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USC Norris Comprehensive Cancer Center
Keck Medicine of USC

USC BRAIN TUMOR CENTER Report

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From the USC BTC Directors

Dear Friends of the USC Brain Tumor Center,

As we enter winter, we do so in a meaningful year—the **5th anniversary of the USC Brain Tumor Center**. In just five years, this program has grown through the trust of our patients and families, the dedication of our faculty and staff, and the generosity of donors and advocates who believe in our mission. Together, we are advancing what's possible in brain tumor care through innovation, collaboration, and compassion.

This issue begins with a remarkable patient story: five years tumor-free after a complex meningioma diagnosis. Her journey is a testament to the power of advocacy, informed choice, and expert, human-centered care. We are honored she entrusted her care to Dr. Gabriel Zada, and we celebrate this milestone with her and her family.

Because **meningioma** remains an underfunded and often overlooked frontier, we are also highlighting what meningioma is and the meningioma research underway at the USC Brain Tumor Center. Building on a promising genetic and epigenetic discovery, the Zada Lab has launched a **$1M Meningioma Advancement Campaign** to accelerate precision drug discovery and advance early-phase clinical trials aimed at transforming this breakthrough into new treatments—and ultimately, a cure.

We are also thrilled to announce the arrival of the newest and most advanced **Gamma Knife® Esprit**, offering frameless radiosurgery, available to patients beginning February 23, 2026. To illustrate the real-world impact of this technology, we are honored to share Niki Kozak's story of how state-of-the-art radiosurgery offered new hope.

This Winter Edition also spotlights outstanding faculty, including **Dr. David Tran**, and an article that highlights emerging innovations in **glioblastoma** research—exploring whether electric fields may help supercharge the immune system's attack on this aggressive disease.

Finally, we are proud to share important Center updates, including Dr. Zada's appointment as **Editor of *Neurosurgical Focus***. We also look forward to coming together on March 27, 2026, at the **3rd Annual Southern California Brain Tumor Conference**, featuring our extraordinary keynote speaker, **Dr. Patrick Soon-Shiong** and leading experts from across Southern California's top institutions sharing the newest research and breakthroughs aimed at finding better treatments and ultimately, a cure for brain cancer.

Thank you for being part of this community and this mission. We are honored to care for you and determined to keep pushing the field forward.

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

Five Years Tumor-Free: A Story of Advocacy, Choice, and Survival

Karen Ross

In April 2021, as the world continued to navigate the uncertainty of the COVID-19 pandemic, my own life came to an abrupt halt. Months earlier, I had been diagnosed with a benign brain tumor located at the base of my skull, a meningioma. Leading up to the diagnosis, I experienced persistent migraines, visual disturbances, and chronic nausea—symptoms I initially attributed to the demands of single motherhood and managing a busy law practice.

After months of declining health, I underwent an MRI. The imaging revealed a tumor measuring just over two centimeters. While small in size, its location made it exceptionally complex and potentially life-threatening. In that moment, everything changed.

I approached my diagnosis the same way I had approached my legal career: with diligence, research, and an unwavering commitment to understanding every available option. I consulted experts, reviewed medical literature, and interviewed ten neurosurgeons at leading tertiary care institutions across the country. Eight advised against surgical intervention due to the tumor's proximity to a critical vein, recommending stereotactic radiosurgery instead. While I respected those opinions, I sought a path that offered the possibility of complete tumor removal.

Ultimately, I placed my trust in **Dr. Gabriel Zada, M.D.**, a board-certified neurosurgeon and internationally recognized expert in brain, skull base, and pituitary surgery at Keck Hospital of USC. Dr. Zada believed total resection was achievable. On April 7, 2021—just over eight weeks after my diagnosis—I underwent a craniotomy, with three children and an active law practice in Las Vegas, Nevada.

Continues on page 2

"Five Years Tumor-Free" ***continued***

The weeks preceding surgery were marked by intense anxiety, insurance appeals, and careful planning to ensure continuity for my family and my clients. Like many patients, I discovered that navigating the healthcare system during a serious diagnosis can be as daunting as the illness itself. USC was in constant contact with me on their efforts to obtain approval.

On the morning of surgery, COVID-19 restrictions required my family and me to say goodbye at the hospital doors. I carried with me the weight of motherhood, responsibility, and uncertainty—yet also a very deep faith in my care team. In the moments before surgery, Dr. Zada stood beside me, offering calm reassurance and presence. He assured me that he and his team would be focused on fighting for me and my family over the next few hours. That human connection mattered as much to me as the technical excellence that would follow.

When I awoke in the intensive care unit, I learned the surgery had been a success. I was alive and the tumor had been completely removed.

Recovery, however, had its challenges. Months of occupational therapy followed as I relearned balance, coordination, and overall confidence. While the most debilitating symptoms had resolved, I experienced changes in my executive functioning, heightened anxiety, and ultimately gained a profound realization that brain surgery often leaves invisible injuries and while my tumor was gone, this was now about adaptation.

Through this process, I learned the importance of acknowledging what patients carry beyond the operating room: the emotional, cognitive, and identity shifts that accompany neurological trauma. I also learned the power of community, multidisciplinary care, and compassionate medicine.

