

# the department of neurological surgery at ucsf

2012 year in review

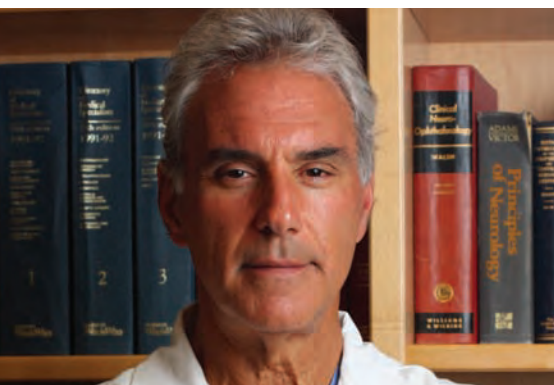
University of California  
San Francisco

**UCSF**

Neurological Surgery



# letter from the chair



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Dear Colleagues:

In these pages you will find some of this year's major accomplishments from the Department of Neurological Surgery at UCSF. A new national clinical trial for a brain tumor vaccine developed by Dr. Andrew Parsa (page 4). A new program to streamline multidisciplinary care for patients with sports concussions and brain injuries (page 8). A new laser treatment protocol for medically refractory epilepsy (page 12). But I would particularly like to note the outstanding progress made by our Quality and Safety Program, led by Dr. Catherine Lau (page 26). The efforts of this program resulted in a 2012 Healthgrades Neurosurgery Excellence Award, recognizing the best in patient safety.

I am also honored to be serving as the 81st president of the American Association of Neurological Surgeons (AANS), which has provided me with a platform to address quality and safety in neurosurgery at a national level.

This year, the NeuroPoint Alliance – established by the AANS in 2008 – began the pilot program for the National Neurosurgery Quality and Outcomes Database (N<sup>2</sup>QOD). The purpose of this database is to track quality of surgical care for the most common neurosurgical procedures, as well as provide practice groups and hospitals with an infrastructure for prospective data collection and self-assessment. The Department of Neurological Surgery at UCSF is one of 28 groups participating in the pilot program.

In addition to allowing us to compare the relative effectiveness of therapies and related quality-of-life measures, the N<sup>2</sup>QOD will be critical for justifying payment for neurosurgical procedures in a new era of healthcare that will heavily weight quality and performance. For better or worse, the medical community as a whole needs to begin gathering robust data that provide evidence for the value of our interventions to insurance companies and lawmakers. We also need to ensure that we are involved in defining the benchmarks for success.

In the Department of Neurological Surgery, our neurospinal disorders group has become especially involved in performing

quality and cost analysis studies (page 23). A recent analysis done in conjunction with their colleagues in the Department of Orthopaedic Surgery revealed that for surgeries planned to be performed over two or more stages, the later stages are categorized as readmissions under the "all-cause readmissions" metric used by Medicare. With the launch of Medicare's new program to penalize medical institutions based on readmission rates, this will be an important issue for government to address.

Patient satisfaction is also a critical part of evaluating care, and I would like to congratulate our adult neuro-oncology team for winning the UCSF Medical Center's Pinnacle Award for an unprecedented fifth year in a row. The Pinnacle Award recognizes the outpatient service with the highest patient satisfaction scores. The neuro-oncology team has also been joined by a remarkable group of philanthropists, led by Randi Murray, Cathy Podell, and Marritje Greene, in creating a new program aimed at supporting caregivers (page 3). The importance of providing support for caregivers of patients with serious or terminal illness cannot be overemphasized. The Caregiver Program will provide one-on-one support from a social worker trained specifically to guide families suffering with the diagnosis of a brain tumor.

I am very proud of the work done this year to make the experience for patients and their families the best it can be. That mission will continue to drive everything we do in the Department of Neurological Surgery.

Mitchel S. Berger,  
MD, FACS, FAANS

Kathleen M. Plant Distinguished Professor  
and Chairman

Department of  
Neurological Surgery

Director, UCSF  
Brain Tumor Center

# brain tumor center



Brain Tumor Center supporters Randi Murray, Mairitje Greene, Ira Glass, and Cathy Podell.

“We are so grateful for the tireless efforts of this dedicated group of philanthropists. Without fundraising it is difficult to establish programs specifically aimed at providing support to caregivers. Their work will make the road easier for other families dealing with the diagnosis of a brain tumor.”

– Susan Chang, director of neuro-oncology

## Brain Tumor Center at UCSF Establishes Program for Caregivers with Support from Dedicated Donors and Activists

On April 21, 2012 Ira Glass, host and producer of National Public Radio’s “This American Life,” talked to supporters of the UCSF Brain Tumor Center about the loss of his brother-in-law Gordon Murray to brain cancer at a benefit that raised \$1.2 million to establish a new program to help patient caregivers. “I know how lucky we were that he was able to receive the outstanding care he did at UCSF,” said Mr. Glass. “It really is an extraordinary institution.”

The fundraising efforts were led by Mr. Glass’ sister Randi Murray, Cathy and Mike Podell, and Mairitje and Jamie Greene.

The money raised will fund three years of operations costs that includes a dedicated social worker to assist the caregivers of

patients with brain tumors treated at UCSF. Family members are often overwhelmed by the emotional toll and responsibility that comes with caring for a loved one with a brain tumor. By providing them with the resources and support that they need, patients often have better outcomes.

## Neuro-Oncology Service Enters UCSF ‘Hall of Fame’ for Patient Satisfaction

The Neuro-Oncology Service was given the UCSF Medical Center Pinnacle Award for an unprecedented fifth year in a row, making it the first service to be inducted into the Pinnacle Award Hall of Fame. The Pinnacle Award recognizes the UCSF medical service with the best patient satisfaction scores for outpatient care.

The Division of Neuro-Oncology consistently receives top scores for patient satisfaction.



## faculty

### Adult Neuro-Oncology

- Nicholas Butowski MD
- Susan Chang MD
- Jennifer Clarke MD, MPH
- Michael Prados MD

### Adult Brain Tumor Surgery

- Manish Aghi MD, PhD
- Mitchel Berger MD
- Edward Chang MD
- Sandeep Kunwar MD
- Michael McDermott MD
- Andrew Parsa MD, PhD

### Neuropsychology

- Caroline Racine PhD

### California Center for Pituitary Disorders

- Manish Aghi MD, PhD
- Lewis Blevins, Jr. MD
- Sandeep Kunwar MD

**Research Laboratories**

Manish Aghi MD, PhD  
Oncolytic viral therapies;  
vascular biology of glioma

Aruturo Alvarez-Buylla PhD  
Developmental neuroscience;  
stem cell biology

Krystof Bankiewicz MD, PhD  
Drug delivery strategies; gene therapy

Arnau Benet MD  
Surgical anatomy; novel surgical  
approaches

Mitchel Berger MD  
Brain mapping; molecular and  
genetic basis of brain tumors

Gabriele Bergers PhD  
Angiogenesis; tumor invasion

Soonmee Cha MD  
Neuroimaging

Joseph Costello PhD  
Functional genomics

Nalin Gupta MD, PhD  
Pediatric brain tumors;  
cell-cell interactions

Daphne Haas-Kogan MD  
Cell signaling; genetic mutations;  
therapeutic irradiation enhancement

C. David James PhD  
Molecular biology of CNS cancers;  
rodent model testing of  
experimental therapeutics

Andrew Parsa MD, PhD  
Immunotherapy

Claudia Petritsch PhD  
Brain cancer stem cells;  
asymmetric stem cell division;  
novel tumor suppressor genes

Joanna Phillips MD, PhD  
Neuropathology; interaction between  
tumor cells and the microenvironment

Russell Pieper PhD  
Signal transduction; models of human  
gliomagenesis and drug resistance

David Rowitch MD, PhD  
Central nervous system development;  
tumorigenesis

William Weiss MD, PhD  
Mouse models of human brain tumors;  
cell signaling

John Wiencke PhD  
Biomarker development and  
application in brain tumor etiology

Margaret Wensch MPH, PhD  
Genetic and molecular epidemiology  
of adult glioma

Shichun Zheng PhD  
Molecular neuroepidemiology

**National, Randomized  
Phase II Clinical Trial of  
Heat-Shock Protein  
Vaccine for Brain Tumors**

In a multicenter phase 2 clinical trial, a brain cancer vaccine tailored to individual patients by purifying heat shock proteins from their own tumors has proven effective at extending their lives by several months or longer.

The trial was initiated by principal investigator Andrew Parsa MD, PhD, who worked to develop the personalized vaccines with biotechnology company Agenus, Inc. The results were presented this year in a plenary session at the annual meeting of the American Association of Neurological Surgeons.

The trial found that the vaccine, given to more than 40 patients, extended survival by several months when compared to 80 other patients who were treated at the same hospitals and received standard therapy—47 weeks compared to 32 weeks. Several of the patients who received the vaccine have survived for more than a year.

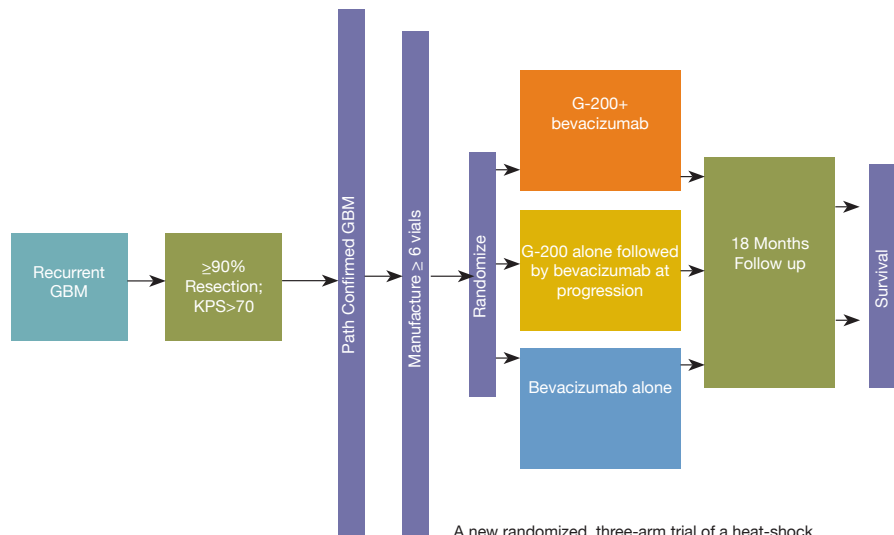
These promising results have provided the rationale for a three-arm, randomized clinical trial to determine effectiveness of the vaccine combined with the drug bevacizumab (an anti-vascular therapy now considered to be standard of care for recurrent glioma) compared to the

effectiveness of bevacizumab or the vaccine alone. The trial will be conducted through the Alliance for Clinical Trials in Oncology – a national cooperative group funded by the National Cancer Institute.

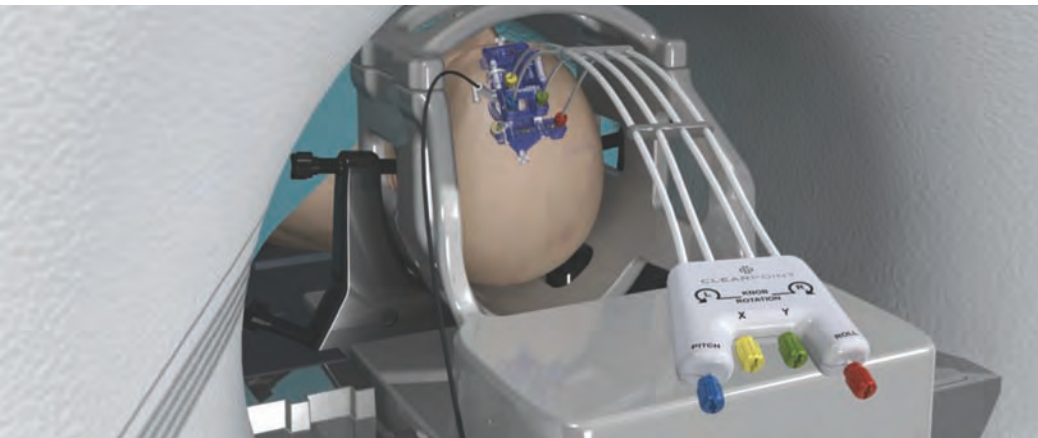
Initial funding for the trial was derived in part from UCSF's Specialized Program of Research Excellence (SPORE) for brain tumors, which has been continually awarded to the Brain Tumor Research Center by the NCI since 2002.

During the most recent funding cycle of the SPORE grant, Dr. Parsa and BTRC principal investigator Russell Pieper PhD examined the role of the brain tumor microenvironment in modulating tumor vaccine efficacy. Their work has shown that the tumor is not only influenced by the microenvironment, but actively manipulates it to support its own survival.

