In this Summer issue of the USC BTC Newsletter, we have a lot of exciting updates to share with our supportive community. We are excited that a major announcement is on the horizon for the USC BTC and cannot wait to share it with our readers in our next issue.

In this issue, we want to introduce our amazing Clinical Care Staff Team who is the backbone of the BTC. Having a strong clinical care team is essential to provide personalized, multi-disciplinary and disease-focused care to our brain tumor and cancer patients. They are an integral part of the USC Brain Tumor Center team. We all work collectively towards providing the most streamlined care for our patients and towards our ultimate goal of finding a cure for brain tumors.

At the USC Brain Tumor Center, our staff understands the difficulties that brain tumor patients and their families often face. To help make these journeys easier, the center offers multiple options that care for the whole patient — not just their diagnosis. Our team of clinicians, nurses and researchers strives to provide the best patient experience for patients and their families that choose us as their site for brain tumor care.

Our multidisciplinary involvement across Keck Medicine, the Keck School of Medicine of USC, the Norris Comprehensive Cancer Center, LAC + USC and CHLA keeps us focused on continuing our mission of advancing research, education, and the best clinical care for our brain tumor patients.

The USC Brain Tumor Center also collaborates with partners across the nation. This Summer, The USC Brain Tumor Center and The Cleveland Clinic hosted the 33rd Annual Brain Tumor Update and the 13th Annual Symposium on Brain Metastases and Spine Tumors. The hybrid symposium was held at the JW Marriot and was a 2-day packed joint event covering the latest treatment strategies for the most commonly occurring brain and spine tumors, as well as emerging technologies. Expert speakers from across the nation represented disciplines including Neuro-Oncology, Neurosurgery, Radiation Oncology, Neurology, Pathology, Neuro-Radiology and Translational Medicine.

The USC BTC Research Advancement Core continues to make strides on our ongoing BTC Core research projects. Under the

Meet Our Brain Tumor Center Clinical Care Staff

Rebekah Ghazaryan BSN, RH, PHN has degrees in both Biology (UCI) and Nursing (West Coast University) as well as a Public Health Certification. Rebekah prides herself on her extensive knowledge of caring for neurosurgical patients. She has solely specialized and dedicated her nursing career, thus far, in the neuroscience field. Taking acute critical care of post-operative neurosurgical patients intrigued Rebekah to see how patients thrive once discharged, which sparked her transition from a bedside RN to the Clinical RN Coordinator for the USC Brain Tumor Center. “I want patients to know and understand that myself and the team are with them in every step of this journey. We will rejoice in their victories and help them overcome their hurdles. I take pride in being a part of the USC Brain Tumor Center.”

Nancy Hart MSN, RN, CPON is the Nurse Navigator for the USC Brain Tumor Center. Nancy received her MSN from Vanderbilt University. Her interest in working with patients with cancer began early in her career while working the night shift. After providing direct care at the bedside, Nancy’s focus has moved to Care Management, Clinical Research, and more recently, management of Clinical Operations. “I was confident the experiences from my previous roles prepared me for the responsibilities of the new Nurse Navigator position with the Brain Tumor Center. Working with the collaborative BTC team makes the weight of our work so much lighter. I look forward to helping make each day a little bit easier for our patients.”

Jinsy Rogers LCSW, OSW-C received her Master’s in Social Welfare at UCLA. She has 12 years of experience in medical social work and has worked at Keck for 10 years. When she was assigned to the Neuro ICU and Neuro Medical/Surgical Unit a decade ago, she had met her calling. She has been with the USC Brain Tumor Center for 2 years and is a certified Oncology Social Worker. Meeting patients
“From the Director” continued

leadership of BTC Scientific Director Dr. Josh Neman, we are honing an efficient workflow to collect patient’s tumors resected by USC BTC neurosurgeons and rapidly assess genomic signatures and drug testing, with the goal of developing the most advanced personalized treatments.

We also continue to offer a vast 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.

This amazing research would not be possible without the support of our donors, grateful patients and families who choose to fund early-stage research that can then be utilized as a catalyst for larger NIH grants and investigations. It is not without the partnership and support of gracious donors that rapid translational and unrestricted pilot research can enable new, early discoveries that promote successful future grant applications.

