

New Interventional MRI System Developed to Improve Surgery for Movement Disorders

Deep brain stimulation (DBS) has been used for over a decade to treat movement disorders such as Parkinson's disease, essential tremor, and dystonia. It has become the gold standard for surgical care of these diseases; over 40,000 patients have had DBS devices implanted worldwide. DBS uses a pulse generator implanted in the chest, similar to a pacemaker, to deliver pulses to specific regions of the brain via a permanently implanted electrode. The traditional method of surgical implantation involves placement of a stereotactic head frame and an awake implantation procedure using a technique known as microelectrode recording (MER). During MER, the surgeon passes small microelectrodes into the region of the intended target and observes the pattern of neuronal activity to physiologically confirm accurate placement of the stimulating electrode. Although this technique is widely used, it is technically demanding, time consuming, and often difficult for patients to tolerate.

Interventional MRI (or iMRI) allows surgeons to take advantage of MR imaging in real time by performing procedures inside the scanner itself. Paul Larson MD, assistant professor of neurological surgery, and Philip Starr MD, PhD, Dolores Cakebread Endowed Chair and associate professor of neurological surgery, were both involved with this technology during its development in the 1990s. In 2002, they began to think about how to perform DBS

using this technique at UCSF. The subthalamic nucleus (STN) is by far the most common brain target for DBS in Parkinson's disease and is visible on 1.5T MR images. In traditional DBS surgery, MER is used to map the STN and locate the center of its motor region, the area which has been shown to be effective in reducing symptoms when stimulated. With iMRI, the surgeons can see this region directly and can place the DBS electrode without the need for MER.

In conjunction with Alastair Martin PhD in the Department of Radiology, Jill Ostrem MD in the Department of Neurology, and others, Starr and Larson developed a technique of implantation using a modified but commercially available skull-mounted aiming device and custom-made, MR-compatible surgical instruments. After validating the techniques with numerous phantom studies, they began performing iMRI implantations in patients in 2004. To date they have implanted 67 electrodes in 36 patients using this technique. iMRI DBS has several distinct advantages over traditional implantation methods. There is no need for a stereotactic frame and no need for the patients to be awake and off of their Parkinson's medications, so patients tolerate the procedure well. The procedure time is half that of traditional MER-guided implantation, and since MER is not necessary there is only one brain penetration needed in the vast majority of cases. The shorter operative times and

fewer brain penetrations may lead to less confusion postoperatively, particularly in older patients. It may ultimately result in a lower hemorrhage risk as well, but this remains to be established.

In 2008, Larson, Starr, and Martin partnered with the medical device company SurgiVision to develop new technologies for the iMRI DBS technique. This includes an MRI-compatible, skull-mounted aiming device and MR coils specifically designed to provide optimal imaging during surgery. They have also developed a software environment that will standardize the implantation procedure on different MRI platforms. The new software environment will stream data from any manufacturer's 1.5T MRI scanner and guide the surgeon through the implantation procedure using a specially designed graphical interface. The software will also improve accuracy by automating some steps that were previously dependent on the user. The UCSF group and SurgiVision will be testing and validating the new system this spring and summer.

Martin AJ, Larson PS, Ostrem JL, Sootsman WK, Talke P, Weber OM, Levesque N, Meyers J, Starr PA. Placement of deep brain stimulator electrodes using real-time high-field interventional magnetic resonance imaging. *Magn Reson Med* 2005;54(5):1107-1114.

Martin AJ, Larson PS, Ostrem JL, Starr PA. Interventional magnetic resonance guidance of deep brain stimulator implantation for Parkinson disease. *Top Magn Reson Imaging* 2008;19(4):213-221.

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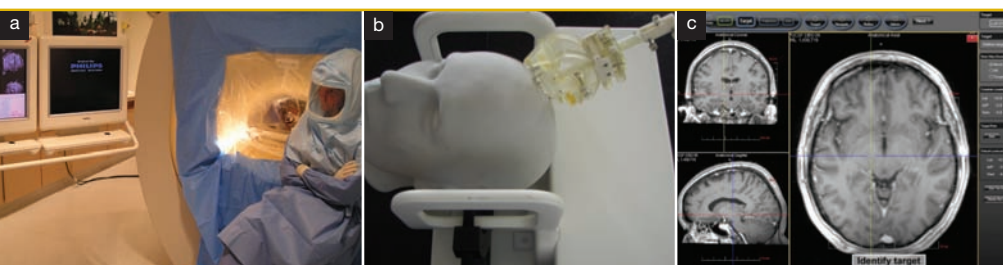
Neurological Surgery

