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 Directors

As we look back at 2022, we are quite proud of the accomplishments that the USC Brain Tumor Center (USC BTC) achieved in the way of advancing research, recruitment, education, and clinical care for our brain tumor patients. Our team has set our goals and expectations even higher for 2023 and we will continue to stay focused on growth and sustainability of the BTC. We will also continue to strive in providing the best patient experience for all families and patients that choose USC as a destination site for brain tumor care. We are especially excited about the recent opening of the **USC Norris CCC GMP** facility to facilitate **CAR-T cell delivery** for brain tumors at USC Norris, and the promise this approach brings to patients and families in 2023.

The USC BTC wrapped up 2023 with a live and virtual **Brain Tumor Research Retreat** on December 9th that showcased an unprecedented amount of new and innovative science being led by 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. The keynote address was delivered by Adrienne Boire MD PhD (Geoffrey Beene Junior Faculty Chair, Memorial Sloan Kettering Cancer Center), whose translational research focuses on brain and leptomeningeal metastases.

We are constantly assessing what more we can do for our patients and to drive towards a cure for brain tumors. In this newsletter we are highlighting one of the most advanced technologies we offer to patients with Brain Tumors- **LITT (or Laser Interstitial Thermal Therapy)**. LITT has demonstrated safety as a minimally invasive surgical approach to treating primary brain tumors and is a viable option for patients with new and recurrent brain tumors including glioblastoma, other primary central nervous system (CNS) neoplasms, brain metastases, and radiation necrosis.

We will continue to offer the ever growing **USC BTC Caregiver Support group**, led by Jinsy Rogers LCSW, on a monthly basis. We will also continue to offer access to all our clinical trials and will focus on enhancing our portfolio in order to make available, alternative advanced investigational options for our patients with different types of brain tumors. This year, we expect to see new trials opened at the BTC that are based on intranasal delivery of drugs to brain and skull base tumors, as well as novel immunotherapy and CAR-T cell trials for brain tumors.

We 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 outstanding care in 2023 and always.

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U.S. News & World Report Best Hospital Ranking - doximity

In early 2023, solicitations to vote for the annual US News and World Report Best Hospital ranking will start. Please consider voting for USC Neurology and Neurosurgery. Your vote for USC Brain Tumor Center physicians is an endorsement of our work on your patients' behalf. Patients see this ranking as an important credential for an institution. Your support is another way of reassuring your patients that you have referred them to a preeminent institution.

As a valued partner, we are committed to maintaining your trust and look forward to working with you this year.

Brain Tumors: Your Guide to Navigating Through Our System

By Rebekah Ghazaryan RN, BSN, PHN, RN Clinical Coordinator, USC Brain Tumor Center

It is a daunting experience to attempt to navigate through the medical nuances once diagnosed with a brain tumor. Where do I begin? What do I need to see the neurosurgeon? What does surgery entail? Here is a quick guide on how we can make this process as simple as possible for you.

For most brain tumors, surgery is the first line of treatment, but can vary depending on the tumor type, the size of the tumor, and location. For some tumors, it is recommended that continued monitoring is the best route.

Preparing to see our Neurosurgeons

- Most appointments with our neurosurgeons are accommodated within 48-72 hours
- In determining whether a brain tumor will benefit from surgery, radiation, or observation it is important that we have the necessary imaging to make the most meaningful recommendations for you.
- Neuroimaging is one of the most important pieces of the puzzle and can vary from:

Continues on page 2

"Brain Tumors: Your Guide to Navigating..." ***continued***

- MRI (Magnetic Resonance Imaging) – gold standard when diagnosing most types of brain tumors
- CT Scan (Computerized Tomography)

• Medical records – only records pertaining to your current diagnosis:
- Imaging reports
- Notes from the referring MD

Surgery and Expectations

Surgical resection is the most common treatment done on brain tumors, but remember, that may not be the first treatment recommendation as every brain tumor case is different. Below is a list of types of brain surgeries that can be done to best identify the pathology of your tumor and the removal of the mass.

Craniotomy and resection of the brain tumor – this can take anywhere from 3-6 hours with a recovery period of 2-3 days in the hospital*

Biopsy of the tumor – 2-3 hours and up to 1-2 days in the hospital*

Transsphenoidal Resection – 2-3 hours and 1-2 days of hospitalization*

The most important key to remember in all of this is that the size and location of the tumor is a one of the chief deciding factors of whether you will need surgery. If a tumor is in a more eloquent area of the brain or abuts certain imperative nerves and structures – surgery may take longer, and recovery will vary.

