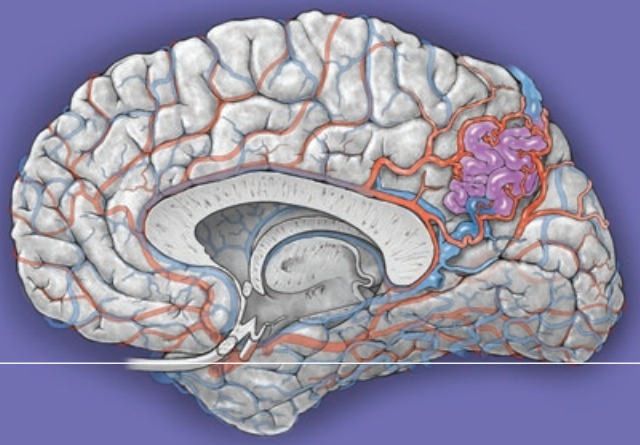
UCSF Neurosurgery News

UCSF Department of Neurological Surgery



Volume 14

Arteriovenous Malformations in the Brain

Treatment versus Observation and a New Imaging Technique for Assessing Risk of Future Rupture

For patients with a hemorrhagic arteriovenous malformation (AVM), the risks of neurological morbidity and mortality are similar to those of a ruptured aneurysm, and reported mortality rates are as high as 20%. Surgical treatment is generally advised for these AVMs because they carry a relatively high risk of subsequent hemorrhage.

Less straightforward are treatment decisions for unruptured AVMs. As with other brain lesions, improvements in imaging techniques over the past four decades have substantially increased the number of incidentally detected AVMs. Symptomatic patients with unruptured AVMs most often experience headaches or seizures. A less common indicator can be similar to a transient ischemic attack that occurs when the AVM takes oxygenated blood away from normal brain tissue; a scenario aptly named 'steal.'

According to the American Association of Neurological Surgeons, the odds of an unruptured AVM bursting are approximately four percent per year. But despite these relatively low odds, the consequences, including neurological deficit, seizures and death, are severe enough to warrant a close look at intervention. "At UCSF we have the full range of treatment options and the experience to guide patients and their families to the best choice – whether that be observation or some combination of radiosurgery, embolization, and microsurgery," says Michael Lawton, MD, chief of vascular neurosurgery.

While successful AVM surgery can result in definitive cure, it is one of the most technically demanding neurosurgical procedures. An AVM can occur anywhere in the brain and each tangle of arteries and veins is unique, requiring careful planning that accounts for all of the affected vasculature.

"Every procedure needs to be tailored to the individual anatomy of the patient and the lesion," says Lawton, who has resected 750 AVMs and written the book on AVM surgery. His best-selling textbook *Seven AVMs: Tenets and Techniques for Resection* details the situations encountered most often during microsurgical procedures and provides a guide for advanced practitioners.

A multicenter study of patients with unruptured AVMs (known as the ARUBA trial) reported a 33% rate of morbidity and mortality among those undergoing treatment and only a 10% rate among those followed with observation.[1] Two published UCSF case series, however, showed no difference in morbidity and mortality between surgery and observation, suggesting that the ability to judiciously select AVMs for surgery and the technical skills to remove them safely can provide a better alternative than observation in some cases.[2,3] This is especially true of surgery for low-grade AVMs, which has a high cure rate and low complication rate.

In the ARUBA trial, patients were randomized to receive treatment or observation, and treatment could include embolization, radiosurgery, microsurgery, or combinations

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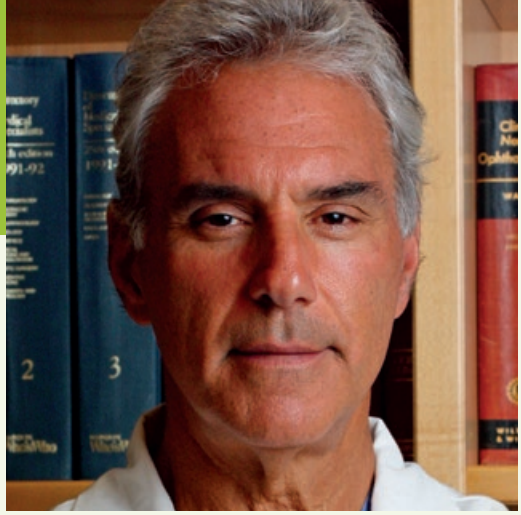
Looking to the Future



Over the last 15 years, a trend in treatment for cerebrovascular disorders has been a movement towards less invasive procedures. Endovascular procedures, embolization, and radiosurgery have all become valuable additions to our armamentarium, both alone and as adjuncts to surgery. For many patients, this is a positive development. Procedures that require less experience and can be performed by more physicians expand the options for treatment.