Our Advancement Liaisons for the USC Brain Tumor Center are charged with identifying and cultivating philanthropic relationships that can ultimately lead to additional financial support for the Center, it’s clinicians and its research, and also work closely with the members of the USC Brain Tumor Advisory Council who voluntarily assist in promoting the growth of the USC BTC by offering their advice, time, talents, and support in advancing the established goals of the Center.

We are very proud of the cutting edge and evidence-based care that we deliver at the USC BTC, 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
Professor of Neurological Surgery, Otolaryngology, and Internal Medicine
Director, USC Brain Tumor Center
gzada@usc.edu

“Clinical Care Staff” continued

and their families where they are and walking alongside them as they experience the ups and downs of their illness has been deep passion for her. Our patients are more than their diagnoses, and as a social worker, she is able to have a human touch and explore the psychosocial aspect in having a brain tumor. “Being a social worker with the USC Brain Tumor Center has been such a rewarding and unique experience for me. It is a special role to be invited into a very personal space in my patient’s lives and help them cope with the ups and downs of having a brain tumor.”

Jinsy and Nancy run the USC Brain Tumor Center Patient Caregiver group. This group provides the opportunity for family and friends of patients with brain tumors to come together and find common ground to help each other. It meets the Second Thursday of each month 4-5:00p.m.

Tania Vartanians, MS, PA-C earned her undergraduate degree from UC, Santa Barbara and her MS in Physician Assistant studies from Western University of Health Sciences. She has been a PA for 16 years and has spent 12 of those years working directly with cancer patients. In 2020, she joined the USC Brain Tumor Center and is proud to be a part of such a strong multidisciplinary team. “My goal is to provide compassionate care, support and encouragement to our patients and their families to help them navigate and succeed in their cancer care.”

After graduating with her Bachelor of Science in Molecular Biology and Biotechnology from California State University, Fullerton, Vanessa Mach, BS started her career at Keck hospital of USC. She currently holds the role as a coordinator at the Neurosurgery department. Vanessa strives on improving quality of life for individuals and works diligently to achieve that goal. “As a coordinator, I take pride in the work that has been accomplished over the year to achieve the optimal experience for Brain Tumor patients. Ensuring the smooth coordination of appointments for patients provided me with fulfillment and accomplishment working with the Brain Tumor Center at USC.”

The promise of personalized brain tumor treatment

From the operating room to the scientific laboratory and back to the clinic.

At the USC Brain Tumor Center (BTC), part of the work we do is to collect patient’s tumors resected by BTC member neurosurgeons with the goal of developing better targeted and personalized treatments. Thus far, in just a short period of time, we have collected 116 different brain tumors – ranging from primary tumors which start off in the brain itself (i.e meningioma, gliomas, pituitary adenoma) to tumors which spread to the brain (metastases) (Figure 1). BTC scientists then process and grow living tumor cells (Figure 2) at the BTC core labs (Martirosian V et al, Current Protocols, 2021). We then characterize them to determine the various genetic and proteomic expression changes (Figure 3) which allows these cancer cells to grow.

Currently, BTC scientists are utilizing these cultured patient-derived lines to run drug screens from 491 FDA-approved compounds. This drug compound library that has been preselected by USC BTC scientists has many repurposed drugs which are able to cross the blood-brain-barrier and modulate the tumor microenvironment.

It is our collective goal to optimize the process of tumor specimen collection from the operating room to the growth and testing of these compounds on living cancer cells in our BTC laboratory, per patient, in order to truly provide a personalized treatment for our brain tumor patients.

Josh Neman, PhD
Scientific Director, USC Brain Tumor Center
Assistant Professor, Departments of Neurological Surgery, Physiology & Neuroscience
Member, Norris Comprehensive Cancer Center

![Figure 1. Collection of different brain tumors, ranging from primary to metastatic tumors.](image1)

![Figure 2. Example of spheres grown from individual glioblastoma cells taken from a USC BTC patient.](image2)

![Figure 3. Characterization of individual USC BTC patients with brain metastases from breast, lung, colon, melanoma, renal cell carcinoma.](image3)
2022 Annual Brain and Spine Tumor Symposium

On July 29-30, USC hosted the annual Brain and Spine Tumor Symposium jointly with the Cleveland Clinic at the JW Marriott Anaheim. The meeting was a resounding success featuring many of our own experts studying brain and spinal tumors.

