

USC BRAIN TUMOR CENTER

Report

Volume 2 • Issue 1

WINTER 2022

From the Director



As we look back at 2021, we are quite proud of the accomplishments that the **USC Brain Tumor Center (USC BTC)** achieved in the way of advancing research, education, and clinical care for our brain tumor patients. Our team has set goals and expectations very high for 2022 and we will continue to stay focused on growth and sustainability of the USC BTC. We will also continue to strive to provide the best patient experience for all families and patients that choose USC as a destination site for brain tumor care.

The USC BTC wrapped up 2021 with a live and virtual **Brain Tumor Research Retreat** on December

10 that showcased an unprecedented amount of new and innovative science being led by USC BTC members. The USC BTC team—including trainees, administrators, researchers, clinicians, and staff — along with members of the community-at large gathered this year to share and discuss our visions for the future of brain tumor research and care. Visiting Neurosurgeon **Dr. Michael Sughrue** from Sydney, Australia gave an impressive lecture on connectomics and tractography in brain tumor surgery, and Keynote speaker **Dr. David Tran** from the University of Florida gave a wonderful lecture on computational analysis and immunotherapy in brain tumors.

Our USC BTC Team continues to rapidly grow, and in 2021 we added several members to our team of over 70 individuals working together for our common purpose. This year, I have the distinct pleasure of introducing our newest team member, **Dr. Lindsay Hwang**, assistant professor of Radiation-Oncology, who specializes in treating benign and malignant tumors of the Central Nervous System. Dr. Hwang brings extensive experience in today's most advanced modalities in radiation oncology and stereotactic radiosurgery. The radiation oncology team, led by **Dr. Eric Chang**, Chairman of Radiation Oncology at the Keck School of Medicine and the USC Norris Comprehensive Cancer Center, is a critical centerpiece of the multi-disciplinary team at the USC BTC.

We are constantly assessing what more we can do for our patients and to drive towards a cure for brain tumors. Last year we introduced the **USC BTC Caregiver Support group**, led by **Jinsy Rogers LCSW**, that allows patients' caregivers to connect with each other on a monthly basis, and we will continue to offer this excellent addition this year. We also offer a vast clinical trial portfolio that grew exponentially in 2021, and will continue to hone this in an effort to provide alternative advanced investigational options for our patients with different types of brain tumors.

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. We look forward to continuing to provide unsurpassed care in 2022 and always.

Gabriel Zada, MD, MS, FAANS, FACS

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

Lindsay Hwang, M.D. joins the USC Brain Tumor Center

The USC Brain Tumor Center is pleased to announce **Dr. Lindsay Hwang**, as our newest member of the **USC Brain Tumor Center** and the Department of Radiation Oncology.

Dr. Lindsay Hwang is a radiation oncologist and specializes in treating benign and malignant tumors of the central nervous system (CNS). She received her undergraduate degree in Human Biology from the University of California, San Diego and her medical degree from Case Western Reserve University School of Medicine. She completed her radiation oncology residency at USC and served as chief resident in her final year. She was awarded the **RSNA Roentgen Resident Research Award** for her research in brain metastases and patient advocacy.



As a radiation oncologist, Dr. Hwang cherishes the privilege of guiding her patients through the vulnerable journey of cancer diagnosis and cancer care. Her goal is to deliver comprehensive, safe radiation treatment while developing a relationship of trust built on scientific expertise, empathy and consideration for patients and their families as whole individuals. Through the USC Brain Tumor

Center, she is able to combine her passion for patient care while advancing the field through collaboration and clinical trials.

"Dr. Lindsay Hwang has a prominent role at the USC Brain Tumor Center because she is

very passionate about providing outstanding care for patients with brain tumors, as well as involving herself in research and educational activities that will help ameliorate patient suffering caused by brain tumors. She is leading clinical trial investigations into 7 Tesla MRI to better understand how this advanced neuroimaging can be used to help melanoma patients with metastatic brain disease. She is an exceptionally kind, compassionate, and empathetic physician who always stands ready to advocate for the best care of her patients," **Dr. Eric Chang**, Chairman, Radiation Oncology, Keck School of Medicine, USC Norris Comprehensive Cancer Center.