But for complex cases, there is no substitute for microsurgery. In experienced hands, surgery produces the most durable results for aneurysms and AVMs, and it remains the only treatment option for cavernous malformations.

With the trend towards less invasive treatments, fewer young neurosurgeons are adopting this subspecialty and an increasing number of patients from all over the country are referred to specialized centers like UCSF for surgery. Our cerebrovascular case volume has risen every year for the last decade and we currently have one of the busiest practices in the nation.

At UCSF, we continue to emphasize a surgical approach in both our clinical practice and our residency training program. Considering the serious morbidity and mortality associated with cerebrovascular disorders, I believe it is critical that the neurosurgical community continues to provide patients with this expertise as part of the full continuum of care.

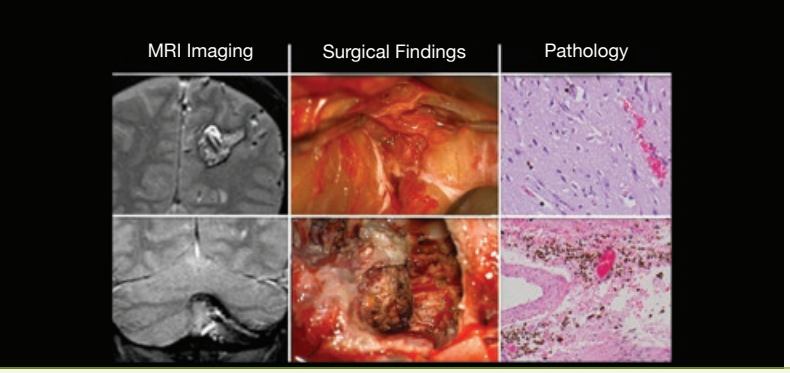
Mitchel S. Berger, MD

Berthold and Belle N. Guggenhime Professor and Chair

**Director,
Brain Tumor Center**

**Department of
Neurological Surgery, UCSF**

UCSF



Two AVMs that appeared unruptured on standard MR images actually showed evidence of silent hemorrhage when removed. Blood products seen during surgery and hemosiderin staining indicate previous bleeding, which is a risk factor for future rupture (top panel, hemosiderin grade 1; bottom panel, hemosiderin grade 4).[4]

"At UCSF, we have the full range of treatment options and the experience to guide patients and their families to the best choice."

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of these treatments. But being able to identify those AVMs most likely to rupture changes the risk-benefit ratio and enables physicians to better counsel their patients.

Selecting the Riskiest AVMs for Treatment

AVMs at increased risk for rupture are those with deep venous drainage, in a deep location in the brain, or in patients with a prior history of hemorrhage. Currently there are no reliable data on anatomical features of AVMs that can predict their rupture.

Another feature linked to a major rupture are the so-called silent hemorrhages or microruptures that happen with some AVMs. In this case the AVM leaks small volumes of blood but doesn't burst or cause overt symptoms that a patient would report, such as headache. The leakage cannot be seen on standard MR images, so these AVMs are typically classified as unruptured with no prior bleeding.

When Lawton and his colleagues examined tissue from 242 resected AVMs, they found that 29% of the unruptured AVMs had evidence of silent hemorrhaging (shown by staining with hemosiderin).[4] "If one in three patients with an unruptured AVM actually has evidence of prior bleeding, that's significant and we need to be able to identify them and offer them more aggressive treatment," says Lawton. In addition to putting patients at a higher risk for a major rupture, over time the buildup of blood created by a slow-leaking AVM can lead to neurological deficits or seizures.

Advanced Imaging to Detect Silent Hemorrhage

Cerebrovascular researchers at UCSF, led by Helen Kim, PhD, and David Saloner, PhD, have been studying ferumoxytol-enhanced MRI to image brain AVMs and determine if active inflammation correlates with silent hemorrhage and a more dangerous natural history of the disease. Ferumoxytol is an iron oxide nanoparticle that is taken up by macrophages that migrate to sites of inflammation in the brain, in this case an AVM. The degree of macrophage infiltration has been strongly correlated to the presence of hemosiderin, and imaging experts believe it may be a useful surrogate to detect silent hemorrhages.