Drs. Pieper and Parsa discovered that the immunosuppressive surface protein B7-H1, which is overexpressed in most glioblastoma cells, mediates the elimination of immune cells when they come into contact with the tumor. They have also gathered evidence that an immune response is further hampered by tumor-specific activation of phosphatidylinositol 3-kinase (PI3K). A future trial combining the heat shock protein vaccine with a PI3K inhibitor in patients with B7-H1-suppressed tumors is a goal of the next phase of the UCSF Brain Tumor SPORE.



A new randomized, three-arm trial of a heat-shock protein vaccine combined with bevacizumab will be offered through the Alliance for Clinical Trials in Oncology



The ClearPoint MRI-compatible clinical system for convection enhanced delivery of nanoparticles to brain tumors was developed through a collaboration between the medical device company SurgiVision and UCSF faculty Philip Starr MD, PhD, Paul Larson MD, and Alistair Martin PhD.

Parsa AT, Crane C, Han S, Kivett V, Fedoroff A, Butowski N, Chang S, Prados M, Clarke J, Berger M, McDermott M, Aghi M, Sloan A, Bruce J. A phase 2 multicenter trial of autologous heat shock protein peptide vaccine (HSPPC-96) for recurrent glioblastoma multiforme (GBM) patients shows improved survival compared to a contemporary cohort controlled for age, KPS and extent of resection. Presented at: American Association of Neurological Surgeons Annual Scientific Meeting; April 17, 2012; Miami, FL.

### Clinical Trial Testing Convection Enhanced Delivery of Toca 511 is Enhanced by Real-Time Imaging

The UCSF Brain Tumor Research Center is offering a phase 1 clinical trial of Toca 511 – a new treatment regimen for recurrent glioblastoma that combines attributes of gene therapy and chemotherapy.

Patients take the non-toxic oral drug 5-fluorocytosine (5-FC) and then a retrovirus carrying the enzyme cytosine deaminase (CD) is injected directly into the tumor. The retrovirus spreads throughout the tumor by replicating itself in dividing tumor cells, while the CD it carries converts the 5-FC that has accumulated in the tumor cells into cytotoxic 5-fluorouracil (5-FU).

A key component of success for this new therapy will be to ensure that the initial infusion of the retrovirus is spreading throughout the target region. Neurosurgeons are now able to monitor the infusion of the retrovirus in real time using the ClearPoint system, which was developed at UCSF and uses an MR-compatible skull mounted device for performing implantation of deep brain stimulator electrodes or drug infusion cannulae in the MR scanner.

Using convection enhanced delivery – developed and refined in the laboratory of Krystof Bankiewicz MD, PhD – a pressure

gradient at the tip of the cannula pushes interstitial fluid out of the way, enabling coverage of larger brain volumes than could be achieved by diffusion alone.

In 2012, the trial's principal investigator Manish Aghi MD, PhD has successfully used ClearPoint to monitor infusion in two patients and will be following them in the coming months to assess safety, tolerability, and preliminary efficacy.

This trial has been developed by Tocagen Inc., and study sites include UCSF, UCLA, UCSD, and Cleveland Clinic.

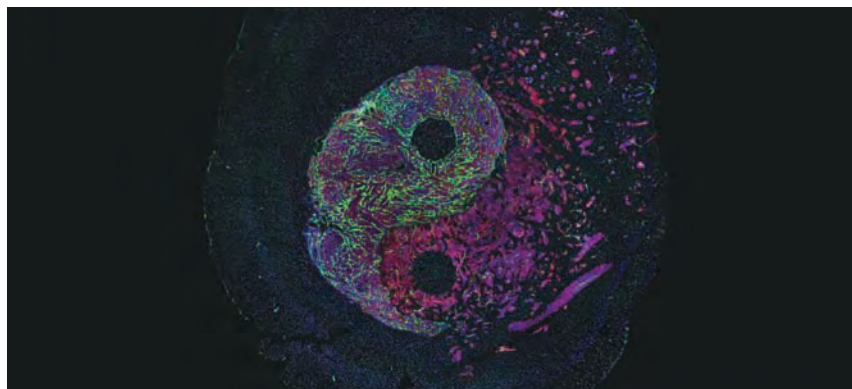
### c-MET Inhibitors Offer Potential for Augmenting Anti-VEGF Therapy in Brain Tumors

The laboratory of principal investigator Gabriele Bergers PhD has recently focused on events that drive migration of tumor cells in patients being treated with vascular endothelial growth factor (VEGF) inhibitors, such as bevacizumab.

VEGF inhibitors target the increase in angiogenesis that occurs in highly vascular tumors, such as glioblastoma. While most patients experience beneficial effects of treatment, those effects are largely and transient and tumors invariably recur. In a subset of patients, VEGF blockade is associated with recurrent tumors that have a more diffuse and infiltrative growth pattern, which makes them difficult to resect.

The Bergers lab has now identified the molecular mechanisms by which VEGF ablation causes enhanced invasion, demonstrating that VEGF directly and negatively regulates tumor cell invasion through formation of a novel cMet:VEGFR2 receptor complex, which suppresses HGF-dependent c-Met phosphorylation and tumor cell migration. Consequently,

The yin and yang of vascular endothelial growth factor (VEGF) signaling. Murine glioblastomas that overexpress VEGF are highly proliferative and angiogenic, but have well-defined, circumscribed borders (left side). At the opposite extreme, murine glioblastomas deficient in VEGF are nonangiogenic, slower growing, but highly invasive (right side). Tumor cells are red, blood vessels are green, and nuclei are blue.



VEGF blockade restores or increases c-Met activity in GBM cells in a hypoxia-independent manner while inducing an EMT-like program.

These findings support combined treatment strategies targeting both VEGF and c-Met in glioblastoma patients in order to overcome pro-invasive resistance and prolong survival.

Lu KV, Chang JP, Parachoniak CA, Pandika MM, Aghi MK, Meyronet D, Isachenko N, Fouse SD, Phillips JJ, Cheres DA, Park M, Bergers G. VEGF inhibits tumor cell invasion and mesenchymal transition through a MET/VEGFR2 complex. *Cancer Cell* 2012; 22(1):21-35.

## Magnetic Resonance Spectroscopy Detects Oncometabolite Associated With Improved Survival in Low-Grade Tumors

A team of UCSF neuroimaging specialists led by Sarah Nelson PhD has used advanced magnetic resonance spectroscopy techniques to detect a novel molecular marker that could be useful in predicting outcome and evaluating new treatments for patients with low-grade glioma.

Dr. Nelson and her colleagues gathered image-guided tissue samples from patients with recurrent gliomas that had been grade II at initial diagnosis and analyzed them for the presence of mutations in the IDH1 gene. Studies in the last two years have shown that more than 70 percent

of patients with low-grade gliomas have such mutations and that their presence is associated with longer survival.

The IDH1 mutations have been shown to cause an increase in production of the oncometabolite 2-hydroxyglutarate (2HG), which the research team was able to measure in the tissue samples using the nuclear magnetic resonance technique of proton high-resolution magic angle spinning spectroscopy. 2HG is present in extremely small quantities and UCSF is one of the only institutions with the technology sensitive enough to measure it.

There was an 86.4% concordance between the detection of 2HG in the spectra with the presence of the IDH1 mutation. The 2HG was correlated with cellular density and other vivo parameters that may be useful in designing new methods for evaluating non-invasively in patients whether recurrent tumors have remained grade II or undergone malignant transformation to a higher grade.

Further work is underway at UCSF to translate these findings to the in vivo setting by using a clinical MR scanner. Noninvasive monitoring of 2HG in the clinic may help physicians better predict patient survival, gauge cancer recurrence, make follow-up treatment decisions, and assess response to therapy.

Elkhaled A, Jalbert LE, Phillips JJ, Yoshihara HAI, Parvataneni R, Srinivasan R, Bourne G, Berger MS, Chang SM, Cha S, Nelson SJ. Magnetic resonance of 2-hydroxyglutarate in IDH-mutated low-grade gliomas. *Sci Transl Med* 4(116):116ra5.

## Genome Sequencing Zeroes in on Risk for Developing Oligodendroglioma and IDH1/2-Mutated Astrocytoma

Groundbreaking new research from the UCSF Brain Tumor Research Center and the Mayo Clinic has shown that certain subtypes of gliomas are connected to specific inherited variation in a small, non-coding region of the genome.

Building on their previous work demonstrating that single nucleotide polymorphisms (SNPs) at 8q24 near CCDC26 are inherited risk loci for oligodendroglial tumors and astrocytomas with mutated IDH1 or IDH2, the research team has now shown that the low-frequency SNP rs55705857 within 8q24.21 is the SNP most strongly associated with tumor formation.

The variant in rs55705857 substitutes guanine for adenosine and is about 6 times more common in people who have these types of tumors than people who do not.

The findings, published this year in *Nature Genetics*, suggest that the variant in rs55705857 either contributes to IDH1/2 mutation or interacts with IDH1/2 mutation to facilitate development and progression of glioma. Although the exact function of the variant is unknown, it is located in a highly conserved region and may effect gene regulation as a non-coding or microRNA.

The study was jointly led by epidemiologists Margaret Wrensch PhD, and John Wiencke, PhD, professors in

the Department of Neurological Surgery at UCSF, and Robert Jenkins, MD, PhD, professor of Laboratory Medicine in the Department of Laboratory Medicine and Pathology and the Division of Laboratory Genetics at the Mayo Clinic. The collaboration between these investigators resulted from interactions through the NCI Specialized Program of Research Excellence (SPORE) for brain tumors, and the next phase of the UCSF SPORE will continue this comprehensive project on integrative genomics of glioma survival.

Jenkins RB, Xiao Y, Sicotte H, Decker PA, Kollmeyer TM, Hansen HM, Kosel ML, Zheng S, Walsh KM, Rice T, Bracci P, McCoy LS, Smirnov I, Patoka JS, Hsuang G, Wiemels JL, Tihan T, Pico AR, Prados MD, Chang SM, Berger MS, Caron AA, Fink SR, Halder

C, Ryneerson AL, Fridley BL, Buckner JC, O'Neill BP, Giannini C, Lachance DH, Wiencke JK, Eckel-Passow JE, Wrensch MR. A low-frequency variant at 8q24.21 is strongly associated with risk of oligodendroglial tumors and astrocytomas with IDH1 or IDH2 mutation. *Nat Genet* 2012;44(10):1122-5.

### New Surgical Anatomy Laboratory Explores Minimally Invasive Approaches to Brain, Skull Base, and Cerebrovascular Lesions

A new laboratory at UCSF is focused on developing more effective surgical strategies to treat complex cranial lesions with less impact to patients' quality of life.

Surgical anatomist and principal investigator Arnau Benet MD performs surgical simulations in postmortem specimens and produces digital 3-D anatomic images for surgical planning, development of novel surgical approaches, and educational activities.

In collaboration with otolaryngologists Ivan El-Sayed MD and Larry Lustig MD and neurosurgeons Michael Lawton MD, Mitchel Berger MD, Michael McDermott MD, and Manish Aghi MD, PhD, Dr. Benet is exploring ways of optimizing surgical routes via endoscopic minimally invasive techniques to complex skull base regions. The laboratory is also working to develop minimally invasive transcranial microsurgical approaches to the skull base and subcortical structures using image-guided dissection.

Ivan El-Sayed MD, Arnau Benet MD, and Manish Aghi MD, PhD simulate a surgical procedure through the endonasal corridor.



# brain & spinal injury center

8

## faculty

### Neurotrauma

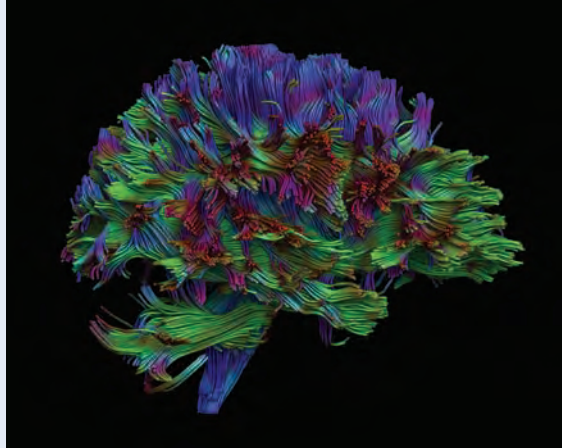
San Francisco General Hospital

Geoffrey Manley MD, PhD

Michael Huang MD

Shirley Stiver MD, PhD

Vincent Wang MD, PhD



Diffusion tensor imaging of a mild traumatic brain injury.