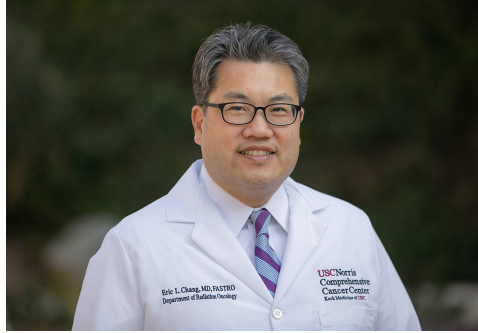
She brings extensive experience in today's most advanced modalities in radiation oncology to treat patients with CNS malignancies. She specializes in **Gamma Knife** and other radiosurgery techniques, which use noninvasive, precise, focused beams of radiation to treat tumors. She also has expertise in **intensity-modulated radiation therapy (IMRT)**, **image-guided radiation therapy (IGRT)**, and **stereotactic body radiation therapy (SBRT)**, among others.

Meet Dr. Eric Chang

Dr. Chang is the Medical Director of Radiation Oncology at USC Norris Comprehensive Cancer Center and a member of the USC Brain Tumor Center Team.

Dr. Chang is considered a world authority in the use of advanced radiation therapy techniques in the treatment of a variety of benign conditions and malignant tumors of the central nervous system. He is highly experienced in handling both routine cases, and the most complex cases requiring radiotherapeutic evaluation in a multi-disciplinary setting of experts comprising neuro-radiation oncologists, neurosurgeons and neuro-oncologists, and neuro-radiologists.

Dr. Chang received his undergraduate degree in Biology from the Massachusetts Institute of Technology and medical doctorate degree from Harvard Medical School. His internship in medicine at the California Pacific Medical Center at UC San Francisco and residency training was conducted at the Harvard Joint Center for Radiation Therapy, in Boston, Massachusetts. He has held research leadership roles including having served as member and Chair of the M. D. Anderson Cancer Center Clinical Research Committee (CRC). He served as the 2011 CNS track leader for the American Society for Clinical Oncology (ASCO) Scientific Program Committee, and member of the ASCO Cancer Education Committee. Dr. Chang has served as the co-leader for the



American Society of Radiation Oncology (ASTRO) brain metastasis guidelines development task force and as a member of the Annual Program Committee of the Educational Council of ASTRO. He is a current Chair of the American Radium Society Appropriate Use Committee (AUC) for Brain. He has been listed in the Best Doctors Directory. Dr. Chang led a phase III randomized controlled trial on brain metastasis published in the *Lancet Oncology* 2009 which is starting to change the practice patterns for metastatic brain disease. Dr. Chang has been selected as a plenary speaker for past meetings of ASTRO and the American Association for Neurological Surgeons (AANS). He has authored or co-authored over 150 peer-reviewed papers and abstracts.

In addition to his leadership roles at Keck Medicine of USC, Dr. Chang also serves as the Medical Director of the Radiation Oncology Service at Children's Hospital Los Angeles.

Dr. Chang will be inducted as a Fellow into the American Radium Society (FARS) founded in 1916, the oldest society devoted to the study and treatment of cancer.

USC Brain Tumor Center Annual Research Retreat 2021

By Josh Neman, PhD, Scientific Director, USC Brain Tumor Center

The annual **USC Brain Tumor Center Cancer Center Retreat** was held in person at the USC Health Sciences Campus and virtually on December 10, 2021. The USC brain tumor team—from trainees, to administrators, researchers, clinicians, and faculty, along with members of the community-at large—came together this year, to share our visions for the future of brain tumor research and care. The meeting was kicked off by Center Director's (Drs Zada and Neman) reports on both clinical and scientific progress. The scientific sessions began with selected presentations from faculty covering major topics highlighting new insights into brain tumor biology and treatments, including **1)** approaches for accelerating precision medicine for brain tumors, **2)** the utilization of liquid biopsies for diagnostic and drug discovery in brain metastasis, **3)** the role of the nervous system in brain metastasis, and **4)** intranasal drug delivery to brain tumor. Visiting Neurosurgeon Dr. Michael Sughrue from Sydney, Australia gave an impressive lecture on connectomics and tractography in brain tumor surgery and Keynote Speaker David Tran MD PhD (Chief of the Division of Neuro-Oncology, McKnight Brain Institute at the University of Florida), whose translational research focuses on unlocking fate-based immunity in brain tumor, gave a wonderful lecture on computational analysis and immunotherapy in brain tumors.

