Skull base and cerebrovascular surgery are ranked among the most difficult of the surgical subspecialties. Neurosurgeons must create corridors through tiny spaces between nerves, arteries and bone to access tumors and vascular lesions. Successfully navigating these critical structures requires a masterful grasp of neuroanatomy.

“As a surgeon you cannot always rely on technology,” says Roberto Rodriguez Rubio, MD, director of UCSF’s Skull Base and Cerebrovascular Laboratory (SBCVL). “If you do, you might miss something that could result in a neurological deficit for your patient.”

In creating new anatomical models and surgical simulations, the SBCVL is currently at the forefront of developing minimally invasive routes to complex disorders and creating an entirely new way for students, residents and faculty to experience the relationship between different structures in the brain.

“Surgical simulation is a broad category,” explains Rodriguez Rubio. “Many of the models we create use donors [cadaveric models], but we also create simulations with virtual reality, augmented reality, 3D printed models and holographic display.”

Clinical Innovation

Neurosurgeons and otolaryngologists at the SBCVL are continually exploring new corridors that provide better exposure and less risk of injury. Perhaps nowhere has this exploration yielded more clinical applications than in the relatively new field of minimally invasive skull base surgery, which involves the use of an endoscope to navigate tiny corridors through the nasal passages and sinuses.

At UCSF Medical Center, head and neck surgeons and neurosurgeons often operate together on the same patient, combining expertise on navigating both the sinuses and brain tissue. In the past, many lesions of the skull base were considered inoperable or could only be accessed through large, transfacial operations that left patients with significant disfigurement and morbidity. But over the last decade, routes through the endonasal corridor to the clivus, infratemporal fossa, foramen magnum, paranasal sinuses and intracranial lesions have all been described.

In the realm of cerebrovascular disorders, Adib Abla, MD, chief of vascular neurosurgery, describes how anatomic dissections are revealing less invasive exposures for high-risk procedures that would usually need large incisions.

“Right now in the lab we are looking at how to perform a V3 vertebral artery bypass with a common carotid artery donor,” he says. “This has not previously been characterized and could be a safer way to achieve the same good outcome.”

The rules regarding surgery in eloquent regions of the brain are also evolving through research at the SBCVL. Rodriguez’s detailed models of white matter anatomy aim to identify landmarks for functional and anatomical correlation.

“Broca’s area has been described for over 150 years and we used to completely avoid eloquent areas,” says Rodriguez Rubio. “But now we have transopercular approaches to gliomas, which previously would have been prohibited. Using brain mapping, we are creating these small windows that you can approach them through safely.”
Looking to the Future

I am very pleased to share that UCSF has recently been ranked among the top three neurosurgery and neurology programs in the nation by U.S. News & World Report’s 2018-19 survey of Best Hospitals. UCSF Medical Center has also been ranked the best hospital in California and sixth nationwide. These designations are a reflection of the commitment by our faculty and staff to deliver the best service we can to our patients and referring doctors.

UCSF offers the accumulated expertise of multidisciplinary teams, as well as the most cutting-edge technologies and treatments for central nervous system disorders. We pride ourselves on quick responses to requests for referrals or peer-to-peer consultations, and aim to provide a valuable resource to your practice.

We have recently introduced a complimentary online physician consult process for adult and pediatric brain tumor cases, which you can find at btc.ucsf.edu. It features secure upload of imaging and physician notes, and we will provide a response to your query within two days. Simply navigate to Physician Tools and select Request an Online Consult. You can also sign up for our clinical trials e-newsletter to get updates on the latest brain tumor clinical trials available at UCSF for adults and children.

UCSF adult neurosurgery clinics are also available in Marin, Napa and Oakland to provide easy coordination with local physicians and convenient access for patients in those areas. We have also recently partnered with John Muir Health to offer neurosurgery evaluations at the new Berkeley Outpatient Center, a center for primary and specialty care serving patients in the East Bay.

As always, we greatly appreciate the opportunity to work with you in the care of your patients and look forward to partnering with you in the future.