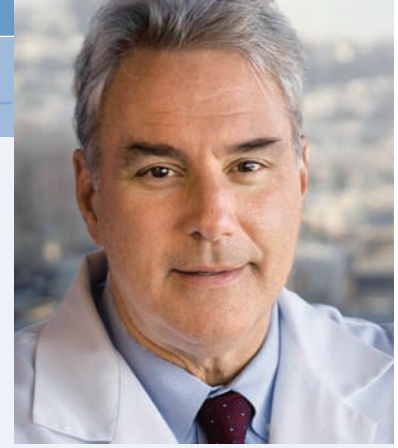
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a The interventional MRI suite at UCSF Medical Center.

b The ClearPoint software allows the surgeon to view the MR images in different orientations to guide DBS electrode implantation.

c The SmartFrame mounts on the patient's skull and helps guide the DBS electrode into the brain.





Treatment for movement disorders – like Parkinson's disease, dystonia, or tremor – was once exclusively medical, but technologies have evolved that permit remarkable improvement for patients who are treated surgically. In 2001, one of six national Parkinson's Disease Research, Education and Clinical Centers (PADRECC) was established at the San Francisco Veterans Affairs Medical Center, and it has since become one of the largest referral centers for movement disorder surgery in the United States. The surgical movement disorders program is led by Philip Starr MD, PhD and Paul Larson MD who have expertise in stereotactic and functional neurosurgery, including deep brain stimulation (DBS), which has dramatically transformed the quality of life of many patients suffering with Parkinson's disease. In 2008, they were joined by clinician-scientist Daniel Lim MD, PhD, a former resident in the Department who trained under Larson and Starr in stereotactic neurosurgical techniques.

While the advent of new technology has helped lessen the severity of patients' symptoms, we continue to invest in research to improve treatments and attack the underlying disease. One way we are improving existing treatments is by making them less invasive. Starr and Larson have recently partnered with the medical device company SurgiVision to develop the first system using interventional MR imaging for DBS (page 1). The new technology obviates the need for a stereotactic frame, reduces the number of brain penetrations to one, and shortens operating times.

In the laboratory, we are leading studies to understand the pathophysiology of movement

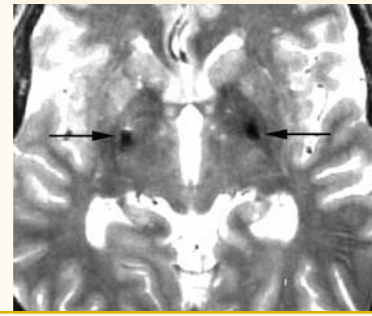
disorders, define new surgical targets, and develop novel treatments. A major source of excitement arising from basic science studies has been the advancement of gene therapy. A recently completed phase I study for Parkinson's disease, led by Michael Aminoff MD in the UCSF Department of Neurology, demonstrated the safety of convection-enhanced delivery (CED) of the gene for the enzyme aromatic L-amino acid decarboxylase (AADC). This enzyme converts L-dopa (the standard medical therapy for Parkinson's disease) into dopamine. CED infusion of viral vectors carrying the gene for AADC was pioneered in the laboratory of Krystof Bankiewicz MD, PhD over decades of research using animal models of Parkinson's disease, and if the therapy is successful, patients may require less medication to achieve the same level of symptom control, reducing dose-related side effects. Although it was not a randomized, controlled trial, all 10 patients enrolled in the phase I study showed significant improvement in off-label Unified Parkinson's Disease Rating Scale scores. These results are encouraging and warrant further investigations in placebo-controlled clinical trials.

While gene therapy has suffered from a variety of setbacks in past trials, including those for movement disorders, we are optimistic that with continued investigation, the hurdles of this promising treatment strategy will be overcome. Starr and Bankiewicz are also collaborating with Nutan Sharma (Massachusetts General Hospital) to explore an animal model of DYT1+ dystonia created by convection-enhanced delivery to the brain of viral vectors expressing the mutant Tor1A gene.

Stem cell research is yet another promising avenue for scientific investigation, and recent changes in laws regarding funding has opened the floodgates for numerous studies involving the use of stem cells to treat neurological disorders. The Buck Institute (led by Xianmin Zeng PhD) and a team at UCSF (led by Lim, Aminoff, and William Marks MD of the Department of Neurology) have recently applied for funding to design a phase I transplantation therapy trial testing dopaminergic neurons derived from human embryonic stem cells. If the grant is funded, UCSF may someday be one of first sites at which human embryonic stem cells are used for the treatment of Parkinson's Disease.

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Typical DBS lead location in the putamen in a patient with dystonia



Dystonia: Surgical Treatment and Advances in Pathophysiology

Dystonia is the third most common movement disorder, after Parkinson's disease and essential tremor.

