

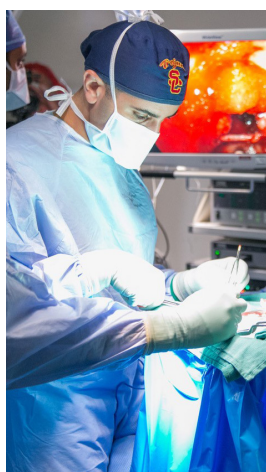
USC BRAIN TUMOR CENTER

Report

Volume 1 • Issue 4

AUTUMN 2021

From the Director



With regard to advancing clinical care and research, I am delighted to share with you that the **USC Brain Tumor Center (BTC)** continues to make strides on behalf of our brain tumor patients. Our multidisciplinary team of clinicians, scientists, engineers, and dedicated administrators continue to stay focused on the key goals for growth and sustainability of the BTC. We continue to strive in providing our patients the best experience regarding their care and continuing of care with our team.

During the past year we have invested in our **Brain Tumor Center Tissue Core**

where we are focusing on a multidisciplinary approach to tailor personalized treatment plans for patients with cancer. We seek to combine patient-derived data from the fields of molecular biology, neuro-imaging, and high-throughput drug screening with FDA approved drugs to find targeted treatments to best benefit our patients. The utilization of already approved drugs allows for immediate benefit to the patient.

In this issue, I am excited to share one of my patient's success story that coincides with the 5-year anniversary of her surgery and care at the USC Brain Tumor Center.

In addition, you will find our extensive clinical trials portfolio which provides patients, who have a variety of brain tumors, with advanced investigational options for their conditions. We also continue to focus on numerous advances in research that are being realized across our campuses and partnering institutions and include several high impact publications, some of which are profiled in this issue.

We are proud of our accomplishments over the past year and as always, I want to thank you for your support of the 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

Professor of Neurological Surgery, Otolaryngology, and Internal Medicine
Director, USC Brain Tumor Center
gzada@usc.edu

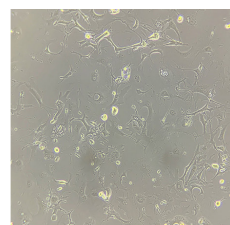
USC Brain Tumor Center Establishes Brain Tumor Tissue Core Bank

As the USC Brain Tumor Center, we pride ourselves on providing state-of-the-art clinical services and the highest quality healthcare for all our patients. Our multi-disciplinary team engages in thorough discussions to prepare a treatment plan best serving the patient's needs. We also recognize the importance of the growing field of personalized medicine and the benefit it provides to patient care.

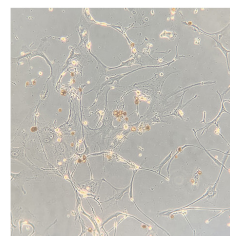
As such, we have recently added a research component to our services tasked with establishing a brain tumor tissue bank - collecting samples that will be processed for cell line establishment, drug screening, and RNA sequencing studies. The tissue core will be critical in providing personalized data which can be used along with guidance from our medical team to make clinical decisions on a patient-by-patient basis.

Although the goal of the core is research oriented, we believe this work will yield translational results with direct patient benefit.

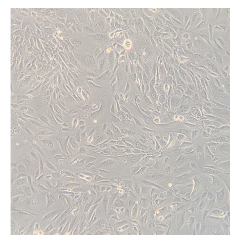
We have established a procedure where resected tumor samples are immediately processed by the tissue core for RNA sequencing and more importantly, for establishment of tumor cells. Tumor cells grown in the laboratory will then be subjected to a panel of 1600 FDA approved drugs and the sensitivity to each of these drugs will be determined. Considering these drugs are already approved for in human use, our goal is then to inform our neuro-oncologists of the screening results, who will then use this data along with other parameters to make treatment decisions personalized for the patient. In the future, the data collected from patient samples will be used to predict how certain tumors will behave genetically and how they will respond to certain drug classes - thereby improving our understanding of the complex biology of brain tumors and our ability to treat them.