On April 7, 2026, I mark five years tumor-free. In that time, I have returned to the practice of law, passed the Florida Bar Examination, and had the privilege of supporting other brain tumor patients as they navigate their own diagnoses. I have also been present for the milestones that once felt uncertain: watching my eldest son graduate as a high school Valedictorian and attend the University of Florida; celebrating my middle son's Bar Mitzvah; and seeing my youngest, Aiden—now proudly bearing the Hebrew name Aiden Gabriel—grow and thrive.

My journey reinforced the importance of patient advocacy, informed consent, and access to specialized care. It is also a testament to what is possible when medical excellence is paired with humanity.

Dr. Zada will forever remain our family's hero.

Keck Medicine of USC to Celebrate Grand Opening of Gamma Knife® Esprit

Keck Medicine of USC is the only academic medical center in Los Angeles offering the newest and most advanced Gamma Knife® Esprit with frameless radiosurgery—bringing next-generation precision, without incision, to brain tumor patients. Join us as we celebrate the Grand Opening on February 23, 2026.

Keck Medicine of USC is proud to announce the arrival of the newest and most advanced Gamma Knife® Esprit with frameless radiosurgery—expanding access to next-generation precision care for patients facing complex brain tumors and other neurological conditions. As the only academic medical center in Los Angeles offering this technology, Keck Medicine of USC continues to advance the USC Brain Tumor Center's mission to deliver world-class, multidisciplinary care paired with leading-edge innovation.

"Gamma Knife® Esprit provides unparalleled precision and flexibility to give fractionated frameless radiosurgery and advances our vision for precision radiation medicine—targeting brain lesions using highly focused pencil shaped beams with remarkable accuracy that allows us to preserve surrounding healthy brain tissue to the greatest extent possible," said **Eric Chang, MD, Chair of Radiation Oncology**. "This new Gamma knife Esprit technology allows us to design a treatment plan that is tailored to meet the unique and complex needs of patients presenting with a variety of brain conditions."

Gamma Knife® radiosurgery is a highly targeted form of **stereotactic radiosurgery (SRS)** designed to treat select conditions in the brain. Using advanced imaging and sophisticated treatment planning, multiple focused beams converge on the target—helping limit radiation exposure to surrounding healthy tissue. Because it is non-invasive, Gamma Knife treatment does not require a surgical incision and is often performed on an outpatient basis, depending on each patient's care plan.

Three things to know about Gamma Knife® radiosurgery:

- **No incision:** A non-invasive approach that does not involve traditional surgery.
- **High precision:** Focused beams converge on the target to treat select brain lesions while helping spare healthy tissue.
- **Meaningful clinical impact:** Used in carefully selected cases for brain tumors (including many metastases) and other neurologic conditions—guided by advanced imaging for accuracy.

We look forward to celebrating our 30-year history of performing gamma knife and this milestone of being able to offer the newest Gamma Knife® Esprit that will further strengthen the comprehensive care and innovation available through Keck Medicine of USC and the USC Brain Tumor Center.

What Is a Meningioma?

By Gabriel Zada, MD (for our patients and families)

Hearing the word "tumor" is frightening—full stop. If you've recently been told you have a meningioma, I want you to know two things right away: you are not alone, and we have effective, well-established ways to manage this diagnosis.

A simple definition

A meningioma is a tumor that grows from the meninges—the thin protective membranes that cover the brain and spinal cord. Because meningiomas arise from these coverings (rather than from brain tissue itself), their impact depends to a high degree on the tumor's location, size, growth rate, and relationship to nearby nerves and blood vessels.

Are meningiomas cancer?

Most meningiomas are benign (non-cancerous) and slow-growing. Some are discovered incidentally, meaning they show up on an MRI or CT scan that was done for another reason.

That said, "benign" doesn't always mean "harmless." A slow-growing tumor can still cause symptoms if it presses on important structures, especially in sensitive areas like the skull base, near the optic nerves (vision), or close to brain regions that control movement, balance, or speech. Meningiomas may invade, or grow into, normal surrounding tissues, which limits the ability of surgery or radiation to completely and safely eradicate or cure them.

Common symptoms

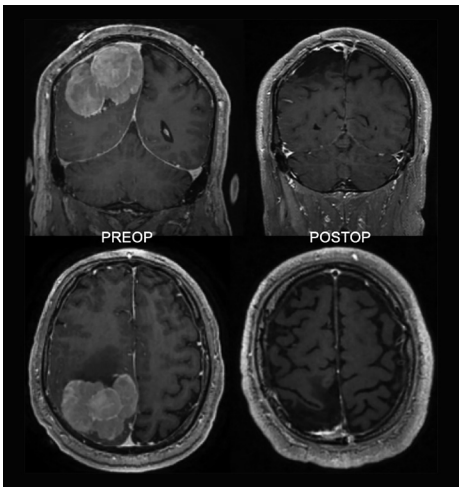
Symptoms vary widely and often reflect where the tumor is located. Some people have no symptoms at all. Others may experience:

- Headaches
- Seizures
- Vision changes
- Weakness or numbness
- Balance difficulties or dizziness
- Memory, concentration, or personality changes

How we diagnose and "grade" a meningioma

Diagnosis begins with MRI imaging (often with contrast) to understand the tumor's size, location, and features that can suggest how active it might be.

If surgery is performed, a pathologist examines the tissue and assigns a grade, which helps us estimate the likelihood of recurrence and whether additional treatment (like radiation) might be helpful.



Treatment options

There is no single "right" treatment for every meningioma. The best plan is the one that fits your tumor and your life.

