

The Official Newsletter of the

Keck Medicine of USC

USC Brain Tumor Center

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**USC Norris Comprehensive
Cancer Center**

Keck Medicine of USC

USC BRAIN TUMOR CENTER

Report

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From the Director



This Spring Issue of the USC Brain Tumor Center Newsletter coincides with **Brain Tumor Awareness Month** (May). Raising awareness about brain tumors is of course vital to all brain tumor and cancer patients, and to our community as a whole. The USC Brain Tumor Center (BTC) staff understands the challenges that brain tumor patients and caregivers often face. To help make the journey easier, the BTC offers multiple options that care for the whole patient — not just their diagnosis. Our team of clinicians, nurses and researchers strives to provide the most streamlined and holistic patient experience that opt for brain tumor care at USC. Our multidisciplinary involvement across **Keck Medicine**, the **Keck School of Medicine of USC**, the **Norris Comprehensive Cancer Center (Norris CCC)**, and **Children's Hospital Los Angeles** keeps us focused

on continuing our mission of advancing research, education, and clinical care for all brain tumor patients. In this issue, we are excited to share work being done by several members of our team, including exciting research updates pertaining to the pioneering use of **blue light endoscopy** and **5-ALA optical fluorescence** for glioma surgery, and **advanced neuro-imaging algorithms** used for detection and grading of brain tumors.

The **USC BTC's collaboration with the Norris CCC**, an NCI-designated Comprehensive Cancer Center, is imperative to the clinical care of brain tumor and cancer patients, working relationships with oncologists and radiation oncologists, and clinical trials. With our integral collaboration and cross-center support of translational research, the USC BTC and Norris CCC are pursuing cutting-edge research and joint clinical trials that will develop next generation treatments for brain tumor patients. We offer direct access to several early phase and multi-institution clinical trials developed by USC BTC scientists and physicians. Only through these collaborative means can we work towards our goal of finding a cure for brain tumors.

Earlier this year, we launched the inaugural **USC Brain Tumor Center Advisory Council**, comprised of a selected group of dedicated and resourceful individuals with a primary focus on directing future growth of the USC BTC. This group is comprised of patients, family members and community leaders whom collaborate to provide invaluable insight and advice that will help the BTC obtain the support required to pursue cutting edge research and continue its rapid growth.

In this issue, we introduce our readership to the pioneering work being done by **Dr. Mark Shiroishi** and the advanced neuro-imaging center at LONI using 7 Tesla MR imaging. Dr. Shiroishi is the Director of Neuro-Radiology at the USC Brain Tumor Center and an international authority on clinical and advanced brain tumor imaging, and leads the imaging evaluation in our weekly multi-disciplinary Brain Tumor Board. We are one of few centers in the U.S. to have 7T MRI capability for clinical use in order to uncover new structural and functional biomarkers in brain tumor patients that have never been seen before and may revolutionize brain tumor care.

We are constantly assessing what more we can do for our patients and to drive towards a cure for brain tumors. Our **USC BTC Caregiver Support Group**, led by **Jinsky Rogers LCSW**, allows patients' caregivers to connect with each other on a monthly basis. Our **Patient**

Continues on page 2

USC BTC USC Norris Partnership

Led by Dr. Gabriel Zada, a member of the USC Norris **Genomic and Epigenomic Regulation Program**, the USC Brain Tumor Center is paving the way towards longer-term control and cures for a variety of brain tumors via streamlined, multidisciplinary clinical care, access to the latest clinical trials, and cutting-edge translational research. Our partnership with the USC Norris Comprehensive Cancer Center (USC Norris CCC) is imperative to advancing innovative brain cancer research and the clinical care of brain cancer patients.



As one of only 51 **NCI-Designated Comprehensive Cancer Centers** in the nation, USC Norris is a magnet for the best minds in cancer research, education, and delivery of patient-centered care. Through the new Rosalie and Harold Rae Brown Center for Cancer Drug Development, USC Norris is transforming groundbreaking discoveries from its laboratories into new cures. The translation of cancer research to the clinic enables our multi-disciplinary clinical teams to provide the latest evidence-based care at the Norris Cancer Hospital, Keck Medicine, and LA County Hospital, a public safety net hospital, as well as outpatient clinics throughout Los Angeles and Orange counties. In 2021, USC Norris renewed its comprehensive designation by the NCI, earning an exceptional rating, the best score in the history of the Cancer Center and one of the best in the nation.

