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neurosurgery news

Cerebrovascular Disorders: Inside the Operating Room and the First Pre-clinical Model of Arteriovenous Malformation

Dr. Michael Lawton's operating room is cool, dim, and quiet. The only light comes from a single overhead surgical lamp and from the bright bulb of an operating microscope. The microscope has two sets of eyepieces that allow Dr. Lawton, chief of vascular neurosurgery at UCSF, and neurosurgical resident Matthew Tate to peer into a tiny opening in their patient's cerebellum and begin their search for a small cavernous malformation that is causing imbalance, dyscoordination, and double vision.

A cerebral cavernous malformation is an abnormal cluster of enlarged capillaries or veins that have weak endothelial linings prone to leaking blood. Like its relatives the arteriovenous malformation (AVM) and the aneurysm, the cavernous malformation is a type of cerebrovascular disorder that can cause bleeding in the brain, seizures, or neurological deficits. It may also remain asymptomatic and not require any treatment.

MR images taken before surgery indicate that the malformation Dr. Lawton is looking for is situated in the cerebral peduncle, an area of the brainstem that houses the upper motor neurons and important fiber tracts. Nearly one third of the lesions in Dr. Lawton's surgical experience have been found in the brainstem.

Beginning in the cerebellum, he carefully cuts through the clear, filmy arachnoid membrane, causing the cerebral spinal fluid to drain out of the subarachnoid space and opening up a surreal landscape. He works his way past the white bands of the lower cranial nerves, through brambles of veins no thicker than strands of angel hair pasta, skirting the glistening, pink vertebral artery with its extending tentacle, PICA. When he arrives at the cerebral peduncle, he makes a tiny incision into the tissue, releasing a rush of blood. "Do you see that? That's the hematoma," he says. Visiting neurosurgical fellows watch on a screen that displays what Dr. Lawton views through the microscope. In a normal peduncle, the incision would only have found more tissue. But the bleeding has signaled the site of the cavernous malformation. Delving further into the tissue Dr. Lawton alights upon the mass and begins to separate it from the dura using miniscule surgical instruments he has designed himself. On the screen, the malformation is a sickly greenish hue, distinguishing it from the surrounding healthy tissue, and it is quickly removed without violating the normal parts of the brain.

Cerebrovascular disorders are rare but serious conditions that are generally associated with high mortality and morbidity. The majority of aneurysms, for instance, are only discovered once they rupture and patients are taken to the hospital with subarachnoid hemorrhage. Following rupture, roughly 40 percent of patients do not survive the first 24 hours and there is a high probability of the aneurysm re-bleeding or for new aneurysms to form after the hemorrhage has been treated. Surgery for an aneurysm then becomes a chance to defuse a ticking bomb; the most important thing to know is which wire to clip.

Clipping aneurysms is a specialty of Dr. Lawton's. In his career, he has repaired close to 3,000 of them using this technique and says that the survival rate for patients who live long enough to receive treatment is approximately 80%. By inserting metal clips at the base of the aneurysms, neurosurgeons can stop the flow of blood into the aneurysm sac, preventing it from filling and bursting. Although anatomy is generally conserved, each person's brain presents its own unique set of challenges, and there are many types of aneurysms to contend with.

Aneurysms typically form on the trunks of arteries, as opposed to their fine branches, and often at the junctions where they fork. They can manifest as one simple sac protruding off the wall of the artery like a ripe berry or a complicated mass wrapped around vital structures of the brain. These more complicated aneurysms may require multiple clips at different sites where blood enters them or may require complete occlusion of the vessel and a bypass operation for the necessary blood flow to be re-routed. Clipping an aneurysm requires extraordinary skill and experience, but when successful, restores proper flow through the artery and permanently repairs the aneurysm.

Some aneurysms can also be treated through an endovascular procedure called coiling, which

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Surgical removal is the only treatment for cavernous malformations and is often curative.

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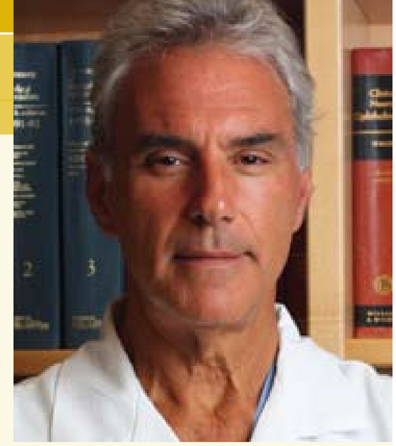
looking to the future



In 2005, the International Subarachnoid Hemorrhage Trial compared neurosurgical clipping to endovascular coiling for the treatment of ruptured aneurysms. The results of the trial indicated that coiling was safer than clipping, but that clipping was a more definitive treatment. While many centers have abandoned surgery since the advent of endovascular techniques, the debate that has ensued over which procedure is best has made it clear to me that there is a need for both options. In the future, neurosurgeons will need both interventional and surgical training. Our Chief of Vascular Neurosurgery, Michael Lawton MD, is currently completing an endovascular fellowship, allowing him to better guide his patients through the process of deciding which procedure is best for them individually.