Its hallmark is excessive muscle activity, in particular, simultaneous contraction of muscle groups that normally oppose each other. It has numerous clinical manifestations, ranging from severe, life-threatening juvenile onset generalized forms to adult onset focal dystonias such as spasmodic torticollis and blepharospasm. Its pathophysiology is poorly understood.

The UCSF center for the surgical treatment of movement disorders is one of the two busiest centers in the United States for the surgical treatment of dystonia. Working with Jill Ostrem MD from the Department of Neurology, UCSF neurosurgeons have performed deep brain stimulation (DBS) for various forms of dystonia in over 80 patients. Our center is the first to describe the technique of microelectrode-guided DBS in awake patients.¹

The accepted brain target for DBS in dystonia has been the major outflow nucleus of the basal ganglia, the globus pallidus internus (GPi). However, our group has shown that, in adult onset focal dystonias, GPi-DBS may be associated with subtle deficits (slowness) in previously normal body parts.^{2,3} Funded with a seed grant from the Benign Essential Blepharospasm Research

Foundation (BEBRF), Ostrem and Philip Starr MD, PhD, associate professor of neurological surgery, are conducting a pilot trial of an alternative target in dystonia, the subthalamic nucleus (STN).⁴

Understanding the pathophysiology of dystonia has been a primary interest of Starr's basal ganglia physiology laboratory. Using single unit recording techniques in humans undergoing awake neurosurgery, his group has defined the abnormalities in single unit neuronal firing in three basal ganglia nuclei, the GPi,^{5,6} the STN, and the external pallidum.⁷ In 2008, these physiology studies were extended to include cortical function, assessed using electrocorticography techniques. Working with a Doris Duke fellow in the Starr laboratory, Andrea Crowell, the group has discovered characteristic oscillation frequencies in both the cortex and basal ganglia that appear to encode the dystonic phenotype.⁸ The Starr laboratory has also recently received a grant from the Dystonia Medical Research Foundation to investigate STN and motor cortex local field potentials in patients with dystonia. These studies are helping to decode the pathophysiology of dystonia, provide a window on function of the basal ganglia, and may lead to new targets for the treatment of this mysterious disorder.

1. Starr PA, Turner RS, Rau G, et al. Microelectrode-guided implantation of deep brain stimulators into the globus pallidus internus for dystonia: techniques, electrode locations, and outcomes. *J Neurosurg* 2006;104(4):488-501.
2. Berman BD, Starr PA, Marks WJ Jr, Ostrem JL. Induction of bradykinesia with pallidal deep brain stimulation in patients with cranial-cervical dystonia. *Stereotact Funct Neurosurg* 2009;87(1):37-44.
3. Ostrem JL, Marks WJ Jr, Volz MM, Heath SL, Starr PA. Pallidal deep brain stimulation in patients with cranial-cervical dystonia (Meige syndrome). *Mov Disord* 2007;22(13):1885-1891.
4. Ostrem JL, Volz MM, Starr PA. Deep brain stimulation (DBS) of the subthalamic nucleus (STN) in patients with segmental and focal cervical dystonia [abstract]. *Mov Disord* 2008;23(suppl 1):S380.
5. Starr PA, Rau GM, Davis V, Marks WJ Jr, Ostrem JL, Simmons D, Lindsey N, Turner RS. Spontaneous pallidal neuronal activity in human dystonia: comparison with Parkinson's disease and normal macaque. *J Neurophysiol* 2005;93(6):3165-3176.
6. Chang EF, Turner RS, Ostrem JL, Davis VR, Starr PA. Neuronal responses to passive movement in the globus pallidus internus in primary dystonia. *J Neurophysiol* 2007;98(6):3696-3707.
7. Sani S, Ostrem JL, Shimamoto S, Levesque N, Starr PA. Single unit "pauser" characteristics of the globus pallidus pars externa distinguish primary dystonia from secondary dystonia and Parkinson's disease. *Exp Neurol* 2009; 216(2):295-259.
8. Crowell A, Ostrem JL, Shimamoto S, Starr PA. Cortical and subthalamic local field potentials in primary dystonia. Presented at: 15th quadrennial meeting of the World Society of Stereotactic and Functional Neurosurgery; May 24-27, 2009; Toronto, Canada.

selected publications

Glass GA, Ku S, Ostrem JL, Heath S, Larson PS. Fluoroscopic, EMG-guided injection of botulinum toxin into the longus colli for the treatment of anterocollis [published online ahead of print February 26, 2009]. *Parkinsonism Relat Disord* doi:10.1016/j.parkreldis.2009.01.006

Martin AJ, Larson PS, Ostrem JL, Starr PA. Interventional magnetic resonance guidance of deep brain stimulator implantation for Parkinson disease. *Top Magn Reson Imaging* 2009;19(4):213-221.