UCSF's PlaySafe Program works with school districts across the Bay Area to treat and provide education about concussion and brain injury.

## Transforming Research and Clinical Knowledge in Traumatic Brain Injury II (TRACK-TBI II)

Scientists at the UCSF Brain and Spinal Injury Center, led by Geoffrey Manley MD, PhD, are implementing the second phase of their prospective, longitudinal study of traumatic brain injury patients, called TRACK-TBI II.

Their previous trial – TRACK-TBI – tested and refined the Common Data Elements (CDE) for Traumatic Brain Injury, which were developed with neuroscientists from the NIH and U.S. Department of Defense to provide new standards for reporting and defining brain injuries across studies. There are currently no validated outcome measures to inform patients about their prognoses or any classification schemes that take into account the pathophysiological mechanisms that lead to neurological deficit.

Collaborating with the University of Pittsburgh Medical Center, the University Medical Center Breckenridge, and Mount Sinai Rehabilitation Center, investigators at UCSF established data repositories for clinical informatics, biospecimens, neuroimaging, and neurocognitive outcome assessments.

In TRACK-TBI II, the data collection will be extended to 10 sites across the United States with the goal of providing clinicians and researchers with current information that links genomic data, imaging characteristics, neurocognitive outcomes, quality-of-life measures, and patient-specific demographic information.

The NIH and U.S. Department of Defense now require the CDE to be used in all future clinical trials for traumatic brain injury. The TRACK-TBI repository is also serving as the initial test dataset for the launch of the Federal Interagency Traumatic Brain Injury Research (FITBIR) informatics system. When fully implemented, FITBIR will provide access to high quality, curated data on a bioinformatics platform that will accelerate the ability of researchers to collaborate and compare results across studies.

The emphasis on data sharing and development of common research tools across institutions and disciplines echoes a recent report by the National Academy of Sciences calling for large-scale data networks to be developed for all diseases. The report, "Toward Precision Medicine: Building a Knowledge Network for Biomedical Research and a New Taxonomy of Disease," outlines a vision in which the most current research findings and patient data for a given disease are entered into a central, interactive data repository that can be accessed by clinicians and scientists. It would allow research to be more tightly integrated into clinical care and speed the implementation of personalized treatment strategies.

## Comprehensive Care for Sports Concussions and Head Injuries

The Bay Area Concussion and Brain Injury Program at UCSF is a new multidisciplinary collaboration among clinicians from UCSF Medical Center, UCSF Benioff Children's Hospital, and

San Francisco General Hospital to provide coordinated care for patients with sports concussions or other head injuries.

The program includes a monthly clinic where patients are seen by experts from many fields, including sports medicine, physical medicine and rehabilitation, neuropsychology, neuroradiology, neurology and neurosurgery.

Highlights of the Bay Area Concussion and Brain Injury Program:

- We use a team approach to treat each patient, involving experts from a wide range of specialties
- Patients can be seen by all the specialists they need at a single clinic visit
- Through UCSF's PlaySafe Program, we work with school districts across the San Francisco Bay Area to treat and raise awareness about concussion and brain injury. Athletes at participating schools receive:
  - Comprehensive evaluation by a sports medicine physician trained in management of concussion
  - Detailed step-by-step return to play progression program
  - Consultation and communication with the school's certified athletic trainer or official



## BASIC Laboratories

Michael Beattie PhD  
central nervous system repair

Jacqueline Bresnahan PhD  
central nervous system repair

Adam Ferguson PhD  
bioinformatics

John Fike PhD  
neurogenesis and traumatic brain injury

Jialing Liu PhD  
neurogenesis and functional recovery

Geoffrey Manley MD, PhD  
basic, translational, and  
clinical traumatic brain injury research

Linda Noble-Haeusslein PhD  
neuroinflammation in traumatic brain  
and spinal cord injury

S. Scott Panter PhD  
cellular injury following stroke and  
hemoglobin-based neurological injury

Susanna Rosi PhD  
chronic neuroinflammation;  
learning and memory

## Spinal Cord Injury May Be Tempered by Available Anti-inflammatory Drug

With a grant awarded this year from the U.S. Department of Defense, Linda Noble-Haeusslein PhD will study an approved nonsteroidal anti-inflammatory drug (NSAID), which also functions as a sheddase for the molecule L-selectin, in the treatment of spinal cord injury (SCI).

Over the past 10 years Dr. Noble-Haeusslein and her colleagues Steven Rosen PhD and Sang Mi Lee PhD have been studying the role of the leukocyte adhesion molecule L-selectin in the inflammatory process following SCI. They have shown that knocking out L-selectin in mice substantially improves locomotor recovery after sustaining an SCI, making it a promising therapeutic target.

The team has now identified a candidate sheddase of L-selectin, which temporarily “sheds” the molecule from the surface of the leukocyte, to be further studied as a potential therapy. The sheddase is an existing FDA-approved NSAID that would be repurposed for treating SCI. The new research will focus on defining the optimal dosing and therapeutic window for administering the drug.

Dr. Steven Rosen is a professor of anatomy at UCSF and Dr. Lee is a postdoctoral fellow in the BASIC laboratories of Michael Beattie PhD and Jacqueline Bresnahan PhD.

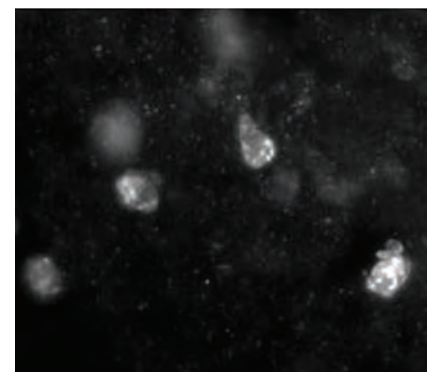
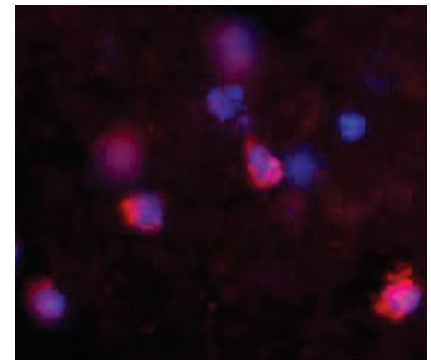
## Understanding Traumatic Brain Injury in the Developing Brain

One of the main challenges in treating children who suffer brain injuries is that they often develop social as well as cognitive problems. In a new five-year study funded by the National Institute for Neurological Disorders, postdoctoral fellow Bridget Semple PhD and principal investigator Linda Noble-Haeusslein PhD will study how neutrophil elastase may not only cause local tissue damage following injury, but also impair normal development of the brain.

Unlike adults, children experience a prolonged trafficking of neutrophils into the brain following injury. Neutrophils release proteases, such as neutrophil elastase, that can damage tissue. In adult mouse models of brain injury, neutrophils clear the brain within 24-48 hours of the insult. In the pediatric models, neutrophils linger for up to two weeks.

The developing brain does not adequately express many of the neuroprotective molecules of the adult brain, such as antioxidants, and may be especially vulnerable to extended exposure to neutrophils. While it has been shown that the expression of neutrophil elastase in the injured brain worsens outcome, Drs. Semple and Noble-Haeusslein will for the first time examine its impact on social and cognitive functions in a mouse model.

Top: Neutrophils are present in the injured developing brain, demonstrated here by immunolocalization of myeloperoxidase (red), which is located in granules in these leukocytes. Bottom: A detailed view of the granules commonly found in the cytoplasm of neutrophils.



# vascular neurosurgery

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Neurosurgeons from UCSF provide treatment and training in Guadalajara, Mexico.

## Project Altruista: Advancing Neurosurgery in Mexico

In July 2012, a team of neurosurgeons and volunteers from UCSF and Johns Hopkins traveled to Guadalajara, Mexico as part of Project Altruista to perform six pro-bono surgeries at a civil hospital servicing underprivileged patients.

Led by Michael Lawton MD, chief of vascular neurosurgery at UCSF, and Alfredo Quiñones-Hinojosa MD, director

of the pituitary tumor center at Johns Hopkins and former neurosurgery resident at UCSF, the team collaborated on the cases with Mexican neurosurgeons and residents to provide training on advanced neurosurgical techniques.

With donated equipment and limited resources, they successfully performed a wide range of complex procedures, including hemispherectomy for epilepsy and resections for deep cavernous

malformation; temporal horn arteriovenous malformation; acoustic neuroma; craniopharyngioma; and medulloblastoma.

To get involved or find out more about Project Altruista, contact Dr. Lawton at: [LawtonM@neurosurg.ucsf.edu](mailto:LawtonM@neurosurg.ucsf.edu)

Michael Lawton MD engages with Mexican residents and neurosurgeons during the second year of Project Altruista.



“Our mission is small and fledgling, but unique: working with the local neurosurgeons, providing for the needy, and focusing on the complex cases with the greatest teaching impact.”

— Michael Lawton MD, chief of vascular neurosurgery at UCSF

## faculty

### Vascular Neurosurgery

Michael Lawton MD

Michael Huang MD

Michael McDermott MD  
(Gamma Knife radiosurgery)

### Cerebrovascular Research Laboratories

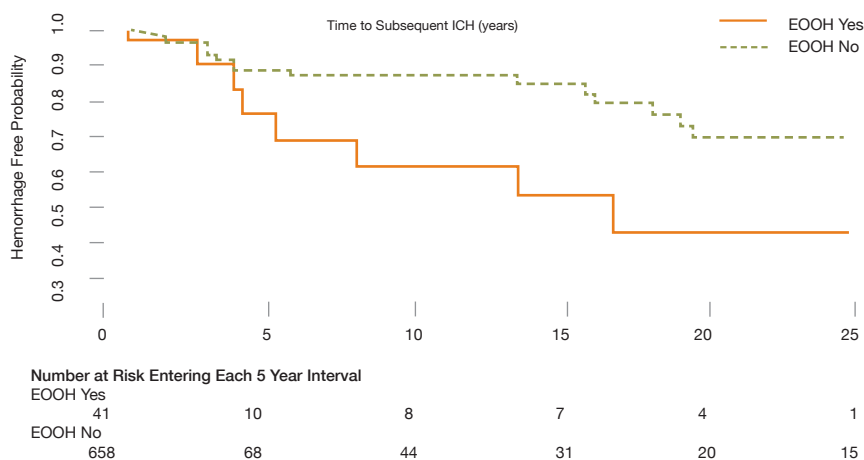
Arnau Benet MD  
surgical anatomy; novel surgical approaches

Michael Lawton MD  
pathophysiology of arteriovenous malformation; hemodynamics of aneurysms; radiation-induced arteriopathy

Jialing Liu PhD  
neurogenesis and functional recovery after stroke

S. Scott Panter PhD  
animal models of stroke and traumatic brain injury

William L. Young MD  
pathophysiology of arteriovenous malformation; hemodynamics of aneurysms; predictors of brain hemorrhage in patients with arteriovenous malformations



Survival analysis of new intracranial hemorrhage (ICH) after diagnosis by evidence of old hemorrhage (EOOH).  
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### Silent Microhemorrhaging of Asymptomatic Arteriovenous Malformations Increases Risk of Intracranial Hemorrhage

Approximately half of all brain arteriovenous malformations (AVM) are asymptomatic when detected. In managing these AVMs, physicians weigh the risks of treatment against the risk of intracranial hemorrhage (ICH). But there have been few reliable predictors of how likely an asymptomatic AVM is to rupture.

In a new study by the UCSF Center for Cerebrovascular Research, investigators found that ‘silent’ microhemorrhages — asymptomatic bleeding in the lesion — are associated with a higher rate of subsequent ICH. The research team first became interested in this possibility when they observed microbleeding in their new animal model of AVM. Analyzing human surgical tissue collected through the UCSF Brain AVM Study Project confirmed that patients with symptomatic ICH also had evidence of older bleeds, likely from silent hemorrhaging of an asymptomatic lesion.

These findings pave the way for developing new risk-stratification schemes for patients with asymptomatic AVMs and the UCSF Vascular Neurosurgery Service is beginning to implement iron-sensitive MRI sequences that can detect the presence of microhemorrhages in patients.

Guo Y, Saunders T, Su H, Kim H, Akkoc D, Saloner DA, Hetsch SW, Hess C, Lawton MT, Bollen AW, Pourmohamad T, McCulloch CE, Tirhan T, Young WL. Silent intralesional microhemorrhage as a risk factor for brain arteriovenous malformation rupture. *Stroke* 2012;43(5):1240-46.

