tae Life Sciences

The Promise of Biologically Targeted Brain Cancer Treatment

How BNCT will improve outcomes for the most difficult-to-treat cancers

INTRODUCTION

Difficult-to-Treat Cancers Present an Open Door for Innovation

Advances in cancer treatment options have reduced many early diagnoses of common cancers from a death sentence to a major inconvenience. But many of the most lethal cancers continue to take lives because conventional methods can't effectively target the cancer cells without causing substantial collateral damage.

A malignant brain tumor, for example, is the archetype of a terminal diagnosis. It's easy to intuitively recognize how the critical tissues and structures of the brain are particularly sensitive to invasive cancer growth. But the most promising research in the treatment of brain cancers and many of the other most difficult-to-treat cancers centers on new methods of biologically targeting cancer cells. These rapidly developing treatments use the specific biology of the cancer cells to deliver focused and amplified cancer-killing effects—without damaging surrounding healthy cells and tissues.

As the evidence behind these hyper-targeted treatments continues to grow—and technological innovations make them practical and accessible in more clinical settings—biologically targeted treatments will not only redefine the prognosis for the most deadly and difficult-to-treat cancers, but also have the potential to change how all forms of cancer are treated.

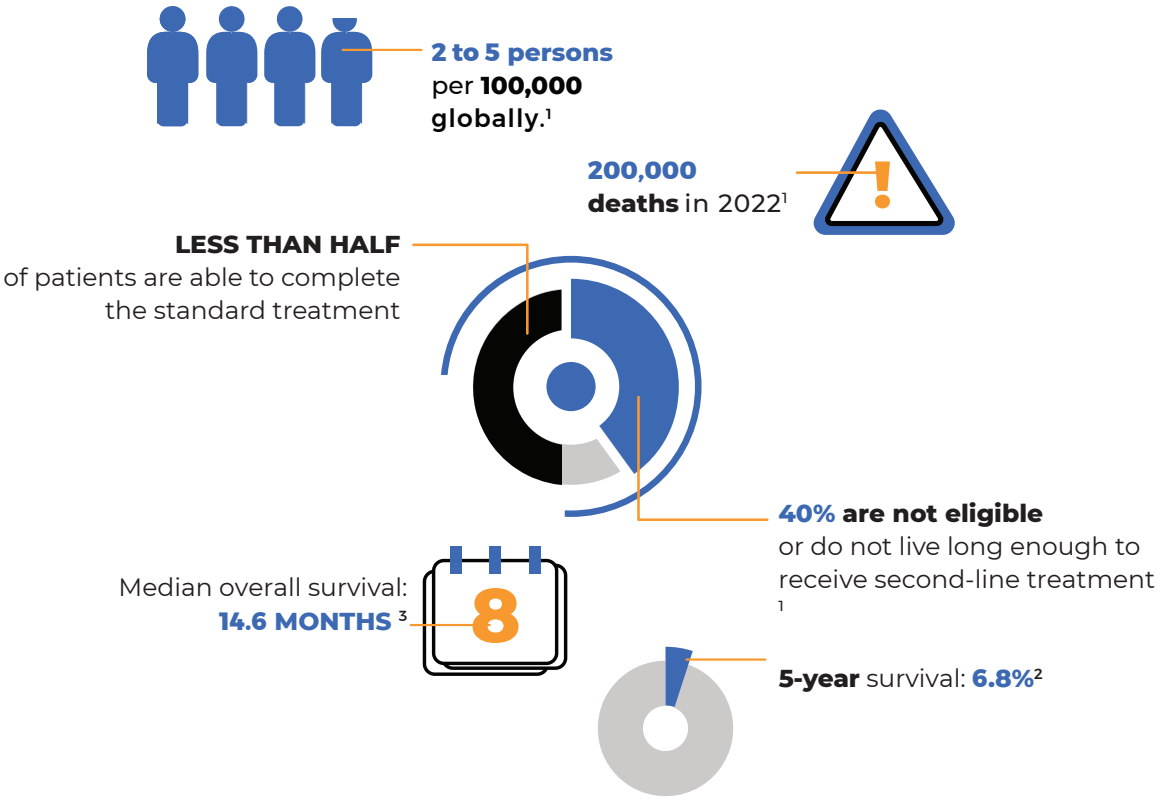
Hyper-targeted treatments have the potential to change how all forms of cancer are treated.