Richardson RM, Larson PS, Bankiewicz KS. Gene and cell delivery to the degenerated striatum: status of preclinical efforts in primate models. *Neurosurgery* 2008;63(4):629-644.

Marks WJ Jr, Ostrem JL, Verhagen L, Starr PA, Larson PS, Bakay RA, Taylor R, Cahn-Weiner DA, Stoessl AJ, Olanow CW, Bartus RT. Safety and tolerability of intraputamenal delivery of CERE-120 (adeno-associated virus serotype 2-neurturin) to patients with idiopathic Parkinson's disease: an open-label, phase I trial. *Lancet Neurol* 2008;7(5):400-408.



Paul Larson MD, assistant professor of neurological surgery, has clinical interests in stereotactic and functional neurosurgery, particularly with regard to movement disorders and psychiatric disorders. He has been involved in the development and evolution of novel surgical methods for deep brain stimulator implantation, including frameless techniques and the use of high-field, real-time intraoperative magnetic resonance imaging (MRI). He has extensive surgical experience in the use of intraoperative MRI for a number of neurosurgical applications.

During his residency, Dr. Larson was extensively involved in the development of the Norton Hospital intraoperative MRI program, and spent a year in the Speed School of Engineering's Computer Vision and Image Processing Lab studying the basic science of CT and MR image analysis and 3D modeling.

Dr. Larson's research interests include neurostimulation, gene therapy, and other neurorestorative therapies for a variety of neurological diseases, including movement disorders and psychiatric disorders. He is also involved in studies using high-field MR brain imaging for clinical and basic science research. His basic science interests include MR research and the development of new technologies to perform functional neurosurgery using real-time MRI.



selected publications

Sanai N, Berger MS. Glioma extent of resection and its impact on patient outcome. *Neurosurgery* 2008;62(4):753-764.

Sanai N, Mirzadeh Z, Berger MS. Functional outcome after language mapping for glioma resection. *N Engl J Med* 2008;358(1):18-27.

Sanai N, Alvarez-Buylla A, Berger MS. Neural stem cells and the origin of gliomas. *N Engl J Med* 2005;353(8):811-822.

Sanai N, Tramontin AD, Quiñones-Hinojosa A, Barbaro NM, Gupta N, Kunwar S, Lawton MT, McDermott MW, Parsa AT, Manuel-García Verdugo J, Berger MS, Alvarez-Buylla A. Unique astrocyte ribbon in adult human brain contains neural stem cells but lacks chain migration. *Nature* 2004;427(6976):740-744.

Nader Sanai MD was born in Tehran, Iran and raised in Palo Alto, California. He attended UCSD as an undergraduate, where he double-majored in Animal Physiology & Neuroscience and French Literature. His initial interest in neurosurgery stemmed from his family's experience caring for his mother's sister, who died from a glioma.

In 1998, Sanai entered the UCSF School of Medicine, where he first joined the laboratory of Dennis Deen PhD in the Brain Tumor Research Center and was selected as the first recipient of the Diane D. Ralston & Henry J. Ralston Scholarship for Research in Neurosciences. In 2001, he was awarded a Howard Hughes Medical Institute (HHMI) Research Training Fellowship to conduct research in the laboratory of Arturo Alvarez-Buylla PhD, studying adult neural stem cells in the human brain. Among various basic science honors, Sanai received the Edwin F. Boldrey Award for Basic Science Research from the San Francisco Neurological Society, served as Guest Editor for the Neural Stem Cells issue of the

journal *Neurosurgery Clinics of North America*, and is currently an Associate Editor for the journal *BMC Cancer*.

Sanai began his neurosurgical training at UCSF in 2004, and under the mentorship of his advisor, Mitchell Berger MD, he has conducted a number of studies focusing on surgical neuro-oncology, intraoperative language mapping, and the biology of gliomagenesis. Within surgical neuro-oncology, his area of clinical specialization has also extended into lesions of the skull base. Among various clinical honors, Sanai received the Kaiser Award for Clinical Research from the San Francisco Neurological Society and the Dandy Clinical Fellowship from the Congress of Neurological Surgeons.

