering bacterial hosts for enhanced production of protein biologics. His research interests are to:
1) understand the contribution of extracellular matrix to cancer spread and metastasis into the brain
2) develop novel radiopharmaceuticals and nanoparticle solutions for targeted tumor radioablation and multimodal imaging.

Steve Swenson, PhD
Dr. Swenson’s research interests are to develop and translate to the clinic novel anti-cancer therapeutics. He has extensive experience with animal models of human disease and injury. His current research projects include:
1) Development of integrin targeted radiotherapy for the treatment of gliomas
2) Identification of the breakdown products in Periethyl alcohol derivatives of tamoxifen (TMO)

3) Development and evaluation of a novel treatment strategy for melanoma involving a triglucuate of periferyl alcohol-TMZ-Indolise (triple compound)
4) Assisting team members with identification of drug level uptake and tissue specificity
5) Development and testing of novel ovarian cancer therapies delivered intraperitoneally.

Weijun Wang, MD
Dr. Wang has more than 10 years of experience as an oncologist, and a certified clinical research professional for human gliomas treatment. Dr. Wang has extensive experience in establishing varied human disease animal models, including experimental orthotopic metastatic brain tumor, Parkinson’s disease, and nasopharyngeal carcinoma. Currently, Dr. Wang focuses on translational research under the guidelines of SOPs, FDA and ICH/ISEE regulations in the development of innovative drug delivery system target and new chemotherapeutic agents for CNS related disorders, like, viral vector mediated gene therapy for stage IV glioblastoma Multiforme (GBM), novel agents for neurodegenerative Parkinson’s disease, and to apply molecular imaging for brain tumor monitoring.

C O L L A B O R A T I O N S

Florence M. Holman, PhD
Dr. Holman is Professor of Pathology. Dr. Holman’s research interests are as the mechanisms of drug resistance in glioblastoma (GBM). The administration of temozolomide (TMZ), current standard of care, usually results in the development of tumor resistance and eventual tumor recurrence. She is interested in identifying the effects of different novel, newly synthesized, drugs directly on the tumor-initiating cells, the glioma stem cells (GSC), resulting in tumor invasion and progression. She is also interested in the functional characteristics of the brain tumor vasculature and the blood-brain barrier, and how these cells interact with the GBM cells and glioma stem cells. Understanding the mechanism of drug activity on the GSC and the brain vasculature will lead to identifying effective drugs for treatment of GBM.

Francis S. Markland Jr., PhD
Dr. Markland is Professor of Biochemistry and Molecular Biology. He is internationally recognized for the isolation and characterization of proteins from snake venom, and has studied a number of clinically relevant proteins from venom over the past 45 years. Presently, his research examines the translational therapeutic and diagnostic potential of recombinant peptides whose structures are based on a class of agents known as disintegrins that were originally isolated from snake venom. Their therapeutic efficacy is based on binding with high affinity and specificity to proteins on the surface of tumor cells, leading to inhibition of their invasive capacity. His research has shown, using mouse models of human breast, prostate, ovarian cancer and glioma, that disintegrins serve as very effective therapeutic agents and dramatically inhibits tumor invasion, dissemination and angiogenesis. There are a number of patents surrounding his technologies and more are in progress. Finally, a recombinant version of a fibronectin-metalloprotease ligand that disintegrins serve as very effective therapeutic agents and dramatically inhibits tumor invasion, dissemination and angiogenesis. There are a number of patents surrounding his technologies and more are in progress. Finally, a recombinant version of a fibronectin-metalloprotease ligand that was originally isolated from snake venom that disintegrins serve as very effective therapeutic agents and dramatically inhibits tumor invasion, dissemination and angiogenesis. There are a number of patents surrounding his technologies and more are in progress. Finally, a recombinant version of a fibronectin-metalloprotease ligand that was originally isolated from snake venom that disintegrins serve as very effective therapeutic agents and dramatically inhibits tumor invasion, dissemination and angiogenesis. There are a number of patents surrounding his technologies and more are in progress. 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Axel H. Schönthal, PhD
Dr. Schönthal is Associate Professor of Molecular Microbiology & Immunology, and Molecular Pharmacology & Toxicology. Dr. Schönthal is a cancer biologist with 25 years of experience in the areas of molecular oncology and anticancer drug development in preclinical models. His laboratory is pursuing cross-disciplinary approaches to understand the mechanisms that drive tumor growth and determine chemoresistance. His current research projects are focused on mesenchymal tumors, which can arise from primary tumor growth inside the brain (such as glioblastoma) or from metastatic spread of other cancer types (such as breast cancer or lung cancer) into the brain. Infratotal tumors are especially hard to treat, because many therapeutic agents do not cross the blood-brain barrier and therefore are unable to enter the brain. With the use of animal models, his research team is exploring novel approaches to overcome these treatment obstacles with the goal to develop new methods and novel drugs that are more effective against tumors inside the brain.