According to the University Hospital Consortium database, UCSF has the busiest vascular neurosurgery practice in California and is in the top 10 in the nation (we are first in the nation for aneurysm clipping). We have also recently been joined by talented neurosurgeon Michael Huang MD, who completed a fellowship in skull base and cerebrovascular surgery at the University of South Florida.

In the laboratories of the UCSF Center for Cerebrovascular Research, our faculty is performing some exciting research into the pathophysiology of cerebrovascular disease and the future of medical therapies (see pages 2- 3). One of these studies is being led by Tomoki Hashimoto MD, who has been given an R01 award from the NIH to study why aneurysms occur more frequently in post-menopausal women and the potentially protective effect of estrogen. The results may lead us closer to understanding how biochemistry influences the pathology of this disease and how to develop therapies against it. Another area of research interest is stem cell therapy and preliminary studies are being planned in animal models to see how stem cells behave in the environment of a cerebrovascular disorder.

Mitchel S. Berger MD

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involves threading a catheter into the aneurysm and packing it full of platinum wires to form a plug. Coiling is less invasive than surgery and patients generally have shorter hospital stays and recovery times. But it carries the risk that over time the intense blood flow at the weakened portion of the arterial wall may pack the wire back, causing the aneurysm to reform and potentially burst. In such cases the aneurysm may need to be re-coiled or clipped.

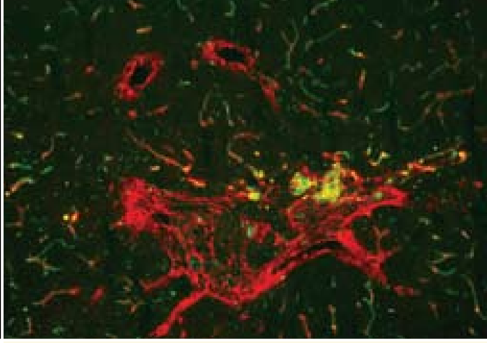
Dr. Lawton, who is completing an endovascular fellowship to hone the coiling technique, believes it is important to be able to offer patients both options. "Being able to perform both procedures allows me to better guide my patients through the decision and give them continuity of care," he says. Some types of aneurysms, however, may not be suitable for coiling. Lawton has recently detailed these aneurysms in his book *Seven Aneurysms: Tenets and Techniques for Clipping*.[1] Now in its second printing and a Spanish translation, the textbook describes the types of aneurysms that are better treated with microsurgery.

But what makes people at risk for developing cerebrovascular disorders in the first place? This is a question that Dr. Lawton and his colleague William L. Young, director of the UCSF Center for Cerebrovascular Research, have been examining in the laboratory. Together with a team of investigators from the Departments of Anesthesia, Neurological Surgery, and Neurology, they have been looking at the hemodynamics involved in these disease processes to better predict their behavior and determine their natural history.

First Model of Arteriovenous Malformation

The first animal model of brain AVM that recapitulates key features of the human disease was recently created under the direction of Dr. Young and Dr. Hua Sua at the UCSF Center for Cerebrovascular Research.[2] The model — in the adult mouse — manipulates the genotype known to

Abnormal connections between veins and arteries form in the brains of adult mice in a new experimental model of arteriovenous malformation. A large abnormal dysplastic vascular structure is shown here; green lectin marks endothelial cells and red platelet-derived growth factor receptor ß marks a profusion of pericytes covering the structure.



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cause the human disease hereditary hemorrhagic telangiectasia (HHT) type 2. Approximately 2% of AVMs are thought to be inherited and the vast majority of these are found with HHT. HHT type 2 is associated with mutations in activin receptor-like kinase 1 (ALK1). In the new model, the gene for ALK1 is conditionally deleted in a localized area of the brain (the basal ganglia) and a viral vector containing vascular endothelial growth factor (VEGF) is used to simultaneously stimulate new vessel growth. Both an increase in VEGF and ALK1 deletion are necessary for the formation of AVMs in the mice.

A unique attribute of the new model is that the AVMs form in adult mice, demonstrating that it is not necessarily a developmental disease. “Almost every textbook describes AVM as a congenital disorder,” says Dr. Young. “But there is very little evidence for that and the adult onset in our study shows experimental proof of principle that AVM is not necessarily a developmental phenotype.”