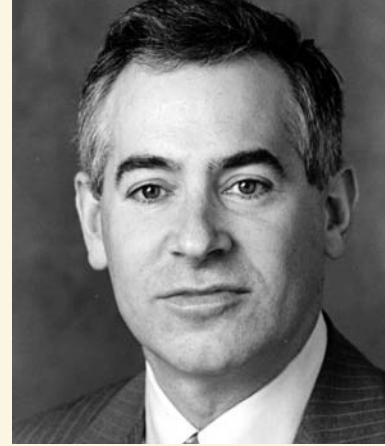
After finishing his neurosurgical training at UCSF in 2009, Sanai will complete a fellowship in skull base surgery with Robert F. Spetzler MD at the Barrow Neurological Institute in Phoenix, AZ. He then anticipates a career in academic neurosurgery as both a surgical neuro-oncologist and neural stem cell scientist.

Philip Starr MD, PhD, is the Dolores Cakebread Endowed Chair and associate professor of neurological surgery. His particular specialty interests lie in the area of movement disorders, including Parkinson's disease, tremor, and dystonia. He has fellowship training in microelectrode-guided surgery of movement disorders, which he completed at Emory University in Atlanta, Georgia. Starr's research interests include physiology of the basal ganglia, clinical trials of novel surgical therapeutics in movement disorders, and the use of interventional magnetic resonance imaging (iMRI) for functional neurosurgery.

Working together with William Marks MD and Jill Ostrem MD in the Department of Neurology in a joint UCSF-San Francisco Veterans Affairs Hospital Medical Center study, Starr is an investigator for the largest formal clinical trial of deep brain stimu-

lation (DBS) currently taking place in North America: "A Randomized Trial of Best Medical Therapy versus Deep Brain Stimulation of the Globus Pallidus or Subthalamic Nucleus for Parkinson's Disease." This is a six-center trial jointly funded by the Department of Veterans Affairs and the National Institutes of Health. Starr also conducts NIH-funded research on pallidal physiology in patients with dystonia.

The goal of Starr's research laboratory is to understand the pathophysiology of movement disorders by recording electrical activity in humans undergoing microelectrode-guided basal ganglia surgery in the awake state. Data gathered are used to confirm, refute, or expand upon existing models of basal ganglia function and dysfunction, to identify possible new surgical targets, and to provide a better understanding of the mechanism of action of brain stimulation.



selected publications

Chang EF, Turner RS, Ostrem JL, Davis VR, Starr PA. Neuronal responses to passive movement in the globus pallidus internus in primary dystonia. *J Neurophysiol* 2007;98(6):3696-3707.

Starr PA, Kang GA, Heath S, Shimamoto S, Turner RS. Pallidal neuronal discharge in Huntington's disease: support for selective loss of striatal cells originating the indirect pathway. *Exp Neurol* 2008;211(1):227-233.

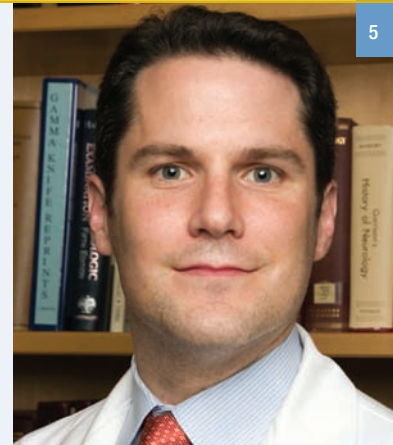
Sillay KA, Larson PS, Starr PA. Deep brain stimulator hardware-related infections: incidence and management in a large series. *Neurosurgery* 2008;62(2):360-366.

Sani S, Ostrem JL, Shimamoto S, Levesque N, Starr PA. Single unit "pauser" characteristics of the globus pallidus pars externa distinguish primary dystonia from secondary dystonia and Parkinson's disease. *Exp Neurol* 2009; 216(2):295-259.

James Waldron MD received his undergraduate degree from Rice University in Houston, TX and attended medical school at the University of Texas, Southwestern School of Medicine in Dallas, TX, where he graduated first in his class. While at UT Southwestern he completed a summer research fellowship in the laboratory of Nobel laureates Michael Brown MD and Joseph Goldstein MD, studying cholesterol metabolism. After graduation he completed an internship in Internal Medicine at Brigham and Women's Hospital, Harvard Medical School, followed by a period of time in the business sector working as a consultant in the healthcare practice of McKinsey & Company.