USC Meningioma 7



USC BBM 5



USC AO 1

Josh Neman, PhD

Assistant Professor, Neurosurgery
Scientific Director, USC Brain Tumor Center

Vahan Martirosian, PhD

USC Brain Tumor Center



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

On the 5-Year Anniversary of My Brain Tumor Surgery

By Kelly Poland Self ('03)

My name is Kelly Poland Self ('03) and in November of 2016 I was happily married to my college sweetheart Joseph Self ('03) and together we were raising our two young girls. On a trip back to London over Thanksgiving to pack up our flat, where we had been living for the previous three years, my life was forever changed by a grand mal seizure. After an immediate flight back to Los Angeles and an appointment with a neurologist followed by a battery of tests, within three days I was told that I had a brain tumor, specifically a Glioma. Many months and pathology reports later we would learn of the official diagnosis of an Anaplastic Astrocytoma.

In the fog of such terrifying news and all of the unknowns and 'what ifs' it was clear that the first step was to get this mass out of my head and the most critical part of that process was deciding who I would trust, quite literally, with my life. My husband and I knew that this decision was critical and that we had to explore every available option. Thankfully we live in Los Angeles and are surrounded by many wonderful hospitals and talented doctors. Being a Trojan alumni in addition to being the daughter of two alums, Keck USC was obviously on our list and through the gift that is the Trojan Network I ended up sitting in a room with Dr. Gabriel Zada six days after my initial diagnosis.

At a moment when I could not have been more terrified of dying and missing the future with my husband getting to watch our beautiful daughters grow up it was immediately clear that Dr. Zada was the right person to entrust with one of the most important decisions I have ever made. Based on all of our research we knew that he had the necessary skills to perform the operation but what was even more clear in that first meeting was his compassion for our family and his understanding of my top priority of being a healthy mom.

Thanks to Dr Zada and his team at Keck, after a year of radiation and chemotherapy, I have been living the wonderfully healthy and normal life that I was so terrified I would lose. While I am not an expert I feel very confident in saying that my positive outcome is due primarily to the success of my surgery performed by Dr. Zada.

In the years since that initial meeting I have been fortunate to spend more time with the one man who has literally "been inside my head" and through this have come to appreciate Dr. Zada's passion for his craft and his desire and vision to make a significant impact in the brain tumor world through the Brain Tumor Center at Keck USC. Our family has so much to be grateful for from our experience with Dr Zada and we look forward to supporting the future of his important work and the creation of the new USC Brain Tumor Center.

Keck Medicine of USC
The USC Department of Neurological Surgery

USC Brain Tumor Center

Annual Research Retreat

FRIDAY, DECEMBER 10, 2021

1:00 - 5:00pm

HOSTED BY Gabriel Zada, MD, MS AND Josh Neman, PhD

Keynote Speaker

DAVID TRAN, MD, PHD

CHIEF OF THE DIVISION OF NEURO-ONCOLOGY IN THE DEPARTMENT OF NEUROSURGERY
ASSOCIATE DIRECTOR OF THE PRESTON A. WELLS, JR. BRAIN TUMOR CENTER
MCKNIGHT BRAIN INSTITUTE OF THE UNIVERSITY OF FLORIDA COLLEGE OF MEDICINE

Presentations by

FRANCES CHOW, MD

SHAHAB ASGHARZADEH, MD

ASHLEY S. MARGOL, MD, MS

MIN YU, MD, PHD

PETER KUHN, PHD

JOSH NEMAN, PHD

LOCATION: USC Health Sciences Conference Center,
Hyatt House USC
1616 San Pablo Street (North of Alcazar Street)
(IN PERSON AND VIRTUAL)

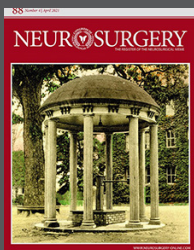
Please register at:

<https://www.eventbrite.com/e/usc-brain-tumor-center-annual-research-retreat-tickets-212632137447>

Poster Session to follow.