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The internationally-renowned LAC+USC Acute Care Surgery (ACS) service collaborates closely with Neurosurgery. The American College of Surgeons in their report of LAC+USC Level 1 Trauma Center certification in the Spring of 2015 singled out Neurosurgery as a major contributor to excellent trauma management. The internationally-renowned LAC+USC Acute Care Surgery (ACS) service collaborates closely with Neurosurgery. The American College of Surgeons in their report of LAC+USC Level 1 Trauma Center certification in the Spring of 2015 singled out Neurosurgery as a major contributor to excellent trauma management.

Surgeries for cranial and spinal trauma are done almost daily. The majority of beds in our 18-bed Neuroscience Intensive Care Unit (NSICU) are usually occupied by traumatic brain and spinal cord-injured patients. The Neurocritical Care Service (3 Neurology and 2 Neurosurgery Attending) manages non-operative neurotrauma victims in the Surgical as well as in the NSICU. Invasive intracranial pressure (ICP) monitors (intracranial bolts and external ventricular drains) are placed by neurosurgical residents (junior supervised by senior) and on any day 4-8 TBI patients’ ICPs are being monitored in the NS or Surgical ICU.

Local hospitals in Los Angeles and surrounding counties with more limited neurosurgical expertise frequently stabilize and then transfer TBI and SCI patients to USC’s Keck Hospital for “higher level of care”.

Nerve injuries are managed in collaboration with both Orthopedic and Plastic Surgery. Neurosurgery runs a weekly “Nerve” clinic. Nerve injuries are also seen in Orthopedic Hand and Plastics clinics.

The LAC+USC Neurotrauma Team is led by Dr. Peter Gruen, Neurotrauma Liaison (also Director of Neurosurgical Care) to the ACS-accredited Trauma Service. Other members include three Neurosurgery Attending full-time at LAC+USC, Drs. Esha Christian, Frank Attenello, and Alexander Tuchman. In addition Dr. Arun Amar (Neurosurgery) provides Neurotrauma and Neurocritical Care services with colleagues Drs. Gene Sung, Natasha Renda, Nerses Sanossian, and Sabin Bulic of Neurology. There are also 2 Neurocritical Care Fellows.

Neurotrauma Critical Care Multidisciplinary Senior Attending Rounds complement daily morning Team Rounds every day. Neurontensive Nursing education and training is the focus of quality improvement in the Neuroscience ICU. Our nurses are comfortable with the care of the most complex neurotraumatic injuries.

The 4th Annual Neurotrauma Critical Care Symposium, a 4-hour review of Recent Advances, was a great success with attendees not only from LAC+USC but also from several Southern California hospitals, medical schools, and pre-med programs.

The LAC+USC Traumatic Brain Injury (TBI) Clinic began seeing patients 8 years ago and has seen several hundred mild-moderate TBI victims. Two studies of diffusion tensor imaging (DTI) have been done enrolling patients from the LAC+USC TBI Clinic, one of which was funded by the United States Department of Defense.

Other research projects in progress include a patient family information project to improve communication and reduce anxiety, a study looking at inferior vena cava ultrasound volume for management of volume status in patient with traumatic brain and spinal cord injury. We are also looking at compliance with National Brain Injury Foundation Guidelines for the Management of Severe Brain Injury. In 2001, USC Neurosurgery published a paper in Neurosurgery about brain death declarations at LAC+USC with suggestions for improvement in the process that have been adopted by many hospitals that treat TBI – a follow up paper is currently in preparation for publication.

Since moving into the new Los Angeles County Hospital 8 years ago we have used a portable head CT scanner in the NSICU operated by Dr. Gruen with the assistance of two of our level providers.
The USC Spine Center at Keck School of Medicine of USC merges innovative research with multidisciplinary services to provide customized treatment plans for varied and complex problems of the spine. Neurosurgery together with Orthopedic Surgery and Rehabilitative Medicine work together as a collaborative team to handle some of the most complex spine issues.

