## (10)
# 硼中子捕獲治療在台灣的現況與未來的展望
## Current Status and Perspective of BNCT in Taiwan

時　　間：114 年 6 月 28 日(星期六) 08:20~12:00
地　　點：臺北榮民總醫院 中正樓 B1 腫瘤醫學部會議室

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| ***08:20-08:30*** | ***Opening Remarks*** | 劉裕明副教授<br>Yu-Ming Liu |
| | **座長：顏上惠 醫師 (Sang-Hue Yen)** | |
| 08:30-09:20 | 硼中子俘获療法（BNCT），新一代帶電粒子療法<br>Boron Neutron Capture Therapy (BNCT). Next Generation Charged Particle Therapy | 松村 明教授<br>Akira Matsumura<br>(日本) |
| 09:020-09:45 | 硼中子捕獲治療在國內的現況與未來的展望<br>Current and Future Perspective of BNCT in Taiwan | 顏上惠教授<br>Sang-Hue Yen |
| 09:45-10:10 | 18F-BPA 的現況與未來發展<br>The Current Status and Perspective of 18F-BPA | 林可瀚醫師<br>Ko-Han Lin |
| ***10:10-10:30*** | ***Coffee Break*** | |
| | **座長：黃品逸 醫師 (Pin-I Huang)** | |
| 10:30-11:00 | 台灣加速器硼中子捕獲癌症治療的發展<br>Development of Accelerator-based Boron Neutron Capture Therapy in Taiwan | 陳韋霖博士<br>Wei-Lin Chen |
| 11:00-11:30 | 臺灣第一台加速器型硼中子捕獲治療進行恩慈療法的初步結果<br>Preliminary Outcomes of Compassionate Use of First Accelerator-Based Boron Neutron Capture Therapy(AB-BNCT) in Taiwan | 吳元宏醫師<br>Yuan-Hung Wu |
| 11:30-12:00 | 中子捕獲增強粒子治療（NCEPT）：現況發展、可行性評估與未來展望<br>Neutron Capture Enhanced Particle Therapy (NCEPT): Current Development, Feasibility Assessment, and Future Perspective | 劉晉昇技師<br>Ching-Sheng Liu |
| ***12:00-12:05*** | ***Closing Remarks*** | 王令瑋醫師<br>Ling-Wei Wang |

# Boron Neutron Capture Therapy (BNCT). Next generation charged particle therapy

# 硼中子俘获療法（BNCT），新一代帶電粒子療法

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Boron Neutron Capture Therapy (BNCT) represents a dual-modality radiation treatment utilizing 10B compounds that selectively accumulate in tumor cells. When exposed to epithermal neutrons, these compounds undergo nuclear reactions, generating alpha and Li particles. Essentially, BNCT can be viewed as targeted charged particle therapy for tumor cells.

First proposed by Locher in 1937, BNCT has since undergone numerous clinical trials using research nuclear reactors. Recent technological advancements have enabled the transition to accelerators, making BNCT feasible in hospital settings. In 2020, BNCT was approved as an insurance-covered medical treatment for recurrent head and neck cancer following successful clinical trials in Japan.

BNCT shows promise for treating various cancers including malignant brain tumors (e.g., glioblastoma, malignant meningioma), melanoma, angiosarcoma, breast cancer, lung cancer, and chest wall cancer. To expand the BNCT in medical institutions, it is necessary to expand the clinical indications in these type of cancers.

Looking ahead, the development of more effective boronated drugs is crucial for optimizing BNCT efficacy. The shift from basic drug research to translational research, encompassing clinical marketing strategies, is now imperative. This lecture explores current challenges and future directions in BNCT, emphasizing the pivotal role of drug development and translational research in advancing clinical outcomes.

# Current and future perspective of BNCT in Taiwan

# 臺灣硼中子捕獲治療現在及未來展望

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Boron Neutron Capture Therapy (BNCT) development in Taiwan began over 30 years ago. Despite major advances in radiation oncology—such as 3DCRT, IMRT, IGRT, and proton/carbon ion therapy—external beam radiotherapy remains limited by its impact on surrounding normal tissues. BNCT, a targeted, intra-tumoral high-LET therapy, offers a promising solution to this challenge.

Since 2007, the THOR research team and Taipei Veterans General Hospital (Taipei VGH) have collaborated on BNCT clinical development, with a strategic focus on expanding accelerator-based BNCT (AB-BNCT) across major medical centers. To date, Taipei VGH has conducted over 600 BNCT treatments—including clinical trials and compassionate-use cases—utilizing both reactor-based and Taiwan-developed AB-BNCT platforms.