Case Study of an Aggressive Brain Cancer: Glioblastoma

One of the most aggressive and lethal forms of brain cancer, glioblastoma, offers an insightful case study that reveals a much more complex, frustrating, and, yet, hopeful picture. A deeper look at glioblastoma illuminates why brain cancers, along with nearly all head and neck cancers, present unique challenges in treatment; where conventional treatments hit hard limits in effectiveness; and how innovative, biologically targeted treatments like boron neutron capture therapy (BNCT) show exciting promise.

Overview of glioblastoma

Glioblastoma is the most common type of malignant brain or central nervous system (CNS) tumors, accounting for roughly half of all malignant CNS tumors in adults.[1]



A poor prognosis

Unlike most other cancers, there is no localized and surgically curable form of glioblastoma. This means all diagnoses of glioblastoma are considered grade 4, even when caught early. The standard of care was established more than 15 years ago: surgery, then radiotherapy and concurrent drug therapy. Patients who do not want or are not eligible for surgery may also undergo chemotherapy before radiotherapy treatment.

A high rate of recurrence—and low survival

Recurrence of glioblastoma is virtually guaranteed—even among those healthy enough to complete first-line treatment.

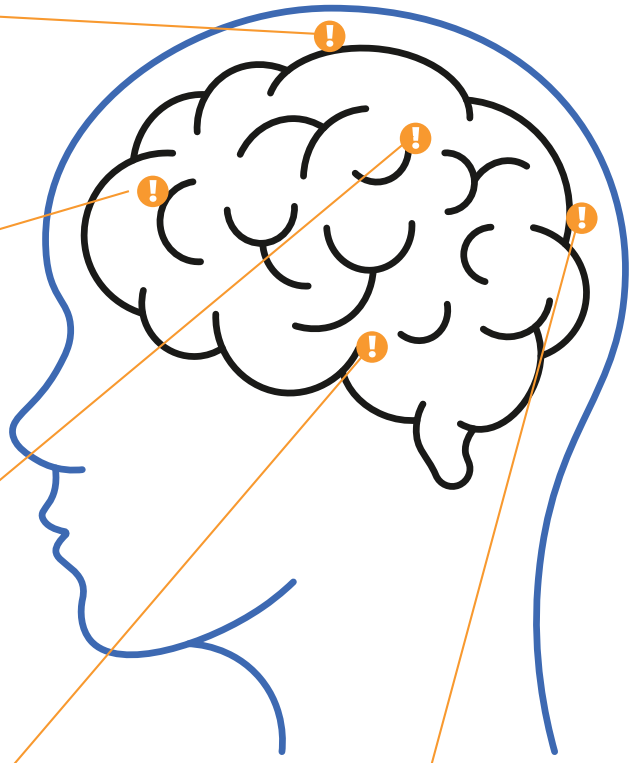
1. https://www.gliocure.com/en/patients/glioblastoma/#:~:text=The%20number%20of%20new%20cases,the%20aging%20of%20the%20population.
2. https://www.frontiersin.org/articles/10.3389/fonc.2021.748061/full
3. https://www.nature.com/articles/s41598-020-68011-4

Why Is Glioblastoma So Difficult to Treat?

Several factors converge to present unique challenges in the treatment of this aggressive and lethal form of cancer:[3]

Location of cancer

Clinicians face the huge challenge of mitigating collateral damage to the brain and CNS—damage that can result in significant quality-of-life-reducing side effects of cognitive impairment and functional dependence.



Blood-brain barrier

The blood-brain barrier (BBB) restricts 100% of macromolecules and nearly 98% of smaller molecules from reaching the brain, including many anticancer drugs.

Highly infiltrative cancer

Glioblastoma spreads into normal brain tissue, making it very difficult to define clear margins so clinicians can remove the primary growth without leaving cancer cells behind at the edges.

Brain-tumor barrier

Glioblastoma has a complex tumor structure that protects the cancer cells. This hinders uniform distribution of drugs and creates an immunosuppressive microenvironment within the tumor, making immunotherapies ineffective.

Heterogeneous cellular composition

Related to the complex tumor structure, not all cells in a glioblastoma are the same. This limits the efficacy of targeted therapies that can work on only a specific subset of the tumor cells.