Building upon the longstanding excellence of our USC Spine Center, the vision for the Spine Center is to deliver comprehensive and appropriate world-class care for patients, train the next generation of physician scientists, expand basic and clinical research programs, and develop new treatments and therapeutic approaches, including protein and stem cell therapies and cutting-edge surgical procedures.
Our spine specialists are dedicated to developing new techniques and instrumentation for spine surgery. We participate in clinical trials that assess the best treatment regimen. Our goal is to develop new and effective approaches to alleviate spine and back pain for our patients.

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The Spine Center at Keck School of Medicine of USC understands and treats the varied and complex clinical problems that are associated with the neck and the back. Together, our team of experts are able to customize each patient’s treatment plan with his or her specific needs and condition in mind. Unique to the USC Spine Center is true comprehensive, coordinated care. We offer our patients a conservative approach to spine care providing the most appropriate treatment options, both nonsurgical and surgical, tailored to each patient’s specific need. As part of our complete range of comprehensive care, our services also include diagnostic testing, pain management and occupational therapy.

Our spine specialists are committed to providing appropriate and individual spine care. Our physicians are accomplished in performing a full range of spine surgical procedures from minimally invasive to the most complex.

Unique to the USC Spine Center is true comprehensive, coordinated care. We provide diagnostic testing, pain management, psychological counseling, physical therapy, occupational therapy and a wide variety of surgical procedures such as microdiscectomy, cervical and lumbar spine fusion and artificial disc replacement.

Our Multidisciplinary Approach
The multidisciplinary team at the USC Spine Center of Keck Medicine of USC provides solutions for the varied and complex clinical problems that are associated with the neck and back. Our surgeons in orthopaedic surgery and neurological surgery work together with physical therapists, occupational therapists, rehabilitation physicians, radiologists, psychologists and physician assistants, taking a team approach to diagnose and treat back and spine issues.

Together, our experts are able to customize each patient’s treatment plan with his or her specific needs and condition in mind.

Our Leadership
The USC Spine Center of Keck Medicine of USC is led by Co-Directors John C. Liu, MD, and Jeffrey C. Wang, MD, both of whom are leaders in the field of spine treatment and research. They bring an unmatched level of experience to our center.

Our Physicians
We have an experienced group of spine surgeons who are accomplished in performing minimally invasive and the most complex spine surgery procedures. Our doctors are recognized as leaders in the field, appearing in U.S. News & World Report, Pasadena Magazine’s “Top Doctors” and Best Doctors.

Our Specialties
Unique to the USC Spine Center is true comprehensive, coordinated care. We provide diagnostic testing, pain management, psychological counseling, physical therapy, occupational therapy, and a wide variety of surgical procedures such as microdiscectomy, cervical and lumbar spine fusion and artificial disc replacement.

We also offer advanced diagnostic testing and treatment plan design for patients experiencing high acuity conditions such as spine tumor and advanced spine deformities. Our team of specialists will collaborate to determine the best approach of care for every patient.

Additionally, our spine specialists are dedicated to developing new techniques and instrumentation for spine surgery. We also participate in clinical trials that assess the best treatment regimen. Our goal is to develop new and effective approaches to alleviate spine and back pain for our patients.

USC patient, Julie LaFuent's en bloc surgery to resect a large osteosarcoma from her sacrum, pelvic bone, and sciatic notch, which took place at USC Norris Cancer Hospital, took two days to complete. Credit: Katie Neilh and photography by Philip Channing, USC Norris Cancer Report.
RESEARCH

The Spine Center’s multidisciplinary research program partners with investigators from the USC Viterbi School of Engineering, The Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research at USC, and the USC Norris Comprehensive Cancer Center. With these partners, the Spine Center is harnessing the power of bench-to-bedside research and clinical care to develop new treatments for spinal cord injury, arthritis of the spine, the aging spine, soft tissue calcification, and spine regeneration.

Research priorities include:
• Enhancing surgical procedures and developing minimally invasive surgical techniques for spinal disorders, including spinal cord injuries
• Analyzing and improving long-term patient outcomes
• Utilizing stem cell and gene therapies for the treatment of neurological and spinal disorders
• Understanding and utilizing bone growth proteins to inhibit and cure cancerous tumor growth
• Advancing biomedical engineering technology to develop non-invasive spine surgery using high-intensity, focused ultrasonic waves
• Developing biological therapies for artificial disc replacements (fused fusion of the spine)
• Creating bioengineered pressure sensors that monitor movement and impact in the spine
• Exploring new therapeutic approaches to alleviate pain and suffering in complex cases relating to the aging spine

PUBLICATIONS

2015-2016 select publications from a total of 28 spine papers.

