The Official Newsletter of the
Keck Medicine of USC
USC Brain Tumor Center
Patient referrals, (844) 33-**BRAIN** (844-332-7246)

USC Norris Comprehensive Cancer Center
Keck Medicine of USC

USC BRAIN TUMOR CENTER Report

Volume 5 ▪ Issue 1
WINTER 2025

From the USC BTC Directors

As we step into 2025, we are thrilled to share with you the latest developments from our last newsletter. The USC Brain Tumor Center continues to focus on its mission of providing exceptional and innovative brain tumor care to all patients who face a brain tumor diagnosis, we are also focused on finding a cure for brain tumors. 2024 was an incredibly productive year and we are confident that 2025 will be even more impactful.

We are thrilled to kick of this newsletter by celebrating the outstanding achievements of our multidisciplinary team. **Dr. David Tran**, USC BTC co-director, division chief of neuro-oncology at the Keck School of Medicine of USC, a member of the Tumor Immunology and Microenvironment Program at the USC Norris Comprehensive Cancer Center, and his team, including neuropathologists, computational biologists, and neurosurgeons at Keck Medicine of USC, received a multi-million dollar grant from **California Institute for Regenerative Medicine** that will propel our research efforts toward finding a cure for brain tumors. We extend heartfelt congratulations to everyone involved.

We would like also to congratulate **Dr. Eric Chang** and **Dr. Mark Shiroishi** on their publications in two prestigious sources. Last, but certainly not least, **Dr. Frances Chow**, was honored as the recipient of the "Caregivers Apply Restorative Efforts" grant. This grant aims to support restorative and well-being efforts for healthcare providers.

Collaboration is critical in the fight against brain tumors. On December 6th, 2024, the USC Brain Tumor Center hosted the **2nd Annual Southern California Brain Tumor Conference**. This highly anticipated event fostered an electrifying atmosphere of discovery and collaboration, as experts from across Southern California gathered to share groundbreaking research and innovative treatments in the fight against brain tumors. Education also plays a pivotal role in advancing our mission. At the conference we proudly recognized the top 3 research posters highlighting innovative research.

Additionally in this winter issue, we include an educational piece on brain tumor resection. When our patients are given a brain tumor diagnosis, we strive to provide them with all the information necessary so that they are well informed and prepared for their treatment journey.

The USC Brain Tumor Center continues to expand its extensive clinical trial portfolio, with several new trials for glioblastoma, brain metastases, and meningiomas. These studies provide hope for patients and their families.

This year marks the **5th anniversary of the USC Brain Tumor Center**, a milestone made possible by the incredible support of our community and donors. Your generosity fuels our mission, drives innovation and brings us closer to a cure. Together we are making a lasting impact, thank you for being a part of this journey.

We look forward to continuing in making a difference in the lives our brain tumor patients and their families.

Heal on!

Gabriel Zada, MD, MS, FAANS, FACS
Co-Director, USC Brain Tumor Center

David D. Tran, MD, PhD
Co-Director, USC Brain Tumor Center

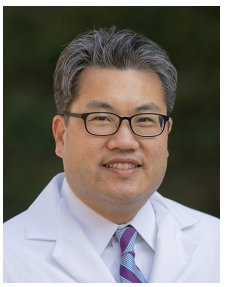
Josh Neman, PhD
Scientific Director, USC Brain Tumor Center

New Grant Funds First-of-its-kind Gene Therapy to Treat Aggressive Brain Cancer

The California Institute for Regenerative Medicine (CIRM) has awarded a $6 million grant to USC investigators pioneering a new first-of-its-kind genetic therapy for glioblastoma, a severe form of brain cancer. The treatment would be the first gene therapy for glioblastoma to use a novel, more precise delivery system that is less likely to harm non-cancerous cells. Congratulations to Dr. David Tran USC Brain Tumor Center Co-Director and his team, including neuropathologists, computational biologists, and neurosurgeons at Keck Medicine of USC.