1) **Observation (Active Surveillance).** If a meningioma is small, not causing symptoms, and appears slow-growing, it may be safest to monitor with scheduled imaging. Many patients do very well with careful observation.
2) **Surgery.** Surgery is often recommended when a tumor is causing symptoms, growing over time, or threatening important neurological function. The goal is to remove as much tumor as safely possible—while protecting nearby nerves, blood vessels, and brain tissue. In many cases, surgery offers excellent long-term control.
3) **Radiation-Based Therapy.** For tumors in high-risk locations, for residual tumor after surgery, or for tumors that recur, focused radiation (including stereotactic radiosurgery such as the Gamma Knife) can be a powerful tool. Radiation may be used alone or as part of a combined plan.

Research at the USC Brain Tumor Center: advancing meningioma care

At the USC Brain Tumor Center, our commitment to meningioma patients extends beyond excellent clinical care—we are also conducting extensive, ongoing research to improve outcomes and expand treatment options. Our teams are working across multiple fronts, including:

- Refining surgical approaches and techniques to maximize tumor removal while protecting neurological function - especially for complex skull base tumors.
- Studying tumor biology, genetics, and epigenetics to better understand why some meningiomas grow, recur, or behave more aggressively than others.
- Improving prediction and personalization, with the goal of tailoring surveillance schedules and treatment plans to the unique features of each tumor.
- Building research infrastructure and collaboration, so that discoveries in the lab translate more quickly into better care for patients.
- Finding drugs that can treat meningiomas effectively without the need for surgery or radiation.

In my own work as a surgeon-scientist, I focus on a central question: How can we make meningioma care more precise, safer, and more individualized?

Some meningiomas are soft, while others are fibrous or calcified; Tumor "consistency" can affect both the surgical plan and the safest pathway to removal. My colleagues and I have worked on ways to standardize how we describe and predict tumor consistency before surgery, so we can better plan our approaches and learn from outcomes across patients. At the same time, our research interest in molecular and genetic drivers supports the broader movement toward more personalized predictions of tumor behavior and smarter treatment strategies over time.

The most important message

A meningioma diagnosis can be serious, however it is also highly manageable in most cases. The next steps should feel clear, not rushed:

1. Understand what the tumor is doing now.
2. Estimate what it is likely to do next.
3. Choose the plan that best aligns with your long-term health and quality of life.

Zada Lab aims to raise $1M to advance precision medicine in meningioma treatment


Nicole Measles

Under the leadership of Gabriel Zada, MD, MS, FAAN, Surgical Director of the USC Brain Tumor Center, the **Zada Lab** has identified a **powerful genetic and epigenetic signal** that appears to drive the development of meningioma, the most common primary intracranial tumor, affecting tens of thousands of patients each year. This discovery provides one of the clearest biological entry points to date for developing targeted therapies for a disease that has long resisted meaningful innovation.

To translate this breakthrough into patient impact, the Zada Lab has launched a $1 million initiative to accelerate precision-drug discovery and advance the early-phase human clinical trials aimed at curing meningiomas by directly targeting this newly uncovered signal.

Despite major advances in cancer therapeutics, benign brain tumors such as meningiomas remain an overlooked frontier. While many malignant tumors have been the primary target of investment and rapidly evolving treatment options, meningiomas receive only a fraction of the nominal research funding allocated to other brain tumor types. As a result, patients continue to face long-term neurological consequences, and the field lacks effective emerging drugs or immunotherapies capable of altering the disease course. Early progress in this research has been made possible by a dedicated community of patients and donors. Now, the Zada Lab is calling on the broader brain tumor community to help propel this work into its next phase transforming a scientific breakthrough into a viable cure for meningioma.

For any questions related to supporting the USC BTC, please contact: **Nicole Measles, Director of Development**, Email: **Nicole.measles@med.usc.edu**, Mobile: **(213) 806-0693**.

When melanoma spread to her brain and lungs, Niki Kozak turned to the experts of the USC Stereotactic Radiosurgery Center, where innovative treatment would save her life

By 2013, Niki Kozak, a radio host and promotions director, had been living with melanoma for six years. She was first diagnosed with early-stage melanoma in 2007. The disease had brought its share of challenges to the avid outdoorswoman, but otherwise, she was thriving.

> *"I had a supportive husband, a young adult son launching his own successful life, an adorable little dog and a fat orange cat, a job that paid me to talk and give stuff away, and weekends on my bike with friends," Niki says. "I was in the best shape of my life, both mentally and physically."*

Then one morning in April 2013, while hosting her morning country music show, Niki suffered a seizure on-air. She was taken to her local emergency room, which delivered a deeply troubling update: her melanoma had metastasized to her brain, lungs and soft tissues, making her a stage IV cancer patient.

Niki had lost both parents to cancer, so she was determined to get the best care possible. Niki's husband, Frank, had been deeply impressed by the exceptional level of coordinated care he witnessed at the USC Norris Comprehensive Cancer Center, part of Keck Medicine of USC, when his own mother was undergoing treatment there.

For Niki and Frank, the decision on where to get treatment was easy. Niki reached out to the USC Norris Comprehensive Cancer Center. She says knowing that it is a National Cancer Institute-designated Comprehensive Cancer Center also contributed to their choice.

Their faith was well-founded. "My care team was built, coordinated and in contact with us before we even knew what treatments I was going to need," Niki says. Her treatment regimen soon began and would take place at both Keck Hospital of USC and USC Norris Cancer Hospital.