The model is also the first in which it will be possible to screen drugs for clinical trials. Few non-surgical treatments for AVM exist, although a pilot study at UCSF has shown that the drugs doxycycline and minocycline are well tolerated and could be studied in larger trials.[3]

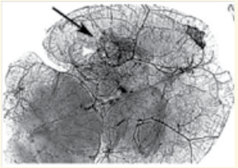
Similar to findings in their model of aneurysms, the UCSF researchers see evidence that vascular remodeling may be responsible for the formation of AVMs. As the body forms new vessels, there is an increase in chemicals released by the vascular wall and bone-marrow derived cells, such as matrix metalloproteinases. These proteolytic enzymes degrade structural elements of the blood vessel wall and are critical in the processes of inflammation and angiogenesis. “You can think of it like new construction,” says Dr. Young. “To renovate a city block, you must tear down the buildings that are there. To grow new blood vessels, you must break down the structural proteins of the old wall.” If the new construction goes awry, arteries and veins can form abnormal connections (an AVM). While the exact mechanism for this is unknown, compounds that block inflammation and angiogenesis could interfere with the abnormal connecting process and many are already FDA-approved for other diseases. Among them are tetracyclines, statins, and anti-angiogenic compounds such as VEGF inhibitors and the drug thalidomide, which is given to patients with HHT to stop nose bleeds. The Center’s NIH Program Project Grant is also studying other molecules that could be useful, such as the anti-angiogenic nuclear transcription factor Hox A5.

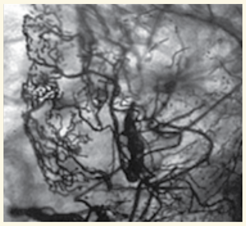
In addition to providing a platform for testing new therapies, the new model will be used to identify similarities between sporadic AVMs and those caused by genetic disorders. With Dr. Young as the program director, UCSF is the coordinating center for the Brain Vascular Malformation Consortium, part of the NIH Rare Diseases Clinical Research Network. This program is examining several brain disorders linked to abnormal brain angiogenesis and associated with hemorrhagic stroke. One of the projects is the first large-scale study to compare the natural history of HHT AVMs to that of the more common sporadic, non-inherited AVMs.

1. Lawton MT. Seven Aneurysms: Tenets and Techniques for Clipping. Thieme New York, NY, 2011

2. Walker EJ, Su H, Shen F, Choi EJ, Oh SP, Chen G, Lawton MT, Kim H, Chen Y, Chen W, Young WL. Arteriovenous malformation in the adult mouse brain resembling the human disease. Ann Neurol 2011;69(6):954-62.

3. Frenzel T, Lee CZ, Kim H, Quinnine NJ, Hashimoto T, Lawton MT, Guglielmo BJ, McCulloch CE, Young WL. Feasibility of minocycline and doxycycline use as potential vasculostatic therapy for brain vascular malformations: pilot study of adverse events and tolerance. Cerebrovasc Dis 2008;25(1-2):157-63.





Large tangled vessels resembling a diffuse arteriovenous malformation formed in the brains of adult mice at the site where viral vectors were injected to induce vascular endothelial growth factor overexpression and cause conditional deletion of the Alk-1 gene (black arrow).[2]

selected publications

Chang EF, Gabriel RA, Potts MB, Berger MS, **Lawton MT.** Supratentorial cavernous malformations in eloquent and deep locations: surgical approaches and outcomes. J Neurosurg 2011;114(3):814-27.

Lawton MT, Kim H, McCulloch CE, Mikhak B, Young WL. A supplementary grading scale for selecting patients with brain arteriovenous malformations for surgery. Neurosurgery 2010;66(4):702-13.

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

Sanai N, Tarapore P, Lee AC, **Lawton MT.** The current role of microsurgery for posterior circulation aneurysms: a selective approach in the endovascular era. Neurosurgery 2008;62(6):1236-53.

Lawton MT, Quiñones-Hinojosa A, Chang EF, Yu T. Thrombotic intracranial aneurysms: classification scheme and management strategies in 68 patients. Neurosurgery 2005;56(3):441-54.

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 the busiest cerebrovascular service on the West Coast for over 14 years, he has experience in surgically treating nearly 3,000 brain aneurysms and over 500 AVMs. He is also trained in the endovascular treatment of aneurysms.

Dr. Lawton conducts his research at the UCSF Center for Cerebrovascular Research, a collaborative research group funded by a program project grant from the NIH 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 efficacy of aneurysm, AVM, and bypass surgery.

He has published over 250 peer-reviewed articles, over 40 book chapters, and two textbooks, including his single-author book, *Seven Aneurysms: Tenets and Techniques for Clipping.* 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.

focus on faculty

selected publications

Richardson RM, Kells AP, Rosenbluth KH, Salegio EA, Fiandaca MS, Larson PS, Starr PA, Martin AJ, Lonser RR, Federoff HJ, Forsayeth JR, Bankiewicz KS. Interventional MRI-guided putaminal delivery of AAV2-GDNF for a planned clinical trial in Parkinson's disease. Mol Ther 2011;19(6):1048-57.

Richardson RM, Kells AP, Martin AJ, Larson PS, Starr PA, Piferi PG, Bates G, Tansey L, Rosenbluth KH, Bringas JR, Berger MS, Bankiewicz KS. Novel platform for MRI-guided convection-enhanced delivery of therapeutics: preclinical validation in nonhuman primate brain. Stereotact Funct Neurosurg 2011;89(3):141-51.

Richardson RM, Freed CR, Starr PS. Pallidal neuronal discharge in Parkinson's disease following intraputamenal fetal mesencephalic allograft. J Neurol Neurosurg Psychiatry 2011;82(3):266-71.