In 2002, Waldron joined the laboratory of Andrew Parsa MD, PhD in the Brain Tumor Research Center at UCSF as a postdoctoral research associate studying glioma immunology and the underlying mechanisms that allow gliomas to escape the immune system. Waldron continued to work closely with Parsa

after becoming a resident in the Department of Neurological Surgery, winning the Preuss Award for Brain Tumor Research at the Congress of Neurological Surgeons in 2006 and receiving an NIH National Research Service Award to support a year of dedicated research in glioma immunology. Waldron was selected to receive the Integra Foundation Award at the 2009 Annual Meeting of the American Association of Neurological Surgeons for his work looking at preoperative embolization of skull base tumors. Waldron's academic and clinical interests have broadened to include the treatment of cerebrovascular disease. He has worked closely with Michael Lawton MD developing skills in open cerebrovascular surgery and publishing on the surgical treatment of previously coiled aneurysms and the removal of cavernous malformations from the basal ganglia. After graduation, Waldron will pursue an endovascular fellowship at Stanford University, and focus his academic efforts on the development of endovascular drug-delivery techniques.



selected publications

Waldron JS, Lawton MT. The supracarotid-intrafrontal approach: surgical technique and clinical application to cavernous malformations in the anteroinferior Basal Ganglia. *Neurosurgery* 2009;64(3 Suppl):86-95.

Waldron JS, Halbach VV, Lawton MT. Microsurgical management of incompletely coiled and recurrent aneurysms: trends, techniques, and observations on coil extrusion. *Neurosurgery* (In Press).

Parney IF, Waldron JS, Parsa AT. Flow cytometry and in vitro analysis of human glioma-associated macrophages. Laboratory investigation. *J Neurosurg* 2009;110(3):572-582.

Parsa AT, Waldron JS, Panner A, Crane CA, Parney IF, Barry JJ, Cachola KE, Murray JC, Tihan T, Jensen MC, Mischel PS, Stokoe D, Pieper RO. Loss of tumor suppressor PTEN function increases B7-H1 expression and immunoresistance in glioma. *Nat Med* 2007;13(1):84-88.

Manish Aghi MD, PhD, assistant professor of neurological surgery, has been awarded a James S. McDonnell Foundation Grant for \$450,000 over 4 years for the project “Identifying and overcoming glioblastoma resistance to treatments targeting vascular endothelial growth factor.” He has also been granted a Specialized Programs of Research Excellence Career Development Award from the National Institutes of Health (NIH) for the project “Identifying and overcoming mechanisms of resistance to antivascular agents in human glioblastoma.”

Krystof Bankiewicz MD, PhD, Kinetics Foundation Chair in Translational Research and professor of neurological surgery, and his colleagues have successfully administered adeno-associated virus (AAV)-based gene therapy vectors to specific areas of the primate cortex by infusing the vectors into the thalamus via convection enhanced delivery. The gene therapy vectors efficiently disperse through axons that connect the thalamus and the cortex.

Kells AP, Hadaczek P, Yin D, Bringas J, Varenika V, Forsayeth J, Bankiewicz KS. Efficient gene therapy-based method for the delivery of therapeutics to primate cortex. *Proc Natl Acad Sci USA* 2009;106(7):2407-2411

Nicholas Barbaro MD, professor of neurological surgery, has received a \$21 million grant from the NIH to fund the Radiosurgery or Open Surgery for Epilepsy (ROSE) Trial – a phase III randomized clinical trial of Gamma Knife® radiosurgery for mesial temporal sclerosis.

Mitchel S. Berger MD, Kathleen M. Plant Distinguished Professor and chairman of the Department of Neurological Surgery, has been honored with the prestigious Winn Prize from the Society of Neurological Surgeons. The Winn Prize acknowledges outstanding clinical and/or translational research conducted by an academic neurosurgeon.

Edward Chang MD, resident in the Department of Neurological Surgery, received the Ronald L. Bittner Award at the 2009 Annual Meeting of the American Association of Neurological Surgeons (AANS) for the research article “Multi-institutional validation of the University of California at San Francisco Low-Grade Glioma Prognostic Scoring System.”

Jacqueline Bresnahan PhD, adjunct professor of neurological surgery, has been appointed chair of the Scientific Advisory Board for the Christopher and Dana Reeve Foundation.

Dean Chou MD, assistant professor of neurological surgery, and **Vincent Wang MD, PhD**, resident in the

Department of Neurological Surgery, have developed a new surgical technique for placing expandable cages from the back. The approach avoids dissecting the pleura, potentially preventing pulmonary issues when putting in these cages.

Chou D, Wang VY. Trap-door rib-head osteotomies for posterior placement of expandable cages after transpedicular corpectomy: an alternative to lateral extracavitary and costotransversectomy approaches. *J Neurosurg Spine* 2009;10(1):40-45.

Joseph Costello PhD, associate professor of neurological surgery, has been awarded a grant for \$12 million over the next 5 years as part of the new NIH Roadmap Epigenomics Program. Costello will lead the Integrated Epigenetic Maps of Human Embryonic and Adult Cells project in conjunction with Marco Antonio Marra PhD at the British Columbia Cancer Agency.