In a pilot study, the UCSF group showed that ferumoxytol could reliably image macrophages that were infiltrating an AVM.[5] Now they are enrolling patients with unruptured AVMs in a larger study to validate the technique and gather evidence for whether it should be routinely implemented for every patient that arrives at the hospital with an unruptured AVM. These sophisticated techniques could ensure a safer future for patients with dangerous but resectable AVMs who might otherwise be told that they don't need surgery.

1. Mohr JP, Parides MK, Stapf C, et al. Medical management with or without interventional therapy for unruptured brain arteriovenous malformations (ARUBA): a multicenter, non-blinded, randomised trial. **Lancet** 2014;383(9917):614-21.

2. Rutledge WC, Alba AA, Nelson J, Halbach VV, Kim H, Lawton MT. Treatment and outcomes of ARUBA-eligible patients with unruptured brain arteriovenous malformations at a single institution. **Neurosurg Focus** 2014;37(3):E8.

3. Potts MB, Lau D, Abla AA, Kim H, Young WL, Lawton MT; UCSF Brain AVM Study Project. Current surgical results with low-grade brain arteriovenous malformations. **J Neurosurg** 2015;122(4):912-20.

4. Abla AA, Nelson J, Kim H, Hess CP, Tihan T, Lawton MT. Silent arteriovenous malformation hemorrhage and the recognition of "unruptured" arteriovenous malformation patients who benefit from surgical intervention. **Neurosurgery** 2015;76(5):592-600.

5. Hasan DM, Amans M, Tihan T, Hess C, Guo Y, Cha S, Martin AJ, Lawton MT, Neuwelt EA, Saloner DA, Young WL. Ferumoxytol-enhanced MRI to image inflammation with human brain arteriovenous malformations: a pilot investigation. **Transl Stroke Res** 2012;3 (Suppl 1):166-73.

Residency Program Graduates

Tene A. Cage, MD, was born and raised in Santa Clara, California. She attended Harvard University as an undergraduate where she graduated cum laude with a degree in biology and a certificate in neurobiology. She completed a senior thesis on cortical neuron differentiation for which she received summa cum laude honors. After graduation, she spent time in Ghana, West Africa conducting research on women's social experiences after medical illness.

Cage then entered the UCSF School of Medicine in 2003 where she became interested in neurosurgery. During medical school, she was awarded the American Brain Tumor Association (ABTA) Medical Student Fellowship, the UCSF Genentech Foundation Fellowship, and the Howard Hughes Medical Institute Research Fellowship to conduct research in the laboratories of Jeanette Hyer, PhD, and Nalin Gupta, MD, PhD, with collaboration from Arturo Alvarez-Buylla, PhD, investigating developmental patterns of medulloblastoma dissemination. She was awarded the Lucien J. Rubenstein award from the ABTA and the Young Investigator Award from the Pediatric Brain Tumor Foundation for this work. Cage graduated from medical school with Alpha Omega Alpha Honors and began her neurosurgical training at UCSF in 2010.

During her residency, she continued to develop an interest in pediatric and adult brain tumors and has conducted several clinical studies in these populations. In 2014, she joined the laboratory of William Weiss, MD, PhD, to investigate the role of MYCN signaling in mouse models of medulloblastoma. She was also recognized for providing outstanding clinical care to her patients with the Howard Nafzigger UCSF Neurosurgery Resident Award in 2013 and the Exceptional Physician Award from UCSF Medical Center in 2015.

Upon graduating from residency in 2016, Cage plans to begin a fellowship at Zuckerberg San Francisco General Hospital with Geoffrey Manley, MD, PhD. She will also complete a Master's Degree in Clinical Research at UCSF, during which time she will continue to explore her interest in neuro-oncology, focusing her research on health disparities in neurosurgical and neuro-oncological care. She then anticipates a career in academic neurosurgery where she hopes to continue to combine her interest in neuro-oncology and her commitment to addressing health disparities in neurosurgery.

Residency Program Graduates' Selected Publications

Cage TA, Chanthery Y, Chesler L, Grimmer M, Knight Z, Shokat K, Weiss WA, Gustafson WC. Downregulation of MYCN through PI3K inhibition in mouse models of pediatric neural cancer. Front Oncol 2015;5:111.

Cage TA, Clark AJ, Aranda D, Gupta N, Sun PP, Parsa AT, Auguste KI. A systematic review of treatment outcomes in pediatric patients with intracranial ependymomas. J Neurosurg Pediatr 2013;11(6):673-81.

Cage TA, Samagh SP, Mueller S, Nicolaides T, Haas-Kogan D, Prados M, Banerjee A, Auguste KI, Gupta N. Feasibility, safety, and indications for surgical biopsy of intrinsic brainstem tumors in children. Childs Nerv Syst 2013;29(8):1313-9.