Richardson RM, Ostrem JL, Starr PA. Surgical repositioning of misplaced subthalamic electrodes in Parkinson's disease: location of effective and ineffective leads. Stereotact Funct Neurosurg 2009;87(5):297-303.

Richardson RM, Barbaro NM, Alvarez-Buylla A, Baraban SC. Developing cell transplantation for temporal lobe epilepsy. Neurosurg Focus 2008; 24(3-4):E17.

Mark Richardson MD, PHD completed undergraduate studies at the University of Virginia, majoring in environmental sciences, before obtaining an MS degree in physiology from the Medical College of Virginia (MCV). He then entered the MD/PhD program at MCV, where he developed an interest in adult neurogenesis while working with tissue resected during epilepsy surgery, leading to a pre-doctoral NIH National Research Service Award and initiation of a program to isolate neural progenitor cells from patients with brain injuries.

Dr. Richardson continued to develop his interest in functional and restorative neurosurgery after beginning training at UCSF in 2005. He has worked closely with Paul Larson MD and Philip Starr MD, PhD to develop an expertise in deep brain stimulation surgery and with Nicholas Barbaro MD in epilepsy surgery. In 2009, Richardson received a post-doctoral NIH National Research Service Award to gain experience with the delivery of therapeutic biologics to the non-human primate brain. During a year in the laboratory of Krys Bankiewicz MD, PhD, he was instrumental in the development and preclinical testing of a protocol for an upcoming gene therapy clinical trial for Parkinson's disease.

After completing residency in June 2011, Dr. Richardson has become Director of Adult Epilepsy Surgery and Co-Director of Functional Neurosurgery at the University of Pittsburgh Medical Center. His Translational Neurobiology Laboratory will merge studies of hippocampal neurogenesis in the human brain with non-human primate experiments to develop drug delivery strategies for neuromodulation in the temporal lobe.

William L. Young MD is the James P. Livingston Professor and vice chair of the Department of Anesthesia and Perioperative Care at UCSF. He is also professor of neurological surgery and neurology, and the director of the Center for Cerebrovascular Research (CCR). The CCR, a core group of UCSF faculty and staff pursuing various lines of inquiry in clinical neuroscience, focuses on improving our understanding of issues and problems in cerebrovascular disease using an integrative strategy of clinical and basic science approaches. A primary focus is vascular malformations of the brain, such as arteriovenous malformations and aneurysms that can result in hemorrhagic stroke. Dr. Young received his medical degree from the Indiana University School of Medicine and his clinical training at New York University. After subspecialty training in neurosurgical anesthesiology and post-doctoral training in circulatory physiology at Columbia University College of Physicians and Surgeons in New York, he joined the faculty there in 1985, where he was professor of anesthesiology, neurological surgery and radiology prior to moving to UCSF in 2000. He directs an NIH-funded research program in cerebrovasular disease, currently serves on the editorial boards of *of Stroke, BMC Neurology,* and *Anesthesiology,* and is the Review Articles editor of the *Journal of Neurosurgical Anesthesiology.*

selected publications

Walker EJ, Su H, Shen F, Choi EJ, Oh SP, Chen G, Lawton MT, Kim H, Chen Y, Chen W, **Young WL.** Arteriovenous malformation in the adult mouse brain resembling the human disease. Ann Neurol 2011;69(6):954-62.

Gao P, Chen Y, Lawton MT, Barbaro NM, Yang GY, Su H, Ling F, **Young WL.** Evidence of endothelial progenitor cells in the human brain and spinal cord arteriovenous malformations. Neurosurgery 2010;67(4):1029-35.

Su H, Kim H, Pawlikowska L, Kitamura H, Shen F, Cambier S, Markovics J, Lawton MT, Sidney S, Bollen AW, Kwok PY, Reichardt L, **Young WL**, Yang GY, Nishimura SL. Reduced expression of integrin alphavbeta8 is associated with brain arteriovenous malformation (BAVM) pathogenesis. Am J Pathol 2010;176(2):1018-27.

Gao P, Zhu Y, Ling F, Shen F, Lee B, Gabriel RA, Hao Q, Yang GY, Su H, **Young WL.** Nonischemic cerebral venous hypertension promotes a pro-angiogenic state via HIF-1 downstream genes and leukocyte-derived MMP-9. J Cereb Blood Flow Metab 2009;29(8):1482-90.

Chen Y, Zhu W, Bollen AW, Lawton MT, Barbaro NM, Dowd CF, Hashimoto T, Yang GY, **Young WL.** Evidence of inflammatory cell involvement in brain arteriovenous malformations. Neurosurgery 2008;62(6):1340-9.

Michael Sughrue MD attended undergraduate studies at the University of Oklahoma in Norman, OK and medical school at Columbia University College of Physicians and Surgeons in New York, where he graduated Alpha Omega Alpha. While at Columbia, he first became interested in the complement cascade while working in the lab of E. Sander Connolly MD.