3. https://www.dovepress.com/recurrent-glioblastoma-ongoing-clinical-challenges-and-future-prospect-peer-reviewed-fulltext-article-OTT

The Limitations of Conventional Treatments

A 2021 meta-analysis focused on recurrent treatment of glioblastoma provides an overview of the state of conventional cancer treatments, indicating both the clinical benefits and limitations of each type of treatment, as briefly summarized below.




Surgery

Even as the standard first line of treatment for glioblastoma, surgery has major limitations:

Eligibility: Many patients are ineligible for surgery as a first-line treatment, and just 20 – 30% of relapsed patients are eligible for a second surgery.[4]

Negative quality-of-life impacts: Brain surgery presents the risk for several cognitive and functional side effects.[5]

Lack of clear margins: Surgery will always require a near-impossible calculation of conservative and aggressive excision, with major potential effects to quality of life.[4]

Drug Therapies

The meta-analysis concluded that no drug therapy is yet showing significant near-term promise.

Radiation therapy

While another essential part of the standard of care for glioblastoma, conventional radiation therapy presents two inherent limitations:

Lack of clear margins: The highly infiltrative nature of glioblastoma makes it difficult to achieve clean margins, risking negative quality-of-life impacts.

Brain tissue is not tolerant of irradiation: Studies have demonstrated that the dose required to achieve local control of glioblastoma "exceeds the accepted tolerance of normal brain tissue."[6]

Immunotherapies

Despite glioblastoma research around four types of immunotherapies , the meta-analysis concludes that, "unfortunately, initial results with immunotherapy have been disappointing."[4]

An Underlying Challenge: Creating Biologically Targeted Treatments

As summarized above, the conventional treatment options for glioblastoma carry significant efficacy and quality-of-life concerns. Novel treatments set out to improve these outcomes by using the specific biology of the cancer cells as a targeting mechanism, aiming for the ultimate goal of delivering treatment directly to the cancer cells—and only the cancer cells.

4. https://www.dovepress.com/recurrent-glioblastoma-ongoing-clinical-challenges-and-future-prospect-peer-reviewed-fulltext-article-OTT
5. https://www.cancer.org/cancer/brain-spinal-cord-tumors-adults/treating/surgery.html#:~:text=Complications%20during%20or%20after%20any,to%20help%20lessen%20this%20risk
6. https://tcr.amegroups.com/article/view/1119/html#:~:text=Abstract%3A%20Boron%20neutron%20capture%20therapy,the%20surrounding%20normal%20brain%20tissue.