When Julie Anne Lafuente, 23, was diagnosed with a malignant tumor that involved her spine, it wasn’t her first battle against cancer. As a toddler, she had been successfully treated for a yolk sac tumor with a regimen that included radiation. In fact, her doctors believe that the radiation she received as a two-year-old was likely the cause of her most recent bout with the disease.

After consulting with an orthopedic specialist and a neurosurgeon at her primary hospital, Julie was referred to Patrick Hsieh, MD at the USC Spine Oncology Program. “We have a unique spine center that includes treatment for spine tumors far beyond the capability of most institutions,” says Hsieh. “Our program offers the most advanced surgical, radiosurgical, and chemoradiation treatment options to preserve neurologic function and to achieve a cure when possible.”

The majority of spine tumors are metastatic tumors that originate elsewhere in the body. But for primary spine tumors, such as osteosarcomas, like Julie’s tumor, USC is one of only a handful of centers in the country to offer a radical resection procedure called Total En Bloc Spondylectomy. Since most primary spinal tumors have a poor response rate to chemotherapy and radiation, complete and radical tumor excision is necessary to obtain long-term survival for patients and to provide them with the hope for cure.

“The traditional method for dealing with most spinal tumors, including primary spinal tumors, was to go inside the tumor and remove as much of it as possible from the inside without increasing the risk of spinal cord or vascular injury. The downside is that you are always leaving microscopic cells behind, putting the patient at high risk for tumor recurrences, which will shorten life expectancy,” says Hsieh, who has extensive experience with metastatic and primary spinal tumors. “With this more advanced technique of en bloc tumor excision, we take the tumor out in whole, along with a rim of surrounding healthy tissues, essentially eliminating the risk of leaving any microscopic disease behind.”

This type of radical surgical removal of tumors in the spine is considered to be the most complex and technically demanding procedure by neurosurgeons, spine surgeons and orthopedic surgeons. Julie’s en bloc surgery, which took place at USC Norris Cancer Hospital, took two days to complete. Julie recovered at the Keck Hospital of USC for nearly a month and completed another month of rehabilitation at a transitional care unit. Julie’s surgery involved a large multidisciplinary team of specialists and surgeons, including Hsieh, Wesley G. Schoeler, MD, a plastic and reconstructive surgeon, and Andreas M. Kaiser, MD, a colorectal surgeon, among others.

“I’m feeling very good” says Julie, who is recovering at a remarkable rate. “In comparison to how I was before surgery, I’m 100 percent better. I know that’s not quite true, but I believe I’m better.” Hsieh concurs. “I am very happy with Julie’s surgical results. She is doing really well and is disease free at this point.”

For Julie, the future is very clear. “I can see my future,” she says. “I can see my work expanding, and I can see myself starting a family — adopting kids and getting married. I can see all that, and I think because I can see my future, it helps me be positive now — this is just one more thing I have to get through.”

Credit: Katie Neith and photography by Van Urfalian, USC Norris Cancer Report

Martin Pham, MD and Patrick Pelosi, MD
The USC Radiosurgery Center, co-directed by Gabriel Zada, MD (Neurosurgery) and Eric Chang, MD (Radiation Oncology) has been among the nation’s preeminent radiosurgical centers for more than four decades, and continues to innovate in the application of radiosurgical treatments for brain, spine and systemic diseases. The multidisciplinary center includes neurosurgeons, radiation oncologists, physicists and medical oncologists, and uses cutting-edge radiosurgery capabilities including the most advanced Gamma Knife, Cyberknife and TrueBeam technologies. Having access to these three modalities for stereotactic radiosurgery allows USC physicians to individualize treatment plans for a wide variety of diseases with the utmost accuracy and safety. As the only institution in Southern California to offer these three technologies in one location, our physicians are able to provide patients with the best possible course of treatment. Each one is designed to support more favorable results while minimizing both side effects and length of treatment. All of these procedures are conducted without an incision or general anesthesia, and without the need for a hospital stay.

USC physician-scientists have been among the pioneers of radiosurgical treatments for the past several decades, having treated over 6,000 brain lesions in the past two decades. Our program remains in the forefront of innovative applications of radiosurgical treatments for brain, spine and systemic diseases. Many of the innovations in stereotactic surgery were invented or refined at Keck Medicine of USC. The technology that preceded the original CyberKnife® robotic surgical system was invented at USC. Additionally, our physicians helped create stereotactic frames for the head and other equipment that made navigation through the skull, brain and spine more precise during Gamma Knife® procedures.