Post-Operative Expectations

Once you are discharged home or to your next recovery destination, please rest assure, you will always be in direct contact with one of our neurosurgery RNs who will be guiding you in post-operative incisional care, post-op appointments and overall, the next steps. Here at USC Brain Tumor Center, you are never alone. You can reach someone 24 hours/7 days a week.

Post-Op Appointment Expectations

We will usually see you 7-10 days post-surgery in our clinic which is located adjacent to the main hospital here at Keck. By the date of your appointment, we will have your pathology details and your case will have been discussed in our multidisciplinary conference.

What do you mean by multidisciplinary?

USC Brain Tumor Center is comprised of multiple neurosurgeons, neuro-oncologists, radiation oncologists,

neurosurgery RNs, neuro pathologists, and neuro social workers all of which are involved in your care and meet weekly to discuss brain tumor cases and the best approach to your treatment plan.

Your post-op appointment will be encompassed by providers and clinicians who specialize in brain tumors and are leading experts in their field.

Once you are discharged from the neurosurgery team, our Brain Tumor RN Navigator will hold your hand and assist with all your follow-up appointments and will be your go to person during your treatment.

We here at USC Brain Tumor Center understand the journey that lays ahead of you is challenging but have confidence that we are the best at what we do and will guide you every step of your way.

*These are average times and days in hospital, but will vary depending on post-operative recovery as every case and patient is different.

USC Brain Tumor Center Annual Research Retreat 2022

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 on December 9, 2022. 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 presentation from faculty covering major topics highlighting new insights into brain tumor biology and treatments, including:

- USC Brain Tumor Center Personalized Medicine Initiative
- Developing epigenetic approached to therapy for pediatric gliomas
- Imaging biomarker strategies for clinical trials in brain tumors,
- Precision medicine in radiation oncology
- Tumor microenvironment in brain metastases

With the keynote address given by Adrienne Boire, MD PhD (Geoffrey Beene Junior Faculty Chair, Memorial Sloan Kettering Cancer Center), who's translational research focuses on brain and leptomeningeal metastases.

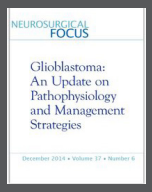
I wish to thank all those who attended this extraordinary event and continue to help our scientific and clinical community in developing a deeper understanding of brain tumors in order to help out those effected with this devasting disease.

Laser Interstitial Thermal Therapy (LITT) for Brain Tumors

At the USC Brain Tumor Center, we will design a treatment plan customized to your type of tumor and focused on your well-being goals. Treatment options for unresectable new and recurrent brain tumors remain limited. One of the newest interventions the USC BTC offers is LITT (or Laser Interstitial Thermal Therapy). LITT has demonstrated safety as a minimally invasive surgical approach to treating primary brain tumors and is a viable option for patients with new and recurrent brain tumors including glioblastoma, other primary central nervous system (CNS) neoplasms, brain metastases, and radiation necrosis. LITT may be selected in lieu of surgical resection in appropriate patients. It can be used in conjunction with radiation treatment, Tumor Treating Fields, and systemic therapy, especially in patients who are at high risk for surgical resection due to tumor location in eloquent regions or poor functional status.

How does LITT work? LITT employs a fiber optic coupled laser delivery probe stabilized via stereotaxis to deliver thermal energy that induces coagulative necrosis in tumors to achieve effective cytoreduction. The blood-brain barrier (BBB) is a major limiting factor for drug delivery in brain tumors. LITT has also been shown to induce transient disruption of the peri-tumor BBB. Overcoming this barrier will be key for the development of new therapies and for the repurposing of existing anti-cancer drugs that are known to be highly lethal against brain tumor cells but have had limited clinical use in brain tumor patients due to their lack of BBB penetrance. Numerous large studies have demonstrated the safety and efficacy of LITT against various CNS tumors, and as the literature continues to grow on this novel technique, so will its indications. Notably, emerging data suggest that LITT may induce immunogenic cell death, creating a potential synergy with existing cancer immunotherapy.

SELECTED PUBLICATIONS



Stereotactic laser ablation of high-grade gliomas.

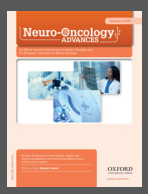
Hawasli AH, Kim AH, Dunn GP, Tran DD, Leuthardt EC. *Neurosurg Focus. 2014 Dec;37(6):E1. doi: 10.3171/2014.9.FOCUS14471.*

Evolving research has demonstrated that surgical cytoreduction of a high-grade glial neoplasm is an important factor in improving the prognosis of these difficult tumors. Recent advances in intraoperative imaging have spurred the use of stereotactic laser ablation (laser interstitial thermal therapy [LITT]) for intracranial lesions. Among other targets, laser ablation has been used in the focal treatment of high-grade gliomas (HGGs). The authors review the research on stereotactic LITT for the treatment of HGGs and provide a potential management algorithm for HGGs that incorporates LITT in clinical practice.