Mitchel S. Berger, MD
Berthold and Belle N. Guggenhime Professor and Chair
Director,
Brain Tumor Center
Department of Neurological Surgery, UCSF

New Brain Tumor Center Website Offers Online Consults for Physicians

The UCSF Brain Tumor Center has launched a new website that makes it easy for physicians to request an online consult with the brain tumor specialists at UCSF. The online consult service includes:

- Fast, secure upload of patient data, including medical records and scans
- Prompt response times
- Access to adult and pediatric brain tumor specialists
- Both surgical and medical consults

Visit btc.ucsf.edu to request a consult or find out more about our services for physicians.
By having a realistic model to try new techniques on, surgeons at the SBCVL can rapidly receive feedback on the result of any maneuver. “The laboratory is like a time machine,” says Rodriguez Rubio. “I can go back and forth on the steps of a surgical technique. I can stop at step three and see what happens if I jump to step six. And then go back to see if there is a way to get to step three straight from step one. That’s how we start designing new corridors. At the end it’s not just beautiful dissections and models, but how we can apply this and make it meaningful.”

The Future of Medical Education

While faculty working in the SBCVL blaze new paths in the clinical setting, the lab has also become a valuable resource for medical students, research fellows and neurosurgery residents. Compared to flat images in a textbook, 3D models give a better sense of the actual distance between central nervous system structures. And as technologies improve and new ones become available, students can not only view the neuroanatomy more realistically, but experience and interact with it in a virtual environment.

For instance, wearing virtual reality headsets, trainees and surgeons can immerse themselves in an actual patient’s anatomy, enabling them to practice the surgery ahead of time and plan the safest route. In most hospitals, a trainee may have the opportunity to practice a procedure on a cadaver once before performing it in the operating room on a real patient. With the opportunity to practice in a surgical simulation lab, they can hone their skills over more time and enter the operating room with more confidence in their ability to safely perform the procedure.

In order to recreate the environment a surgeon would encounter during a real case, the operating microscope, surgical navigation systems and surgical instruments in the SBCVL are the same state-of-the-art models used in UCSF’s operating rooms.

The SBCVL’s dual mission of innovation and education is perhaps best embodied in its research fellowship program. To date, 33 fellows from 11 countries have graduated from the program, publishing widely on surgical techniques, neuroanatomical education practices, and modeling. By bringing their new expertise back to their home institutions, they serve as ambassadors for the program and will go on to train a new generation of surgeons and anatomists worldwide using the most advanced technologies. For Rodriguez Rubio, this is the true heart of the lab’s mission. “What is the point of this knowledge if you cannot apply it to patients and share it with others?”
Neurosurgery News & Notes

UCSF Neurosurgery and Neurology Ranked #3 in the Nation on U.S. News & World Report’s 2018-19 List of Best Hospitals

UCSF Named Clinical Center of Excellence for Cerebral Cavernous Malformation

On June 2, 2018, the Angioma Alliance named UCSF a Clinical Center of Excellence in Cerebral Cavernous Malformation. UCSF is the only institution in California, and one of only six in the nation, to earn this designation. Angioma Alliance Clinical Centers are recognized by the Angioma Alliance as providing high-quality interdisciplinary care for adult and pediatric patients with both sporadic and familial cerebral cavernous malformation. Led by Adib Abla, MD, and Nerissa Ko, MD, the UCSF Clinical Center of Excellence in Cerebral Cavernous Malformations includes a coordinated team of nationally recognized and specially trained physician experts from multiple specialties.

A coronal MRI shows a cavernous malformation of the brainstem in the right pons.

McDermott Neuro-Oncology Scholars Program

Neurological Surgery faculty member Michael McDermott, MD, has established a new fund to support multidisciplinary advanced training in brain tumor care and research. Upon completing a UCSF neuro-oncology fellowship in June, Sarah Lapointe, MD, became the first McDermott Neuro-Oncology Scholar and is currently beginning an additional fellowship with the University of Toronto.

Specialized Neurosurgical Care at the New Berkeley Outpatient Center

John Muir Health and UCSF Health have opened their first joint medical center for primary and specialty care. The Berkeley Outpatient Center provides patients in Berkeley, Oakland, Emeryville and the surrounding areas with a wide range of health care services, including evaluations by UCSF neurosurgeons. Imaging and lab services will also be available, so patients can stay in one location for their care.
New Programs at the UCSF Brain Tumor Center

Generous support from donors to the UCSF Brain Tumor Center has launched three new programs in 2018.

Sheri Sobrato Brisson Brain Cancer Survivorship Program

A brain tumor diagnosis and treatment can continue to affect patients long after the active phase of therapy has ceased. The Sheri Sobrato Brisson Brain Cancer Survivorship Program was developed to provide comprehensive rehabilitation and long-term follow-up to assist patients with returning to work and achieving the best quality of life possible. A personalized care plan includes strategies to improve any existing motor, language or cognitive deficits and evolves over time to meet the changing needs of each survivor.