To learn more, please visit the Keck School of Medicine of USC Newsroom by clicking **HERE**.

Adult CNS Radiation Oncology, Principles and Practice: Second Edition



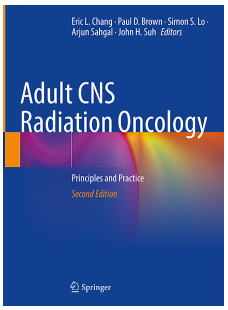
Eric Chang, MD

This new edition of *Adult CNS Radiation Oncology, Principles and Practice* elucidates the radiation therapy protocols and procedures for the management of adult patients presenting with primary benign and malignant central nervous system tumors.

With the development of new treatment strategies and rapid advancement of radiation technology, it is crucial for radiation oncologists to maintain and refine their knowledge and skills.

Dedicated exclusively to adult CNS radiation oncology, this textbook explores CNS tumors ranging from the common to the esoteric as well as secondary cancers of metastatic origin.

The first half of the book is organized anatomically: tumors of the brain, spinal cord, leptomeninges, optic pathway, ocular choroid, and skull base.

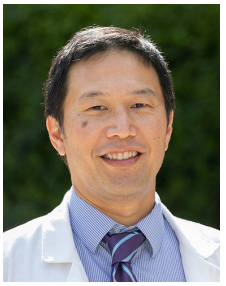


The second half covers primary CNS lymphoma, rare CNS tumors, metastatic brain disease, vascular conditions of the CNS, radiation-associated complications, and radiation modalities.

This new edition is updated throughout and includes several new chapters, including: palliative radiation therapy for leptomeningeal disease, preoperative treatment for brain metastases, advanced neuroimaging for brain tumors, and MR-LINAC for brain tumors. Each chapter provides guidance on treatment field design, target delineation, and normal critical structure tolerance constraints in the context of the disease being treated.

Learning objectives, case studies, and Maintenance of Certification Self-Assessment Continuing Medical Education-style questions and answers are incorporated throughout the book.

The Quantitative Imaging Biomarkers Alliance (QIBA) Profile for Dynamic Susceptibility Contrast MRI Quantitative Imaging Biomarkers for Assessing Gliomas



Mark Shiroishi, MD

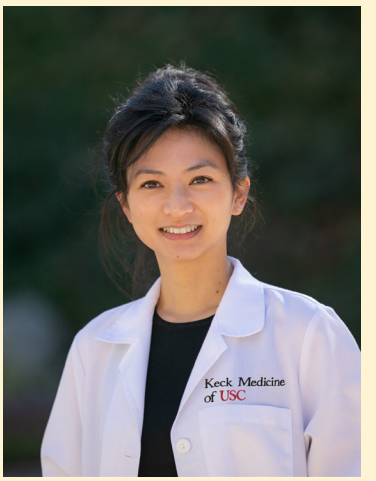
Congratulations to Dr. Mark Shiroishi on his most recent brain tumor perfusion paper in *Radiology*, the highest impact factor journal in clinical radiology.

While dynamic susceptibility contrast (DSC)-MRI measures of relative cerebral blood volume (rCBV) are a well-established advanced MRI method to monitor therapeutic response and disease progression in glioma patients, its quantification and reproducibility across patients, devices and software remains challenging.

The Radiological Society of North America (RSNA) DSC-MRI Biomarker Committee of the Quantitative Imaging Biomarkers Alliance developed a Profile that defines statistics-based claims for the precision of longitudinal measurements.

Surprisingly little is known about this topic and, based on the little data that currently exists, our work has shown is that an increase of 182% or more in rCBV of a glioma compared to baseline indicates that a real increase has occurred; a decrease of 64% or more compared to baseline suggests that a real decrease has occurred.

However, this is based on a single data-set using older DSC-MRI methods. Larger studies are needed using modern DSC-MRI methods and this knowledge can provide critical insights into clinical care and the design of clinical trials."