Cage TA, Louie JD, Liu SR, Alvarez-Buylla A, Gupta N, Hyer J. Distinct patterns of human medulloblastoma dissemination in the developing chick embryo nervous system. Clin Exp Metastasis 2012;29(4):371-80.

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, Lee AT, Tsai C, Halabi C, Barbaro NM, Auguste KI, Garcia PA, Chang EF. Seizure types and frequency in patients who "fail" temporal lobectomy for intractable epilepsy. Neurosurgery 2013;73(5):838-44.

Englot DJ, Hinkley LB, Kort NS, Imber BS, Mizuiri D, Honma SM, Findlay AM, Garrett C, Cheung PL, Mantle M, Tarapore PE, Knowlton RC, Chang EF, Kirsch HE, Nagarajan SS. Global and regional functional connectivity maps of neural oscillations in focal epilepsy. Brain 2015;138(8):2249-62.

Englot DJ, Nagarajan SS, Imber BS, Raygor KP, Honma SM, Mizuiri D, Mantle M, Knowlton RC, Kirsch HE, Chang EF. Epileptogenic zone localization using magnetoencephalography predicts seizure freedom in epilepsy surgery. Epilepsia 2015;56(6):949-58.

Crane CA, **Han SJ,** Ahn BJ, Oehlke J, Kivett V, Fedoroff A, Butowski N, Chang SM, Clarke J, Berger MS, McDermott MW, Prados MD, Parsa AT. Individual patient-specific immunity against high-grade glioma after vaccination with autologous derived peptides bound to the 96 KD chaperone protein. Clin Cancer Res 2013;19(1):205-14.

Han SJ, Rolston JD, Molinaro A, Clarke JL, Prados MD, Chang SM, Berger MS, Butowski N. Phase II trial of 7 days on/7 days off temozolomide for patients with recurrent high-grade glioma. Neuro Oncol 2014;16(9):1255-62.

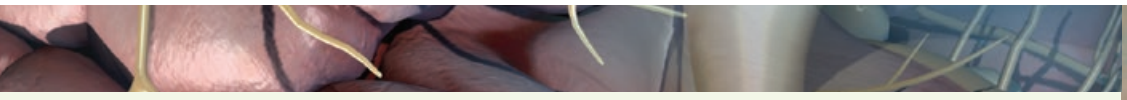
Han SJ, Rutledge WC, Molinaro AM, Chang SM, Clarke JL, Prados MD, Taylor JW, Berger MS, Butowski NA. The effect of timing of concurrent chemoradiation in patients with newly diagnosed glioblastoma. Neurosurgery 2015;77(2):248-53.

Han SJ, Rolston JD, Zygourakis CC, Sun MZ, McDermott MW, Lau CY, Aghi MK. Preventing delays in first-case starts on the neurosurgery service: A resident-led initiative at an academic institution. J Surg Educ 2016;73(2):291-5.

Dario J. Englot, MD, PhD, received his undergraduate degree from the University of Scranton in 2003, where he studied neuroscience, philosophy, and biochemistry. He then earned his PhD in neuroscience (2009) and MD (2010) from Yale University, under the mentorship of Hal Blumenfeld, MD, PhD. His dissertation research used electrophysiology and fMRI to examine the effects of focal seizures on brain networks in rats, and was supported by an NIH F30 grant.

During his neurosurgery residency at UCSF, Englot further developed his interests in epilepsy and functional neurosurgery. His primary clinical and research mentor has been Edward Chang, MD, and he also completed research projects with Mitchel Berger, MD, Michael McDermott, MD, Michael Lawton, MD, and Paul Larson, MD. During the year of his residency that was dedicated to research, Englot worked with Sri Nagarajan, PhD, in UCSF's magnetoencephalography (MEG) laboratory studying functional connectivity in epilepsy patients, work that was supported by an NIH F32 award.

After graduation, Englot will be completing a one-year clinical and research fellowship in epilepsy and functional neurosurgery at Vanderbilt. In July 2017, he will be joining the neurosurgery faculty at Duke with a clinical focus in epilepsy surgery. He plans to continue his research into brain networks in epilepsy, building a human neuroimaging and electrophysiology laboratory at Duke.