### Conditions We Treat

- Brain metastases
- Meningiomas
- Pituitary adenomas
- Acoustic neuromas
- Craniopharyngiomas
- Chondromas
- Trigeminal Neuralgia
- Arteriovenous Malformations

## Stereotactic Radiosurgery

The USC Radiosurgery Center, co-directed by Gabriel Zada, MD (Neurosurgery) and Eric Chang, MD (Radiation Oncology) has been among the nation’s preeminent radiosurgical centers for more than four decades, and continues to innovate in the application of radiosurgical treatments for brain, spine and systemic diseases. The multidisciplinary center includes neurosurgeons, radiation oncologists, physicists and medical oncologists, and uses cutting-edge radiosurgery capabilities including the most advanced Gamma Knife, Cyberknife and TrueBeam technologies. Having access to these three modalities for stereotactic radiosurgery allows USC physicians to individualize treatment plans for a wide variety of diseases with the utmost accuracy and safety. As the only institution in Southern California to offer these three technologies in one location, our physicians are able to provide patients with the best possible course of treatment. Each one is designed to support more favorable results while minimizing both side effects and length of treatment. All of these procedures are conducted without an incision or general anesthesia, and without the need for a hospital stay.

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### 2015-2016 Procedures

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<th>Condition</th>
<th>2015-2016 Procedures</th>
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<td>Brain metastases</td>
<td>Total volume of such radiosurgical cases performed at Keck Medical Center of USC and USC Norris Comprehensive Cancer Center</td>
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STE R E O T A C T I C  R A D I O S U R G E R Y

The USC Stereotactic Radiosurgery Center at Keck Medical Center of USC is considered one of the nation’s leading centers for Gamma Knife® and other incision-free techniques in the treatment of brain and spine tumors. The team has published results showing more than 95 percent tumor control over five years for a majority of tumor types. Using a team approach toward diagnostics and treatment of patients with brain and spine tumors, our multi-disciplinary team offers patients the most advanced and sophisticated radiosurgical treatments.

Every week, neurosurgeons, radiation oncologists, and experienced physicists meet to determine the best treatment options for our patients. The specialists in the program, who include physicians at Keck Hospital of USC and the USC Norris Comprehensive Cancer Center, have performed thousands of procedures with the Gamma Knife® (including the latest Perfexion model), CyberKnife®, and TrueBeam™ Stx. The Gamma Knife® and other radiosurgical modalities are very safe complements to conventional surgery and chemotherapy.

Gamma Knife® radiosurgery is a non-invasive alternative to traditional brain surgery, directing a precise beam of radiation to the targeted area of the brain. For many conditions, treatment using the Gamma Knife® Perfexion – the newest model – is the most accurate form of stereotactic radiosurgery available. With it, 192 beams of cobalt-60 radiation are delivered through the skull to a small and critically located area inside the skull, to stop or alter tissue growth. The Gamma Knife® contains no blade and makes no incision. It combines data from three-dimensional computer imaging studies with a stereotactic head frame to precisely focus radiation.

The Leksell Gamma Knife was installed and made operational at the USC University Hospital in 1994 and upgraded in 2000 with the installation of the Leksell Gamma Knife 3 and again in 2008 with the Leksell Gamma Knife Perfexion. The Gamma Knife procedure is typically delivered on an outpatient basis.

CyberKnife® radiosurgery is a non-invasive alternative to surgery for the treatment of tumors in multiple locations in the body. CyberKnife® treatments also involve no cutting, instead delivering beams of high dose radiation to tumors anywhere in the body with extreme accuracy.

The CyberKnife® system is the world's first and only robotic radiosurgery system designed to treat tumors. Using image-guidance and computer-controlled robotics, the CyberKnife® tracks the tumor's position, detects any tumor or patient movement and automatically corrects treatment delivery.

The TrueBeam™ Stx radiosurgery system is a non-invasive system that delivers powerful radiation to even more precise areas than possible with other technologies, in the head and neck, lung, liver and other areas. The TrueBeam™ Stx system can target tumors and other disorders in areas close to critical structures in the body and direct a precise beam of radiation without harming those structures. In addition, a treatment of radiation therapy using the TrueBeam™ Stx system can take just a few minutes, minimizing patient discomfort.