Frances Chow, MD

Care for the Caregiver

Dr. Frances Chow is a recipient of the Keck Medicine **"Caregivers Apply Restorative Efforts"** grant to support restorative and wellbeing efforts for healthcare providers.

Brain tumor specialists are at a particularly high risk of burnout from the burden of care, rapid turnover of patients, and limited therapeutic options for brain tumors.

The USC Brain Tumor Center was launched in 2020 during the height of the COVID pandemic. Since our inauguration, we have provided top-quality care for hundreds of patients and families challenged by devastating diagnoses.

Dr. Chow's initiative will fund measures to improve teamwork, recognize and appreciate team members, honor patients to provide emotional self-care, and serve as a think tank for initiatives to drive the Brain Tumor Center forward. This project is critical to rejuvenate the work culture, teamwork, and emotional strength of the members of the Brain Tumor Center who continuously strive to serve and improve the lives of patients with brain tumors.

Dr. Frances Chow served as the Wellness & Burnout Committee Chair for the USC Department of Neurology from 2022-2024. She is a strong advocate for physician well-being, leadership development, and performance improvement.

Breaking Barriers in Neuro-Oncology: Highlights from the 2nd Annual Southern California Brain Tumor Conference

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


Josh Neman, PhD

The The 2nd Annual Southern California Brain Tumor Conference, hosted by the USC Brain Tumor Center, took place on December 6, 2024, at the USC Health Sciences Campus, bringing together 158 of the brightest minds in neuro-oncology. This highly anticipated event fostered an electrifying atmosphere of discovery and collaboration, as experts from across Southern California gathered to share groundbreaking research and innovative treatments in the fight against brain tumors.

Eight leading academic and hospital institutions—**USC, CHLA, UCLA, UCI, UCSD, City of Hope, Cedars-Sinai,** and **Pacific Neuroscience Institute**—joined forces to make this event a resounding success. Researchers, clinicians, trainees, administrators, and faculty members engaged in an immersive exchange of knowledge, propelling the field forward with their insights and expertise. The conference featured dynamic discussions that bridged the gap between scientific discovery and clinical application, reinforcing a shared vision for the future of brain tumor treatment and care.

The event was structured into five compelling sessions, each tackling critical aspects of neuro-oncology. The session on High-Grade Gliomas delved into the complexities of genetic heterogeneity and precision medicine. **Katie Grausam, PhD** discussed modeling glioblastoma in immunocompetent mice, while **Frank Furnari, MD**, showcased the potential of human iPSC-derived brain cancer avatars in revolutionizing therapeutic recovery.

The Brain Metastases session was equally fascinating, with **Lisa Anne Feldman, MD, PhD**, presenting on CAR T cell therapy for leptomeningeal disease, a treatment that could redefine the landscape of brain metastasis care. Meanwhile, **Josh Neman, PhD**, shed light on the intricate role of cancer neuroscience, specifically on how brain tumors interact with their microenvironment.

The focus then shifted to Meningioma and Pituitary Tumors, with **Gabriel Zada, MD, MS**, unveiling cutting-edge advancements in minimally invasive cranial neurosurgery. Attendees were also treated to **Garni Barkhoudarian, MD's** presentation on endocrine outcomes after pituitary tumor surgery, highlighting the long-term considerations for patient care beyond the operating room.

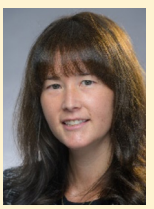
Pediatric brain tumors took center stage in the afternoon session, where **David Rincón Fernandez Pacheco, PhD**, spoke about his insights into G34R gliomas. **Lior Goldberg, MD, MSc**, provided a deep dive into the immunometabolic adaptations of CAR T cells in the CNS, an area of research that could hold the key to new therapeutic breakthroughs.

Perhaps one of the most thoughtful moments of the conference came during the dedicated session on Palliative Care. **Akanksha Sharma, MD**, delivered a moving presentation on how the integration of palliative care into neuro-oncology is reshaping patient outcomes. Her talk underscored the importance of treating not just the disease but the whole person, ensuring that patients receive compassionate, holistic care throughout their journey.