Surgery, innovative radiotherapy and more

Niki's treatment included two craniotomies performed by neurosurgeon **Charles Liu, MD, PhD**.

About a month after Niki's first surgery, she began treatment with the USC Stereotactic Radiosurgery Center. This center, which specializes in innovative radiation oncology treatments for brain and spine tumors, is a multidisciplinary partnership of two Keck Medicine entities: USC Norris Comprehensive Cancer Center and the USC Brain Tumor Center.

Niki began undergoing stereotactic radiosurgery (SRS), which would prove foundational to her treatment. It is an exceptionally precise, targeted radiation procedure. In Niki's case, a device called the Gamma Knife was used to deliver the SRS that would eradicate her brain tumors.

Radiation oncologist **Eric Chang, MD**, ultimately performed 10 rounds of stereotactic radiosurgery on Niki to eliminate a total of 37 tumors. **Gabriel Zada, MD**, co-director of the USC Brain Tumor Center, also oversaw Niki's treatment.

Niki praises Dr. Chang as a pioneer for pushing her SRS treatment beyond what would be customary (to treat just a few tumors). By having more of her tumors treated with SRS, Niki was able to avoid undergoing whole-brain radiation therapy, which can pose some long-term health risks.

> *"If not for Dr. Chang's desire to change the paradigm of limiting SRS's use to 'four lesions or fewer,' I would be facing some lifelong consequences that often result from whole-brain radiation," Niki says. "He pushed boundaries that are now considered new standards."*

For Niki, the SRS process involved an early morning pre-check, followed by anesthesia. Once Niki was unconscious, she would receive intracranial lidocaine shots and be fitted with a head frame. From there, an MRI would map the number and location of tumors to be targeted.

Once in the device, her head frame would be locked into place to restrict her movement. The machine then applied small beams of gamma rays to damage the DNA of the targeted cells, ultimately causing them to shrink and die.

Niki would spend anywhere from 20 minutes to three and a half hours in the machine. Fortunately, she could listen to music while undergoing treatment. The 1960s and 1970s songs she preferred kept her mood up and helped her keep track of how much treatment time remained during each session.

Niki praises her entire care team for making her experience as pleasant as possible. "A great nurse, good music and an anesthesiologist to relieve the pain of the frame placement certainly helped," she says. "Also, every provider I came across was a great listener. It takes a special person to show proper empathy and also make you laugh, even when you have a searing headache and think you might vomit. I feel like I made some lifelong friends there."

She adds: "I've spoken with many patients who have experienced radiosurgery at other institutions around the U.S., and not all seem to follow the same 'patient comfort' process."

This year, Keck Medicine will also start offering SRS treatment via an even more advanced device. It is installing the newest version of the Gamma Knife device, which offers both frame-based and frameless SRS treatment, Dr. Zada says.

Niki's care from Keck Medicine would also go on to include 22 months of immunotherapy using two different types of immunotherapy drugs, a lung lobectomy, subcutaneous lesion removal from dermatologist David Peng, MD, rheumatologic treatment for some immunotherapy side effects, and months of targeted drug therapy.

Bright future ahead

Today, Niki is back to enjoying an active lifestyle, having completed a century bicycle ride, run a marathon and hiked the Italian Alps and the Canadian Rockies.

Since there is no cure for melanoma, she continues annual follow-ups with medical oncologists, brain MRIs with radiation oncologists and dermatology checkups every five or six months.

When meeting people facing their own cancer journeys, Niki makes sure to let them know that having access to a comprehensive cancer center like USC Norris can make a huge difference — not only for the specialized care it provides, but also for the integrated approach that takes extra travel and recordkeeping off a patient's shoulders.

> *"Being treated for cancer and its side effects can feel like a full-time job," she says. "Hauling yourself from location to location while dragging along records, imaging and clinic notes to keep your ring of doctors all in the loop is exhausting. This is where my recommendation for comprehensive cancer centers comes into play. Having a team that can communicate and offer specialized care for all the varied treatments you will need is huge. Having a team 'under one roof' can save you so much stress and headache."*

She also advises patients to rely on their community, whether that includes their medical team, friends or family.

> *"If you don't have support friends or family, ask your doctors about the nurse coordinators who are available," she says. "You can also ask about patient advocates and support groups that the hospital offers or is aligned with. With cancer comes anxiety, even for the calmest individual. Find your people — the ones who hear you, who 'get' you and who make you feel like an appointment is something to look forward to."*

FAQs About Clinical Trials: What Participation Really Involves

By Rebekah Ghazaryan, RN, BSN, PHN, MSN/NP-S; RN Clinical Coordinator - USC Brain Tumor Center | USC Pituitary Center

Rebekah Ghazaryan, RN, BSN, PHN, MSN/NP-S

At the USC Brain Tumor Center, clinical trials are an important part of how we improve care for patients today while shaping the treatments of tomorrow. Many of the therapies now considered "standard of care" were once available only through research studies made possible by patients who chose to participate.

If you or your loved one has been offered a clinical trial, it is completely natural to have questions.

Understanding what participation truly involves can help you make a decision that feels informed, comfortable, and aligned with your goals of care.

Here are some common asked questions regarding clinical trials and their inner workings.

Understanding What a Clinical Trial Is

A clinical trial is a carefully designed research study that evaluates new treatments, new combinations of therapies, or new ways of using existing treatments.