## Technical Refinements in Vascular Neurosurgery: Innovations from UCSF in 2012

### Flash Fluorescence for Middle Cerebral Artery Aneurysms

Distal middle cerebral artery (MCA) aneurysms often require bypass to treat, but their location can make efferent arteries, needed to redirect blood flow, difficult to identify. The flash fluorescence technique uses intraoperative videoangiography and indocyanine green dye to make the efferent arteries fluoresce during surgery. This allows fast and reliable identification of an appropriate recipient artery for bypass.

Rodríguez-Hernández A, Lawton MT. Flash fluorescence with indocyanine green videoangiography to identify the recipient artery for bypass with distal middle cerebral artery aneurysms: operative technique. *Neurosurgery* 2012;70(2 Suppl Operative):209-20.

### Contralateral Clipping of Middle Cerebral Artery Aneurysms

A recent article published by Michael Lawton MD and cerebrovascular fellow Ana Rodríguez-Hernández MD defines

a select patient group that may benefit from contralateral MCA clipping. While this is often a controversial approach to these aneurysms, the more standard approach requires two craniotomies, which some — especially elderly — patients cannot tolerate. The authors define the ideal aneurysms for this procedure as unruptured, having simple necks, projecting inferiorly or anteriorly, associated with short M1 segments, and residing in older patients with sylvian fissures widened by brain atrophy.

Rodríguez-Hernández A, Gabarrós A, Lawton MT. Contralateral clipping of middle cerebral artery aneurysms: rationale, indications, and surgical technique. *Neurosurgery* 2012; 71(1 Suppl Operative):116-23.

### Contralateral Transcingulate Approach to Cavernous Malformations and Arteriovenous Malformations

The contralateral transcingulate approach may be a less invasive and safer route than the contralateral transcassal approach for

lesions located near language and motor areas in the cingulate gyrus and deep white matter of the medial frontal lobe. Neurosurgical resident Jason Davies MD, Rabih Tawk MD, and Michael Lawton MD recently detailed their experience with the technique in 11 patients in the journal *Neurosurgery*.

Davies J, Tawk RG, Lawton MT. The contralateral transcingulate approach: operative technique and results with vascular lesions. *Neurosurgery* 2012; 71(1 Suppl Operative):4-13.

#### Epilepsy Surgery

Edward Chang MD

Paul Larson MD

#### Epilepsy Research Laboratories

Arturo Alvarez-Buylla PhD

Scott Baraban PhD



UCSF is now offering the Visualase™ thermal ablation system for surgical treatment of epilepsy.

“As a medical community, we are not practicing evidence-based medicine with regard to the treatment of patients who have epilepsy.”  
— Edward Chang, MD, chief of adult epilepsy surgery



### New Minimally Invasive Laser Surgery for Epilepsy Offered at UCSF: the Visualase™ Thermal Ablation System

The UCSF Epilepsy Center is excited to be offering a new minimally invasive system to surgically treat epilepsy. Using interventional MRI technology developed at UCSF, neurosurgeons guide an MR-compatible laser applicator into the brain toward the target lesion that is the source of the patient’s seizures. The laser then heats and destroys the small, well-defined area of abnormal tissue, leaving the surrounding tissue unharmed. Thermal ablation is viewed in real-time on thermal maps that display the distribution of heat and successful target treatment. The entire procedure can be done through a single burr hole. The state-of-the-art procedure has been adopted by select hospitals since 2010.

Patients eligible for thermal ablation must have lesional epilepsy resulting from tumors, hypothalamic hamartoma, or medial temporal lobe sclerosis.

### Brain Surgery for Epilepsy Underutilized

Ten years ago, a landmark clinical trial in Canada demonstrated the unequivocal effectiveness of brain surgeries for treating uncontrolled epilepsy, but since then the

procedure has not been widely adopted — in fact, it is dramatically underutilized according to a study from epilepsy specialists at UCSF.

The study, published in the April 2012 issue of *Neurology*, showed that the number of Americans having the surgery has not changed in the decade since release of the effectiveness study, though surgical treatment is now uniformly encouraged by neurology and neurosurgery professional societies.

The U.S. Centers for Disease Control and Prevention estimates that 2 million Americans have epilepsy. Hundreds of thousands of these men, women and children suffer from uncontrolled seizures, but nationally only a few hundred are treated surgically each year with UCSF performing about 50 of the operations.

Among people who do have the operation, the study found, there are significant disparities by race and insurance status. White patients were more likely to have surgery than racial minorities, and privately insured patients were more likely to undergo surgery than those with Medicaid or Medicare.

“As a medical community, we are not practicing evidence-based medicine with regard to the treatment of patients who have epilepsy,” said Edward Chang, MD, chief of adult epilepsy surgery in the UCSF Department of Neurological Surgery and

## Find out more about utilization of epilepsy surgery:

Englot DJ, Ouyang D, Garcia PA, Barbaro NM, Chang EF. Epilepsy surgery trends in the United States, 1990-2008. *Neurology* 2012;78(16):1200-6.

Englot DJ, Ouyang D, Wang DD, Rolston JD, Garcia PA, Chang EF. Relationship between hospital surgical volume, lobectomy

rates, and adverse perioperative events at US epilepsy centers. *J Neurosurg*. 2012 Oct 26. [Epub ahead of print]. DOI: 10.3171/2012.9.JNS12776.

Engel J Jr, McDermott MP, Wiebe S, et al.; Early Randomized Surgical Epilepsy Trial (ERSET) Study Group. Early surgical therapy for

drug-resistant temporal lobe epilepsy: a randomized trial. *JAMA* 2012;307(9):922-30.

Koubeissi M. Epilepsy surgery: a broken bridge between utility and utilization. *Epilepsy Curr* 2012;12(5):194-6.

the UCSF Epilepsy Center. "There are a lot of people who are taking medications and continuing to have seizures even though they can potentially be seizure-free."

A follow-up study showed that the incidence of perioperative adverse events for epilepsy surgery was significantly higher at low-volume hospitals (12.9%) than at high-volume centers (6.1%), indicating that patients with refractory epilepsy should be referred to a high-volume, comprehensive epilepsy center for surgical evaluation.

## Comparing Electrical Stimulation Devices for Epilepsy – How to Determine the Best Option for Each Patient

A recent study at UCSF compared the efficacy and side effect profiles of three therapies that use electrical stimulation to mitigate seizures: deep brain stimulation (DBS), vagus nerve stimulation (VNS), and the Responsive Neurostimulator (RNS™).

Based on the results of randomized trials, the three devices demonstrated comparable seizure control, and the

right choice should be tailored to patient preferences, age, and type of epilepsy (focal, diffuse, or generalized).

Rolston JD, Englot DJ, Wang DD, Shih T, Chang EF. Comparison of seizure control outcomes and the safety of vagus nerve, thalamic deep brain, and responsive neurostimulation. *Neurosurg Focus* 2012;32(3):E14.

## Predicting Seizure Freedom after Surgery for Epilepsy Caused by Cortical Malformations

Surgery can be an effective option to treat medically refractory epilepsy caused by focal cortical dysplasia, but results have been variable. A recent meta-analysis of published outcomes for resection reported that 55.8% of patients achieve freedom from seizures after surgery.

Factors associated with higher rates of seizure control included: partial seizures, a temporal location, detection with MRI, and a Type II Palmini histological classification. Extent of resection was also an important factor; complete resection of the epileptic foci correlated with greater seizure control.

These findings suggest that improvements in diagnostic imaging and surgical tools will continue to improve rates of seizure freedom in this patient population.

Rowland NC, Englot DJ, Cage TA, Sughrue ME, Barbaro NM, Chang EF. A meta-analysis of predictors of seizure freedom in the surgical management of focal cortical dysplasia. *J Neurosurg* 2012;116(5):1035-41.

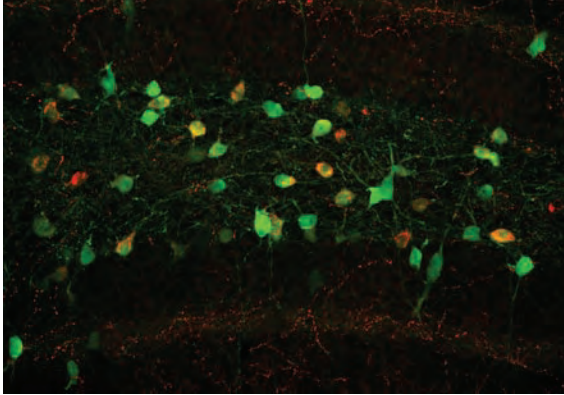
Wang DD, Deans A, Barkovich AJ, Tihan T, Garcia PA, Barbaro NM, Chang EF. Transmantle sign in cortical dysplasia: a unique radiologic entity with excellent prognosis for seizure-control. *J Neurosurg*, In Press.

## Study on Integration of Lab-Grown Interneurons Challenges Prevailing Theory of Cell Fate

Over the past two years, an exciting research program in the Department of Neurological Surgery has been focused on generating interneurons from progenitor cells, which can then be transplanted into the brain to cure epilepsy.

A UCSF study compared vagus nerve stimulation (left), deep brain stimulation (middle), and the Responsive Neurostimulator for treating epilepsy (right).





Hilar region of hippocampus in an epileptic mouse transplanted with GABA progenitor cells. MGE-derived interneurons are shown in green; parvalbumin-positive interneurons are shown in red.

Interneurons secrete the neurotransmitter GABA, which inhibits excitatory circuits in the brain. The absence of GABA may lead to the uncontrolled electrical signaling in the brain that causes epileptic seizures.

With funding from the National Institutes of Health and the California Institute for Regenerative Medicine, the laboratories of Scott Baraban PhD and Arturo-Alvarez Buylla PhD have shown that progenitors derived from the medial ganglionic eminence (MGE) region of adult mouse brains can be transformed into interneurons, produce GABA, and integrate into the neocortex to block spontaneous seizures. They are also investigating the use of embryonic progenitors and whether or not seizures can be blocked in specific genetic models of epilepsy.

The newest results from this research program, published this year in *Nature*, show that there is a threshold for the number of interneurons that can survive and inhibit synaptic events after being transplanted. The number of interneurons

in each transplant experiment varied by 200-fold, but the number of surviving transplants remained the same, expanding the cell population by no more than 35%. The investigators conclude that interneuron cell fate is intrinsically determined, independent of signaling from neurotrophic factors in the local environment. This finding disputes the long-favored neurotrophic hypothesis, which suggests that interneurons are overproduced in the embryonic ventral forebrain and then migrate to the cortex where the excess cells are eliminated through competition for neurotrophic factors.

Establishing the threshold for the number of cells that can survive in the cortex has important implications for planning transplants of MGE progenitors in humans.

Southwell DG, Paredes MF, Galvao RP, Jones DL, Froemke RC, Sebe JY, Alfaro-Cervello C, Tang Y, Garcia-Verdugo JM, Rubenstein JL, Baraban SC, Alvarez-Buylla A. Intrinsically determined cell death of developing cortical interneurons. *Nature* 2012;491(7422):109-13.

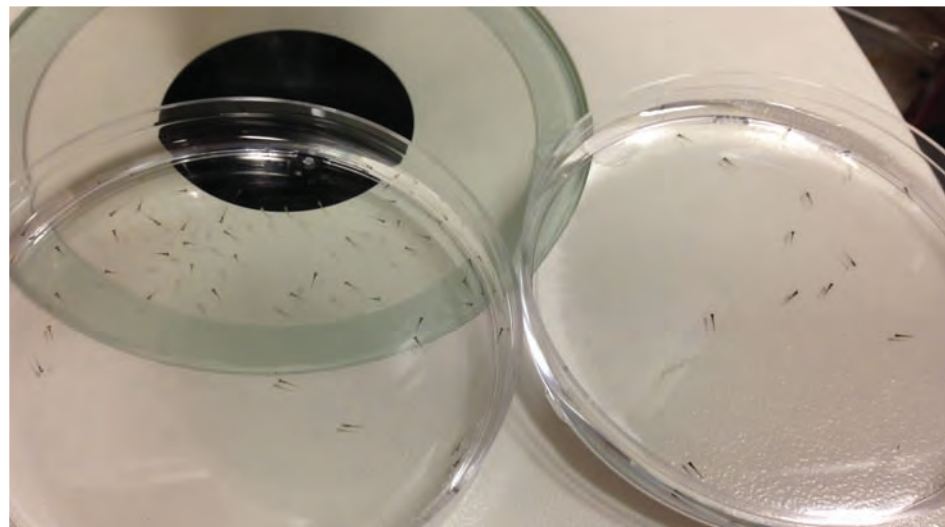
## EUREKA! Prestigious Grant for New Models of Pediatric Epilepsy

Scott Baraban PhD has been awarded a EUREKA grant from the NIH for the project "Using Zebrafish to Advance Our Understanding and Treatment of Epilepsy." Dr. Baraban and his team are using zebrafish mutants featuring a loss-of-function sodium channel mutation to identify molecular targets for therapeutic treatment and screen drug candidates. The epileptic zebrafish display a phenotype similar to monogenic epilepsy disorders primarily seen in children, such as Dravet syndrome and Severe Myoclonic Epilepsy of Infancy.