The USC BTC and USC Norris CCC are critical elements to the clinical care of brain cancer patients, and having numerous team members whom are members of both centers fosters natural translational research, working relationships among treating physicians, and access to lifesaving clinical trials. Early phase, multi-institutional and investigator-initiated clinical trials developed by the USC Norris/BTC scientists and physicians are highly prioritized and, numerous initiatives are currently ongoing and on the horizon, spanning from novel drug therapies, immunotherapy, drug delivery mechanisms such as intranasal therapy, and cutting edge surgical treatments. Only through these highly collaborative means can we continue to work towards our goal of finding a cure for brain cancer.

"From the Director" continued

Research Advancement Core continues to make strides on our ongoing research projects. We also continue to offer a vast and rapidly expanding clinical trial portfolio and will continue to hone this in an effort to provide alternative advanced investigational options for our patients with different types of brain tumors.

We are very proud of the care that we deliver, and we will continue to strive to provide the best patient experience for our patients and their families. I want to thank you for your support of the USC BTC and its mission to provide unsurpassed clinical care to patients from all over the world and to cure brain tumors.

Gabriel Zada, MD, MS, FAANS, FACS

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USC Brain Tumor Center Launches Advisory Council

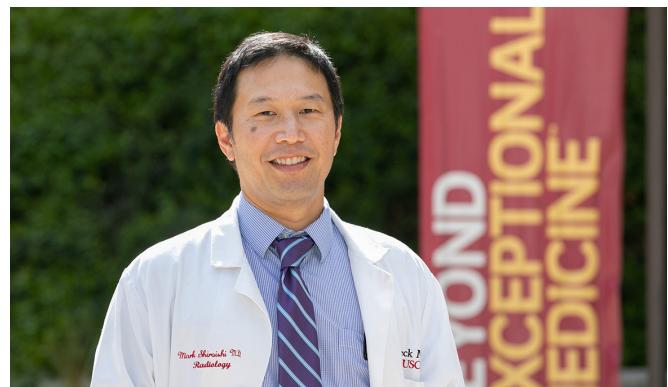
Earlier this year, we launched our inaugural **Brain Tumor Center Advisory Council**, comprised of dedicated and resourceful individuals with a primary focus on promoting the growth of the USC Brain Tumor Center. These amazing volunteers – many of whom have personal testimony with our incredible team – will help lift the Center to new heights by offering their advice, their time, talents, and support in advancing the established goals of the Center. The agenda of our first meeting covered topics like shining the spotlight on the Brain Tumor Center throughout the community, suggestions for increasing our fundraising efforts, and improving our patient experience. The Brain Tumor Center looks forward to welcoming new members to our team. If you or someone you know is interested in joining this team, please contact **Brian Loew** at brian.loew@med.usc.edu.



Gabriel Zada, MD, MS, Kelly Poland Self ('03), and Joseph Self ('03)

USC Brain Tumor Center Donor Spotlight

The USC Brain Tumor Center is honored to have the ongoing support of so many donors and friends. This Spring, we'd like to highlight **Kelly** and **Joe Self** and showcase their amazing generosity. Through a donation made in December of 2021, Joe and Kelly continued their support of clinical care and research at the Center. As members of the Advisory Council and as ambassadors of our mission to the community, the Selfs have helped to raise over \$200,000 to support our incredible team of clinicians and researchers. Thank you, Kelly and Joe, for all that you do and continue to do!



Meet Dr. Mark Shiroishi

Mark S. Shiroishi, M.D., Director of Neuro-Radiology, USC Brain Tumor Center, and Chief of Pediatric Neuroradiology at the Los Angeles County+USC Medical Center

Dr. Shiroishi is an international authority on clinical and advanced brain tumor imaging. He is the Director of Neuro-Radiology at the USC Brain Tumor Center and leads the imaging evaluation at both the multi-disciplinary Brain Tumor Board and Pituitary Tumor Board. He is also the Chief of Pediatric Neuroradiology at the Los Angeles County+USC Medical Center.