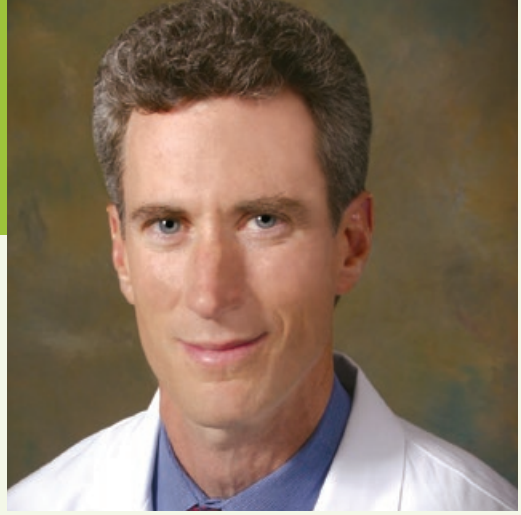
Seunggu Jude Han, MD, received his undergraduate degree in neuroscience from the University of California, Los Angeles. He then attended medical school at UCSF, during which he developed an interest in surgical neuro-oncology and tumor immunology under the mentorship of Andrew Parsa, MD, PhD. Han received support from the Howard Hughes Medical Institute to study mechanisms of immunoresistance in malignant gliomas in the setting of an early phase clinical investigation of a novel vaccine using a heat-shock protein.

Since joining UCSF's neurosurgery residency program, Han has maintained an interest in neuro-oncology, immunotherapy, and clinical trials. He was awarded the Neurosurgery Research and Education Foundation Fellowship to work in the laboratory of Hideho Okada, MD, PhD, studying the immune landscape and exploring novel immunotherapeutic strategies for meningiomas. In collaboration with Nicholas Butowski, MD, and Manish Aghi, MD, PhD, Han is also a co-investigator for an NIH-funded, phase I trial investigating real-time convection enhanced delivery of nanoliposomal irinotecan for recurrent high-grade gliomas. He also developed a strong interest in functional mapping for tackling tumors of eloquent brain under the mentorship of Mitchel Berger, MD.

Han has also served as the resident leader in the Department's quality improvement efforts. He has spearheaded multiple program-specific quality improvement initiatives and published nine peer-reviewed manuscripts in quality improvement research.

Upon graduation, Han will remain at UCSF as the Ho-Hungerford Endowed Neuro-Oncology Fellow in the Department of Neurological Surgery. He will continue to pursue his research in eloquent tumor surgery and clinical trial development.

Focus on Faculty



Michael Lawton, MD, is the Tong-Po Kan endowed chair, professor and vice chair of the Department of Neurological Surgery at UCSF. He is chief of vascular neurosurgery, specializing in the surgical treatment of aneurysms, arteriovenous malformations (AVMs), arteriovenous fistulas, cavernous malformations and cerebral revascularization, including carotid endarterectomy. As chief of one of the busiest cerebrovascular services on the West Coast for over 18 years, he has experience in surgically treating over 4000 brain aneurysms and over 700 AVMs. He also practices the endovascular treatment of aneurysms.

Lawton co-directs and conducts his research at the UCSF Center for Cerebrovascular Research, a collaborative research group funded by grants from the National Institutes of Health that investigates the physiology of cerebral circulation and the pathophysiology of vascular malformations. His basic science investigations study the formation, underlying genetics and rupture of brain AVMs, as well as the hemodynamics, rupture and computational modeling of brain aneurysms. His clinical investigations study the anatomy of microsurgical approaches to vascular lesions and the outcomes of aneurysm, AVM and bypass surgery. He is the principal investigator of an NIH U54 grant and program director of the Brain Vascular Malformation Consortium, a multicenter group studying malformations associated with hereditary hemorrhagic telangiectasia, cavernous malformations and Sturge–Weber Syndrome.

He has published over 450 peer-reviewed articles, over 70 book chapters and 3 textbooks, including *Seven AVMs: Tenets and Techniques for Resection* and *Seven Aneurysms: Tenets and Techniques for Clipping,* which have won numerous awards. His awards include the Young Neurosurgeon Award from the World Federation of Neurological Societies, the Harold Rosegay Teaching Award, and the Diane Ralston Clinical and Basic Science Teaching Award. He has given over 600 invited lectures nationally and internationally, including visiting professorships at over 40 neurosurgical institutions. He has been active in resident teaching, directing the CNS Anatomy Course for Senior Residents, co-directing the American Association of Neurological Surgeons Vascular Skills Course, and directing industry-sponsored anatomy courses. He sponsors an observership in vascular neurosurgery that has hosted more the 100 neurosurgeons and residents nationally and internationally. Finally, he co-founded Mission:BRAIN, a teaching mission to raise the level of neurosurgery practiced in developing countries, and has conducted seven missions in Mexico and the Philippines.