According to the NIH, EUREKA (Exceptional, Unconventional Research Enabling Knowledge Acceleration) grants fund "exceptionally innovative research projects that could have an extraordinarily significant impact on many areas of science."

Scott Baraban PhD studies zebrafish models of epilepsy.

Young wild-type (left) zebrafish are lighter than those with a sodium mutation that mimics Dravet syndrome (right). The zebrafish mutants are used in high-throughput drug discovery assays.



# movement disorders

15



The Starr lab uses electrocorticography to investigate the pathophysiology of movement disorders. Top row, left to right: Nathan Rowland MD (neurosurgery resident), Philip Starr MD, PhD (PI). Bottom row, left to right: Nicki Swann PhD (postdoctoral fellow), Coralie DeHemptinne PhD (postdoctoral fellow), and Elena Ryapolova BS (lab assistant).

## Electrocorticography Reveals Novel Patterns of Cortical Synchronization in Patients with Movement Disorders

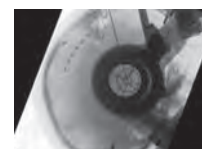
The laboratory of Philip Starr MD, PhD has adapted the technique of electrocorticography, widely used in epilepsy, to study the pathophysiology of movement disorders.

In the past year, Dr. Starr and postdoctoral fellow Coralie deHemptinne showed that in Parkinson's disease, population spike activity in primary motor cortex is excessively coupled to the phase of low frequency rhythms, and this pathological oscillatory synchronization is ameliorated by therapeutic deep brain stimulation.

The work was presented at the 2012 Society for Neuroscience meeting. It reveals fundamental mechanisms by which basal ganglia disease disrupts cortical function, and gives novel insight into mechanisms of deep brain stimulation.

Crowell AL, Ryapolova-Webb ES, Ostrem JL, Galifianakis NB, Shimamoto S, Lim DA, Starr PA. Oscillations in sensorimotor cortex in movement disorders: an electrocorticography study. *Brain* 2012;135(Pt 2):615-30.

DeHemptinne C, Ostrem JL, Garcia P, Chang E, Ryapolova-Webb E, Galifianakis NB, Starr PA. Deep brain stimulation alters aberrant cross frequency coupling in the primary motor cortex of Parkinson disease patients. Presented at the Society for Neuroscience Annual Meeting; October 13-17, 2012; New Orleans, LA.



Intraoperative lateral fluoroscopy showing an electrocorticography electrode inserted over primary motor cortex during deep brain stimulator implantation.

## New Phase I Gene Therapy Trial for Parkinson's Disease Using Real-Time Imaging of Infusate

UCSF will be performing the first gene therapy clinical trial for Parkinson's disease using real-time monitoring of a viral vector infusion with the ClearPoint system. Developed at UCSF, ClearPoint is an MR-compatible skull-mounted aiming device with MR coils designed for optimal imaging during surgery.

### Why real-time imaging?

Previous trials using gene therapy with direct infusion have been hampered by technical limitations. In one study, postmortem tissue from patients who received direct infusion of gene therapy into the putamen revealed that the drug did not cover the entire putamen as was planned, but instead only covered about 15% of the structure, implying that patients did not receive the desired dose of genetic material.

ClearPoint allows real-time visualization of delivery to ensure that a sufficient amount of infusate spreads throughout the target

regions of the brain. It will also allow for monitoring of cannula flow – backflow up along the cannula (and away from the intended target) has been a technical issue in many other trials of direct brain infusions for a variety of neurosurgical disorders.

### What Therapy Will Be Administered?

Patients will receive adeno-associated virus encoding human amino acid decarboxylase (AAV2-AADC). AADC converts oral levodopa to dopamine. If successful, the therapy will decrease dependence on medication and improve symptoms.

### When Will the Trial Begin and How Can My Patients Enroll?

The trial will begin in the Spring of 2013. For more information or to inquire about enrolling a patient, call: (415) 353-2071

This research has been supported by the Michael J. Fox Foundation. Clinical PI: Paul Larson MD; Coordinating PI: Krystof Bankiewicz MD, PhD; Neurology Co-PI: Chadwick Christine, MD.

## faculty

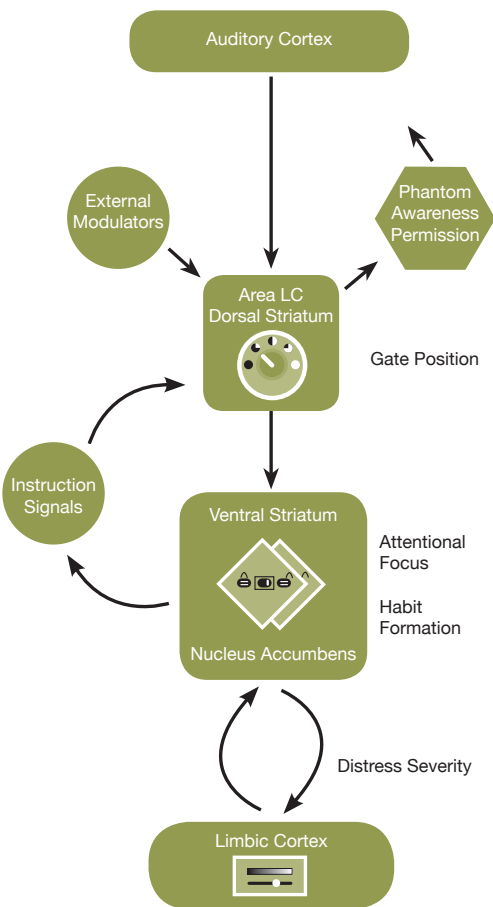
### Movement Disorders Surgery

Philip Starr MD, PhD  
Edward Chang MD  
Paul Larson MD  
Daniel Lim MD, PhD

### Movement Disorders Research Laboratories

Krystof Bankiewicz MD, PhD  
Gene therapy and drug-delivery strategies  
Paul Larson MD  
Neurotransplantation strategies for Parkinson's disease

Philip Starr MD, PhD  
Basal ganglia physiology in movement disorders; neurogenesis and functional recovery



Phantom percept gate control model. Conscious awareness of auditory phantoms is contingent on associated corticostriatal signals passing through area LC of the dorsal striatum. Gate position is determined by restrictive integrity of area LC, strength of phantom percept neural representations, external modulators, and the ventral striatum.

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## Clinical Trial of Deep Brain Stimulation for Tinnitus and a New Paradigm for How the Brain Perceives Sound

UCSF is developing the first pilot study of deep brain stimulation (DBS) for patients with the most severe forms of tinnitus who have not been helped by other available treatment modalities.

The rationale for the study is based on work by UCSF neurosurgeon Paul Larson MD and otolaryngologist Steven Cheung MD, which demonstrated stimulation in a newly discovered region of the caudate nucleus called area LC could modulate loudness of auditory phantoms or create phantoms where none had previously existed. The experiments were performed in patients undergoing DBS for movement disorders who also had tinnitus.

Area LC was not previously thought to be involved in auditory perception, prompting a new model for how the brain perceives sound. Drs. Larson and Cheung propose that the dorsal striatum – home to area LC – gates the perception and loudness of auditory phantoms, and that control of the gate is modulated by the ventral striatum and related circuits.

While most patients become accustomed to chronic tinnitus, 0.5% to 2% of patients experience a drastic decrease in quality of life, including emotional and behavioral problems. Understanding dorsal striatal gate dysfunction may provide insight into the biological underpinnings of how atypical and typical tinnitus differ.

Larson PS, Cheung SW. Deep brain stimulation in area LC controllably triggers auditory phantom precepts. *Neurosurgery* 2012;70(2):398-405.

This work has been nominated for the Tsubokawa Award, given by the World Society for Stereotactic and Functional Neurosurgery to recognize important publications published in the field of functional and stereotactic neurosurgery.

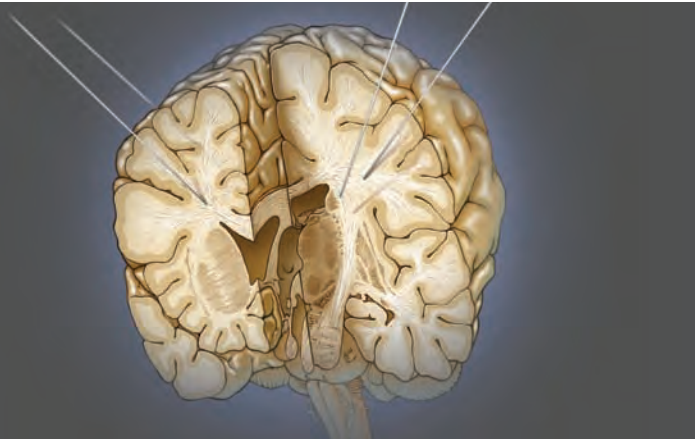
## UCSF Neurosurgery Hosts the 2012 Meeting of the American Society for Stereotactic and Functional Neurosurgery

Under meeting chair Philip Starr MD, PhD and local arrangements host Daniel Lim MD, PhD, the 2012 ASSFN meeting at the San Francisco Fairmont Hotel attracted record attendance (370), a record number of abstracts (170), and record corporate sponsorship.

Keynote addresses were given by UCSF faculty Karunesh Ganguly MD, Adam Gazzaley MD, PhD and Peter Goadsby MD, PhD. Paul Larson MD and Doris Wang MD, PhD gave platform presentations.

Edward Chang MD organized and moderated a satellite symposium on electrocorticography in neuroscience research. Co-director of the UCSF surgical movement disorders program, Jill Ostrem MD, organized a satellite symposium on programming of deep brain stimulators.





Human neural stem cells were injected into four sites of the brain in pediatric patients with Pelizaeus-Merzbacher disease.

## Transplanted Neural Stem Cells Produced Myelin in Phase I Trial

In one of the first neural stem cell transplantation trials ever conducted in the United States, a team led by Chief of Pediatric Neurosurgery Nalin Gupta MD, PhD and Chief of Neonatology David Rowitch MD, PhD showed that neural stem cells successfully engrafted into the brains of patients and appear to have produced myelin.

In the landmark phase I trial, human neural stem cells developed by Stem Cells, Inc., of Newark, California, were injected directly into the frontal lobes of four young boys with an early-onset, often fatal form of Pelizaeus-Merzbacher disease (PMD). In patients with PMD, oligodendrocytes are unable to form myelin, leading to progressive neurological deterioration.

The study, published in *Science Translational Medicine*, demonstrated that neural stem cell transplantation could

be performed in humans. Although only designed as a safety and preliminary efficacy study, additional evidence obtained from detailed MR diffusion data suggested that the transplanted cells are able to produce new myelin in the white matter. These results are encouraging and support the conduct of future studies.

Gupta N, Henry RG, Strober J, Kang SM, Lim DA, Bucci M, Caverzasi E, Gaetano L, Mandelli ML, Ryan T, Perry R, Farrell J, Jeremy RJ, Ulman M, Huhn SL, Barkovich AJ, Rowitch DH. Neural stem cell engraftment and myelination in the human brain. *Sci Transl Med.* 2012;4(155):155ra137.

## New Personalized Medicine Trials for Patients with Pediatric Astrocytomas

In recent years the BRAF<sup>V600E</sup> mutation has been established as a promising therapeutic target in pediatric brain tumors because it is activated in approximately 20% of pediatric tumors but only 3% of adult tumors.

In a recent collaboration between the Pediatric Brain Tumor Center laboratories of David Rowitch MD, PhD and C. David James PhD, investigators found that while the BRAF<sup>V600E</sup> mutation is common in pediatric tumors, it did not form tumors from neural progenitor cells unless it was paired with homozygous deletion of cyclin-dependent kinase inhibitor 2A (CDK2A). The study, published this year in *Proceedings of the National Academy of Sciences*, also demonstrated that combination therapy of BRAF and CDK inhibitors significantly extended survival in a mouse model of pediatric astrocytoma.

Another author of that report, pediatric neuro-oncologist Theodore Nicolaidis MD, is now leading a UCSF study of single-agent vemurafenib (a BRAF inhibitor similar to PLX4720, which was used in the preclinical studies at UCSF) in children with BRAF<sup>V600E</sup> mutant brain tumors. Future trials will focus on combination therapies, the most promising being a combination of vemurafenib and the CDK 4/6-specific inhibitor PD0332991.