The conference concluded with an engaging poster session, where researchers shared their latest findings, further fueling the exchange of ideas and collaborations that will shape the future of brain tumor research. The enthusiasm from the conference was palpable, a testament to the unwavering dedication of the Southern California neuro-oncology community. With another successful year in the books, the Southern California Brain Tumor Conference continues to inspire researchers and clinicians to push the boundaries of what is possible in the fight against brain tumors. The impact of this year's discussions will undoubtedly reverberate in labs and clinics, paving the way for the next wave of transformative breakthroughs.

We look forward to seeing you all at the 3rd conference on March 6th, 2026!

Enabling a brighter outcome for brain tumor patients and their families


Nicole Measles

Thank you for your partnership in 2024. With four years since the official launch of the USC Brain Tumor Center, we are grateful for the community of supporters that have come together to support the progress and growth of our Center team.

As we encounter challenges in our daily lives, especially those impacted in our local communities, your enduring support for the Center and our research mission is what will soon change the trajectory of a brain tumor diagnosis.

We are grateful to the many of you whom stepped up to provide support to our Center last year. Gifts of all sizes enhance the Center's ability to pilot novel research, to offer patient resources, to fund laboratory expenses, and to enable collaborative training and education.

As we launch new laboratories and new clinical trials, we are always pleased to share updates with you and keep you abreast of what is on the horizon in brain tumor care and research. This year, we look forward to launching a virtual series that will feature faculty presenting their latest research advancements live to our community of patient's, donor's, caregivers, and friends—to learn more about projects and initiatives that have been bolstered through your philanthropic support.

For any questions related to supporting the USC BTC, please contact:

Nicole Measles, Director of Development
Email: **Nicole.measles@med.usc.edu**
Cell: **(213) 806-0693**

Poster Winners from the 2nd Annual Southern California Brain Tumor Conference

Education also plays a pivotal role in advancing our mission. Congratulations to our top three Southern California Brain Tumor Conference Poster winners.

1st Place
Sara Barcik Weissman
Laboratory Technician, Department of Radiation Oncology

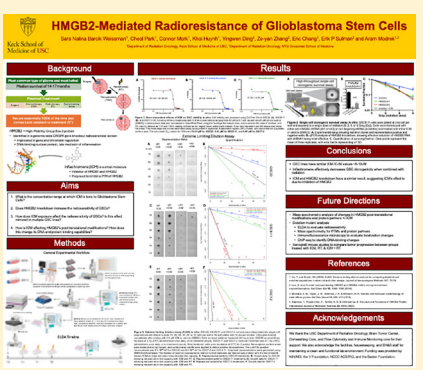
HMGB2-Mediated Radioresistance of Glioblastoma Stem Cells
Glioblastoma (GBM) is a highly aggressive brain cancer that is difficult to treat effectively. Even with surgery, radiation, and chemotherapy, the cancer often comes back and becomes harder to treat with radiation.

To understand why GBM becomes resistant to radiation, we identified a protein called HMGB2 that might play a role.

We tested a drug called Inflachromene (ICM), which targets HMGB2, on cancer stem cells from GBM patients.

The drug reduced the ability of these cells to grow and form tumor-like clusters, especially when combined with radiation.

These findings suggest that HMGB2 helps GBM resist radiation, and targeting it with drugs like ICM could improve treatment. We plan to study how HMGB2 works and how ICM blocks its activity to develop better therapies in the future.