Mark Shiroishi, M.D. gave the first talk on advanced neuroimaging and how fractional tumor burden analysis of perfusion MRI can allow differentiation of post-treatment radiation effects from tumor progression. Frances Chow, M.D. spoke on different types of vaccine therapy including oncolytic viruses, CAR T therapies, and immune checkpoint blockade which could be used for treating glioblastoma.

Vahan Martirosian, Ph.D. reviewed how captured tissues from surgery could be used to establish patient-derived organoid model for drug screening assays to develop a personalized medicine approach to patients. He also described how a key metabolic protein allows medulloblastoma tumor cells to use GABA as an energy source in the cerebrospinal fluid granting them the ability to metastasize. Gabriel Zada, M.D. spoke on using blue light endoscopy for glioma resection while Kyle Hurth, M.D., Ph.D. reviewed the newest WHO blue book classification of brain tumor and C-IMPAC reports.

Frank Attenello, M.D., Ph.D. described the genomic landscape of glioma while Jason Ye, M.D. spoke on emerging applications of radiosurgery. Lindsay Hwang, M.D. presented the latest data on Gamma Tiles used intraoperatively for meningioma, recurrent glioma and brain metastases. Thomas Chen, M.D., Ph.D. presented novel drug delivery platforms for glioma including intranasal delivery.


Closing out the program, Gino In, M.D. discussed immunotherapy for brain metastasis while Jason Ye, M.D. described a unique way of using SRS to manage 4th ventricular brain metastasis (a precarious situation).

There were many more outstanding talks given in this two-day program by our colleagues from Cleveland clinic, and so many were delighted to be able to return to an in-person hybrid on-site meeting to connect, network, exchange information and socialize with like-minded brain and spinal tumor experts.

USC Brain Tumor Center Advancement Liaisons

The Advancement liaisons for the USC Brain Tumor Center are charged with identifying and cultivating philanthropic relationships that can ultimately lead to additional financial support for the Center, its clinicians and its research. In this work, they engage individuals, grateful patients and their families, as well as institutional donors and prospects, who generously choose to direct their philanthropy to support the meaningful work of the USC BTC. Philanthropy can make a significant impact in fueling advances in the field, as we’ve seen through by donors who choose to fund early-stage research that can then be utilized as a catalyst for larger NIH grants and investigations. It is not without the partnership and support of gracious donors that our research can truly thrive and be nimble to follow new discoveries down uncharted paths. In addition, the Advancement liaisons also work closely with the members of the USC Brain Tumor Advisory Council, who assist in promoting the growth and development of the USC BTC by offering their advice, their time, talents, and support in advancing the established goals of the Center.

Nicole Measles - Director of Development, Neurosciences
Nicole joined the Keck Advancement team in May 2022 from UCLA where she held various roles of increasing responsibility over her nine-year tenure. She most recently served as Director of the UCLA Chancellor’s Society, the campus-wide leadership annual giving recognition program. In this role, Nicole worked between annual giving, regional gift officers, campus partners, and events staff to ensure the thoughtful, strategic engagement and cultivation of nearly 5,000 annual households. In addition, she managed overall efforts with the nine Chancellor’s Society volunteer committees and directly staffed the Executive Committee. Nicole received a B.A. in Communication Studies from California State University, Northridge.

Brian Loew - Senior Director of Development, Neurosciences
Brian joined the Keck Advancement team in April 2020. He began working in Development in 2013 as the Director of Development for Patient Programs at UCLA and eventually moved into major gift fundraising for the Neurosciences, as well as the UCLA Operation Mend program, funding reconstructive and plastic surgery and mental health services for post-9/11 veterans who were injured during training, or active combat. Prior to joining USC, he served as the Director of Major Gifts for the Ronald Reagan Presidential Foundation and Institute, which supports the Reagan Presidential Library, the Air Force One Discovery Center, and the Annenberg Presidential Learning Center. Prior to UCLA, Brian served as the Assistant Director of Admission & Enrollment for 6 years at Marist College in Poughkeepsie, NY. Brian received a bachelor’s degree in Public Relations and Political Science, and a Master of Public Administration, both from Marist College.

Brian received a B.A. in Communication Studies from California State University, Northridge.