IMPORTANT MILESTONES:
- 1975: First hospital-based computed tomography (CT) scanner in Los Angeles installed at LAC+USC Medical Center.
- 1979: First imaging directed stereotactic biopsy (B-cell lymphoma), at LAC+USC Medical Center.
- 1979: Stereotactic brachytherapy for malignant lesions of the brain using Iridium-192 radioactive seeds embedded in plastic afterloading ribbons.
- 1986: Linear accelerator (LINAC)-based stereotactic radiosurgery with 4-MV photons at the USC Norris Comprehensive Cancer Hospital and Research Institute, which was the first institution west of Boston to develop a concept through hardware and software research.
- 1992: “Operating Room One” at the USC University Hospital designed to offer frameless capabilities for intraoperative surgery.
- 1994: Leksell Gamma Knife® installed at the USC University Hospital.
- 1995: Stereotactic radiosurgery of the spine.
- 1999: The 1000th patient received stereotactic treatment at the USC.
- 2000: The most advanced Leksell Gamma Knife® Model C installed at the USC University Hospital.
- 2002: USC Norris Cancer Hospital installed the CyberKnife Stereotactic Radiosurgery System.
- 2008: Gamma Knife Perfexion installed at Keck Hospital of USC as the only current Perfexion machine in Los Angeles County.


PUBLICATIONS

2014-2016 select publications from a total of 18 radiosurgical papers.

"Radiotherapy for metastatic disease at the craniospinal junction." *WORLD *Neurosurgery, 2014. Authors: Tsutsumi A, VTC, Chang EL, Kim HT, Hashimoto M, Ayjem M.

"Radiotherapy for metastatic disease at the craniospinal junction." *WORLD *Neurosurgery, 2014. Authors: Tsutsumi A, VTC, Chang EL, Kim HT, Hashimoto M, Ayjem M.


"To stereotactic radiosurgery needed following excision of brain metastasis?" *Neuro-Oncology,* 2016. Authors: Siddiqui A, Bhatnagar S, Tsoo S, Hwang J, Chang EL.


The multidisciplinary USC Neurorestoration Center develops novel strategies to restore injured or diseased nervous system function—caused by Alzheimer’s, epilepsy, multiple sclerosis, traumatic brain injury (TBI) and other neurological issues—by developing new technologies that harness advances in basic neuroscience and neural engineering. The center is a collaborative effort across numerous, stellar institutions in Southern California, from neural engineering research at the USC Viterbi School of Engineering and the California Institute of Technology to clinical programs at Keck Medicine of USC and Rancho Los Amigos National Rehabilitation Center. These high-volume clinical programs function as living laboratories that apply primary and translational research to restore function to the human nervous system with minimal additional risk as compared to standard-of-care treatment.

The management of adult human neurological diseases has traditionally been limited by the belief that there is very little opportunity for recovery after injury. Now, cellular transplantation therapies and other advanced concepts are widely believed to significantly improve neurological function. Biological strategies, advanced neuroprosthetics, robotics, and other products of biomedical engineering have led to a rapidly expanding spectrum of possibilities for additional restorative platforms. These possibilities are based on the explosion of knowledge in the basic neurosciences and neural engineering, areas in which USC has tremendous strengths.
The USC Neurorestoration Center (NRC) was established in December 2013 to physically test innovative neural engineering and basic neuroscience to restore neurological circuitry and function within the human brain. Physicians map, decode and repair basic neural circuitry in the brain, a fundamental departure from current best practices in neurorehabilitation, that rely on pharmacological modulation, external prostheses, compensatory strategies and limited intrinsic neural plasticity.

The center is the “brain child” of Charles Liu, M.D., Ph.D., director, and Christianne Heck, M.D., M.M.M., co-director, who spent more than 10 years seeking the best community partners to move the treatment of neurological disorders beyond traditional surgery and medications. They aim to accomplish this by engineering new technology that restores neurological function while keeping the brain intact.

USC’s approach also presents an alternative to cell-based strategies for regenerative medicine, where success in the brain will be ultimately limited by the ability to restore neural circuitry. The proposed multidisciplinary work will lead to functional maps of the nervous system, highly congruent with the signature of single neurons in epilepsy. Furthermore, the NRC has also established a collaboration with Berislav Zlokovic, MD, PhD, the director of the Zilkha Neurogenetic Institute (ZNI), as well as the center / Neurology & Biophysics, Robert Chow, MD, PhD, who are helping to understand the transcriptomic signature of single neurons in epilepsy. The NRC also established a collaboration with BDS Institute, who are helping to understand the transcriptomic signature of single neurons in epilepsy.

Recently, the NRC was central to the recruitment of Maryam Shamesh, Assistant Professor and holder of the Viterbi Early Career Chair in the Ming Hsieh Department of Electrical Engineering, at the USC Viterbi School of Engineering. Dr. Shamesh’s work involves developing brain-machine interfaces to enhance human decision-making. The CMR also was part of the only California Brain award to Caltech, which is a project created by Drs. Brian Lee with Richard Andersen, the James G. Boswell Professor of Neuroscience at Caltech.