Wolfe Meningioma Program Project

This new research program combines clinical, translational and basic science aims to improve the diagnosis, treatment and biological understanding of meningiomas. The four areas of investigation include:

- Multiparametric diagnostic MRI studies
- Tracking clinical and quality of life outcomes for 3,000 retrospective cases and prospective enrollment in the UCSF Brain Tumor Center database
- Identifying biomarkers of aggressive tumor behavior that can improve predictions regarding prognosis and reveal new therapeutic targets
- Mechanistic studies of how changes to the FOXM1 gene results in aggressive natural history for meningiomas

Glioma Precision Medicine Program

Under this program, five cutting-edge projects explore bold avenues to potentially advance treatment for malignant glioma:

- Matching drug combinations to patients’ individual genetic profiles in a pilot clinical trial
- A new therapy for targeting TERT promoter mutations in cancer cells
- Immunotherapy using CAR T-cells to recognize and kill glioma cells
- Convection-enhanced delivery of a viral gene therapy
- Leveraging data science to link clinical outcomes with genomics and imaging characteristics

Neurological Rehabilitation Specialist Joins UCSF Brain Tumor Center

Neuropsychologist Christina Weyer Jamora, RN, PhD, has joined the UCSF Brain Tumor Center, specializing in the neurocognitive rehabilitation of adults with brain tumors. She also works with brain tumor survivors as part of the new Sheri Sobrato Brisson Brain Cancer Survivorship Program. Her role is to provide baseline neuropsychological assessments for patients, along with developing individual treatment plans for rehabilitative therapies that maximize survival and improve quality of life.
First Demonstration of Feedback-Controlled Deep Brain Stimulation for Parkinson’s Disease

Neurosurgeon Philip Starr, MD, PhD, led a team in the first demonstration of feedback-controlled DBS for Parkinson’s disease using a fully implantable neural device. The system watches for specific neural patterns that indicate motor impairment, then makes real-time adjustments to electrical stimulation levels, based on a patient’s active symptoms. This approach could greatly improve DBS therapy by reducing stimulation-induced side effects. It could also extend the device’s life, prolonging the time before a battery replacement surgery is needed. Efforts are ongoing to evaluate adaptive DBS in a larger-scale trial for Parkinson’s disease treatment.

First Awake Spine Fusions Performed on the West Coast at UCSF

Using a new spinal anesthetic similar to an epidural, patients can now undergo minimally invasive fusions and decompressions in one to three hours and are typically discharged within 24 hours. Ten of the procedures have been performed by neurosurgeon Praveen Mummaneni, MD, over the last year, including the first spinal fusions for awake patients on the West Coast. The side effects of general anesthesia can often linger for a week or more, preventing patients from returning to life and work, and postoperative stays following standard spine surgery can be up to a week. For select patients, awake spinal surgery may offer a faster path to recovery and resumption of daily activities.
**Aggressive Meningiomas Linked to a Single Gene**

A milestone effort to define the molecular profile of aggressive meningioma identified FOXM1 as a key transcription factor driving proliferation and recurrence. A group of investigators led by David R. Raleigh, MD, PhD, examined 280 human meningioma samples collected by UCSF neurosurgeons between 1990 and 2015. Using an array of techniques, including RNA sequencing, whole exome sequencing, DNA methylation profiling, tissue microarrays and targeted gene expression profiling, Raleigh found that heightened activation of the FOXM1 gene was the unifying factor between aggressive meningiomas in both men and women, in older and younger patients, and in meningiomas arising in different parts of the brain. The gene’s activation seems to be an important driver of both newly diagnosed tumors and recurrence following treatment. This finding could help clinicians distinguish earlier between aggressive meningiomas and those more responsive to treatment.


**Open Data Commons for Spinal Cord Injury Research**

Scientists and physicians at UCSF’s Brain and Spinal Injury Center recently participated in launching the first multi-stakeholder, large-scale data-sharing initiative in spinal cord injury research, the Open Data Commons for Spinal Cord Injury, funded by the Craig H. Nielsen Foundation. Explore the open data and find out more about spinal cord injury research at odc-sci.org.

**Human hippocampus at birth. Image: Arturo Alvarez-Buylla**

**Neurogenesis May Be Limited in the Adult Human Brain**

Two recent studies from the laboratory of Arturo Alvarez-Buylla, PhD, have revealed new insights into neurogenesis in the human brain. Tracking the division of neural stem cells over time, the Alvarez-Buylla lab found that most neural stem cells divide symmetrically in a non-self-renewing fashion, limiting the ability to produce new neurons indefinitely. In a separate article, they showed that in the human hippocampus – a region essential for learning and memory and one of the key places where researchers have been seeking evidence that new neurons continue to be born throughout the lifespan – neurogenesis declines throughout childhood and is undetectable in adults.