Dr. Sughrue became a resident in the Department of Neurological Surgery in 2005, and has primarily focused on the treatment and management of skull base tumors and on novel therapies for malignant gliomas. His work has won several awards, including the Bitner award for the top abstract in Brain Tumor Research at the American Association of Neurological Surgeons meeting in 2010, and he received an NIH National Research Service Award to support research in complement biology in gliomas. During his residency, he published over 100 manuscripts in peer-reviewed journals, including many key papers in the area of meningiomas and vestibular schwannoma. He was guest editor of an issue of *Neurosurgery Clinics of North America* on minimally invasive intracranial neurosurgery. After graduating from UCSF, Dr. Sughrue will pursue a fellowship in minimally invasive neurosurgery in Sydney, Australia at the Prince of Wales Hospital with Charles Teo MBBS, FRACS. He will then return to Oklahoma to build the brain tumor center at the University of Oklahoma.

selected publications

Sughrue ME, Rutkowski MJ, Shangari G, Chang HQ, Parsa AT, Berger MS, McDermott MW. Risk factors for the development of serious medical complications after resection of meningiomas. J Neurosurg 201;114(3):697-704.

Sughrue ME, Kaur R, Kane AJ, Rutkowski MJ, Yang I, Pitts LH, Tihan T, Parsa AT. Intratumoral hemorrhage and fibrosis in vestibular schwannoma: a possible mechanism for hearing loss. J Neurosurg 2011;114(2):386-93.

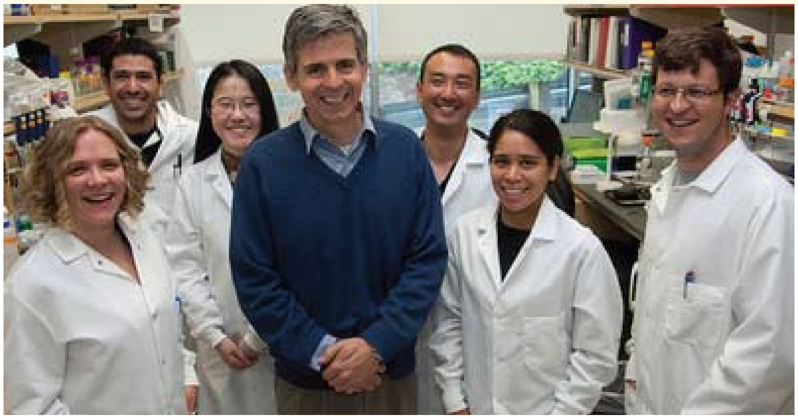
Sughrue ME, Kane AJ, Kaur R, Barry JJ, Rutkowski MJ, Pitts LH, Cheung SW, Parsa AT. A prospective study of hearing preservation in untreated vestibular schwannomas. J Neurosurg 2011;114(2):381-5.

Sughrue ME, Kaur R, Rutkowski MJ, Kane AJ, Kaur G, Yang I, Pitts LH, Parsa AT. Extent of resection and the long-term durability of vestibular schwannoma surgery. J Neurosurg 2011;114(5):1218-23.

Sughrue ME, Kaur R, Rutkowski MJ, Kane AJ, Yang I, Pitts LH, Parsa AT. A critical evaluation of vestibular schwannoma surgery for patients younger than 40 years of age. Neurosurgery 2010;67(6):1646-53.

UCSF Ranked in the Nation's Top 5 Neurosurgery Programs

US News and World Report's 2011-2012 edition of Best Hospitals ranks the neurosurgery and neurology programs at UCSF among the top five in the nation.



Arturo Alvarez-Buylla PhD, recipient of the 2011 Prince of Asturias Award for Technical and Scientific Research, with members of his lab.

Arturo Alvarez-Buylla PhD, professor and Heather and Melanie Muss Endowed Chair of Neurological Surgery, was one of three scientists to receive the 2011 Prince of Asturias Award for Technical and Scientific Research in recognition of his work demonstrating regeneration of neurons in the adult brain.

Christopher Ames MD, associate professor of neurological surgery, has recently been the honored guest of the Australian Spine Society, the Kuwait Neurosurgical Society, and the Korean Spine Society.

Mitchel S. Berger MD, Kathleen M. Plant Distinguished Professor and Chair of Neurological Surgery, has been named president elect of the American Association for Neurological Surgeons (AANS) and will serve in this post until April of 2012.

Ayanabha Chakraborti PhD, postdoctoral fellow in the Fike laboratory, has been selected for NASA Space Radiation Summer School 2011. Only 15 students from laboratories all over the world are selected by NASA every year for this prestigious program. The program is designed to train researchers to tackle the challenges of harmful radiation exposure to humans who will travel on space exploration missions.

Aaron Clark MD, resident in the Department of Neurological Surgery, was awarded first place in the ePoster competition in the category of Tumor at the 2011 AANS Annual Meeting for his abstract "Neurosurgical Management and Prognosis of Patients with Glioblastoma that Progress During Bevacizumab Treatment."