The clinical trial of vemurafenib has been added to the next phase of UCSF's Specialized Program of Research Excellence (SPORE) for Brain Tumors (it is supported by NIH bridge funding that supports SPORE research between project periods). The trial will be part of the first pediatric project of any NIH SPORE program for brain tumors.

The preclinical research was supported by the Pediatric Brain Tumor Foundation.

Huillard E, Hashizume R, Phillips JJ, Griveau A, Ihrie RA, Aoki Y, Nicolaidis T, Perry A, Waldman T, McMahon M, Weiss WA, Petritsch C, James CD, Rowitch DH. Cooperative interactions of BRAFV600E kinase and CDKN2A locus deficiency in pediatric malignant astrocytoma as a basis for rational therapy. *Proc Natl Acad Sci USA* 2012;109(22):8710-5.

## faculty

### Pediatric Neurological Surgery

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Michael Prados MD

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John Fike PhD  
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cell-cell interactions; drug-  
delivery strategies

C. David James PhD,  
Co-director,  
Pediatric Brain Tumor Research Center  
molecular biology of CNS cancer;

analysis of mutant epidermal growth factor  
receptors in malignant gliomas; rodent  
model testing of experimental therapies

Theodore Nicolaides MD  
BRAF oncogenesis in pediatric CNS tumors

Anders Persson PhD  
neural precursors of pediatric brain tumors

Claudia Petritsch PhD  
brain cancer stem cells; asymmetric stem  
cell division; novel tumor suppressor genes

Joanna Phillips MD, PhD  
neuropathology; interaction between  
tumor cells and microenvironment

David Rowitch MD, PhD  
central nervous system development  
and tumorigenesis

William Weiss MD, PhD  
molecular basis of medulloblastoma



### Pacific Pediatric Neuro-Oncology Consortium: a New Clinical Trials Group for Pediatric Brain Tumors

The Pacific Pediatric Neuro-Oncology Consortium (PNOC) is a new network of eight children's hospitals that conduct clinical trials of new therapies for children with brain tumors.

Led by neuro-oncologists Michael Prados MD and Sabine Mueller MD, PhD at UCSF, the consortium focuses on developing personalized medicine that exploits the specific aberrations found in each patient's tumor.

The hospitals that make up PNOC are home to some of the most experienced pediatric neurosurgeons in the nation, and

many PNOC trials are surgically based to validate target inhibition and build a database of tissue for further research on rare types of pediatric brain cancer. Each institution also has scientists actively engaged in laboratory research on pediatric tumor biology who work with clinicians to turn their findings into therapies.

The first PNOC trial will test the mTOR inhibitor everolimus to determine if it is more effective in patients with abnormal activation of the PI3K/Akt/mTOR cell-signaling pathway. The trial is open to patients with recurrent low-grade glioma.

For more information about upcoming trials, visit: [www.pnoc.us](http://www.pnoc.us)



### Participating PNOC Sites:

Seattle Children's Hospital  
University of Washington Seattle

Dorenbecher Children's Hospital  
Oregon Health + Science University

University of Utah

Children's Hospital  
& Research Center Oakland

UCSF Benioff Children's Hospital  
University of California, San Francisco\*

Children's Hospital Los Angeles

UCLA Mattel Children's Hospital  
University of California, Los Angeles

Rady Children's Hospital San Diego  
University of California, San Diego

\* Operations and Data Management Center



Chief of Pediatric Neurological Surgery Nalin Gupta MD, PhD (left) with 2012 Pediatric Brain Tumor Foundation lecturer, James Olson MD, PhD (right).

### The PBTF Institute Research Projects:

#### Spatial, Temporal and Cellular Origins of Pediatric Glioma

Principal Investigators:  
David Rowitch MD, PhD  
and Arturo Alvarez-Buylla PhD

#### MYCN and Medulloblastoma Tumorigenesis

Principal Investigator:  
William Weiss MD, PhD

#### Genetics and Biology of Diffuse Intrinsic Pontine Gliomas

Principal Investigators:  
Nalin Gupta MD, PhD;  
Joanna Phillips MD, PhD;  
and C. David James PhD

### Pediatric Brain Tumor Foundation Renews Support for Institute at UCSF

This year, the Pediatric Brain Tumor Center at UCSF was awarded an additional three years of funding from the Pediatric Brain Tumor Foundation (PBTF) as one of three PBTF Institutes in North America.

The PBTF was founded by Mike and Dianne Traynor in 1991, and their tireless efforts transformed the foundation into the world's largest philanthropic organization dedicated to supporting the search for the causes of and cures for childhood brain cancer. Sadly, Dianne passed away this year. Mike predeceased her in 2009.

To honor their memories, each year UCSF invites an expert on pediatric brain tumors to give a lecture to the campus community

to facilitate education on important topics related to pediatric brain tumor treatment and research.

### Children with Medically Refractory Epilepsy May be Candidates for Permanent Resolution of Seizures by Surgery

Approximately 15% of children with epilepsy have symptoms that cannot be controlled with medication. At UCSF, patients who do not respond after being treated with two different medications are assessed by pediatric epileptologists, neuropsychologists, and pediatric neurosurgeons to determine whether or not they would be good surgical candidates. With successful surgery, children are often seizure free for life.

During surgery, techniques such as electrocorticography and brain mapping are used to identify and avoid injury to sites of language, motor, and sensory function during surgery. By placing electrodes directly on the brain and monitoring its activity, the pediatric epilepsy surgery team can more accurately locate the origin of a patient's seizures than they could with a grid placed on the scalp. This method represents the gold standard for defining the epilepsy network.

A large number of surgical procedures for pediatric epilepsy are offered, including hemispherectomy, corpus callosotomy, vagal stimulation, temporal lobectomy, extratemporal resection, and subpial resection.

### Facts on Pediatric Epilepsy Surgery

- Fifty percent of pediatric patients who undergo surgery for epilepsy have their seizures controlled.
- If seizure foci are located in eloquent cortex, subdural grids can be used to map the foci during

surgery to provide more detailed information about the location and increase the safety of surgery.

- Because younger children usually have a greater chance of functional recovery, an early referral for surgery is best.

- fMRI techniques are being incorporated into clinical use to provide a noninvasive method of localizing language and motor centers in the brain. These techniques help reduce the likelihood of new neurologic deficits resulting from the operation.

# center for management & surgery of peripheral nerve disorders

## faculty

Michel Kliot MD



Tractography allows neurosurgeons to view functioning axons along the surface of a nerve sheath tumor (left) and loss of function in a severed ulnar nerve (right).

## Functioning Axons Sprout to Site of Nerve Injury in New Surgical Procedure Developed at UCSF

Chief of Peripheral Nerve Surgery, Michel Kliot MD, has developed a new surgical procedure to regenerate axons in damaged nerves. Called “side-to-side neurotization,” it involves placing an intact nerve alongside the damaged nerve to allow axons in the functioning nerve to sprout to the site of injury. By making small incisions in the side of each nerve, which avoids cutting across axons and potential axonal pathways, Dr. Kliot and his colleagues create a ‘window’ for the functioning axons to branch out and enter the damaged nerve through.

Standard surgical treatment for this type of injury is to cut and graft a normal nerve onto an injured nerve, which produces some damage in the normal nerve and prevents or reduces the chance for spontaneous regeneration in the injured nerve.

The first patient to undergo side-to-side neurotization at UCSF in July 2012 has regained some function mediated by axons from both the injured and intact

nerve. This novel approach was inspired by the side-to-side vascular repairs performed by Michael Lawton MD, chief of vascular neurosurgery.

## Multidisciplinary Clinic for Neurofibromatosis

Patients with neurofibromatosis (types 1 and 2) are predisposed to a number of CNS tumors, including peripheral nerve tumors. This year UCSF began offering a clinic staffed by specialists in neuro-oncology, neurosurgery, neuropathology, and neurology to evaluate patients with neurofibromatosis and CNS tumors.

The new neurofibromatosis clinic also partners with medical geneticists at the UCSF NF/Ras Pathway Clinic, which provides unique care for patients with syndromes causing germline mutations in genes encoding components of the Ras/mitogen activated protein kinase (MAPK) pathway.

Treatment plans for individuals with neurofibromatosis are developed through coordinated care that takes into account the underlying biology as well as the severity and phenotype produced by the specific mutation in the NF1 or NF2 gene.

## New Developments in Neuro-Imaging Improve Diagnosis and Treatment of Peripheral Nerve Disorders

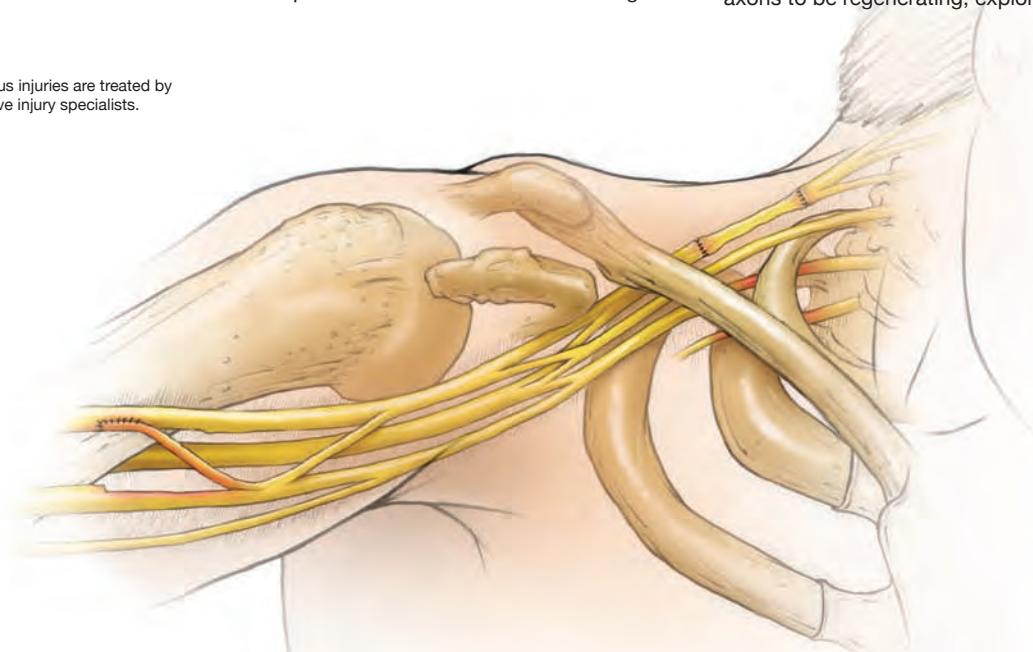
### Diffusion Tensor Imaging

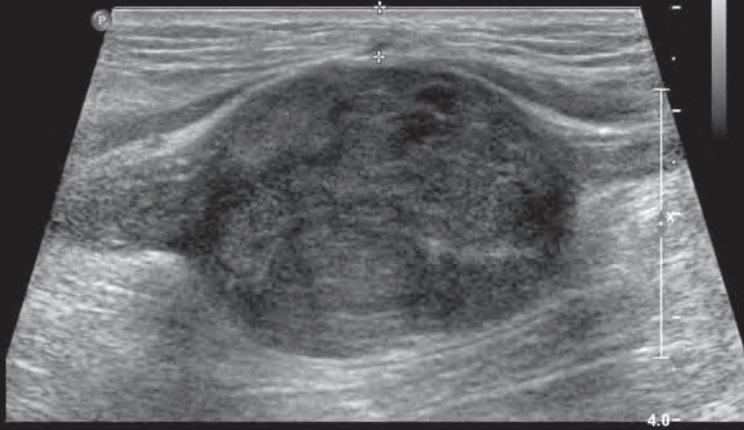
Neuroradiologists Cynthia Chin MD and William Dillon MD are currently using diffusion tensor imaging (DTI) of the peripheral nervous system to visualize axons within peripheral nerves. This cutting-edge technology is allowing UCSF neurosurgeons to visualize:

- where functioning nerve fibers are located on the surface of a nerve sheath tumor to avoid damaging them during surgery
- the extent of nerve fiber damage in injured nerves and any signs of spontaneous regeneration, resulting in fewer exploratory surgeries.

DTI is also being used to monitor axon regeneration following brachial plexus birth injury and to determine if certain nerve roots have been pulled out, or avulsed, from the spinal cord and can no longer be used for repair. If DTI shows axons to be regenerating, exploratory

Pediatric brachial plexus injuries are treated by both pediatric and nerve injury specialists.