Awards and Honors

Mitchel S. Berger, MD, received the Fedor Krause Medal for Excellence from the German Society of Neurosurgery at the organization’s annual meeting in Muenster, Germany. Berger was also selected for the 20th Annual Labatt Brain Tumor Research Centre Academic Lectureship at the University of Toronto.

Edward Chang, MD, was honored as the inaugural William K. Bowes Jr. Biomedical Investigator. Bowes, who was a Distinguished Director of the UCSF Foundation Board of Overseers, created the $50 million endowment to provide select scientists with a five-year funding stream to further their research and drive discovery.

Michael W. McDermott, MD, Halperin Endowed Chair and Vice Chair of Neurological Surgery, has received the Wolfe Family Endowed Professorship in Meningioma Research. This honor recognizes his profound impact on the field of meningioma treatment and research. The new endowed professorship was established through the generous support of the Wolfe Family, who have also funded a new research program funding four specific areas of meningioma research (see page 5).

Edward Chang, MD

Aaron Diaz, PhD, was an invited speaker at the American Association for Cancer Research special conference on Immunobiology of Primary and Metastatic Central Nervous System Cancer. Diaz presented recent research on different populations of tumor-associated macrophages (TAMs) in gliomas, showing that blood-derived TAMs are more immunosuppressive than microglial TAMs and may be more important therapeutic targets.


Stephen Magill, MD, PhD, will give a presentation at the 2018 annual meeting of the Congress of Neurological Surgeons on the paper “Factors Associated with Pre- and Postoperative Seizures in 1033 Patients Undergoing Supratentorial Meningioma Resection,” which has been selected as the Neurosurgery Tumor Paper of the Year.
Geoffrey Manley, MD, PhD, received an honorary doctorate from the University of Kentucky, where he earned his bachelor’s degree, in recognition of his extraordinary achievements in the fields of neurotrauma and clinical informatics.

UCSF Brain Tumor Center Principal Investigator Hideho Okada, MD, PhD, has been granted two new awards from the NIH to study immunotherapy in gliomas. An R01 award will fund a project on immunotherapy to target an epitope derived from a mutation in the isocitrate dehydrogenase gene. With an R35 award, the Okada lab will look at ways to overcome barriers posed by the heterogeneous expression of antigens in gliomas by developing new cell-engineering and antigen-targeting strategies.

Kunal Raygor, MD, was recognized with the William H. Sweet Young Investigator Award from the American Association for Neurological Surgeons for his work examining outcomes of patients with trigeminal neuralgia whose pain recurred after initial treatment with stereotactic radiosurgery (SRS). Raygor and his colleagues found that patients who received microvascular decompression after failed SRS had longer duration of pain relief than those who received repeat SRS. In the group who received repeat SRS, sensory changes following treatment were predictive of better pain control.

Philip Starr, MD, PhD, was selected as the honored guest of the 2018 biennial meeting of the American Society for Stereotactic and Functional Neurosurgery, where he presented his work on bidirectional neural prostheses.

Jacob Young, MD, received the 2018 Krevans Award for Excellence in Patient Care from Zuckerberg San Francisco General Hospital.

The UCSF Brain and Spinal Injury Center (BASIC) was selected for a NIH-NINDS Translational Outcomes Program-Neurotrauma UG3 award to support the development and validation of pathophysiologically based preclinical outcome measures or functional markers that align with practical clinical assessments in spinal cord injury and traumatic brain injury. The grant is one of just five in the nation and was awarded to BASIC investigators Adam Ferguson PhD, Michael Beattie, PhD, Jacqueline Bresnahan, PhD, and Susanna Rosi, PhD.

Geoffrey Manley, MD, PhD, (left) received an Honorary Doctor of Science from his alma mater, University of Kentucky. Manley is pictured here with fellow honoree Tom Hammond (right), sportcaster for NBC.
Jonathan D. Breshears, MD, received his undergraduate degree in biomedical engineering and his medical degree from Washington University in St. Louis. During that time, he developed an interest in neurosurgery and the application of computational methods and technology to neurosurgery. Funded by the Howard Hughes Medical Institute, he spent a year in the lab of Eric C. Leuthardt, MD, developing brain-computer interface technologies, novel brain mapping techniques, and studying the effects of the anesthetic drug propofol on the electrophysiology of the human cerebral cortex.