Coralie de Hemptinne PhD, postdoctoral fellow, and Philip Starr MD, PhD, professor and Dolores Cakebread Endowed Chair of Neurological Surgery, have been awarded a Rapid Response Innovation Award from the Michael J. Fox Foundation for Parkinson's Research for their project "Effect of Deep Brain Stimulation on Cortical Cross Frequency Coupling in Parkinson's Disease: An Electrocorticography Study."

Dario Englot MD, PhD, resident in the Department of Neurological Surgery, received a Resident Research Award from the UCSF Clinical and Translational Science Institute to fund the research project "Anterior Temporal Lobectomy for Medically-Refractory Temporal Lobe Epilepsy: National Trends and Post-operative Seizure Outcomes."

Daniel Lim MD, PhD, assistant professor of neurological surgery, has been awarded a $1.8 million grant by the California Institute for Regenerative Medicine to study new devices for cell transplantation to the brain.

John Fike PhD, professor of neurological surgery, received the John Yuhas Award for Excellence in Radiation Biology from the University of Pennsylvania.

Praveen Mummaneni MD, associate professor of neurological surgery, has been elected to the Society of Neurological Surgeons and served as a guest examiner for the American Board of Neurological Surgery oral board exam.

Neuro-Oncology Service Wins Patient Satisfaction Award

The Neuro-Oncology Service was awarded the UCSF Medical Center Pinnacle Award for the fourth consecutive year. This award recognizes the UCSF medical service with the best patient satisfaction scores for outpatient care.

Fetal Surgery for Spina Bifida More Effective Than Operating After Birth

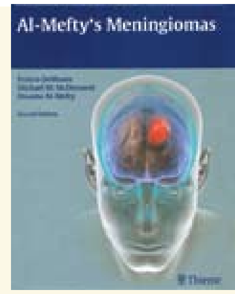
Recently published results from the Management of Myelomeningocele Study showed that prenatal surgery to repair a myelomeningocele reduced the need for shunting after birth and improved motor outcomes at 30 months. This NIH-funded, randomized study was conducted at UCSF, Children's Hospital of Philadelphia, and Vanderbilt University.

Adzick NS, Thom EA, Spong CY, Brock JW 3rd, Burrows PK, Johnson MP, Howell LJ, Farrell JA, Dabrowiak ME, Sutton LN, Gupta N, Tulipan NB, D'Alton ME, Farmer DL; MOMS Investigators. A randomized trial of prenatal versus postnatal repair of myelomeningocele. N Engl J Med 2011;364(11):993-1004.

UCSF Community Extension Clinics Open at Bay Area Hospitals

To better serve our patients in Northern California, the Department of Neurological Surgery at UCSF now has community extension practices at Marin General Hospital in Marin, Queen of the Valley Hospital in Napa Valley, and Saint Francis Memorial Hospital and St. Mary's Medical Center in San Francisco. To refer a patient to a UCSF neurosurgeon at these hospitals, contact Dr. Tarun Arora, director of Community Extension Neurosurgery, at (415) 514-6868.

Just Published



Al-Mefty's Meningiomas, 2nd Edition, edited by Ossama Al-Mefty, Franco DeMonte, and Michael McDermott. Thieme, New York, NY, 2011, 448pp, 554 illustrations.

Several years ago, Dr. Michael McDermott approached Dr. Ossama Al-Mefty about the possibility of a second edition of his meningioma book, originally published in 1990. Dr. Al-Mefty agreed and Dr. McDermott then worked with Dr. Franco DeMonte, Dr. Al-Mefty's first fellow, to recruit a new list of authors and co-edit the second edition. This text is the definitive guide to diagnosis, treatment, and surgery of both intracranial and spinal meningiomas. The second edition provides in-depth information on molecular biology, natural history, and growth rates; details on intraoperative MRI, endoscopic techniques, and radiosurgery; and tackles the issues of caseload management and postoperative quality of life.

New Faculty

The Department of Neurological Surgery is pleased to announce the appointment of Annette Molinaro MA, PhD as associate professor of neurological surgery, specializing in biostatistics. We have also been joined by Tarun Arora MD and Jeffrey Yablon MD, who are leading our neurosurgery outreach clinics in Marin and Napa Valley.

residents' publications

Bloch O, Sughrue ME, Mills SA, Parsa AT. Signaling pathways in cranial chondrosarcoma: potential molecular targets for directed chemotherapy. J Clin Neurosci 2011;18(7):881-5.

Cage TA, Auguste KI, Wrensch M, Wu YW, Gupta N. Self-reported functional outcome after surgical intervention in patients with idiopathic normal pressure hydrocephalus. J Clin Neurosci 2011;18(5):649-54.

Chang EF, **Cheng JS, Richardson RM,** Lee C, Starr PA, Larson PS. Incidence and management of venous air embolisms during awake deep brain stimulation surgery in a large clinical series. Stereotact Funct Neurosurg 2011;89(2):76-82.

Chang EF, **Clark A,** Smith JS, Polley MY, Chang SM, Barbaro NM, Parsa AT, McDermott MW, Berger MS. Functional mapping-guided resection of low-grade gliomas in eloquent areas of the brain: improvement of long-term survival. Clinical article. J Neurosurg 2011;114(3):566-73.