As the USC Brain Tumor Center continues to grow and have a larger and meaningful impact on brain tumor research across Southern California and the nation, we were fortunate to have an inaugural poster session highlighting tools and resources that are available to the research community. Overall, I wish to thank all those who attended this extraordinary event and continue to help our scientific and clinical community in developing a deeper understanding of brain tumors in order to help out those effected with this devastating disease.

Caregiver Support Group of the USC Brain Tumor Center

In August 2021, a great addition to our multidisciplinary care was the launch of our very first caregiver support group, led by **Jinsy Rogers, LCSW** and **Nancy Hart**. Although our hope was that we could meet in person, Zoom meetings seemed to be the safest route taking Covid into consideration.

We had no idea that this would open the door to having caregivers from Bakersfield to South Orange County join us without having to worry about traffic into LA at rush-hour.

We have discussed topics such as strategies to help with day-to-day activities from the caregiver stand-

point and how to cope with a loved one who has a brain tumor during the holidays. We are in awe of the bravery of these care-

givers to be vulnerable and invite us into a very personal and difficult area of their lives. This group has allowed caregivers to connect with each other and know that they are not alone. Not only do they have their medical team

walking beside them through this journey but also other caregivers who experience similar struggles.

We look forward to 2022 and to having educational presentations from our experienced staff at Keck who have worked with brain tumor patients and their families as well as open forum discussions so that our participants can continue to share their ongoing stories.



Jinsy Rogers, LCSW
Licensed Clinical
Social Worker



Nancy Hart,
MSN, RN, CPON
Nurse Navigator

Anyone who would like to participate, please reach out to **Jinsy Rogers** at **323-865-6057** or **Jinsy.Rogers@med.usc.edu**.

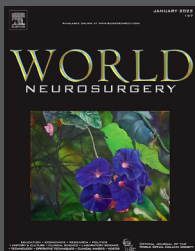
SELECTED PUBLICATIONS



Executive summary from American Radium Society's appropriate use criteria on neurocognition after stereotactic radiosurgery for multiple brain metastases. Michael T. Milano, Veronica L.S. Chiang, Scott G. Soltys, Tony J.C. Wang, Simon S. Lo, Alexandria Brackett, Seema Nagpal, Samuel Chao, Amit K. Garg, Siavash Jabbari, Lia M. Halasz, Melanie Hayden Gephart, Jonathan P.S. Knisely, Arjun Sahgal, Eric L. Chang.

Neuro Oncol. 2020 Dec 18;22(12):1728-1741. doi: 10.1093/neuonc/noaa192. PMID: 32780818 PMCID: PMC7746939 DOI: 10.1093/neuonc/noaa192

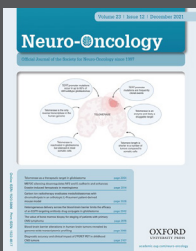
■ The American Radium Society Appropriate Use Criteria brain malignancies panel systematically reviewed (PRISMA [Preferred Reporting Items for Systematic Reviews and Meta-Analyses]) published literature on neurocognitive outcomes after stereotactic radiosurgery for patients with multiple brain metastases (BM) to generate consensus guidelines. For patients with 2-10 BM, SRS alone is an appropriate treatment option for well-selected patients with good performance status.



Systematic Review of Racial, Socioeconomic, and Insurance Status Disparities in Neurosurgical Care for Intracranial Tumors. Jesse Mendoza, Dhiraj J. Pangal, Tyler Cardinal, Phillip A. Bonney, Elizabeth Lechholz-Zey, Ben A. Strickland, Steven Giannotta, Gabriel Zada

World Neurosurg. 2021 Oct 26;158:38-64. doi: 10.1016/j.wneu.2021.10.126. Online ahead of print. PMID: 34710578 DOI: 10.1016/j.wneu.2021.10.126.

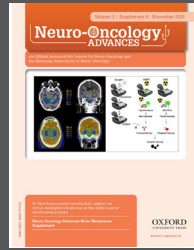
■ The impact of race, socioeconomic status (SES), insurance status, and other social metrics on the outcomes of patients with intracranial tumors has been reported in several studies. However, these findings have not been comprehensively summarized. Significant disparities exist among patients with intracranial tumors, particularly affecting patients of African American race and lower SES. Efforts at the hospital, state, and national level must be undertaken to identify root causes of these issues.