Ultrasound guidance demonstrates the right tibial nerve entering and exiting a tumor.

surgery may be unnecessary. Infants and children with brachial plexus nerve injuries are evaluated by specialists at UCSF's pediatric nerve injury clinic in collaboration with Nalin Gupta MD, PhD, chief of pediatric neurosurgery.

### MR Diffusion

A new application for MR diffusion imaging may allow physicians to non-invasively determine whether nerve sheath tumors are benign or malignant. In preliminary studies at the Center for Management and Surgery of Peripheral Nerve Disorders, tumors with high cellularity (often corresponding to greater malignancy) were shown to have low diffusion coefficients. Clinical research is currently ongoing to precisely correlate findings from MR imaging with histopathology.

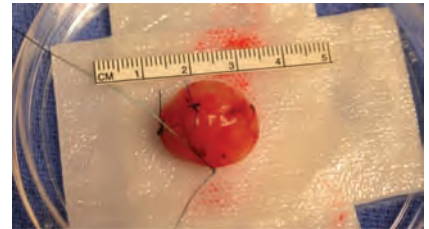
### Intraoperative Ultrasound

UCSF neurosurgeons use a portable ultrasound machine when diagnosing nerve injuries. Ultrasound is playing an increasingly important role in the operating

room by allowing neurosurgeons to more precisely identify nerve pathology and plan surgical trajectories that minimize incision length and tissue dissection, thereby reducing operative time and postoperative discomfort.

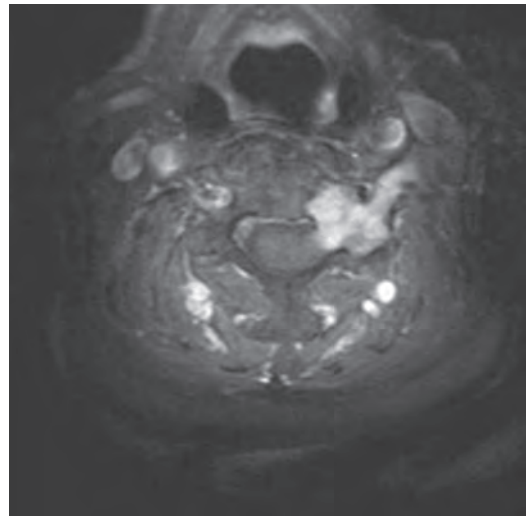
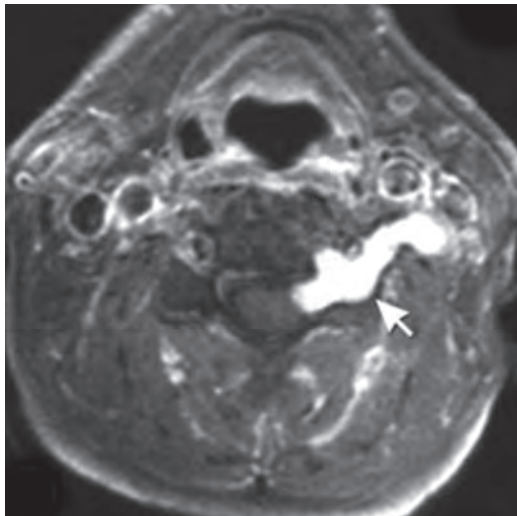
### Research Program on Nerve Sheath Tumor Quiescence

The majority of nerve sheath tumors do not grow beyond their size at initial diagnosis and many can be monitored with serial imaging. A minority of these tumors continue to grow and require surgery, with a small number progressing to malignant tumors. UCSF neuropathologist Tarik Tihan MD, PhD, biochemist Joseph DiRisi PhD, and neurosurgeons Michel Kliot MD and Andrew Parsa MD, PhD are comparing tissue from growing and nongrowing benign nerve sheath tumors to characterize molecular differences that may explain their different natural histories. Understanding why many nerve sheath tumors stop growing on their own could help develop new anti-proliferation strategies.



Sutures on the surface of a resected nerve sheath tumor serve as markers of 3D orientation for neuropathologists correlating MR diffusion imaging with histology.

A dumbbell-shaped tumor of the left C5 nerve, which has stayed the same size for 19 years (Left: MR image from 1993; Right: MR image from 2010). Physicians at UCSF are trying to understand why most nerve sheath tumors stop growing on their own in order to induce quiescence in tumors that continue to proliferate and spread.



# surgical pain management program

22

faculty

Edward Chang MD

Philip A. Starr MD, PhD



Glossopharyngeal neuralgia is a condition that causes severe pain in the tongue, throat, ear and tonsils.

## Glossopharyngeal Neuralgia: Case Report

Treating Physician: Edward Chang MD

### Presentation

A 46-year-old woman presented with long-standing intractable mouth pain for two years. She initially thought it was tooth pain; however, it progressed to include severe throat and ear pain. The episodes were triggered by eating, brushing teeth, talking, and occasionally by sounds. The pain was described as sharp, lancinating, and shock-like — and, therefore, extremely debilitating. She tried several medications including gabapentin, carbamazepine, and lamotrigine, which helped temporarily, but also caused significant side effects.

### Surgery

The patient decided to proceed with surgery to treat her pain. Intraoperatively the PICA artery was found directly adjacent to the glossopharyngeal

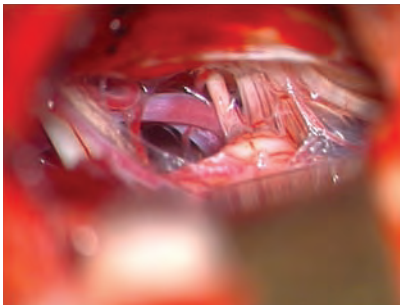
nerve, but did not appear to be causing significant compression. After carefully identifying and then protecting the motor rootlets of the vagus nerve and spinal accessory nerve using electrical stimulation, the glossopharyngeal nerve was transected, as well as the sensory branches of the vagus nerve.

### Postoperative Course

The patient was pain-free after surgery. She experienced transient dysphagia, which improved to baseline in two weeks.

Glossopharyngeal neuralgia is a condition in which there are repeated periods of severe pain in the tongue, throat, ear, and tonsils, which can last from seconds to a few minutes. In most cases, the source of irritation is never found. The most effective drugs are usually anti-seizure medications. In severe cases, surgery can be performed to take pressure off the nerve (microvascular decompression) or to cut the nerve (rhizotomy). Both surgeries are considered highly effective.

Intraoperative photograph showing the 'neurovascular conflict' prior to microvascular decompression for glossopharyngeal neuralgia.



UCSF is home to one of the largest and most comprehensive pain neurosurgery centers in the United States. Patients receive extensive assessments to determine if they are candidates for surgical intervention for their disorders

Neurosurgeons at UCSF work with a variety of other pain specialists at the UCSF Pain Management Center –

designated as a Clinical Center of Excellence by the American Pain Society – to design a therapeutic course that is tailored to each patient. Through the use of specialized surgical procedures, we are often able to deliver pain control in severe cases.

## faculty

Christopher Ames MD

Dean Chou MD

Praveen Mummaneni MD

Philip Weinstein MD

Michel Klot MD  
(chiari malformation)



Neurosurgeon Praveen Mummaneni MD reviews the spinal pathology of his patient with his surgical team before operating.

### Hospitals Overestimate Readmission Rates for Spine Surgery: An Important Issue for Assessing Quality of Care

Neurological and orthopaedic surgeons at UCSF reviewed thousands of hospital admissions for spine problems between 2007-2011 and analyzed “all cause” readmissions, the basis for the Centers for Medicare and Medicaid metric.

Readmission rates can be used to determine a hospital’s quality of care and reimbursements, as they can often reflect hospital-acquired infections or surgical complications. The UCSF investigators found that readmissions were being overestimated by up to 25% because “all cause” readmissions include planned staged surgeries. Many complex spinal surgeries are scheduled to be performed in two or more stages

spaced out during several weeks, and the subsequent surgeries are currently defined as readmissions.

Neurosurgeons Praveen Mummaneni MD, Christopher Ames MD, and Dean Chou MD contributed to the report, presented at the 2012 Annual Meeting of the American Association of Neurological Surgeons.

Amin BY, Tu T-H, Schairer WW, Na L, Takemoto S, Berven S, Deviren V, Ames C, Chou D, Mummaneni P. Pitfalls of calculating hospital readmission rates based on nonvalidated administrative data sets. *J Neurosurg*, In Press.

### Treating Adjacent Lumbar Pathology After Previous Lumbar Surgery

Patients who require fusion of the lumbar spine will often experience a break down in the adjacent level of their spine following

surgery. While some patients with severe deformities and major instability may require further fusion, a recent analysis by UCSF neurosurgeon Dean Chou and colleagues has shown that patients who have degeneration but good spinal alignment following surgery may not need an additional operation.

No previous studies have compared nonoperative and operative management for this patient population. The authors conclude that in the absence of severe disability, nonoperative therapy should be considered as first-line treatment for adjacent segment pathology.

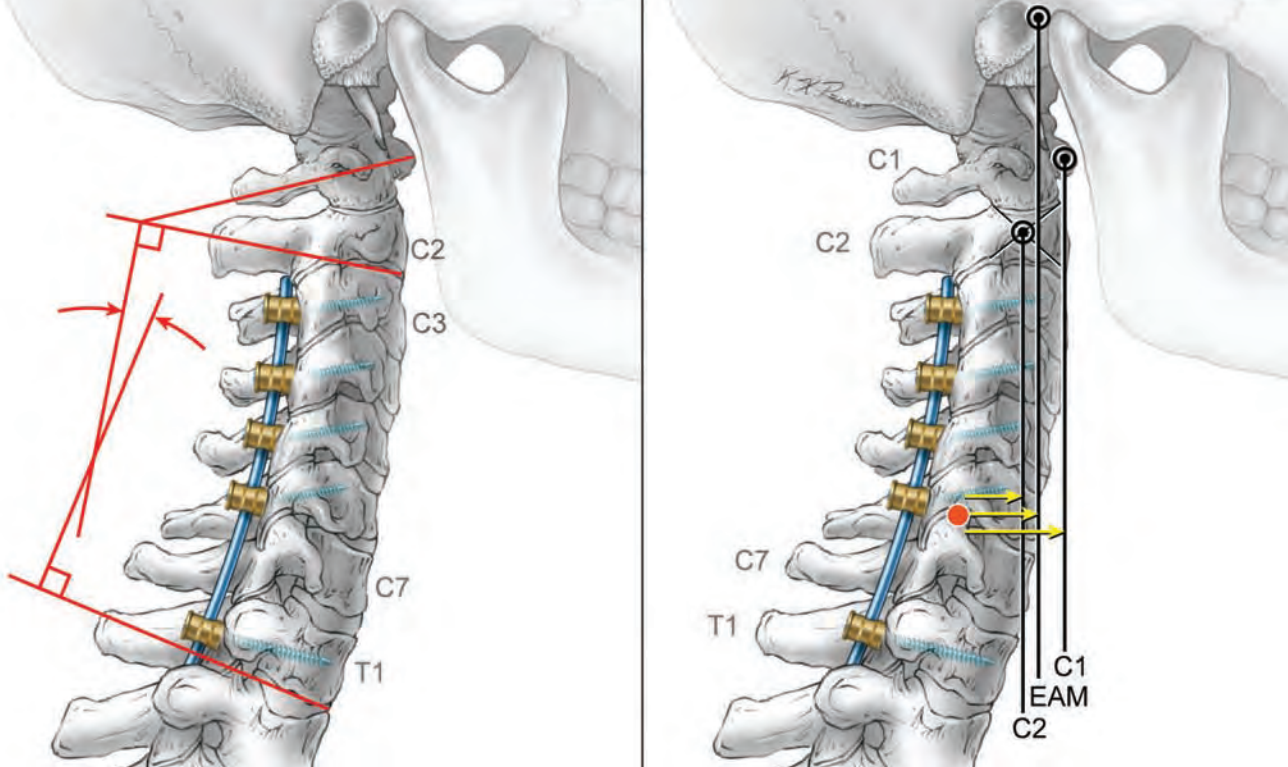
Chou D, Dekutoski M, Hermsmeyer J, Norvell DC. The treatment of lumbar adjacent segment pathology after a previous lumbar surgery: a systematic review. *Spine* (Phila Pa 1976) 2012;37(22 Suppl):S180-8.

### Anterior Cervical Discectomy and Fusion Shown to be a Cost-Effective Procedure

A five-year follow-up of 352 patients receiving anterior cervical discectomy and fusion demonstrated that the procedure was effective at relieving spinal cord compression and provided a durable response. Cost analysis showed that a successful procedure was more cost effective at five years than other nonsurgical interventions, such as a physical therapy or injections.

This work, published in *Spine*, received the first-place award for a clinical research paper at the 2012 annual meeting of the Cervical Spine Research Society.