These studies follow strict scientific and ethical standards to ensure patient safety while advancing medical knowledge.

By the time a treatment reaches a brain tumor clinical trial, it has already undergone years of laboratory testing and earlier phases of human study.

Trials offered to patients are built on a strong foundation of safety data and oversight.

The Meaning of Informed Consent

Before enrolling, you will go through a detailed process called **informed consent**. This is not simply signing a form.

It is a conversation between you and the research team where you will learn:

- The purpose of the study
- What treatments, tests, or procedures are involved
- Potential risks and benefits
- How the study differs from standard treatment
- Your right to ask questions and take time to decide

You are encouraged to review the written consent form at home, discuss it with family, and return with any questions. Participation is always voluntary.

Will You Still Receive Standard Treatment?

Yes. You will never be denied appropriate care. In many brain tumor trials, the study treatment is added to standard therapy.

In others, the new approach is compared to the current standard to determine which is more effective.

Throughout the study, your neuro-oncology team remains fully involved in your care.

Understanding Placebos

The idea of a placebo can be concerning. In brain tumor trials, placebos are rarely used alone.

If a placebo is part of a study, it is typically given **in addition to** standard treatment, never in place of it. This is explained clearly during the consent process.

What Extra Commitments Are Involved?

Participating in a clinical trial often requires:

- Additional blood work or imaging
- More frequent clinic visits
- Careful symptom tracking
- Follow-up after treatment ends

These added steps allow the research team to monitor your safety closely and understand how the treatment is working.

Safety Oversight and Monitoring

Patient safety is the highest priority in any clinical trial. Studies are monitored by multiple oversight groups, including Institutional Review Boards (IRBs), research safety committees, and federal regulatory agencies.

If new safety information emerges, the study can be modified or stopped.

Understanding the Costs

In most cases:

- The study drug or intervention is provided by the trial sponsor
- Standard care costs are billed to insurance as usual
- Research-related tests are covered by the study

Research coordinators review all of this with you in advance so there are no unexpected costs.

The Right to Change Your Mind

Participation in a clinical trial is entirely voluntary. You may withdraw at any time, for any reason, without affecting your relationship with your care team or your access to treatment.

Why Patients Choose to Participate

Patients often share that they participate in trials because they:

- Want access to promising new therapies
- Value contributing to advancements in brain tumor care
- Appreciate the additional monitoring and support from the research team
- Feel empowered being part of the scientific process

Making the Decision That Is Right for You

Deciding whether to participate in a clinical trial is a personal choice.

Your care team will help you understand which trials may be appropriate based on your diagnosis, treatment history, and individual goals.

We encourage you to ask questions, involve loved ones, and take the time you need.

A Partnership in Advancing Care

Clinical trials are not just about research—they are about partnership.

Every patient who participates helps move brain tumor treatment forward, offering hope to future patients while receiving attentive, closely monitored care today.

If you are interested in learning more about clinical trials available through the USC Brain Tumor Center, speak with your provider or a member of our research team at your next visit.

Fight On and Heal On!

USC Brain Tumor Center Spotlight: Dr. David D. Tran, MD, PhD

Dr. Tran is Co-Director, USC Brain Tumor Center, Division Chief, Neuro-Oncology, and Associate Professor of Neurological Surgery & Neurology at the Keck School of Medicine of USC Department of Neurological Surgery.

At the USC Brain Tumor Center, **Dr. David D. Tran** provides specialized care for patients with brain and spinal cord tumors and leads efforts to develop new treatment options through translational and basic research. As **Division Chief of Neuro-Oncology** and **Co-Director of the USC Brain Tumor Center**, Dr. Tran works across disciplines to deliver personalized treatment while accelerating the discovery of next-generation therapies.

Precision medicine, tailored to the individual

Dr. Tran is a physician-scientist who develops treatment plans for tumors of the brain and spinal cord using personalized cancer therapy based on each patient's overall health and disease features, and—in many cases—molecular and genetic profiling. His goal is to match the right therapy to the right patient while maintaining a clear focus on safety and quality of life.

Advancing care through clinical trials and breakthrough approaches

A hallmark of Dr. Tran's work is moving science into options for patients who need them now. He serves as a principal investigator on national and international clinical trials in brain cancer and is recognized for work that brings promising strategies to patients. Recent USC News reporting highlighted studies led by Dr. Tran evaluating Tumor Treating Fields and Laser Interstitial Thermal Therapy paired alongside immunotherapy for glioblastoma, with results suggesting longer survival for select patients.

A translational lab: from bedside questions to therapies

Dr. Tran leads a research program that studies how cancers develop, progress, and resist treatment. The lab integrates clinical observation, computational and systems analysis, and experimental validation to identify actionable targets and move therapies toward the clinic.

As Dr. Tran notes, "*One patient's glioblastoma is different from another patient's glioblastoma*," reinforcing the need for both personalization and strategies that work across patients.

Beyond the white coat

Dr. Tran is fluent in English and Vietnamese and is known for clear, direct communication with his patients and colleagues. He prioritizes listening, shared decision-making, and the outcomes that matter most to patients: time, function, and quality of life.

Learn more / appointments: Dr. David D. Tran's faculty and clinical profiles and lab are available through Keck Medicine of USC and the Keck School of Medicine.