Passed hors d'oeuvres and beverages.

SELECTED PUBLICATIONS

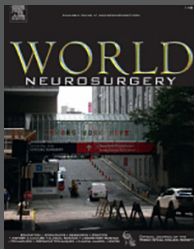


Stereotactic Radiosurgery for Periopic Meningiomas: An International, Multi-center Study.

Bunevicius A, Anand RK, Suleiman M, Nabeel AM, Reda WA, Tawadros SR, Abdelkarim K, El-Shehaby AMN, Emad RM, Chytka T, Liscak R, Sheehan K, Sheehan D, Caceres MP, Mathieu D, Lee CC, Yang HC, Picozzi P, Franzini A, Attuati L, Speckter H, Olivo J, Patel S, Cifarelli CP, Cifarelli DT, Hack JD, Strickland BA, Zada G,

Chang EL, Fakhoury KR, Rusthoven CG, Warnick RE, Sheehan J
Neurosurgery. 2021 Mar 15;88(4):828-837. doi: 10.1093/neuros/nyaa544. PMID: 33475718; PMCID: PMC8517876.

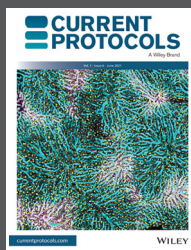
■ Stereotactic radiosurgery (SRS) is increasingly used for management of periopic meningiomas. SRS provides durable tumor control and quite acceptable rates of vision preservation in periopic meningiomas. Margin dose of >12 Gy is associated with improved tumor control, while a dose to the optic apparatus of >10 Gy and tumor progression are associated with post-SRS visual decline.



5-ALA Enhanced Fluorescence-Guided Microscopic to Endoscopic Resection of Deep Frontal Subcortical Glioblastoma Multiforme.

Strickland BA, Zada G
World Neurosurg. 2021 Apr;148:65. doi: 10.1016/j.wneu.2020.12.168. Epub 2021 Jan 13. PMID: 33453427.

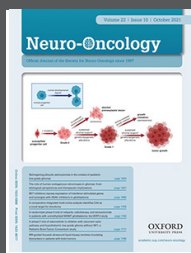
■ Glioblastoma multiforme remains the most common adult primary brain tumor with a life expectancy of 15-18 months following best treatment strategies. 5-Aminolevulinic acid has become a vital tool in the intraoperative identification and differentiation of high-grade glioma as it provides a fluorescent effect capable of distinguishing tumor from normal brain tissue when observed under blue light, which to date has been used primarily via a microscopic light source. However, this effect is attenuated with increasing distance between the blue light source and the tumor, as in the case of deep seated resection cavities. We aimed to overcome this obstacle by using a blue light endoscope as the primary visualization platform, thereby advancing the light source directly into the resection cavity.



Utilization of Discarded Surgical Tissue from Ultrasonic Aspirators to Establish Patient-Derived Metastatic Brain Tumor Cells: A Guide from the Operating Room to the Research Laboratory.

Martirosian V, Deshpande K, Lin M, Jarvis C, Yuan E, Chen TC, Zada G, Giannotta SL, Attenello FJ, Chow F, Neman J.
Curr Protoc. 2021 Jun;1(6):e140. doi: 10.1002/cpz1.140. PMID: 34170630.

■ Current established protocols for propagating tumor cells in vitro are limiting because resections obtained from conventional singular samples limit the diversity in cell populations and do not accurately model the heterogeneous tumor. Utilization of discarded tissue obtained from cavitron ultrasonic surgical aspirator (CUSA) of the whole tumor mass allows for establishing novel cell lines in vitro from the entirety of the tumor. While others have described protocols for establishing patient tumor lines once tissue has arrived in the research lab, a primer from the operating room (OR) to the research lab has not been described before.