He completed his undergraduate, medical school and diagnostic radiology training at UCLA and subsequently completed both a pediatric and adult neuroradiology fellowship at Children's Hospital Los Angeles and Los Angeles County+USC Medical Center/Keck Medical Center of USC, respectively. He recently completed a Master's degree in Clinical, Biomedical and Translational Science and is currently working towards a PhD in Epidemiology in the Department of Population and Public Health Sciences at the Keck School of Medicine of USC. He was recently appointed as Co-Chair Radiological Society of North America (RSNA) Quantitative Imaging Biomarkers (QIBA) Dynamic Susceptibility Contrast MRI Biomarker Committee that strives to establish perfusion MRI metrics as reproducible imaging biomarkers. He was also recently elected as a Fellow of the American Society of Functional Neuroradiology in recognition of his contribution to the field of functional neuroradiology. In addition, he serves on the editorial boards of American Journal of Neuroradiology, BMC Cancer and has received Distinguished Reviewer awards from the American Journal of Neuroradiology and the Journal Magnetic Resonance Imaging. He has received several prestigious grants including an NIH KL2 career development award, NIH Loan Repayment Award and GE Healthcare/RSNA Research Scholar Award. He has given invited presentations at over 45 national and international scientific meetings as well as published more than 60 manuscripts and over 100 conference presentations.

One of his current areas of emphasis are building up the clinical and research neuro-oncology imaging applications of our very unique Siemens Terra 7 Tesla MRI. This is one of the first 7 Tesla MRI scanners approved for routine clinical use in the United States. Dr. Shiroishi is currently nearly through with recruitment for an RSNA grant-funded prospected 7T MRI study of prostate cancer survivors that seeks to understand structural and functional changes of prostate cancer related cognitive impairment. He is also anticipating starting up a similar study in testicular cancer survivors. He is also working with Dr. Danny Wang from the USC Center for Image Acquisition to provide upgrades to the 7T scanner that will allow us to uncover new structural and functional biomarkers in brain tumor patients that have never been seen before and may revolutionize brain tumor care.

Brain Tumor Tissue Core Bank Update

Over the last few months we have made significant strides in our ongoing research projects. First, we have continued to collect samples directly from the operating room for both next-generation sequencing projects and for the establishment of cell lines. We have currently collected over 100 samples spanning both primary brain tumors and brain metastases.

We aim to sequence every sample that is received from the operating room to create a database that will not only be used for research studies but can also be exploited for patient benefit.

Furthermore, we have established numerous cell lines from these specimens which we are currently in the process of validating to ensure

the cells in culture are indeed tumor cells. The latter is important for our future studies, especially our personalized medicine project.

For this project, we have purchased a compound screening library to test compounds on patient specimens to better tailor treatments for patients in hopes of finding a drug which can prolong survival.

Josh Neman, PhD

Assistant Professor, Neurosurgery
Scientific Director, USC Brain Tumor Center

Vahan Martirosian, PhD

USC Brain Tumor Center
Department of Neurological Surgery

SELECTED PUBLICATIONS



2020 Apr 2. PMID: 32241771; PMCID: PMC7144652.

Advanced ADC Histogram, Perfusion, and Permeability Metrics Show an Association with Survival and Pseudoprogression in Newly Diagnosed Diffuse Intrinsic Pontine Glioma: A Report from the Pediatric Brain Tumor Consortium. Vajapeyam S, Brown D, Billups C, Patay Z, Vezina G, Shiroishi MS, Law M, Baxter P, Onar-Thomas A, Fangusaro JR, Dunkel IJ, Poussaint TY. *AJNR Am J Neuroradiol.* 2020 Apr;41(4):718-724. doi: 10.3174/ajnr.A6499. Epub 2020 Mar 2.

■ Diffuse intrinsic pontine glioma is a lethal childhood brain cancer with dismal prognosis and MR imaging is the primary methodology used for diagnosis and monitoring. Our aim was to determine whether advanced diffusion, perfusion, and permeability MR imaging metrics predict survival and pseudoprogression in children with newly diagnosed diffuse intrinsic pontine glioma. ADC histogram, perfusion, and permeability MR imaging metrics in diffuse intrinsic pontine glioma are useful in predicting survival and pseudoprogression.



Improved Glioma Grading Using Deep Convolutional Neural Networks. Gutta S, Acharya J, Shiroishi MS, Hwang D, Nayak KS. *AJNR Am J Neuroradiol.* 2021 Jan;42(2):233-239. doi: 10.3174/ajnr.A6882. Epub 2020 Dec 10. PMID: 33303522; PMCID: PMC7872170.