Nikita DeGurin, specialist in the Department of Neurological Surgery, recently implanted the first tissue-engineered vascular graft made with nanofibrous polymer scaffolds and lined with human embryonic stem cell-derived progenitor cells, replacing a carotid artery in a swine (see photo). This was a joint project with Randell Lee MD, PhD of the Department of Medicine and Song Li PhD of the UC Berkeley Department of Bioengineering.

residents' publications

Chang EF, Clark A, Jensen RL, Bernstein M, Guha A, Carrabba G, Mukhopadhyay D, Kim W, Liau LM, Chang SM, Smith JS, Berger MS, McDermott MW. Multiinstitutional validation of the University of California at San Francisco Low-Grade Glioma Prognostic Scoring System [published online ahead of print March 6, 2009]. *J Neurosurg*. doi: 10.3171/2009.2.JNS081101.

Lim DA, Tarapore P, Chang E, Burt M, Chakalian L, Barbaro N, Chang S, Lamborn KR, McDermott MW. Safety and feasibility of switching from phenytoin to levetiracetam monotherapy for glioma-related seizure control following craniotomy: a randomized phase II pilot study [published online ahead of print January 24, 2009]. *J Neurooncol*. doi: 10.1007/s11060-008-9781-4.

Lu DC, Dhall SS, Mummaneni PV. Mini-open removal of extradural foraminal tumors of the lumbar spine. *J Neurosurg Spine* 2009;10(1):46-50.

Lu DC, Wang V, Chou D. The use of allograft or autograft and expandable titanium cages for the treatment of vertebral osteomyelitis. *Neurosurgery* 2009;64(1):122-30.

Potts MB, Rola R, Claus CP, Ferriero DM, Fike JR, Noble-Haeusslein LJ. : Glutathione peroxidase overexpression does not rescue impaired neurogenesis in the injured immature brain. *J Neurosci Res* 2009;87(8):1848 – 1857.

Quiñones-Hinojosa A, **Chang EF**, Chaichana KL, McDermott MW. Surgical considerations in the management of falcotential meningiomas: advantages of the bilateral occipital transtentorial/transfalcal craniotomy for large tumors. *Neurosurgery* 2009 64(ONS Suppl 1): ons260–ons268.

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):1236-1253.

Sughrue ME, McDermott MW, Parsa AT. Vision salvage after resection of a giant meningioma in a patient with a loss in light perception. *J Neurosurg* 2009;110(1):109-111.

Tate CC, Shear DA, **Tate MC**, Archer DR, Stein DG, Laplaca MC. Laminin and fibronectin scaffolds enhance neural stem cell transplantation into the injured brain. *J Tissue Eng Regen Med* 2009;3(3):208-217.

Wang VY, Deviren V, Ames CP. Reconstruction of C-1 lateral mass with titanium mesh cage after resection of an aneurysmal bone cyst of the atlas. *J Neurosurg Spine* 2009;10(2):117-121.

Yang I, Aranda D, Han SJ, Chennupati S, **Sughrue ME**, Cheung SW, Pitts LH, Parsa AT. Hearing preservation after stereotactic radiosurgery for vestibular schwannoma: A systematic review [published online ahead of print March 20, 2009]. *J Clin Neurosci*. doi:10.1016/j.jocn.2008.09.023

Yang I, Delpolyi A, **Sughrue ME**, Rubenstein J, Bollen AW, Parsa AT. Sarcoidosis of the pineal gland: an unusual presentation of neurosarcoidosis. *J Neurooncol* 2009;91(1):113-116.

John Fike PhD, professor of neurological surgery, has recently received two research grants from the NIH: an R01 award for the study "Radiation and oxidative stress: effects on neurogenesis" and an R21/R33 award for the study "Combined effects of traumatic brain injury and ionizing irradiation on cellular and molecular determinates of cognitive function." He has also been granted a NASA Individual Research Award for the study "Use of a molecular marker of learning and memory to assess effects of 56Fe irradiation on hippocampal-dependent cognition and neurogenesis."

Jialing Liu PhD, associate professor of neurological surgery, has been granted an American Heart Association Established Investigator Award for the project "The recovery of post stroke mild cognitive impairment: an experimental model." She has also been given a VA Research Career Scientist Award for Biomedical Laboratory Research & Development.

Daniel Lim MD, PhD, assistant professor of neurological surgery, and **Arturo Alvarez-Buylla PhD**, Melanie Muss Endowed Chair and professor of neurological surgery, have recently discovered that the gene MLL1 is required for neural stem cells to differentiate into neurons. Using a murine model, Lim and Alvarez-Buylla showed that neural stem cells deficient in MLL1 were able to survive and differentiate into glia, but not neurons.