Clark AJ, Butowski NA, Chang SM, Prados MD, Clarke J, Polley MY, **Sughrue ME,** McDermott MW, Parsa AT, Berger MS, Aghi MK. Impact of bevacizumab chemotherapy on craniotomy wound healing. J Neurosurg 2011;114(6):1609-16.

Deipolyi AR, **Han SJ, Sughrue ME,** Litt L, Parsa AT. Awake far lateral craniotomy for resection of foramen magnum meningioma in a patient with tenuous motor and somatosensory evoked potentials [published online ahead of print July 6, 2011]. J Clin Neurosci. doi:10.1016/j.jocn.2010.12.046.

Englot DJ, Berger MS, Barbaro NM, Chang EF. Predictors of seizure freedom after resection of supratentorial low-grade gliomas. J Neurosurg 2011;115(2):240-44.

Englot DJ, Chang EF, Larson PS. Lead cap localization using ultrasound in deep brain stimulation surgery: technical note. Minim Invasive Neurosurg 2011;54(1):48-9.

Ivan ME, Sughrue ME, Clark AJ, Kane AJ, Aranda D, Barani IJ, Parsa AT. A meta-analysis of tumor control rates and treatment-related morbidity for patients with glomus jugulare tumors. J Neurosurg 2011;114(5):1299-305.

Jahangiri A, Molinaro AM, **Tarapore PE,** Blevins L, Auguste KI, Gupta N, Kunwar S, Aghi MK. Rathke cleft cysts in pediatric patients: presentation, surgical management, and postoperative outcomes. Neurosurg Focus 2011;31(1):E3.

Jian BJ, Sughrue ME, Kaur R, Rutkowski MJ, Kane AJ, Kaur G, Yang I, Pitts LH, Parsa AT. Implications of cystic features in vestibular schwannomas of patients undergoing microsurgical resection [published online ahead of print January 6, 2011]. Neurosurgery. doi: 10.1227/NEU.0b013e318208f614.

Lau D, **Han SJ,** Lee JG, Lu DC, Chou D. Minimally invasive compared to open microdiscectomy for lumbar disc herniation. J Clin Neurosci 2011;18(1):81-4.

Oh MC, Aghi MK. Dopamine agonist-resistant prolactinomas. J Neurosurg 2011;114(5):1369-79.

Potts MB, Jahangiri A, Lamborn KR, Blevins LS, Kunwar S, Aghi MK. Suprasellar Rathke's cleft cysts: Clinical presentation and treatment outcomes [published online ahead of print June 11, 2011]. Neurosurgery. doi: 10.1227/NEU.0b013e318228bcea.

Shear DA, Tate CC, **Tate MC,** Archer DR, Laplaca MC, Stein DG, Dunbar GL. Stem cell survival and functional outcome after traumatic brain injury is dependent on transplant timing and location [published online ahead of print April 6, 2011]. Restor Neurol Neurosci. doi: 10.3233/RNN-2011-0593.

Sughrue ME, Bloch OG, Manley GT, Stiver SI. Marked reduction in wound complication rates following decompressive hemicraniectomy with an improved operative closure technique [published online ahead of print July 11, 2011]. J Clin Neurosci. doi:10.1016/j.jocn.2011.01.016.

Tarapore PE, Sughrue ME, Blevins L, Auguste KI, Gupta N, Kunwar S. Microscopic endonasal transsphenoidal pituitary adenomectomy in the pediatric population. J Neurosurg Pediatr 2011;7(5):501-9.

Tate MC, Kim CY, Chang EF, Polley MY, Berger MS. Assessment of morbidity following resection of cingulate gyrus gliomas. Clinical article. J Neurosurg 2011;114(3):640-7.

Waldron JS, **Oh MC,** Chou D. Lumbar subdural hematoma from intracranial subarachnoid hemorrhage presenting with bilateral foot drop: case report. Neurosurgery 2011;68(3):E835-9.

Yang I, **Han SJ, Sughrue ME,** Tihan T, Parsa AT. Immune cell infiltrate differences in pilocytic astrocytoma and glioblastoma: evidence of distinct immunological microenvironments that reflect tumor biology [published online ahead of print June 10, 2011]. J Neurosurg. doi: 10.3171/2011.4.JNS101172.

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selected recent publications from the department of neurological surgery

Ciesielska A, Mittermeyer G, Hadaczek P, Kells AP, Forsayeth J, Bankiewicz KS. Anterograde axonal transport of AAV2-GDNF in rat basal ganglia. Mol Ther 2011;19(5):922-7.

Chang EF, Wang DD, Perry DW, Barbaro NM, Berger MS. Homotopic organization of essential language sites in right and bilateral cerebral hemispheric dominance. J Neurosurg 2011;114(4):893-902.

Dvorak HF, Weaver VM, Tlsty TD, Bergers G. Tumor microenvironment and progression. J Surg Oncol 2011;103(6):468-74.

Hortopan GA, Baraban SC. Aberrant expression of genes necessary for neuronal development and notch signaling in an epileptic mind bomb zebrafish. Dev Dyn 2011;240(8):1964-76.