Selected Publications

Lawton MT, Rutledge WC, Kim H, Stapf C, Whitehead KJ, Li DY, Krings T, terBrugge K, Kondziolka D, Morgan MK, Moon K, Spetzler RF. Brain arteriovenous malformations. Nat Rev Dis Primers 2015;1:15008.

Kim H, Abla AA, Nelson J, McCulloch CE, Bervini D, Morgan MK, Stapleton C, Walcott BP, Ogilvy CS, Spetzler RF, **Lawton MT.** Validation of the supplemented Spetzler-Martin grading system for brain arteriovenous malformations in a multicenter cohort of 1009 surgical patients. Neurosurgery 2015;76(1):25-31; discussion 31-3.

Han SJ, Englot DJ, Kim H, **Lawton MT.** Brainstem arteriovenous malformations: anatomical subtypes, assessment of "occlusion in situ" technique, and microsurgical results. J Neurosurg 2015;122(1):107-17.

Garcia RM, Ivan ME, **Lawton MT.** Brainstem cavernous malformations: surgical results in 104 patients and a proposed grading system to predict neurological outcomes. Neurosurgery 2015;76(3):265-78.

Rodríguez-Hernández A, Sughrue ME, Akhavan S, Habdank-Kolaczkowski J, **Lawton MT.** Current management of middle cerebral artery aneurysms: surgical results with a "clip first" policy. Neurosurgery 2013;72(3):415-27.

Sughrue ME, Saloner D, Rayz VL, **Lawton MT.** Giant intracranial aneurysms: evolution of management in a contemporary surgical series. Neurosurgery 2011;69(6):1261-70; discussion 1270-1.

Sanai N, Zador Z, **Lawton MT.** Bypass surgery for complex brain aneurysms: an assessment of intracranial-intracranial bypass. Neurosurgery 2009;65(4):670-83.

Lawton MT; UCSF Brain Arteriovenous Malformation Study Project.

Spetzler-Martin Grade III arteriovenous malformations: surgical results and a modification of the grading scale. Neurosurgery 2003;52(4):740-8; discussion 748-9.

Lawton MT. Basilar apex aneurysms: surgical results and perspectives from an initial experience. Neurosurgery 2002;50(1):1-8; discussion 8-10.

Neurosurgery News & Notes

The 11th Annual UCSF Spine Symposium was held in San Francisco on June 3-4, 2016. This popular two-day event, chaired by Praveen Mummaneni, MD, and Shane Burch, MD, saw a record attendance of 125 health care providers. Each year the course emphasizes pioneering trends in diagnostic and therapeutic strategies for patients suffering from spinal disorders and features internationally renowned guest faculty. The symposium is designed for neurosurgeons, orthopedists, nurses, physical therapists, physiatrists, anesthesiologists, pain specialists and primary care providers.

A New Instrument to Measure Quality of Life for Patients with Meningiomas

While quality-of-life studies for aggressive brain tumors like glioblastoma have been increasing over the last decade, there have been few for other tumor types. A new tool developed at UCSF is designed to gather data on quality of life for meningioma patients. Led by **Michael McDermott, MD,** this initiative will be one of the first to look at quality-of-life measures specific to intracranial meningioma sites.

"There can be a significant difference between what surgeons and patients think is a good surgical outcome," says McDermott. "It is important to consider how the treatments we choose affect our patients' daily lives, but currently we have no data to see where we may need to improve."

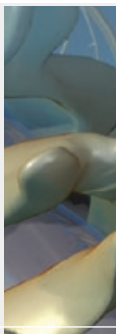
The new tool, called MENG-QOL, is a modified version of the Functional Assessment of Cancer Therapy-Brain and the SF-36 outcome instruments. Following surgery or radiosurgery, patients fill out a web-based questionnaire to rate quality-of-life metrics such as pain, coordination and ability to perform activities of daily living. The tool is currently being used at the UCSF Brain Tumor Center, but McDermott and his colleagues plan to expand the data collection to a total of 10 other sites.

Mitchel S. Berger, MD, Chair of the Department of Neurological Surgery, has been appointed to a Blue Ribbon Panel of scientific experts, cancer leaders and patient advocates that will help to guide the National Cancer Moonshot Initiative. His role will be to help inform the scientific direction and goals of the National Cancer Institute for the initiative.

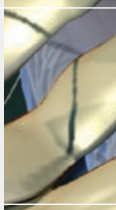
Kurtis Auguste, MD, has been elected to a three-year term as Chief of Surgery by the surgeons at UCSF Benioff Children's Hospital Oakland.