■ Accurate determination of glioma grade leads to improved treatment planning. The criterion standard for glioma grading is invasive tissue sampling. Recently, radiomic features have shown excellent potential in glioma-grade prediction. These features may not fully exploit the underlying information in MR images. The objective of this study was to investigate the performance of features learned by a convolutional neural network compared with standard radiomic features for grade prediction. Convolutional neural networks are able to learn discriminating features automatically, and these features provide added value for grading gliomas. The proposed framework may provide substantial improvement in glioma-grade prediction; however, further validation is needed.



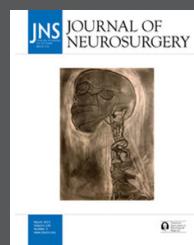
scientific reports

2022 Mar 9;12(1):3806

Automatic differentiation of Grade I and II meningiomas on magnetic resonance image using an asymmetric convolutional neural network. Vassantachart A, Cao Y, Gribble M, Guzman S, Ye JC, Hurth K, Mathew A, Zada G, Fan Z, Chang EL, Yang W. *Sci Rep.* 2022 Mar 9;12(1):3806. doi: 10.1038/s41598-022-07859-0. PMID: 35264655; PMCID: PMC8907289.

■ The Grade of meningioma has significant implications for selecting treatment

regimens ranging from observation to surgical resection with adjuvant radiation. For most patients, meningiomas are diagnosed radiologically, and Grade is not determined unless a surgical procedure is performed. The goal of this study is to train a novel auto-classification network to determine Grade I and II meningiomas using T1-contrast enhancing (T1-CE) and T2-Fluid attenuated inversion recovery (FLAIR) magnetic resonance (MR) images. A novel asymmetric CNN with two differently weighted encoding paths was developed for successful automated meningioma grade classification. Our model outperforms CNN using a single path for single or multimodal MR-based classification.



5-Aminolevulinic acid-enhanced fluorescence-guided treatment of high-grade glioma using angled endoscopic blue light visualization: technical case series with preliminary follow-up. Strickland BA, Wedemeyer M, Ruzevick J, Micko A, Shahrestani S, Daneshmand S, Shiroishi MS, Hwang DH, Attanello F, Chen T, Zada G. *J Neurosurg.* 2022 Mar 18;1-9. doi: 10.3171/2022.1.JNS212562.

■ 5-Aminolevulinic acid (5-ALA)-enhanced fluorescence-guided resection of high-grade glioma (HGG) using microscopic blue light visualization offers the ability to improve extent of resection (EOR); however, few descriptions of HGG resection performed using endoscopic blue light visualization are currently available. In this report, the authors sought to describe their surgical experience and patient outcomes of 5-ALA-enhanced fluorescence-guided resection of HGG using primary or adjunctive endoscopic blue light visualization.

CLINICAL TRIALS: Now Enrolling at the USC Brain Tumor Center

For more information about these clinical trials, please contact **Aida Lozada, Clinical Trials Manager, at Aida.Lozada@med.usc.edu.**

Olaparib in Treating Patients with Advanced Glioma, Cholangiocarcinoma, or Solid Tumors with IDH1 or IDH2 Mutations

This phase 2 trial studies the efficacy of Olaparib in treating patients with recurrent glioma, cholangiocarcinoma, or solid tumors with IDH1 or IDH2 mutations. Olaparib may stop the growth of tumor cells by blocking some of the enzymes needed for cell growth. ClinicalTrials.gov Identifier: NCT03212274

Trial of Enzastaurin Plus Temozolomide During and Following Radiation Therapy in Patients with Newly Diagnosed Glioblastoma with or Without the Novel Genomic Biomarker, DGM1

This study is a randomized, double-blind, placebo-controlled, multi-center trial. Enzastaurin will be added to the standard treatment of radiation and chemotherapy in patients with glioblastoma. Patients will be evaluated for the biomarker DGM1, which in other cancer types was shown to correlate with improved survival upon treatment with Enzastaurin. ClinicalTrials.gov Identifier: NCT03776071

Single Fraction Stereotactic Radiosurgery Compared with Fractionated Stereotactic Radiosurgery in Treating Patients with Resected Metastatic Brain Disease (CTSU- A071801)

This phase 3 trial studies how well single fraction stereotactic radiosurgery works compared with fractionated stereotactic radiosurgery in treating patients with cancer that has spread to the brain from other parts of the body and has been removed by surgery. Single fraction stereotactic radiosurgery is a specialized radiation therapy that delivers a single, high dose of radiation directly to the tumor and may cause less damage to normal tissue. Fractionated stereotactic radiosurgery delivers multiple, smaller doses of radiation therapy over time. ClinicalTrials.gov Identifier: NCT04114981