Ihrie RA, Alvarez-Buylla A. Lake-front property: a unique germinal niche by the lateral ventricles of the adult brain. Neuron 2011;70(4):674-86.

Lee SM, Rosen S, Weinstein P, van Rooijen N, Noble L. Prevention of both neutrophil and monocyte recruitment promotes recovery after spinal cord injury [published online ahead of print June 9, 2011]. J Neurotrauma. doi:10.1089/neu.2011.1860.

Lu DC, Chou D, Mummaneni PV. A comparison of mini-open and open approaches for resection of thoracolumbar intradural spinal tumors. J Neurosurg Spine 2011;14(6):758-64.

Maas A, Menon D, Lingsma H, Pineda J, Sandel EM, Manley GT. Re-orientation of clinical research in traumatic brain injury: Report of a international workshop* on comparative effectiveness research [published online ahead of print May 5, 2011]. J Neurotrauma. doi:10.1089/neu.2010.1599.

Nout YS, Beattie MS, Bresnahan J. Severity of locomotor and cardiovascular derangements after experimental high-thoracic spinal cord injury is anesthesia dependent in rats [published online ahead of print May 5, 2011]. J Neurotrauma. doi:10.1089/neu.2011.1845.

Ohi Y, Qin H, Hong C, Blouin L, Polo JM, Guo T, Qi Z, Downey SL, Manos PD, Rossi DJ, Yu J, Hebrok M, Hochedlinger K, Costello JF, Song JS, Ramalho-Santos M. Incomplete DNA methylation underlies a transcriptional memory of somatic cells in human iPS cells. Nat Cell Biol 2011;13(5):541-9.

Ostrem JL, Racine CA, Glass GA, Grace JK, Volz MM, Heath SL, Starr PA. Subthalamic nucleus deep brain stimulation in primary cervical dystonia. Neurology 2011;76(10):870-8.

Parvataneni R, Polley MY, Freeman T, Lamborn K, Prados M, Butowski N, Liu R, Clarke J, Page M, Rabbitt J, Fedoroff A, Clow E, Hsieh E, Kivett V, Deboer R, Chang S. Identifying the needs of brain tumor patients and their caregivers [published online ahead of print February 11, 2011]. J Neurooncol. doi: 10.1007/s11060-011-0534-4.

Quigg M, Broshek DK, Barbaro NM, Ward MM, Laxer KD, Yan G, Lamborn K; the Radiosurgery Epilepsy Study Group. Neuropsychological outcomes after Gamma Knife radiosurgery for mesial temporal lobe epilepsy: A prospective multicenter study. Epilepsia 2011;52(5):909-916.

Sanai N, Polley MY, McDermott MW, Parsa AT, Berger MS. An extent of resection threshold for newly diagnosed glioblastomas. J Neurosurg 2011;115(1):3-8.

Scheer JK, Tang JA, Buckley JM, Deviren V, Pekmezci M, McClellan RT, Ames CP. Biomechanical analysis of osteotomy type and rod diameter for treatment of cervicothoracic kyphosis. Spine (Phila Pa 1976) 2011;36(8):E519-23.

Sughrue ME, Chang EF, Gabriel RA, Aghi MK, Blevins LS. Excess mortality for patients with residual disease following resection of pituitary adenomas [published online ahead of print April 8, 2011]. Pituitary. doi: 10.1007/s11102-011-0308-1.

Sun H, Le T, Chang TT, Habib A, Wu S, Shen F, Young WL, Su H, Liu J. AAV-mediated netrin-1 overexpression increases peri-infarct blood vessel density and improves motor function recovery after experimental stroke [published online ahead of print June 25, 2011]. Neurobiol Dis. doi:10.1016/j.nbd.2011.06.006.

Wang D, Olman MA, Stewart J Jr, Tipps R, Huang P, Sanders PW, Toline E, Prayson RA, Lee J, J Weil R, Palmer CA, Gillespie GY, Liu WM, Pieper RO, Guan JL, Gladson CL. Downregulation of FIP200 induces apoptosis of glioblastoma cells and microvascular endothelial cells by enhancing Pyk2 activity. PLoS One 2011;6(5):e19629.

Wang Y, Neumann M, Hansen K, Hong SM, Kim S, Noble-Haeusslein LJ, Liu J. Fluoxetine increases hippocampal neurogenesis and induces epigenetic factors but does not improve functional recovery after traumatic brain injury. J Neurotrauma 2011;28(2):259-68.

Zheng S, Houseman EA, Morrison Z, Wrensch MR, Patoka JS, Ramos C, Haas-Kogan DA, McBride S, Marsit CJ, Christensen BC, Nelson HH, Stokoe D, Wiemels JL, Chang SM, Prados MD, Tihan T, Vandenberg SR, Kelsey KT, Berger MS, Wiencke JK. DNA hypermethylation profiles associated with glioma subtypes and EZH2 and IGFBP2 mRNA expression. Neuro Oncol 2011;13(3):280-9.

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