Lim DA, Huang YC, Swigut T, Mirick AL, Garcia-Verdugo JM, Wysocka J, Ernst P, Alvarez-Buylla A. Chromatin remodelling factor Mll1 is essential for neurogenesis from postnatal neural stem cells [published online ahead of print February 11, 2009]. *Nature*. doi: 10.1038/nature07726.

Praveen Mummaneni MD, associate professor of neurological surgery, was elected to Best Doctors in America and was the honored guest of the Taiwan Neurospinal Society in 2008.

Claudia Petritsch PhD, assistant professor of neurological surgery, has been granted a \$30,000 Individual Research Award from the American Cancer Society for the project "Novel regulators of neoplastic progenitor cell transformation."

R. Mark Richardson MD, PhD, resident in the Department of Neurological Surgery, received a Kirschstein National Research Service Award (NRSA) Postdoctoral Fellowship from the National Institute of Neurological Disorders and Stroke for the research project "Effect of AADC gene transfer on L-dopa induced dyskinesia in MPTP monkeys" (Principal Investigator: Krystof Bankiewicz MD, PhD).

James Waldron MD, resident in the Department of Neurological Surgery, received the Integra Foundation Award for his paper "Embolization of skull base meningiomas and feeding vessels arising from the internal carotid artery: feasibility and morbidity in a series of 262 consecutive meningioma patients," presented at the 2009 AANS Annual Meeting.

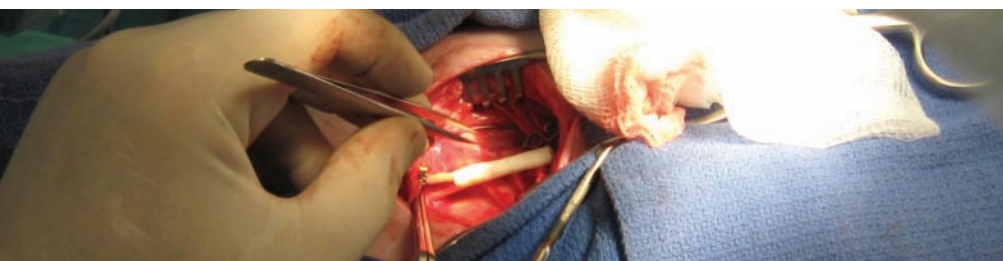
Isaac Yang MD, resident in the Department of Neurological Surgery, received the Leksell Radiosurgery Award from the AANS for the abstract "A systematic analysis of hearing and facial outcomes after Gamma Knife radiosurgery for vestibular schwannoma", presented at the 2009 AANS Annual Meeting. He was also the recipient of a competitive UCSF Clinical and Translational Scientist Training Research Award for his project "Hearing preservation after Gamma Knife radiosurgery for vestibular schwannoma."

The Pediatric Brain Tumor Foundation of the United States (PBTfUS), based in Asheville, North Carolina, has awarded the UCSF Pediatric Brain Tumor Center a 3-year, \$1 million Institute Award for pediatric brain tumor research. This grant will fund studies on stem cell neurobiology, aberrant cell-signaling pathways, and the development of siRNA molecules as therapeutic agents for pediatric brain tumors. UCSF joins Duke University as one of only two fully-funded PBTfUS Institutes in the United States.

New Faculty

The Department of Neurological Surgery at UCSF is pleased to announce the addition of several new faculty members. **Daniel Lim MD, PhD**, has become assistant professor of neurological surgery and principal investigator of a laboratory studying neurogenesis and neural stem cells in the subventricular zone. He also has clinical interests in stereotactic neurosurgery and practices in the surgical movement disorders program. After completing a fellowship in pediatric neurosurgery at the Hospital for Sick Children in Toronto, **Kurtis Auguste MD** joined the Department as an associate physician of neurological surgery and director of pediatric epilepsy surgery. **Jennifer Clarke MD** specializes in novel approaches to the treatment of brain tumors in adult patients and is a member of the Brain Tumor Research Center, focusing on clinical trials for novel therapies and novel imaging methods of characterizing tumors and their response to treatment. **Claudia Petritsch PhD** has joined the Brain Tumor Research Center and established a laboratory studying cell division and differentiation of brain cancer stem cells. She is currently studying regulators of asymmetric stem cell division as potential tumor suppressors and oncogenes by utilizing knock out mice and orthotopic transplantation models. **John Forsayeth PhD** has become an adjunct professor of neurological surgery, and works with Krystof Bankiewicz MD, PhD in developing translational research programs focused on neuro-inflammation and the role of the immune system in Parkinson's Disease.

The first poly (L lactide) nanofibrous polymer graft implanted in a porcine carotid



selected recent publications from the department of neurological surgery

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