Role of Laser Interstitial Thermal Therapy in the Management of Primary and Metastatic Brain Tumors.

Melnick K, Shin D, Dastmalchi F, Kabeer Z, Rahman M, Tran D, Ghiaseddin A. *Curr Treat Options Oncol. 2021 Oct 23;22(12):108. doi: 10.1007/s11864-021-00912-6.*

Laser interstitial thermal therapy (LITT) is a minimally invasive treatment option for brain tumors including glioblastoma, other primary central nervous system (CNS) neoplasms, metastases, and radiation necrosis. LITT employs a fiber optic coupled laser delivery probe stabilized via stereotaxis to deliver thermal energy that induces coagulative necrosis in tumors to achieve effective cytoreduction. LITT has also been shown to induce transient disruption of the blood-brain barrier (BBB), especially in the peritumoral region, which allows for enhanced CNS delivery of anti-neoplastic agents.



A phase II study of laser interstitial thermal therapy combined with doxorubicin in patients with recurrent glioblastoma.

Butt OH, Zhou AY, Huang J, Leidig WA, Silberstein AE, Chheda MG, Johanns TM, Ansstas G, Liu J, Talcott G, Nakiwala R, Shimony JS, Kim AH, Leuthardt EC, Tran DD, Campian JL. *Neurooncol Adv. 2021 Nov 15;3(1):vdab164. doi: 10.1093/noajnl/vdab164.*

The blood-brain barrier (BBB) is a major limiting factor for drug delivery in brain tumors. Laser interstitial thermal therapy (LITT) disrupts the peritumoral BBB. In this study, we examine survival in patients with recurrent glioblastoma (GBM) treated with LITT followed by low-dose doxorubicin, a potent anti-neoplastic drug with poor BBB permeability.

Cancer-Associated Fibroblast Subpopulations With Diverse and Dynamic Roles in the Tumor Microenvironment.

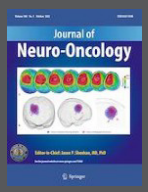
Simon T, Salhia B. *Mol Cancer Res. 2022 Feb;20(2):183-192. doi: 10.1158/1541-7786.MCR-21-0282.*

Close interactions between cancer cells and cancer-associated fibroblasts (CAF) have repeatedly been reported to support tumor progression. Yet, targeting CAFs has so far failed to show a real benefit in cancer treatment, as preclinical studies have shown that such a strategy can enhance tumor growth. The present review aims to provide an in-depth description of the cellular heterogeneity of the CAF compartment in tumors. Through combining information from different cancer types, here we define 4 main CAF subpopulations that might cohabitate in any tumor microenvironment (TME).

Growth hormone secreting pituitary adenomas show distinct extrasellar extension patterns compared to nonfunctional pituitary adenomas.

Pangal DJ, Wishart D, Shiroishi MS, Ruzevick J, Carmichael JD, Zada G. *Pituitary. 2022 Jun;25(3):480-485. doi: 10.1007/s11102-022-01217-z.*

Patterns of extension of pituitary adenomas (PA) may vary according to PA subtype. Understanding extrasellar extension patterns in growth hormone PAs (GHPA) vis-a-vis nonfunctional PAs (NFPAs) may provide insights into the biology of GHPA and future treatment avenues. GHPA and NFPA demonstrate distinct extrasellar extension patterns on MRI. GHPAs show proclivity for inferior extension with bony invasion, whereas NFPAs are more likely to exhibit suprasellar extension through the diaphragmatic aperture. These distinctions may have implications into the biology and future treatment of PAs.



A quantitative characterization of the spatial distribution of brain metastases from breast cancer and respective molecular subtypes.

Mahmoodifar S, Pangal DJ, Cardinal T, Craig D, Simon T, Tew BY, Yang W, Chang E, Yu M, Neman J, Mason J, Toga A, Salhia B, Zada G, Newton PK. *J Neurooncol. 2022 Oct;160(1):241-251. doi: 10.1007/s11060-022-04147-9.*

Brain metastases (BM) remain a significant cause of morbidity and mortality in breast cancer (BC) patients. Specific factors promoting the process of BM and predilection for selected neuro-anatomical regions remain unknown, yet may have major implications for prevention or treatment. Anatomical spatial distributions of BM from BC suggest a predominance of metastases in the hindbrain and cerebellum. We present a novel and shareable workflow for characterizing and comparing spatial distributions of BM which may aid in identifying therapeutic or diagnostic targets and interactions with the tumor microenvironment.