While the Center has received tremendous attention on neuroprosthetics, NRC projects involving human epilepsy tissue are also expanding to involve USC Professor of Psychiatry, James Knowles, MD, PhD and USC Professor of Physiology & Biophysics, Robert Chow, MD, PhD, who are helping to understand the transcriptomic signature of single neurons in epilepsy. Furthermore, the NRC has also established a collaboration with Berislav Zlokovic, MD, PhD to look at the regional BBB transcriptome.

The USC Athletics department is a key component of the minimally invasive neuromodulation effort. There are two Pacific 12 Athletic Conference grants that are in process. The first is PAC-BRAIN, in collaboration with Jack Van Horn, PhD and Meng Law, MD at the Laboratory of Neuro Imaging (LONI) to create a central repository for athletic brain data across the conference using LONI databases. The second is a collaboration with Stanford to develop an advanced accelerometer system to collect cumulative subconcussive force exposure by the brain. The Center’s own accelerometer efforts led by Sami Masri, PhD and Cynthia Blu, PhD serve as third party validation of the Stanford system. The Center will be instigating a clinical trial on a novel eye-tracking technology to detect concussion. Led by Stanford, the NRC is part of a four-center trial to validate this technology. The Center is also working on efforts by the Pac-12 conference, NCAA, and the U.S. Department of Defense to create a care coalition across our conference for head injury. Led by Stanford, we anticipate being included in the first among PAC-12 schools to be folded in.

Two significant areas of new effort for the Center are in minimally invasive neuromodulation and collaborations in the realm of brain health in athletics.

Minimally invasive neuromodulation has been one of three primary points of discussion at BRAIN Initiative PI meetings. The NRC has several studies under development in collaboration with Newport Brain Research Lab - Brain Treatment Center to develop patient-specific strategies to treat a broad spectrum of brain disorders. The first will be on attention deficit hyperactivity disorder (ADHD) involving the USC Department of Athletics and the USC Kortschak Center for Learning and Creativity. Protocols are being finalized for autism in collaboration with Bradley Peterson, MD, PhD and Mark Krieger, MD at Children’s Hospital Los Angeles. The NRC has, likewise, submitted protocols for stroke with Carolee Weinstein, PhD, USC Professor of Biokinesiology and Physical Therapy, and Alzheimer’s Disease, with the Alzheimer’s Disease Research Center.

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The Center will also be expanding our collaborations with our clinical programs. Motivated primarily by the success of David Millett, MD, PhD at Hoag Hospital, Newport Beach, several discussions are ongoing with key decision makers in the South Bay and Bakersfield to further increase the geography of the NRC’s “living laboratory”.

FMR scan used for targeting the implantation location of a neural prosthetic device.
Inspiration

Neural prosthetics have previously been implanted in the brain’s movement center, the motor cortex, allowing patients with paralysis to control the movement of a robotic limb. The motion, however, is delayed and jerky. Now, by implanting neuroprosthetics in the posterior parietal cortex (PPC), a part of the brain that controls not the movement directly but rather the intent to move, Caltech researchers have developed a way to produce natural and fluid movements.

Designed to test the safety and effectiveness of this new approach, the clinical trial was led by principal investigator Richard Andersen, PhD, the James J. Boswell Professor of Neuroscience at Caltech, neurosurgeon Charles Y. Liu, MD, PhD, professor of neurological surgery and neurology at the Keck School of Medicine of USC, and neurologist Mindy Alsen, MD, chief medical officer at Rancho Los Amigos.

The device was surgically implanted in Sorto’s PPC at Keck Hospital of USC in April 2013, and he has since been training with Caltech researchers and staff at Rancho Los Amigos to control a computer cursor and a robotic arm with his mind. The researchers saw just what they were hoping for: intuitive movement of the robotic arm.

Sorto, a single father of two who has been paralyzed for over 10 years, was thrilled with the quick results: “I was surprised at how easily it was to control the robotic arm,” he says. “I remember just having this out-of-body experience, and I wanted to just run around and high-five everybody.”

Keck Medicine of USC surgeons performed the unaccustomed neuroprosthetic implant in a five-hour surgery on April 12, 2013. Liu and his team implanted a pair of small electrode arrays in two parts of the posterior parietal cortex, one that controls reach and another that controls grasp. Each 4-by-4 millimeter array contains 96 active electrodes that, in turn, each record the activity of single neurons in the PPC. The arrays are connected by a cable to a system of computers that process the signals, to decode the brain’s intent and control output devices, such as a computer cursor and a robotic arm.