Learn more at: BTC.keckmedicine.org
The optimal management of brain metastases from gestational trophoblastic neoplasia


Introduction: Gestational trophoblastic diseases and neoplasias (GTDs and GTNs) comprise a spectrum of diseases arising from abnormally proliferating placental/trophoblastic tissue following an antecedent molar or non-molar pregnancy. These can spread to the brain hematogenously in about 10% of patients, mostly in high-risk disease. The optimal management of patients with brain metastases from GTN is unclear, with multiple systemic regimens under use and an uncertain role for radiotherapy. Here, we review the epidemiology, workup, and treatment of GTN with central nervous system (CNS) involvement. Literature searches in PubMed and Google Scholar were conducted using combinations of keywords such as “gestational trophoblastic disease,” “gestational trophoblastic neoplasia,” “choriocarcinoma,” and “brain metastases.” Systemic therapy is the frontline treatment for GTN with brain metastases, and radiotherapy should only be considered in the context of a clinical trial or for resistant/recurrent disease. Surgery has a limited role in palliating symptoms or relieving intracranial pressure/bleeding. Given the highly specialized care these patients require, treatment at a high-volume referral center with multidisciplinary collaboration likely leads to better outcomes. Randomized trials should be conducted to determine the best systemic therapy option for GTN.

Executive summary of American Radium Society’s appropriate use criteria for the postoperative management of lower grade gliomas


Postoperative management of lower grade gliomas (grade 2 and 3) is heterogeneous. The American Radium Society’s brain malignancies panel systematically reviewed and evaluated the literature to develop consensus guidelines addressing timing of postoperative therapy, monotherapy versus combined modality therapy, type of chemotherapy used with radiotherapy, and radiotherapy dose. Thirty-six studies were included. Using consensus methodology (modified Delphi), the panel voted upon representative case variants using a 9-point appropriateness scale to address key questions. Voting results were collated to develop summarized recommendations. While multiple appropriate treatment options exist, these consensus recommendations provide an evidence-based framework to approach postoperative management of lower grade gliomas.

An interdisciplin ary consensus on the management of brain metastases in patients with renal cell carcinoma


Brain metastases are a challenging manifestation of renal cell carcinoma. We have a limited understanding of brain metastasis tumor and immune biology, drivers of resistance to systemic treatment, and their overall poor prognosis. Current data support a multimodal treatment strategy with radiation treatment and/or surgery. Nonetheless, the optimal approach for the management of brain metastases from renal cell carcinoma remains unclear. To improve patient care, the authors sought to standardize practical management strategies. On the basis of the integrated approach of literature review and survey study results, the authors built algorithms for the management of single and multiple brain metastases in patients with renal cell carcinoma. The literature review, consensus statements, and algorithms presented in this report can serve as a framework guiding treatment decisions for patients.

The Abscopal Effect: Systematic Review in Patients with Brain and Spine Metastases

Dhiraj J Pangal, BS, Benjamin Yarovsky, Tyler Cardinal, BS, David J Cote, MD PhD, Jacob Ruzevick, MD, Frank J Attenello, MD, Eric I. Chang, MD, Jason Ye, MD, Josh Neman, PhD, Frances Chow, MD, Gabriel Zada, MD MS. Neuro-Oncology Advances, 19 August 2022, https://doi.org/10.1093/noajnl/vdac132.

The abscopal effect is a rare phenomenon whereby local radiation induces a proposed immune-mediated anti-tumor effect at distant sites. Given the growing use of immunotherapies and systemic immune checkpoint inhibitors in neuro-oncologic practice, we aimed to review prior studies pertaining to this phenomenon in the context of tumor shrinkage both within the central nervous system as well as distant disease sites. A systematic review in accordance with the PRISMA guidelines was conducted to identify all studies which assessed the abscopal effect in patients with treated metastatic cancer to the brain and/or spine. Articles were included if they reported the abscopal effect in patients (case studies) or if the abscopal effect was explicitly analyzed in case series with cohorts of patients with metastatic brain or spine tumors. Abscopal effects can occur following radiotherapy in patients with brain or spine metastases and is thought to be a result of increased anti-tumor immunity. The potential for immune checkpoint inhibitor therapy to be used in combination with radiotherapy to induce an abscopal effect is an area of active investigation.
**USC Is the first to introduce Gamma Tiles to Southern California and is only 1 of two medical centers offering in SoCal**

**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

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**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

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**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

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**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: NCT02704858

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**Clinical Trials Manager, contact**

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**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.
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