SELECTED PUBLICATIONS

Machine Learning-Directed Conversion of Glioblastoma Cells to Dendritic Cell-Like Antigen-Presenting Cells as Cancer Immunotherapy. ***Liu T, Jin D, Le SB, Chen D, Sebastian M, Riva A, Liu R, Tran DD.*** *Cancer Immunol Res. 2024 Oct 1;12(10):1340-1360. doi: 10.1158/2326-6066.CIR-23-0721.*

Immunotherapy has limited efficacy in glioblastoma (GBM) due to the blood-brain barrier and the immunosuppressed or "cold" tumor microenvironment (TME) of GBM, which is dominated by immune-inhibitory cells and depleted of CTL and dendritic cells (DC). Here, we report the development and application of a machine learning precision method to identify cell fate determinants (CFD) that specifically reprogram GBM cells into induced antigen-presenting cells with DC-like functions (iDC-APC). Lastly, we defined a unique CFD combination specifically for the human GBM to iDC-APC conversion of both glioma stem-like cells and non-stem-like cell GBM cells, confirming the clinical utility of a computationally directed, tumor-specific conversion immunotherapy for GBM and potentially other solid tumors.

The EP3-ZNF488 Axis Promotes Self-Renewal of Glioma Stem-Like Cells to Induce Resistance to Tumor Treating Fields. ***Chen D, Le SB, Manektalia H, Liu T, Hutchinson TE, O'Dell A, Salhia B, Tran DD.*** *Cancer Res. 2025 Jan 15;85(2):360-377. doi: 10.1158/0008-5472. CAN-23-3643.*

Tumor treating fields (TTFields) use low-intensity, alternating electric fields to exert antitumor activity and have demonstrated efficacy against multiple cancers, including glioblastoma (GBM). Unfortunately, cancer cells inevitably develop resistance to TTFields, highlighting the need to elucidate the underlying mechanisms to develop approaches to induce durable responses. Using a gene network-based machine learning algorithm, we interrogated TTFields-resistant GBM cells and uncovered a regulatory axis anchored by the prostaglandin E2 receptor 3 (EP3) and the transcription factor zinc finger 488 (ZNF488). The EP3-ZNF488 master regulatory axis in cancer stem-like cells drives resistance to treatments like tumor treating fields, opening avenues for developing strategies to enhance therapeutic efficacy.

Efficacy and safety of adjuvant TTFields plus pembrolizumab and temozolomide in newly diagnosed glioblastoma: A phase 2 study. ***Chen D, Le SB, Ghiaseddin AP, Manektalia H, Li M, O'Dell A, Rahman M, Tran DD.*** *Med. 2025 Sep 12;6(9):100708. doi: 10.1016/j.medj.2025.100708.*

Immune checkpoint inhibitors (ICIs) have shown limited success in glioblastoma due to the tumor's profoundly immunosuppressive microenvironment. Tumor treating fields (TTFields), a non-invasive electric field therapy, activate the type I interferon (T1IFN) pathway via DNA sensor-dependent inflammasomes, promoting in situ immunization against glioblastoma. In this phase 2 study, 31 newly diagnosed glioblastoma patients were enrolled post-chemoradiation to evaluate synergy between TTFields, pembrolizumab, and temozolomide. The primary endpoint was progression-free survival (PFS) compared to case-matched controls treated with TTFields and temozolomide alone. Secondary endpoints included overall survival (OS), response rate, safety, and immune correlates assessed through single-cell transcriptomics and T cell clonotyping of blood and tumor samples. These findings demonstrate synergy between TTFields and ICIs, particularly in patients with high tumor burden, and support further study in larger trials.

Could electric fields supercharge an immune attack on the deadliest form of brain cancer?

A new study led by Keck Medicine of USC researchers may have uncovered an effective combination therapy for glioblastoma, a brain tumor diagnosis with few available effective treatments.

According to the National Brain Tumor Society, the average survival for patients diagnosed with glioblastoma is eight months. The study finds that using **Tumor Treating Fields therapy (TTFields)**, which delivers targeted waves of electric fields directly into tumors to stop their growth and signal the body's immune system to attack cancerous tumor cells, may extend survival among patients with glioblastoma, when combined with immunotherapy (pembrolizumab) and chemotherapy (temozolomide).

TTFields disrupt tumor growth using low-intensity, alternating electric fields that push and pull key structures inside tumor cells in continually shifting directions, making it difficult for the cells to multiply. Preventing tumor growth gives patients a better chance of successfully fighting the cancer.

When used to treat glioblastoma, TTFields are delivered through a set of mesh electrodes that are strategically positioned on the scalp, generating fields at a precise frequency and intensity focused on the tumor. Patients wear the electrodes for approximately 18 hours a day.

Researchers observed that TTFields attract more tumor-fighting T cells, which are white blood cells that identify and attack cancer cells, into and around the glioblastoma. When followed by immunotherapy, these T cells stay active longer and are replaced by even stronger, more effective tumor-fighting T cells.

> *"By using TTFields with immunotherapy, we prime the body to mount an attack on the cancer, which enables the immunotherapy to have a meaningful effect in ways that it could not before," said **David Tran, MD, PhD**, chief of neuro-oncology with Keck Medicine, co-director of the USC Brain Tumor Center and corresponding author of the study. "Our findings suggest that TTFields may be the key to unlocking the value of immunotherapy in treating glioblastoma."*

TTFields are often combined with chemotherapy in cancer treatment. However, even with aggressive treatment, the prognosis for glioblastoma remains poor. Immunotherapy, while successful in many other cancer types, has also not proved effective for glioblastoma when used on its own.