Manish Aghi, MD, PhD, was selected to be scientific program chair of the annual meeting of the Society of Neuro-Oncology. He will also serve on the AANS/CNS Joint Commission on Tumors as treasurer (2016-2018) and chair (2018-2020).

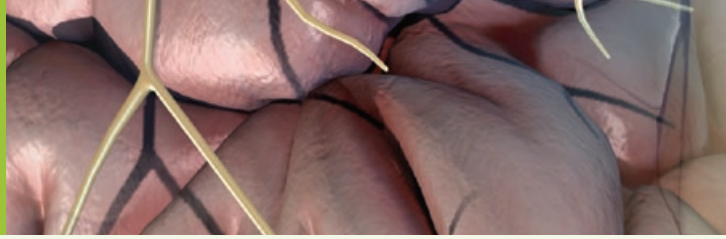
The Scoliosis Research Society (SRS) has nominated **Christopher Ames, MD,** for the both the Whitecloud Award and the Hibbs Award, recognizing his work on novel methods of risk stratification and complication prediction for adult spinal deformity. The award recipients will be announced later this year at the annual meeting of the SRS and at the International Meeting on Advanced Spine Techniques.



Omar Flamenco joins the UCSF Spine Center as our new Practice Manager. He brings over 15 years of management experience working in ambulatory outpatient surgery facilities. He will be managing the neurospine services outpatient clinic.



Praveen Mummaneni, MD, recently served as chair of Spine Summit 2016 – the 32nd Annual Meeting of the AANS/CNS Section on Disorders of the Spine and Peripheral Nerves. He has also recently been named editor in chief of *Journal of Neurosurgery: Spine* and was an editor of the best-selling *Handbook of Spine Surgery, 2nd Edition.*



Scientists at UCSF's Brain and Spinal Injury Center Identify a Potential New Drug to Treat Traumatic Brain Injury

Neurotrophins and their receptors are the focus of many central nervous system injury studies due to their roles in the growth and survival of neurons. p75NTR is a neurotrophin receptor with low specificity that can facilitate both life and death of neurons depending on what molecules it binds to. During early human development expression of p75NTR is high, and then declines in adulthood. However, following CNS injury, its expression increases.

Investigators in the laboratory of **Michael Beattie, PhD,** and **Jacqueline Bresnahan, PhD,** have been looking for a way to block the apoptotic effect of p75NTR expression and simultaneously increase its regeneration effect through neurite outgrowth. They appear to have found it through in vitro studies of EVT901 – a piperazine derivative that blocks binding of pro-nerve growth factors that induce apoptosis. The drug was developed by Sanofi-Aventis and tested in collaboration with UCSF.

The role of p75NTR in growth and survival of neurons depends upon interactions with other receptors. When it interacts with the neurotrophin receptor trkA, it is protective, but when it forms oligomers with some other receptors, like sortilin, it induces apoptosis. EVT901 also inhibits p75NTR oligomerization, possibly further reducing initiation of cell death.

In a separate study, the investigators found that p75NTR may be related to the peripheral inflammatory response – a well-established cause of secondary injury following a primary CNS insult. EVT901 inhibition of p75NTR also blocks the inflammatory response in vivo, and circulation of peripheral pro-inflammatory monocytes was greatly reduced in mice following injury, while their function was better compared to untreated mice. In light of the evidence that EVT901 has a neuroprotective effect following brain injury, a Congressionally Directed Medical Research Programs (CDMRP) grant to study EVT901 in rats has been recommended for funding.

Principal Investigator Michael Beattie, PhD, and Associate Specialist Sangmi Lee, PhD, in the laboratories of the Brain and Spinal Injury Center.

Delbary-Gossart S, Lee S, Baroni M, et al. A novel inhibitor of p75-neurotrophin receptor improves functional outcomes in two models of traumatic brain injury. **Brain.** 2016 Apr 15. [Epub ahead of print].

Lee S, Mattingly A, Lin A, Sacramento J, et al. A novel antagonist of p75NTR reduces peripheral expansion and CNS trafficking of pro-inflammatory monocytes and spares function after traumatic brain injury. **J Neuroinflammation.** 2016;13(1):88.