Neuronal exposure induces neurotransmitter signaling and synaptic mediators in tumors early in brain metastasis. Krutika Deshpande, Vahan Martirosian, Brooke Naomi Nakamura, Mukund Iyer, Alex Julian, Rachel Eisenbarth, Ling Shao, Frank Attenello, Josh Neman

Neuro Oncol. 2021 Dec 21;noab290. doi: 10.1093/neuonc/noab290. Online ahead of print. PMID: 34932815 DOI: 10.1093/neuonc/noab290.

■ Brain metastases (BM) are responsible for neurological decline and poor overall survival. Although the pro-metastatic roles of glial cells, and the acquisition of neuronal attributes in established BM tumors have been described, there are no studies that investigate the initial interplay between neurons and brain-seeking tumor cells. The aim of this study was to characterize early tumor-neuron interactions and the induced CNS-adaptive changes in tumor cells prior to macro-colonization. Tumor-neuron interactions allow for CNS-adaptation early in the course of brain metastasis.

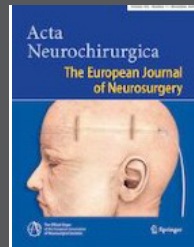


The microenvironment of brain metastases from solid tumors.

Ethan S. Srinivasan, Krutika Deshpande, Josh Neman, Frank Winkler, Mustafa Khasraw
Neurooncol Adv. 2021 Nov 27;3(Suppl 5):v121-v132. doi: 10.1093/oaajnl/vdab121.

■ Brain metastasis (BrM) is an area of unmet medical need that poses unique therapeutic challenges and heralds a dismal prognosis.

The intracranial tumor microenvironment (TME) presents several challenges, including the therapy-resistant blood-brain barrier, a unique immune milieu, distinct intercellular interactions, and specific metabolic conditions, that are responsible for treatment failures and poor clinical outcomes. In this review, we discuss unique aspects of the TME in the context of brain metastases and pathways through which the TME may hold the key to the discovery of new and effective therapies for patients with BrM.

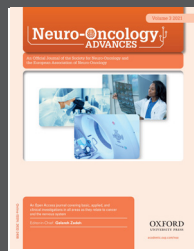


Predictors of readmission after craniotomy for meningioma resection: a nationwide readmission database analysis.

Michelle Lin, Elliot Min, Elliott Orloff, Li Ding, Kerolos Youssef, James Hu, Steven L. Giannotta, William J. Mack, Frank J. Attenello
Acta Neurochir (Wien). 2020 Nov;162(11):2637-2646. doi: 10.1007/s00701-020-04528-x.

■ Meningiomas are the most common

benign primary brain tumors. The mainstay of treatment, surgical resection, is often curative. Given the excellent prognosis of these lesions, minimizing perioperative complications is of the utmost importance. With the establishment of the National Readmissions Database (NRD), researchers are now able to identify variables associated with postoperative complications beyond the index admission. In this study, we sought to identify the leading causes for non-elective readmission and variables associated with increased likelihood of readmission at 30 and 90 days after discharge following a craniotomy for meningioma resection.



Phase I trial of intranasal NEO100, highly purified perillyl alcohol, in adult patients with recurrent glioblastoma.

Axel Schönthal, David Peereboom, Naveed Wagle, Rose Lai, Anna Mathew, Kyle Hurth, Vincent Simmon, Steven Howard, Lynne Taylor, Frances Chow, Clovis da Fonseca, Thomas Chen.
Neurooncol Adv. 2021 Feb 12;3(1):vdab005. doi: 10.1093/oaajnl/vdab005.

■ Better treatments for glioblastoma (GBM) patients, in particular in the recurrent setting, are urgently needed. Clinical trials performed in Brazil indicated that intranasal delivery of perillyl alcohol (POH) might be effective in this patient group. NEO100, a highly purified version of POH, was current good manufacturing practice (cGMP) manufactured to evaluate the safety and efficacy of this novel approach in a Phase I/IIa clinical trial in the United States. Intranasal glioma therapy with NEO100 was well tolerated. It correlated with improved survival when compared to historical controls, pointing to the possibility that this novel intranasal approach could become useful for the treatment of recurrent GBM.

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.

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

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

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

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

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

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

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

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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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**