Carreon LY, Anderson PA, Traynelis VC, Mummaneni PV, Glassman SD. Cost effectiveness of single-level anterior cervical discectomy and fusion five years after surgery [published online ahead of print September 13, 2012]. *Spine* (Phila Pa 1976). 2012 Sep 13. doi: 10.1097/BRS.0b013e318273aee2



Visual representation of the technique used to measure cervical lordosis (left) and cervical sagittal vertical axis (right). Cervical malalignment results in worse outcomes following cervical fusion surgery.

### Standing Regional Cervical Sagittal Alignment Impacts Outcomes After Cervical Fusion Surgery

In a landmark paper published in *Neurosurgery* this year, Christopher Ames MD and his colleagues showed that better sagittal alignment of the cervical spine is correlated with better health-related quality-of-life scores after cervical spine fusion surgery. This study was the first to show that cervical alignment is linked to outcomes in the same way that lumbar sagittal balance is linked to outcomes after lumbar fusion surgery.

As a result of this study, neurosurgeons at UCSF now obtain standing preoperative and postoperative cervical radiographs and 3-foot standing films of all patients undergoing cervical spine fusion. This allows them to better plan ideal postoperative cervical alignment.

This work was presented as a plenary talk at the Joint Section on Spine and Peripheral Nerves at the 2012 Annual Meeting of the American Association of Neurological Surgeons.

Tang JA, Scheer JK, Smith JS, Deviren V, Bess S, Hart RA, Lafage V, Shaffrey CI, Schwab F, Ames CP; ISSG. The impact of standing regional cervical sagittal alignment on outcomes in posterior cervical fusion surgery. *Neurosurgery* 2012;71(3):662-9.

### Minimally Invasive Techniques for Severe Spinal Deformity at All Levels

UCSF is currently offering minimally invasive procedures to treat severe deformity caused by kyphosis or scoliosis. Improvements in instrumentation are allowing neurosurgeons to perform the same operations previously done through open procedures through a minimally invasive approach.

These operations include vertebral column resection for severe rigid deformity and vertebrectomy for tumors that are causing collapse of the spine or deformity. Minimally invasive approaches for these conditions have resulted in less blood loss and lower infection rates among UCSF patients.

### Identifying Patients at Risk for Surgical Site Infection

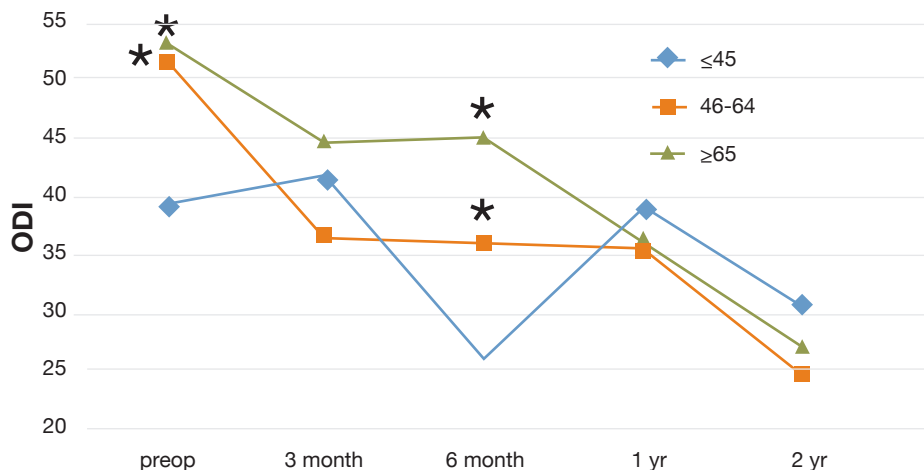
Surgical site infection is often used as a measure of health care quality at large hospitals. A recent analysis by spine neurosurgeons and orthopaedic surgeons at UCSF used administrative claims data to identify the patient population most at risk for developing surgical site infection following spine surgery. The investigators identified a series of procedural and patient-based risk factors, which will help to counsel high-risk patients before surgery.

Abdul-Jabbar A, Takemoto S, Weber MH, Hu SS, Mummaneni PV, Deviren V, Ames CP, Chou D, Weinstein PR, Burch S, Berven SH. Surgical site infection in spinal surgery: description of surgical and patient-based risk factors for postoperative infection using administrative claims data. *Spine (Phila Pa 1976)* 2012;37(15):1340-5.

“Major operations for deformity were the last frontier for minimally invasive surgery.”

– Dean Chou MD





Comparisons in Oswestry Disability Index scores by age groups following surgery for correction of severe deformity. \* = significant difference from ≤45-year-old group; Δ = significant difference from 46 to 64-year-old group.

## Elderly Patients Have Better Health-Related Quality of Life After Major Deformity Surgeries

Health-related quality-of-life (HRQOL) outcomes for elderly patients needing major surgery to correct severe deformities have not been well characterized despite an increasing number of elderly patients seeking treatment for rigid iatrogenic deformities.

In a study done this year by the International Spine Study Group, investigators analyzed the relationship between age and HRQOL for 228 patients who underwent three-column osteotomies – such as pedicle subtraction osteotomies and vertebral column resections.

Interestingly, they found that while elderly patients take longer to recover from surgery, they achieve greater improvement in their HRQOL than younger patients.

UCSF neurosurgeon Christopher Ames MD presented these findings in the plenary session of the annual meeting of the Scoliosis Research Society.

Ames CP, Scheer JK, Smith JS, Gupta MC, Klineberg E, Hart RA, Burton DC, Hostin R, O'Brien MF, Shaffrey CI, Bess S, Schwab F, Deviren V, Kebaish K, International Spine Study Group (ISSG). Outcomes following three-column spinal osteotomies: impact of HRQOL and age on two-year follow up. Presented at the 47th Annual Meeting of the Scoliosis Research Society; September 5-8, 2012; Chicago, IL.

## New Clinic for Chiari Malformation

The Department of Neurological Surgery has opened a specialized clinic to evaluate patients with Chiari malformation, which is often characterized by low-lying cerebellar tonsils. By using cine MRI pulse sequences to evaluate cerebrospinal fluid (CSF) flow dynamics, physicians are able to accurately determine whether there is an obstruction of flow between the brain and cervical spinal cord. Many patients who meet the anatomical criteria for Chiari malformation (cerebellar tonsillar descent below the foramen magnum) do not have blockage of CSF flow. At UCSF, cine MRI studies are a requirement for all patients in order to prevent unnecessary surgeries.

# neurosurgery patient safety & quality improvement program

## faculty

Catherine Lau MD

Rita Mistry MPH

In 2012, the Department of Neurological Surgery received the Healthgrades Neurosurgery Excellence Award, which recognizes hospitals for superior patient safety outcomes in neurological surgery.

The Department of Neurological Surgery's Patient Safety and Quality Improvement Program was formed in 2011 to provide the safest and highest quality patient care based on the principles of clinical, operational, and academic excellence with the overall aim of being a national leader in neurological surgery quality and patient safety.

Led by Catherine Lau MD and Rita Mistry MPH, the program is made up of a multi-disciplinary team of faculty members, residents, nurse practitioners, physician assistants, clinic practice managers, nurses, pharmacists, Infection Control specialists, Service Excellence liaisons, and Medical Center quality improvement and service line representatives. Together, they work on a multitude of projects aimed

at improving the quality of neurosurgical patient care and the patient experience at UCSF Medical Center.

## Creating a Culture of Safety Within Operative Neurosurgery

This year, the Department of Neurological Surgery, in collaboration with the Department of Anesthesia and perioperative nursing staff, developed an educational video on critical perioperative safety TIME OUT and debrief checklists for surgical team members to review prior to and immediately after a surgical procedure. The video focuses on:

- Minimizing errors and improving patient outcomes by simplifying and standardizing neurosurgical perioperative patient safety practices and team communication processes.
- Highlighting critical patient safety checks/precautions (e.g., patient identification, TIME OUT) and team communication practices (e.g., debriefs, hand-offs).

- Fostering a culture of patient safety and promoting improved communication within the perioperative setting.

Find the video under the Quality & Safety section of our website: [neurosurgery.ucsf.edu](http://neurosurgery.ucsf.edu)

Lau CY, Greysen SR, Mistry RI, Han SJ, Mummaneni PV, Berger MS. Creating a culture of safety within operative neurosurgery: the design and implementation of a perioperative safety video. **Neurosurg Focus** 2012;33(5):E3.

## National Neurosurgery Quality and Outcomes Database

Beginning in 2013, the Department of Neurological Surgery will submit data to the National Neurosurgery Quality and Outcomes Database (N<sup>2</sup>QOD), sponsored by the American Association of Neurological Surgeons/ NeuroPoint Alliance. This is the first nationwide effort to collect data on safety, quality, and cost-effectiveness in the field of neurosurgery.

Our educational video "Creating a Culture of Safety Within Operative Neurosurgery" highlights team communication, as well as the critical perioperative safety TIMEOUT and debrief checklists for surgical team members.



## Four Key Areas of Focus in the Neurosurgery Patient Safety and Quality Improvement Program

### Clinical Effectiveness

- Reduce craniotomy and spine surgical site infections
- Reduce medication errors
- Reduce other hospital-acquired conditions: post-op VTE, CA-UTI, VAP, CLABSI, HAPUs, falls
- Lower mortality observed/expected (O/E) ratios
- Improve hand hygiene rates
- Reduce 30-day readmission rates

### Clinical Efficiencies

- Improve discharge before noon
- Improve discharge summary completion timeliness
- Reduce unnecessary laboratory and radiologic testing

### Patient Experience

- Improve inpatient HCAHPS and Press-Ganey scores
- Improve outpatient HCAHPS and Press-Ganey scores

### Resident Engagement

- Quality Improvement (QI) Resident Curriculum
- Resident participation in case review and ongoing departmental QI projects
- Quarterly QI Resident Lunches
- Annual participation in UCSF Graduate Medical Education QI Incentive Project



# ucsf neurological surgery community extension program

## faculty

Tarun Arora MD, Director

Keith B. Quattrocchi MD, PhD, FACS

Corey Raffel MD, PhD

Archimedes Ramirez MD

Jeffrey Yablon MD



Keith Quattrocchi MD, Jillian Payne NP, and Tarun Arora MD work with community physicians to provide high-quality outpatient and inpatient neurosurgical care in Marin, CA.

The Department of Neurological Surgery has formed partnerships with Marin General Hospital, Queen of the Valley Medical Center, and Good Samaritan Hospital to provide extended services to Bay Area residents and physicians.

## Marin

In May 2012, Keith B. Quattrocchi MD, PhD, FACS joined Tarun Arora, director of the Community Extension Program, at Marin General Hospital as a full-time, locally based neurosurgeon. Drs. Quattrocchi and Arora, along with a specialty trained nurse practitioner, skilled outpatient clinic staff, and colleagues at Marin General, work together to seamlessly coordinate state-of-the-art treatment with patients' local medical care.

## Napa Valley

At Queen of the Valley Medical Center in Napa Valley, Jeffrey Yablon MD and Archimedes Ramirez MD treat patients with central nervous system tumors, spinal disorders, cerebrovascular disorders, neurotrauma, minimally invasive spine surgery, spinal instrumentations, and skull base surgery. Both Dr. Yablon and Dr. Ramirez have particular expertise in minimally invasive spine surgery and many years of experience in trauma neurosurgery.

## San Jose

In January 2013, a new pediatric neurosurgery clinic will open at Good Samaritan Hospital in San Jose, led by renowned pediatric neurosurgeon Corey Raffel MD, PhD. Dr. Raffel joins us from Ohio State University, where he served as professor and vice chair. He has also served as chief of pediatric neurosurgery at Nationwide Children's Hospital and been the principal investigator of several research programs aimed at finding new treatments for childhood brain tumors.

Patients with highly complex or unusual disorders requiring the full multidisciplinary care of an academic medical center are offered treatment options at UCSF Medical Center.

UCSF Neurosurgery offers services at Queen of the Valley Medical Center in Napa Valley.



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The UCSF logo is rendered in a teal color. It features the letters 'UCSF' in a bold, sans-serif font. The 'U' and 'C' are connected, and the 'S' and 'F' are also connected. The logo is positioned over a faint, circular seal of the University of California, which includes the text 'UNIVERSITY OF CALIFORNIA' and '1868'.

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San Francisco

*advancing health worldwide™*

University of California  
San Francisco

The UCSF logo is rendered in white. It features the letters 'UCSF' in a bold, sans-serif font. The 'U' and 'C' are connected, and the 'S' and 'F' are also connected. The logo is positioned over a solid yellow background.

Neurological Surgery

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