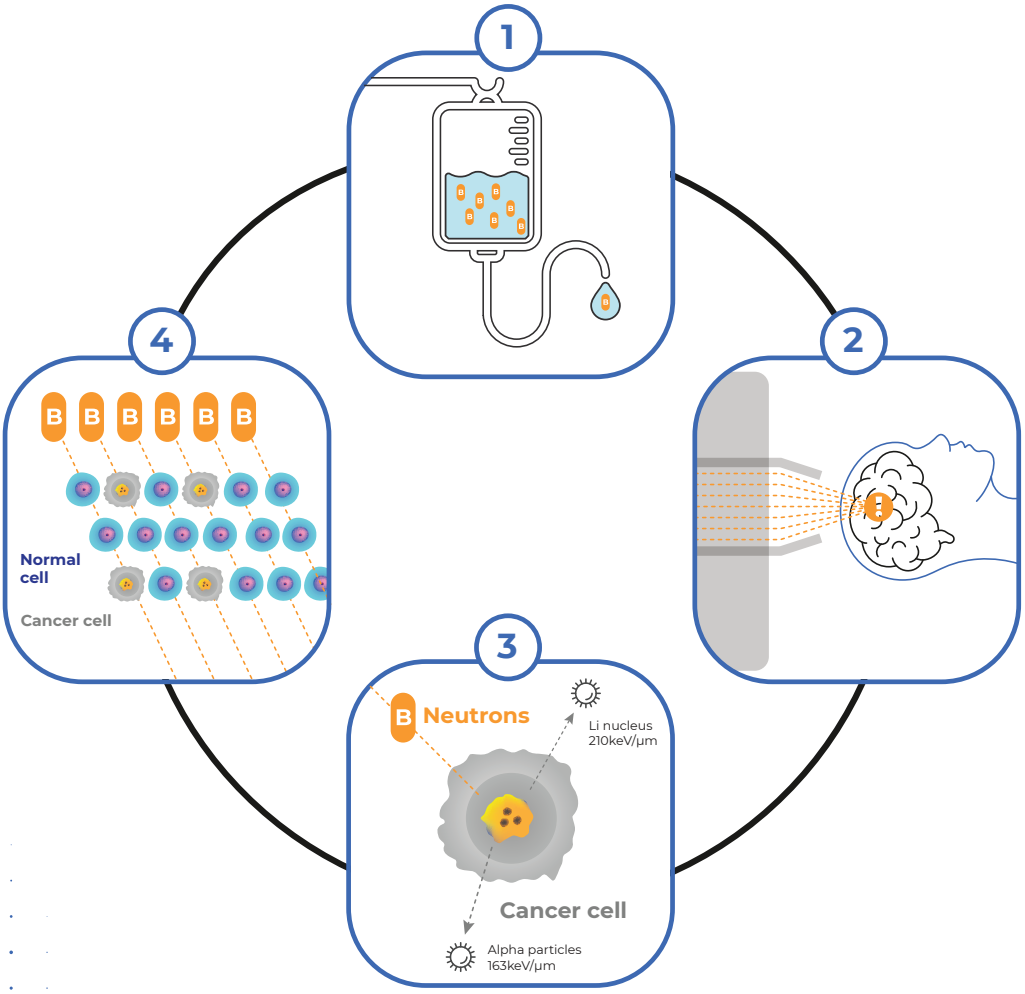
The Emerging Promise of BNCT

One of most promising biologically targeted treatments—boron neutron capture therapy, or BNCT—enhances the proven efficacy of radiotherapy with a tumor-selective targeting mechanism. Unlike many novel treatments, BNCT is not new. The clinical application of BNCT has been performed with reactor-based neutron sources over the past decade, progressively accumulating a strong and wide body of data supporting its safety and efficacy in treatment patients with a variety of advanced tumors—including new and recurrent malignant gliomas (chiefly glioblastomas) and other brain, head and neck, lung, breast, liver, and melanoma cancers, and metastatic disease.

Now, with the shift from reactor- to accelerator-based neutron sources, the potential of BNCT is able to be delivered in a hospital setting to offer cancer patients a new, safe treatment option. Several studies have successfully demonstrated that accelerator-based BNCT (AB-BNCT) is safe and effective.

How BNCT works

BNCT is a two-part treatment that uses non-toxic targeted drugs to actively transport the naturally occurring element boron-10 to the cancer cells—and then delivers low-intensity radiation to trigger an amplified reaction within cancer cells. This reaction generates potent alpha and lithium-7 particles within a limited path length (one-cell diameter) that destroy the cancer cells.



Advantages of BNCT

BNCT offers several distinct benefits over conventional treatment options:

Greater cancer-killing effectiveness
By significantly increasingly the therapeutic ratio, BNCT is three times more destructive to cancer cells than conventional radiotherapy.

BNCT is
3X **MORE DESTRUCTIVE TO CANCER CELLS THAN**
conventional radiotherapy

Protecting quality of life
By enabling a higher therapeutic ratio, BNCT solves the predominant challenge of conventional radiotherapies (and most other drug therapies): achieving effective cancer control while significantly reducing side effects and protecting patients' quality of life during and after treatment.

EFFECTIVE CANCER CONTROL
while significantly
REDUCING SIDE EFFECTS

Treating beyond the margins
The biological targeting of cancer cells gives BNCT the potential to treat undetected metastases in the local region of the tumor during the same treatment session—which cannot be accomplished with conventional radiotherapy.

BNCT can treat
UNDETECTED METASTASES
in the local region of the tumor

Clinical efficiency
The hyper-focused BNCT treatments deliver a high dose of cancer-killing radiation in 1 – 2 treatments—compared to the 20 – 30 treatment sessions of conventional radiotherapy, and similarly high number of treatments for many existing drug therapies. This dramatic reduction in treatment sessions yields significant benefits from a clinical efficiency and cost-effectiveness standpoint, while also making BNCT a much less disruptive treatment for patients.