“Those arrays are very small so their placement has to be exceptionally precise, and it took a tremendous amount of planning, working with the Caltech team to make sure we got it right,” said Liu, who also is director of the USC Neurorestoration Center and associate chief medical officer at Rancho Los Amigos. “Because it was the first time anyone had implanted this part of the human brain, everything about the surgery was different: the location, the positioning and how you manage the hardware. Keep in mind that what we’re able to do—the ability to record the brain’s signals and decode them to eventually move the robotic arm—is critically dependent on the functionality of these arrays, which is determined largely at the time of surgery.”

Although he was able to immediately move the robot arm with his thoughts, after weeks of imaging, Sorto refined his control of the arm. Now, Sorto is able to execute advanced tasks with his mind, such as controlling a computer cursor; drinking a beverage, making a hand-shaking gesture; and performing various tasks with the robotic arm. He says the study has inspired him to continue his education and pursue a master’s degree in social work.

“This study has been very meaningful to me,” says Sorto. “It gives me great pleasure to be part of the solution for improving paralyzed patients’ lives. I joke around with the guys that I want to be able to drink my own beer—to be able to take a drink at my own pace, when I want to take a sip out of my beer and not have to ask somebody to give it to me. I really miss that independence. I think that if it were safe enough, I would really enjoy grooming myself—shaving, brushing my teeth. That would be fantastic.”

“Typically, spinal cord injury patients undergo surgery that stabilizes the spine but generally does very little to restore motor or sensory function,” Liu explained. “With this study, we are testing a procedure that may improve neurological function, which could mean the difference between being permanently paralyzed and being able to use one’s arms and hands. Restoring that level of function could significantly improve the daily lives of patients with severe spinal injuries.”

Two weeks after surgery, Sorto began to show signs of improvement. Three months later, he’s able to feed himself, use his cell phone, write his name, operate a motorized wheelchair and hug his friends and family. Improved sensation and movement in both arms and hands also makes it easier for him to care for himself, and to envision a life lived more independently.

“As of 50 days post-treatment, Kris has gained significant improvement in his motor function, up to two spinal cord levels,” Dr. Liu said. “In Kris’ case, an unusual spinal cord means a large difference between using your hands to brush your teeth, operate a computer or do other things you wouldn’t otherwise be able to do, so having this level of functional independence cannot be overstated.”

“All I’ve wanted from the beginning was a fighting chance,” said Boesen, who has a passion for repairing and driving sports cars and was studying to become a life insurance broker at the time of the accident. “But if there’s a chance for me to walk again, then heck yeah! I want to do anything possible to do that.”

In early April, a surgical team from Keck Hospital of USC carefully injected 10 million AST-OPC1 cells directly into Boesen’s cervical spine. Nearly six weeks later, he was discharged and returned to Bakersfield to continue his rehabilitation. Doctors reviewed his progress at seven days, 30 days, 60 days and 90 days post-injection, and Boesen can look forward to detailed assessments after 180 days, 270 days and one year.

The pioneering surgery is the latest example of how the emerging fields of neurorestoration and regenerative medicine may have the potential to improve the lives of thousands of patients who have suffered a severe spinal cord injury.

The stem cell procedure Boesen received is part of a Phase 1/2a clinical trial that is evaluating the safety and efficacy of escalating doses of AST-OPC1 cells developed by Fiorement, California-based Asterias Biotherapeutics. AST-OPC1 cells are made from embryonic stem cells by carefully convering them into oligodendrocyte progenitor cells (OPCAs), which are cells found in the brain and spinal cord that support the healthy functioning of nerve cells. In previous laboratory studies, AST-OPC1 was shown to produce neurotrophic factors, stimulate vascularization and induce remyelination of denuded axons. All are critical factors in the survival, growth and conduction of nerve impulses through axons at the injury site, according to Edward Whithill III, chief medical director of Asterias and lead investigator of the study, dubbed “SCiStar.”

To qualify for the clinical trial, enrollees must be between the age of 18 and 69, and their condition must be stable enough to receive an injection of AST-OPC1 between the 14th and 30th days following injury.

Keck Medical Center is one of six sites in the United States that is authorized to enroll subjects and administer the clinical trial dosage.

Credit: Alisson Trindade, USC Health Sciences Media Relations, Jessica Stoller-Conrad and Deborah Williams-Hedges from Caltech.
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