However, in this study, adding immunotherapy to TTFields and chemotherapy was associated with a 70% increase in overall survival. Notably, patients with larger, unresected (not surgically removed) tumors showed an even stronger immune response to TTFields and lived even longer.

This suggests that, when it comes to kick-starting the body's immune response against the cancer, having a larger tumor may provide more targets for the therapy to work against.

Using alternating electric fields to unlock immunotherapy

Pembrolizumab, the immunotherapy used in this study, is an immune checkpoint inhibitor (ICI), which enhances the body's natural ability to fight cancers by improving T cells' ability to identify and attack cancer cells.

However, there are typically few T cells in and around glioblastomas because these tumors originate in the brain and are shielded from the body's natural immune response by the blood-brain barrier. This barrier safeguards the brain by tightly regulating which cells and substances enter from the bloodstream. Sometimes, this barrier even blocks T cells and other therapies that could help kill brain tumors.

Optune, tumor treating fields therapy device. (Graphic/Courtesy of Novocure)

This immunosuppressive environment inside and around the glioblastoma is what makes common cancer therapies like pembrolizumab and chemotherapy significantly less effective in treating it. Tran theorized the best way to get around this issue was to start an immune reaction directly inside the tumor itself, an approach known as in situ immunization, using TTFields.

This study demonstrates that combining TTFields with immunotherapy triggers a potent immune response within the tumor — one that ICIs can then amplify to bolster the body's own defense against cancer.

> *"Think of it like a team sport - immunotherapy sends players in to attack the tumor (the offense), while TTFields weaken the tumor's ability to fight back (the defense). And just like in team sports, the best defense is a good offense,"* said Dr. Tran, who is also a member of the USC Norris Comprehensive Cancer Center.

Study methodology and results

The study analyzed data from **2-THE-TOP**, a **Phase 2 clinical trial**, which enrolled 31 newly diagnosed glioblastoma patients who had completed chemoradiation therapy. Of those, 26 received TTFields combined with both chemotherapy and immunotherapy. Seven of these 26 patients had inoperable tumors due to their locations — an especially high-risk subgroup with the worst prognosis and few treatment options.

Patients in the trial were given six to 12 monthly treatments of chemotherapy alongside TTFields for up to 24 months. The number and duration of treatments were determined by patients' response to treatment. The immunotherapy was given every three weeks, starting with the second dose of chemotherapy, for up to 24 months.

Patients who used the device alongside chemotherapy and immunotherapy lived approximately 10 months longer than patients who had used the device with chemotherapy alone in the past.

Moreover, those with large, inoperable tumors lived approximately 13 months longer and showed much stronger immune activation compared to patients who underwent surgical removal of their tumors.

> *"Further studies are needed to determine the optimal role of surgery in this setting, but these findings may offer hope, particularly for glioblastoma patients who do not have surgery as an option,"* said Dr. Tran.

Moving the research forward

Keck Medicine is participating in the multicenter **Phase 3 clinical trial** to validate the efficacy of TTFields with immunotherapy and chemotherapy. Tran, who has been researching TTFields for more than a decade, serves as the chair of the steering committee for this trial. **Frances Chow, MD**, neuro-oncologist with USC Norris, is the principal investigator of the Keck Medicine study site.

This Phase 3 trial, currently open at 28 sites across the United States, Europe, and Israel, aims to enroll over 740 patients through April 2029, including those with gross total resection, partial resection or biopsy-only tumors to assess the extent of how surgically removing tumors influences immune response.

Keck School of Medicine of USC authors of this study include **Dongjiang Chen, PhD**, assistant professor of research neurological surgery; **Son Le, PhD**, assistant professor of research neurological surgery; **Harshit Manektalia**, research programmer; **Ming Li, PhD**, professor of research population and public health sciences; and **Adam O'Dell**, research lab specialist. **Ashley Ghiaseddin, MD**, and **Maryam Rahman, MD, MS**, colleagues from the University of Florida, also contributed to this work.

This study was funded by a grant from Novocure, which manufactures Optune, the TTFields device used in this study. Dr. Tran has received honoraria from Novocure for consultant work. Dr. Chen and Dr. Tran are inventors of two patent applications related to work reported in this study.

Winter Newsletter Spotlight: Keynote Speaker Announcement

The USC Brain Tumor Center is proud to announce Dr. Patrick Soon-Shiong as the Keynote Speaker for the 3rd Annual Southern California Brain Tumor Conference, taking place March 27, 2026 at the USC Health Sciences Campus

Dr. Patrick Soon-Shiong (MBBCh, MSc, FRCS(C), FACS) is a South African–American surgeon, scientist, and entrepreneur whose work over the past three decades has shaped modern cancer treatment, immunotherapy, and digital health. He is best known for inventing the chemotherapy drug Abraxane and Anktiva and for leading efforts to merge biotechnology, genomics, and advanced computing into new forms of medical care. Trained as a surgeon, he began his career at UCLA, where he performed the institution's first whole-organ pancreas transplant and pioneered the world's first transplant of encapsulated islet cells into a patient with Type 1 diabetes. These early successes reflected his long-standing interest in solving complex disease by combining biology with emerging technologies. During his decade as Chair of the California NanoSystems Institute, he oversaw work in nanomedicine, advanced chip manufacturing, and high-speed network connectivity, helping lay the foundation for many of the technology-driven medical initiatives he would later build.