2nd Place
Angela Tang-Tan
Keck School of Medicine of USC, M.D. Class of 2026, Dean's Research Scholar, Department of Neurosurgery

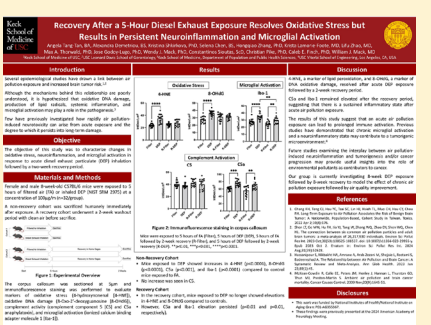
Recovery After a 5-Hour Diesel Exhaust Exposure Resolves Oxidative Stress but Results in Persistent Neuroinflammation and Microglial Activation
Air pollution exposure has been linked with increased brain tumor risk, but the mechanisms behind this are not well understood.

We sought to investigate how air pollution causes cellular damage and immune system activation in the brains of mice, which may contribute to tumor development.

We exposed mice to 5 hours of diesel exhaust or clean air, followed by a 2-week washout period with clean air.

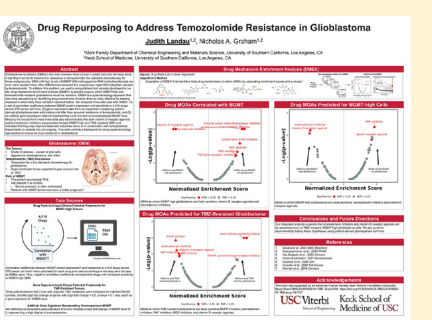
We found that DNA damage and lipid peroxidation resolved after 2 weeks of washout, while complement and microglial activation remained elevated.

We demonstrated a sustained inflammatory state after acute air pollution exposure, which may contribute to the development of brain tumors in the long term.



3rd Place
Judith Landau
PhD Candidate, Mork Family Department of Chemical Engineering and Materials Science USC

Drug Repurposing to address Temozolomide Resistance in Glioblastoma
New therapeutic options are desperately needed for glioblastoma, the most common and deadly type of brain tumor that occurs in adults. My poster shows how I implemented a computational tool called "Drug Mechanism Enrichment Analysis" (DMEA) to identify FDA-approved drugs that could be repurposed for treating glioblastoma resistant to the commonly-used therapeutic temozolomide (TMZ). To accomplish this goal, I tested three sets of data: (1) the correlation between levels of the protein MGMT (which causes resistance to TMZ) and drug sensitivity in hundreds of cancer cell lines, (2) gene expression profiles of cancer cells before and after acquiring resistance to TMZ, and (3) a synthetic data set representing cancer cells with a very high expression of MGMT. The results predicted that two classes of drugs – bromodomain inhibitors and vitamin D receptor agonists – will specifically kill temozolomide-resistant, MGMT-high glioblastoma. I am currently experimentally testing these drugs in the lab on cancer cells taken from glioblastoma patients to evaluate them as potential treatments for these tumors.



What Does "Gross Total Resection" Mean in Neurosurgery?

By Rebekah Ghazaryan, RN, BSN, PHN, FNP-S

Rebekah Ghazaryan, RN, PHN, FNP-S

The When someone undergoes brain or spinal surgery, especially for a tumor, you might hear the term "gross total resection" mentioned by doctors. But what exactly does this mean? Let's break it down in simple terms.

What Is a Resection?

In neurosurgery, a "resection" means the removal of something. When a surgeon talks about resecting, they're talking about cutting out part of the body—in this case, brain or spinal tissue. This usually happens when there's a tumor, abnormal tissue, or something that's causing a problem. The goal is to remove as much of it as possible to help the patient.

Gross Total Resection Explained

The word "gross" in medical terms refers to something that's visible to the naked eye. So, when a doctor says "gross total resection," they are describing the removal of "all visible" parts of a tumor or abnormal tissue. The surgeon aims to take out everything that can be seen during the surgery, leaving nothing behind that could cause future problems. It's like cleaning off a countertop and making sure nothing is left on the surface.

Why Is Gross Total Resection Important?

The goal of gross total resection is to make sure the surgery has done its job by removing all of the tumor or abnormal tissue. This helps reduce the risk of the problem coming back. For some patients, this could mean they have a much better chance of recovery or a longer, healthier life.