Enhanced brain delivery and therapeutic activity of trastuzumab after blood-brain barrier opening by NEO100 in mouse models of brain-metastatic breast cancer.

Wang W, He H, Marín-Ramos NI, Zeng S, Swenson SD, Cho HY, Fu J, Beringer PM, Neman J, Chen L, Schönthal AH, Chen TC
Neuro Oncol. 2021 Oct 1;23(10):1656-1667. doi: 10.1093/neuro/naab041.

■ The antitumor efficacy of human epidermal growth factor receptor 2 (HER2)-targeted therapies, such as humanized monoclonal antibody trastuzumab (Herceptin®, Roche), in patients with breast-to-brain cancer metastasis is hindered by the low permeability of the blood-brain barrier (BBB). NEO100 is a high-purity version of the natural monoterpene perillyl alcohol, produced under current good manufacturing practice (cGMP) regulations, that was shown previously to reversibly open the BBB in rodent models. Here we investigated whether NEO100 could enable brain entry of trastuzumab to achieve greater therapeutic activity.

BRAIN TUMOR PATIENT CAREGIVER SUPPORT GROUP

The USC Brain Tumor Center now offers a monthly support group to caregivers of patients living with a brain tumor

We are excited to announce the launch of our brain tumor caregiver support group. This group will provide the opportunity for family and friends of patients with brain tumors to come together and find common ground to help each other. We hope that each participant will come away feeling more supported in caring for their loved ones and have a safe space to discuss the challenges and victories in being a caregiver.

When: Second Thursday of each month 4-5:00p.m. Location: Remote, via Zoom

Contact for Zoom link: Jinsy Rogers, LCSW, (323) 865-6057, Jinsy.Rogers@med.usc.edu

For more information, please contact Jinsy Rogers or Nancy Hart, Nurse Navigator, RN, (844) 332-7246, Nancy.Hart@med.usc.edu

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.

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

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

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

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

Standard Chemotherapy vs Chemotherapy Guided by Cancer Stem Cell Test in Recurrent Glioblastoma (CSCRGBM)

This study will confirm the utility of chemosensitivity tumor testing on cancer stem cells (ChemolD) as a predictor of clinical response in malignant brain tumors such as recurrent glioblastoma and anaplastic astrocytoma. Patients with an unlimited number of recurrences and multifocal disease are candidates for this study. ClinicalTrials.gov Identifier: NCT03632135

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

Study to Evaluate Eflornithine + Lomustine vs Lomustine in Recurrent Anaplastic Astrocytoma (AA) Patients (STELLAR)

The purpose of this study is to compare the efficacy and safety of eflornithine in combination with Lomustine, compared to Lomustine taken alone, in patients whose Anaplastic Astrocytoma has recurred/ progressed after radiation and temozolomide chemotherapy. ClinicalTrials.gov Identifier: NCT02796261

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

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

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

USC Brain Tumor Center

1441 Eastlake Avenue
Los Angeles, CA 90033

Patient referrals, (844) 33-BRAIN (844-332-7246)

USC has the highest volume of neurosurgical brain tumor cases of any academic center in SoCal.

- California's Office of Statewide Health Planning and Development (OSHPD),
Calendar Year 2019, most recent data available.

We Are the USC Brain Tumor Center

NEUROSURGERY

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Josh Neman, PhD
Frank Attenello, MD, MS
Steven Giannotta, MD
Cheng Yu, PhD
Oscar Aurelio, PhD
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Camelia Danilov, PhD
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Vahan Martirosian, PhD
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David Craig, PhD
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Daniel Weisenberger, PhD

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Sandy Leong, BSN, RN, CCRP
Aida Lozada, MA

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USC Brain Tumor Center



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To refer a patient, please call **(844) 33-BRAIN (844-332-7246)**

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**