Cancer-killing radiation in
1 – 2 TREATMENTS
compared to the
20 – 30 TREATMENT SESSIONS
with conventional radiotherapy

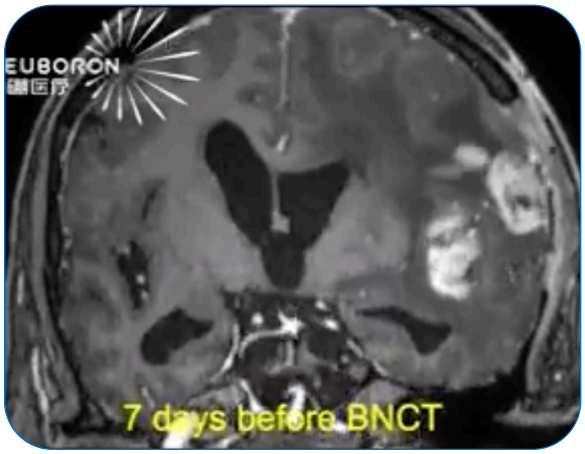
TAE Life Sciences: Bringing the Promise of BNCT to Life

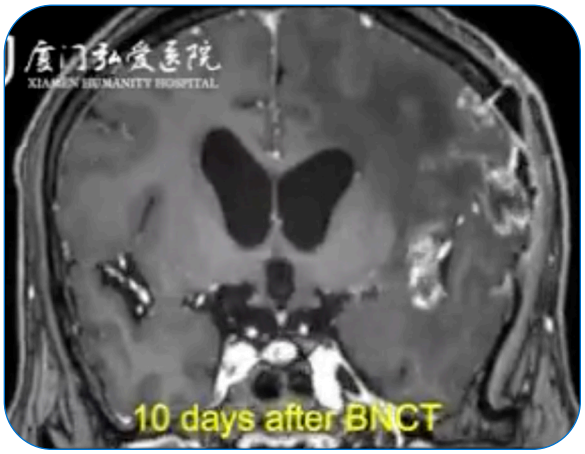
The growing body of research on BNCT demonstrates the strong momentum behind this promising modality as an effective treatment for the most deadly and difficult-to-treat cancers. To move BNCT forward, a 2021 comprehensive review of the clinical applications and potential of BNCT identified two areas for focus: developing better target drugs and lowering barriers to adoption of the technology needed to deliver BNCT.

As the recognized leader in BNCT treatment technology, TAE Life Sciences is leading the charge in advancing BNCT—and is the only company actively working on both of these fronts:

Accelerating the development of better target drugs
TAE Life Sciences has invested heavily in accelerating a pipeline of drugs that can improve the biological targeting of BNCT. These next-generation target drugs will improve the therapeutic ratio of boron in the cancer cells with minimal damage to healthy tissue—enabling improved BNCT outcomes while expanding the application of this transformative treatment to more indications and more patients.

In the most recent study, a 2022 clinical trial at the Xiamen Humanity Hospital in China, 12 patients received BNCT using Neuborn MedTech Neupex™ Sytem, a comprehensibe BNCT solution that includes TAE Life Science's accelerator-based neutron source. These patients diagnosed with recurrent glioma, head and neck, and melanoma cancers received AB-BNCT treatments lasting less than one hour, with interim results suggesting encouraging tumor control.[7]





7. https://www.businesswire.com/news/home/20230227005355/en/China-Performs-First-Cancer-Patient-Treatments-in-the-Xiamen-Humanity-Hospital-Using-Novel-Accelerator-based-Radiation-Oncology-Therapy-BNCT

Making BNCT practical and accessible

Within the last decade, the development of a new breed of accelerator-based neutron sources brought BNCT out of the research realm and into hospital and clinical settings. Yet cost remains the biggest barrier to adoption. TAE Life Sciences (TLS) directly attacked this barrier with the introduction of the Alphabeam Neutron Treatment System—a first-of-its-kind comprehensive BNCT platform that offers a compact, reliable, and economical solution for the clinical implementation of BNCT. TLS is collaborating with leading cancer treatment and research centers around the world to deploy the Alphabeam system, and TLS is rapidly enhancing the platform to make BNCT more accessible and practical for a much broader range of hospitals and clinical settings.

Bringing life-saving treatment to more patients

In working to bring the promise of BNCT to life, TLS is pursuing a critical mission: Expanding the application of BNCT to make this powerfully precise, biologically targeted radiotherapy a first-line treatment for all types of cancer—and engineering the practical technologies that will empower more clinicians to bring these life-saving and life-changing treatments to more patients, every day.

Note: The TAE Life Sciences device and drugs are in development and not available for sale or commercial use

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