However, while the term sounds great, there are some challenges. Tumors in the brain or spine can sometimes be very tricky to remove completely because they are located near critical structures, like blood vessels or nerves. In those cases, doctors might need to leave behind small parts of the tumor to avoid damaging something important.

How Is Gross Total Resection Different from Other Types of Resection?

Not every surgery results in a gross total resection. Sometimes, doctors can't remove the entire tumor for various reasons. For example:

- The tumor might be in a very delicate area.
- The tumor could be too large or spread out to be removed completely.
- There may be risks of bleeding or harming essential parts of the brain or spine.

If a surgeon can't remove all of the tumor, it might be called a "subtotal resection" or "partial resection."

What Happens After a Gross Total Resection?

After surgery, doctors will keep a close watch on the patient. They may run tests, like MRIs or CT scans, to make sure there's no sign of the tumor coming back. In some cases, other treatments like radiation or chemotherapy may be recommended to ensure that any small cells that weren't visible during surgery are eliminated.

In Conclusion.....

In simple terms, a gross total resection means the surgeon has removed all of the tumor or abnormal tissue they can see during the surgery. It's an important goal in neurosurgery to help patients recover, but there are cases where removing everything isn't possible. Either way, the aim is always to help the patient live a better, healthier life.

If you or a loved one is facing neurosurgery, it's always a good idea to discuss any questions with your neurosurgeon and the team to fully understand the surgery and what outcomes you can expect.

Hosted by Keck Medicine of USC

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.

TVAX BIOMEDICAL®

Newly Open: USC partners with TVax Biomedical to open the TVI-Brain-1 cancer vaccine

The USC Brain Tumor Center is now recruiting patients to a phase 2b personalized vaccine-based immunotherapy trial for newly diagnosed glioblastoma. TVI-Brain-1 (TVax Biomedical) is a treatment that uses each patient's own cancer cells collected during surgery to create a cancer-targeting vaccine. When the body is exposed to the vaccine, it stimulates T cells, which are harvested from the blood and are subsequently stimulated, expanded, and infused back to the patient. ClinicalTrials.gov identifier NCT05685004.

	Trial	Interventions	Phase
	Glioblastoma		
1	DB107-RRV, DB107-FC, and Radiation Therapy With or Without Temozolomide (TMZ) for High Grade Glioma	• DB107-RRV + DB107-FC + Standard Therapy	Phase 1/2A
2	EF-41/KEYNOTE D58: Phase 3 Study of Optune Concomitant With Temozolomide Plus Pembrolizumab in Newly Diagnosed Glioblastoma	• Optune + Pembrolizumab + Standard Therapy • Optune + Placebo + Standard Therapy	Phase 3
3	GammaTile and Stupp in Newly Diagnosed GBM (GESTALT)	• GammaTile + Standard therapy • Standard therapy	Phase 4
4	Multi-Center Randomized Controlled Phase 2b Clinical Trial to Evaluate the Safety and Efficacy of TVI-Brain-1 Combined with Conformal Radiotherapy and Temozolomide Compared to Standard Therapy as a Treatment for Newly Diagnosed O6-Methylguanine Methyltransferase Negative (MGMT Unmethylated) Grade 4 Astrocytoma (GBM)	• TVI-Brain-1 + Radiation + Temozolomide • Standard therapy	Phase 2b
5	A Phase 1/2 Study of Selinexor and Temozolomide in Recurrent Glioblastoma	• Selinexor + Temozolomide • Temozolomide	Phase 1/2
6	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
7	Study of NEO212 (Temozolomide-Perillyl Alcohol Conjugate) in Advanced Brain Cancer	• NEO212 (oral)	Phase 1
	Meningioma		
8	An Open-Label, Phase 2 Study of NEO100 in Participants with Residual, Progressive or Recurrent High-grade Meningioma	• Perillyl alcohol (inhaled)	Phase 2
9	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**