Patrick Soon-Shiong, MBBCh, MSc, FRCS(C), FACS

In the 1990s, his research led to the creation of Abraxane, a drug that uses albumin nanoparticles to deliver chemotherapy more effectively to tumors. Approved by the FDA for breast, lung, and pancreatic cancers, Abraxane became the first nanoparticle-based chemotherapy and one of the few treatments to extend survival in metastatic pancreatic cancer. Through his companies American Pharmaceutical Partners and Abraxis BioScience, he brought Abraxane from concept to global use before the companies were acquired for nearly $9 billion. For this work, he received major recognition, including honors from the Vatican and the Franklin Institute.

With the formation of NantWorks in 2011, Dr. Soon-Shiong expanded his focus from therapeutics to building an integrated ecosystem of biotechnology, genomics, artificial intelligence, and digital infrastructure. He had already acquired the National LambdaRail fiber network to link supercomputing centers for medical data analysis, and he worked to combine high-speed connectivity with advanced imaging and diagnostics. His collaboration with UCLA scientist Bahram Jalali led to STEAM, an ultrafast optical imaging technology capable of capturing events too fast for conventional cameras. This work helped propel the use of AI in real-time cellular analysis and medical diagnostics.

At the same time, he became a leader in personalized cancer medicine. His companies NantHealth and NantOmics developed platforms to sequence a patient's DNA, RNA, and proteins to guide individualized treatment decisions. He also expanded into proteomics which added mass spectrometry–based tumor analysis to his diagnostic portfolio. This "panomic" approach—integrating genomic and protein-level information—became central to his vision for precision oncology.

Immunotherapy has been another major focus of his work. Through ImmunityBio, he developed new therapies that activate the immune system to fight cancer. One such therapy, Anktiva (N-803), an IL-15 superagonist, received FDA approval in 2024 for bladder cancer and is now being explored across multiple tumor types. Combined with natural killer cell therapies, it represents a new strategy to stimulate the body's own immune defenses against difficult-to-treat cancers.

His interests in technology also extend to semiconductors and photonics. Starting with Tensorcom's low-power 60-GHz wireless chips, he has pursued ways to overcome the limits of traditional data processing. This led to investment in thin-film lithium niobate, a promising material for ultrafast optical communication. In 2025, his team was granted a U.S. patent for manufacturing next-generation lithium-niobate modulators capable of operating at extremely high speeds, a step toward more energy-efficient computing and communication systems.

Beyond science and technology, Dr. Soon-Shiong has played a prominent role in business, philanthropy, and public service. He leads the Chan Soon-Shiong Family Foundation, has supported major research and medical institutions, and has served in advisory roles at national and international levels. In 2018 he acquired the Los Angeles Times and San Diego Union-Tribune to preserve independent journalism, and he has long been a part-owner of the Los Angeles Lakers. Across all these efforts, his work reflects a consistent theme: the belief that the convergence of biology, computing, and engineering can transform healthcare. Whether through new drugs, diagnostic platforms, or digital infrastructure, he has sought to bring scientific breakthroughs to patients in ways that are practical, scalable, and globally accessible.

We are honored to welcome Dr. Soon-Shiong and look forward to the insight and momentum his keynote will bring to our shared mission—accelerating discovery and improving outcomes for patients and families.

Dr. Gabriel Zada appointed Editor of *Neurosurgical Focus*

The Department of Neurological Surgery at the Keck School of Medicine of USC is proud to announce that **Gabriel Zada, MD**, has been appointed **Editor of *Neurosurgical Focus***, a premier peer-reviewed journal of ***The Journal of Neurosurgery*** Publishing Group and the American Association of Neurological Surgeons (AANS).

Dr. Zada is an internationally recognized leader in neurosurgery with expertise in skull base surgery, pituitary and parasellar tumors, and multidisciplinary brain tumor care.

He is widely respected for his contributions as a surgeon-scientist, educator, and mentor, and for his longstanding commitment to advancing neurosurgical scholarship.

As Editor, Dr. Zada will lead the journal's vision through high-impact thematic issues highlighting emerging science and evolving surgical practice.

His appointment also marks a return of ***Neurosurgical Focus*** to USC, where it was founded 30 years ago by his mentor, **Dr. Martin H. Weiss**, former Chair of the Department of Neurological Surgery.

We congratulate Dr. Zada on this well-deserved honor and look forward to the continued impact of his leadership on the global neurosurgical community.

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	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	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
4	A Phase 1/2 Study of Selinexor and Temozolomide in Recurrent Glioblastoma	• Selinexor + Temozolomide • Temozolomide	Phase 1/2
5	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
6	Study of NEO212 (Temozolomide-Perillyl Alcohol Conjugate) in Advanced Brain Cancer	• NEO212 (oral)	Phase 1
	Meningioma		
7	An Open-Label, Phase 2 Study of NEO100 in Participants with Residual, Progressive or Recurrent High-grade Meningioma	• Perillyl alcohol (inhaled)	Phase 2
8	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
9	MOMENTUM-1: A Randomized, Open-Label, Phase 2 study of [^{177}Lu] Lu-DOTATATE in Adults with Progressive Intracranial Grade 1-3 Meningioma	• Radionuclide 177 Lu • Standard therapy	Phase 2

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