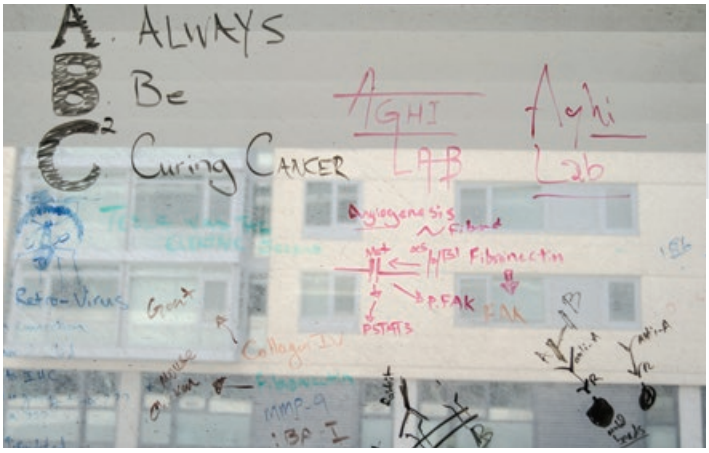
Joint Commission Re-certification for Traumatic Brain Injury

Zuckerberg San Francisco General Hospital has been re-certified by the Joint Commission for traumatic brain injury. The newly redesigned trauma center features an expanded neuro ICU, including state-of-the-art monitoring equipment and 3T MRI scanners.

The UCSF Brain and Spinal Injury Center (BASIC), based at Zuckerberg General Hospital, continues to lead translational neurotrauma research through several national and international initiatives to collect data on imaging, biomarkers and outcomes. The Transforming Research and Clinical Knowledge (TRACK) studies for TBI and SCI are expansive partnerships with the public and private sectors to create common repositories for these data. A grant application for TRACK-SCI, led by principal investigators **Michael Beattie, PhD,** and **Sanjay Dhall, MD,** was recently recommended for federal funding by the Congressionally Directed Medical Research Programs.

For more on TRACK-TBI and TRACK-SCI, visit brainandspinalinjury.org

UCSF neurosurgery resident **Doris Wang, MD, PhD,** received the AANS/CNS Stereotactic and Functional Neurosurgery Resident Award for her abstract "Comparison of GPi Local Field Potential Characteristics in Patients Parkinson's Disease, Craniocervical Dystonia, and Generalized Dystonia." The award was presented by Aviva Abosch, MD, PhD, president of the American Society for Stereotactic and Functional Neurosurgery and UCSF Neurological Surgery alumnus.



Writing on the Wall: the Aghi Lab investigates the microenvironment of brain tumors and members keep their goals in sight on a writable window.

Research Awards in the Aghi Lab

Neurosurgeon **Manish Aghi, MD, PhD,** is serving as a mentor for several new research awards given to members of his lab, showcasing some of the talent and ingenuity of the students, residents and postdoctoral scholars in the Department of Neurological Surgery. It is partially due to their achievements that the Department has remained first in NIH funding among academic neurosurgery programs for over a decade.

• MD/PhD student **Arman Jahangiri** was awarded an F31 grant from the NIH for the study "ß1 integrin/c-Met: a receptor complex driving invasive resistance to anti-angiogenic therapy in glioblastoma." Jahangiri also won the Journal of Neuro-Oncology Award at the 2016 meeting of the American Association of Neurological Surgeons for an abstract written with Aghi entitled "From Bench to Bedside: NIH Funding for Neurosurgeons from 1991 to 2015."

• Postdoctoral scholar **Garima Yagnik, PhD,** received a T32 grant from the NIH for the study "Role of Matrix Metalloproteinase 9 (MMP) in Resistance to Anti-angiogenic Therapy."

• UCSF medical student **Daniel Hoffman** was awarded a Howard Hughes Medical Institute fellowship for the study "Role of Oxidized MIF in Glioblastoma Invasiveness and Tumor Microenvironment."

U.S. Patent Issued to Starr Lab for Device to Treat Movement Disorders

The laboratory of **Philip Starr, MD, PhD,** is focused on understanding the brain network abnormalities underlying movement disorders and how therapeutic interventions correct those abnormalities. In 2014, Starr and members of his lab used electrocorticography to discover a pattern of abnormal synchronization in the electrical spiking of neuronal populations in the motor cortex of patients with Parkinson's disease. They were able to show that treatment with deep brain stimulation ameliorates symptoms of the disease by disrupting this abnormal synchronization.

Now Starr and his colleagues are developing a system that can measure excessive cortical synchronization in a patient's brain so that the settings of deep brain stimulation devices can be adjusted automatically. Current deep brain stimulators deliver constant stimulation to the brain, which can cause side effects.

A new U.S. patent – for "Methods and Systems for Treating Neurological Movement Disorders" – has been issued for the system to Starr, **Jill Ostrem, MD, Coralie de Hemptinne, PhD, and Nicole Swann, PhD.**