An Open-Label, Phase 1/2A Dose Escalation Study of Safety and Efficacy of NEO100 in Recurrent Grade IV Glioma

NEO100-01 is a Phase 1/2A open-label study of perillyl alcohol (NEO100) in patients with recurrent glioma. NEO100 is delivered four times a day by intranasal administration using a nebulizer and nasal mask for up to 6 months. There is no placebo arm. This is the first nasal administration in the US. ClinicalTrials.gov Identifier: NCT02704858

Stereotactic Radiosurgery (SRS Compared with Collagen Tile Brachytherapy

This trial is a randomized controlled study comparing the efficacy and safety of intraoperative radiation therapy using GammaTile versus SRS 3-4 weeks following metastatic tumor resection. GammaTile is a biocompatible permanently implanted system composed of a collagen "tile" that contains 4 Cesium-131 (Cs-131) titanium-encased sources. ClinicalTrials.gov Identifier: NCT04365374

Pivotal, Randomized, Open-label Study of Optune® Concomitant with RT & TMZ for the Treatment of Newly Diagnosed GBM (EF-32)

This study will test the effectiveness and safety of Optune® given concomitantly with radiation therapy and temozolomide in newly diagnosed glioblastoma, compared to radiation therapy and temozolomide alone. In both arms, Optune® and maintenance temozolomide are continued following radiation therapy. Optune® is a medical device that has been approved for the treatment of recurrent and newly diagnosed glioblastoma by the FDA in the United States. ClinicalTrials.gov Identifier: NCT04471844

New Trial Opening Soon

A Phase 2, Open-Label, Single-Arm, Multicenter Study to Evaluate the Efficacy and Safety of Pemigatinib in Participants With Previously Treated Glioblastoma or Other Primary Central Nervous System (CNS) Tumors Harboring Activating FGFR 1-3 Alterations (FIGHT-209).

A Study of Selinexor in Combination with Standard of Care Therapy for Newly Diagnosed or Recurrent Glioblastoma

This is a global multicenter, open-label, randomized study to evaluate a combination regimen with or without Selinexor. The study will independently evaluate 5 different combination regimens in participants with newly diagnosed or recurrent glioblastoma. ClinicalTrials.gov Identifier: NCT04421378

Observation or Radiation Therapy in Treating Patients with Newly Diagnosed Grade II Meningioma That Has Been Completely Removed by Surgery (NRG-BN003)

This randomized trial studies how well radiation therapy works compared with observation in treatment patients with newly diagnosed grade II meningioma that has been completely removed by surgery. Radiation therapy uses high energy x-rays to kill the tumor cells and shrink tumors. ClinicalTrials.gov Identifier: NCT03180268

A Phase I/II Study of Nivolumab plus or minus Ipilimumab in Combination with Multi-Fraction Stereotactic Radiosurgery for Recurrent High-Grade Radiation-Relapsed Meningioma

This trial studies the side effects and best dose of nivolumab when given together with multi-fraction stereotactic radiosurgery with or without ipilimumab in patients with recurrent grade II-III meningioma. Immunotherapy with the checkpoint inhibitors nivolumab and ipilimumab may help the immune system attack cancer and interfere with tumor growth and spread. Stereotactic radiosurgery is a specialized radiation therapy that delivers a single, high dose of radiation directly to the tumor and may cause less damage to normal tissue. ClinicalTrials.gov Identifier: NCT3604978

New Trial Opening Soon

An Open-Label, phase 2 study of NEO100 in participants with residual, progressive or recurrent high-grade meningioma.

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Brain Tumor Awareness Month is nationally recognized in the United States during the month of May.
Join us in the fight against Brain Cancer by raising awareness and bringing attention to the critical need
to find and provide effective brain treatment options for those impacted by a brain tumor diagnosis.

<https://app.mobilecause.com/vf/USCBTC>

We Are the **USC Brain Tumor Center**

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Make a Gift. Because of your support, we can provide Exceptional Medicine. Please contact **Brian Loew**, Senior Director of Development, Neurosciences, at Brian.Loew@med.usc.edu or visit www.keckmedicine.org/btc-donations

For more information about brain tumor clinical trials, please contact **Aida Lozada**, Clinical Trials Manager, at Aida.Lozada@med.usc.edu

Please email us with your questions at BTC@med.usc.edu

Learn more at: BTC.keckmedicine.org