During residency, Breshears’ research accomplishments included characterizing the spatiotemporal structure of spontaneous neural activity in the human superior temporal gyrus – an area critical for speech perception, building probabilistic maps of speech function in the human brain to improve surgical resections, and identifying the cortical site for laryngeal control. This work was funded by an F32 award from the NIH and done under the guidance of Edward Chang, MD. Over the course of training, Breshears’ clinical interests evolved to include skull base surgery for tumors and vascular lesions. Under the mentorship of Philip Theodosopoulos, MD, Michael McDermott, MD, and Adib Abla, MD, he focused on developing the surgical skills for safely addressing lesions in this complex anatomical region. His published research on vestibular schwannoma treatment has been presented at national meetings of the Congress of Neurological Surgeons and the North American Skull Base Society.

Upon graduation, Breshears will be completing a one-year skull base oncology fellowship at MD Anderson Cancer Center in Houston, TX.

Joseph A. Osorio, MD, PhD, completed his undergraduate education at the University of California, Irvine in Civil Engineering. He then earned a PhD in Bioengineering within the joint graduate group at the University of California, Berkeley/UCSF, with a focus on translational research in brain tumor imaging developing MR spectroscopy sequences for brain tumor patients under the mentorship of Sarah Nelson, PhD. He then attended both medical school and residency at UCSF.

During residency at UCSF, Osorio developed an interest in spine surgery, particularly adult spinal deformity and spinal axis tumors. He was recognized by the faculty for his outstanding performance in clinical, research, and teaching with the Krevan’s Award for surgical intern of the year in 2013, the best senior research paper award in 2018, and the Harold Rosegay resident teaching award in 2018. His primary clinical research was focused upon the understanding and prevention of spine complications following spinal deformity operations.

After graduation in 2018, Osorio will be completing a one-year adult and pediatric comprehensive spine fellowship at New York-Presbyterian/Columbia University in New York, NY.
Martin Rutkowski, MD, received his undergraduate degree in religious studies from Brown University, and then went on to complete his medical degree at the University of California, Los Angeles. While in medical school he completed a Doris Duke research fellowship under Andy Parsa, MD, PhD, where he studied how the complement cascade promotes the development and growth of glioblastoma. He also contributed a number of publications on outcomes research for numerous skull base and primary central nervous system neoplasms. While in residency at UCSF, he maintained a strong interest in brain tumors, neuroendocrinology, and skull base neurosurgery. He worked closely with mentors Manish Aghi, MD, PhD, Sandeep Kunwar, MD, Michael McDermott, MD, and Philip Theodosopoulos, MD, on all facets of operative and perioperative brain tumor management. He developed a particular interest in pituitary disease and neuroendocrine disorders, and chose to spend his research year in the Brain Tumor Research Center with Manish Aghi where he examined how tumor associated macrophages contribute to the proliferative and invasive characteristics of pituitary adenoma. This work was sponsored by the PRESCIENT postdoctoral program, a yearlong UCSF fellowship supporting early translational research focused on precision medicine.

His clinical interest in skull base neurosurgery led to a fellowship with Gabriel Zada, MD, and Steven Giannotta, MD, at the University of Southern California where he will continue to develop expertise in open and minimally invasive, endoscopic skull base neurosurgery as a clinical fellow during the 2018-19 academic year.

Selected Publications:

Derek Southwell, MD, PhD, grew up in Minneapolis, Minnesota, and attended college at the Massachusetts Institute of Technology. In 2002 Derek entered the medical scientist training program at UCSF, where he later earned his PhD (in neuroscience, 2009) and MD (2011) degrees. Southwell began neurosurgery residency at Stanford University, and then returned to UCSF in 2013 for the remainder of his post-graduate training. Southwell is interested in functional neurosurgery, as well as basic and translational neuroscience research. His graduate thesis, which was conducted in the laboratory of Arturo Alvarez Buylla, PhD, focused on the biology of cortical interneurons, a cell type with unique capacity to integrate into the nervous system following transplantation. During residency, Southwell continued to explore this area or research, studying the effects of interneuron transplantation in models of neuropsychiatric disease with Vikaas Sohal, MD, PhD. Additionally, he has conducted clinical research in areas such as brain mapping, glioma resection, and deep brain stimulation.

Following his graduation, Southwell will begin professorships in neurosurgery and neurobiology at Duke University, where he will practice functional neurosurgery and conduct lab research in translational neuroscience.

Selected Publications:
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Selected Recent Publications from the Department of Neurological Surgery