Leveraging Molecular and Immune-Based Therapies in Leptomeningeal Metastases.

Wilcox JA, Boire AA. *CNS Drugs. 2023 Jan;37(1):45-67. doi: 10.1007/s40263-022-00975-5.*

Leptomeningeal metastases represent an aggressive stage of cancer with few durable treatment options. Improved understanding of cancer biology, neoplastic reliance on oncogenic driver mutations, and complex immune system interactions have resulted in an explosion in cancer-directed therapy in the last two decades to include small molecule inhibitors and immune checkpoint inhibitors. A number of retrospective studies and promising prospective trials provide evidence of leptomeningeal activity of several small molecule and immune checkpoint inhibitors and underscore potential areas of further therapeutic development for patients harboring leptomeningeal disease.

CLINICAL TRIALS:
Now Enrolling at the USC Brain Tumor Center

Have you or someone you know recently been diagnosed with a brain tumor? Choosing the right treatment can be challenging. To find out more about our breakthrough treatments, contact our specialized brain tumor team at (844) 33-BRAIN (844-332-7246) or email frances.chow@med.usc.edu.

A Phase ½ Trial of Selinexor and Temozolomide in Recurrent Glioblastoma

Selinexor is a novel first-in-class XPO1 inhibitor with potent anti-tumor activity. Preclinical studies demonstrate that selinexor blocks nuclear export, impairs DNA repair, and triggers tumor cell death. Through the National Cancer Institute's (NCI) Cancer Therapy Evaluation Program, Dr. Frances Chow led a team of cancer biologists, pharmacists, and translational scientists to develop a clinical trial to evaluate the safety and efficacy of temozolomide in combination with selinexor in recurrent glioblastoma.

This study is supported by the National Institutes of Health (NIH) and is currently enrolling at USC and across the Experimental Therapeutics Clinical Trials Network (ETCTN).

	Trial	Interventions	Phase
	Brain Metastasis		
1	Stereotactic Radiosurgery (SRS) Compared with Collagen Tile Brachytherapy	• GammaTile • Stereotactic radiosurgery	Phase 1
2	Single Fraction Stereotactic Radiosurgery Compared with Fractionated Stereotactic Radiosurgery in Treating Patients with Resected Metastatic Brain Disease (CTSU-A071801)	• Single fraction SRS • Fractionated SRS	Phase 3
	Glioblastoma		
3	A Phase 1/2 Study of Selinexor and Temozolomide in Recurrent Glioblastoma	• Selinexor + Temozolomide • Temozolomide	Phase 1/2
4	An Open-Label, Phase 1/2A Dose Escalation Study of Safety and Efficacy of NEO100 in Recurrent Grade IV Glioma	• Perillyl alcohol (inhaled)	Phase 1/2A
5	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 Tumors Harboring Activating FGFR 1-3 Alterations (FIGHT-209).	• Pemigatinib	Phase 2
6	Prospective Randomized Placebo-Controlled Trial of SurVaxM Plus Adjuvant Temozolomide for Newly Diagnosed Glioblastoma (SURVIVE)	• SurVaxM + Standard therapy • Placebo + Standard therapy	Phase 2
7	Enzastaurin Plus Temozolomide During and Following Radiation Therapy in Patients with Newly Diagnosed Glioblastoma with or Without the Novel Genomic Biomarker, DGM1	• Enzastaurin + Standard therapy • Standard therapy	Phase 3
8	GammaTile and Stupp in Newly Diagnosed GBM (GESTALT)	• GammaTile + Standard therapy • Standard therapy	Phase 4
9	Pivotal, Randomized, Open-label Study of Optune® Concomitant with RT & TMZ for the Treatment of Newly Diagnosed GBM (EF-32)	• Optune + Standard therapy • Standard therapy	N/A
	Meningioma		
10	A Phase 1/2 Study of Nivolumab Plus or Minus Ipilimumab in Combination with Multi-Fraction SRS for Recurrent High-Grade Radiation-Relapsed Meningioma	• SRS+Nivolumab+Ipilimumab • SRS+Nivolumab	Phase 1/2
11	An Open-Label, Phase 2 Study of NEO100 in Participants with Residual, Progressive or Recurrent High-grade Meningioma	• Perillyl alcohol (inhaled)	Phase 2
12	Observation or Radiation Therapy in Patients with Newly Diagnosed Grade II Meningioma That Has Been Completely Removed by Surgery (NRG-BN003)	• Radiation • Standard therapy	Phase 3

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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**