In parallel, Taipei VGH introduced carbon ion therapy in recent years, demonstrating efficacy in managing radioresistant and complex tumors. With AB-BNCT system installation underway and clinical implementation expected by 2027, the hospital aims to integrate BNCT and carbon ion therapy—both high-LET modalities—to enhance therapeutic outcomes.

Past BNCT progress was hindered by limited neutron sources from research reactors and the slow development of AB-BNCT systems. Recent advances, including hospital-based facilities, have facilitated translational research and broadened clinical access. Ongoing clinical trials are essential to establish robust evidence and expand BNCT indications, potentially enabling its adoption as a first-line treatment for select cancers.

With over 15 years of clinical BNCT experience, Taipei VGH is positioned to lead Taiwan's innovation in combining BNCT with radiotherapy and immunotherapy. These efforts will strengthen Taiwan's role in the global cancer treatment landscape and contribute to meaningful therapeutic advancements.

# The current status and perspective of 18F-BPA

# 18F-BPA 的現況與未來發展

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18F-BPA (Boronophenylalanine, FBPA) is a crucial boron-based drug tracer in Boron Neutron Capture Therapy (BNCT), used for preoperative imaging guidance and therapeutic evaluation. Currently, FBPA is primarily employed in PET scans to detect the distribution and absorption of boron compounds in tumors, ensuring the accuracy and efficacy of boron neutron capture reactions. In clinical applications, FBPA-PET provides reliable pre-treatment assessments for BNCT in patients with high-grade malignant brain tumors, head and neck cancers, and other recurrent cancers.

However, the clinical use of FBPA has recently been limited by constraints in radiopharmaceutical production capacity and regulatory restrictions, hindering its widespread application. This discussion will explore the historical development of FBPA, the challenges currently faced in clinical applications, and its future prospects.

# Development of accelerator-based boron neutron capture therapy in Taiwan

# 臺灣加速器硼中子捕獲癌症治療的發展

**Wei-Lin Chen, Yen-Wan Hsueh Liu, Kuan-Yan Huang Chen-Yu Fan, Zhen-Fan You Shengkai Lin, Wei-Lun Huang, Zi-Wei Liu**

**陳韋霖 薛燕婉 黃冠諺 樊振宇 游鎮帆 林聖凱 黃偉倫 劉子維**

*Heron Neutron Medical Corp. Zhubei City, Hsinchu, Taiwan, ROC*

*禾榮科技股份有限公司*

Heron Neutron Medical Corporation has been working on the design and installation for an accelerator-based boron neutron capture therapy (BNCT) facility in Taiwan. The site selection was done on August 2019. The location is nearby the China Medical University Hsinchu Hospital. The site construction began in November 2021. The floor area is 35 m by 35 m, an underground two-story-high building. The AB-BNCT system provides two beamlines and two irradiation rooms for an optimal utilization for patient treatment. Other medical area includes boron drug injection room, blood boron analysis room, preparation room and treatment control room. The site planning with shielding design and activation analysis was performed to ensure the radiation safety of the facility outside the concrete bunker for the public and for the working staff.

The permission for the construction of this high energy radiation facility was granted in January 2022 by Atomic Energy Council (AEC). The main magnet of cyclotron was moved-in in November 2022. The building construction was completed in May 2023, followed by installation of cyclotron beamline, and beam shaping assembly. Permission of commissioning was granted by AEC in September 2023. In system commissioning, a series of tests and verifications were conducted including testing items following IEC standards and performance of epithermal neutron beam. The system showed good operation stability under the projected clinical scenario. Heron obtained medical device certificate for neutron irradiation system in June 2024. Additionally, continuous development of in-house dose engine for treatment planning calculation shows that in the future treatment planning of BNCT can be completed in a desirable short time.

The success of the Heron AB-BNCT irradiation system has accelerated the development of BNCT in Taiwan. It is Heron's aim to become a total solution provider for BNCT. The boron drug BPA developed by Heron is now in the clinical trial phase. The TFDA's IND approvals for recurrent meningioma, malignant brain tumors, and recurrent head and neck cancers were obtained in September 2024, February 2025, and March 2025, respectively. BNCT in Taiwan is on its way to become a regular treatment modality for hard-to-treat cancers.

# Preliminary outcomes of compassionate use of first accelerator-based boron neutron capture therapy(AB-BNCT) in Taiwan

# 臺灣第一台加速器型硼中子捕獲治療進行恩慈療法的初步結果

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**Background:** Despite significant advances in systemic therapies and radiotherapy in recent years, many patients continue to experience treatment failure and suffer from symptoms associated with local and/or metastatic tumors. Since 2017, our institute has been administering reactor-based boron neutron capture therapy (BNCT) on a compassionate use basis for a range of diseases. Following the TFDA's approval of accelerator-based BNCT(AB-BNCT) in May 2024 in Taiwan, we initiated the compassionate use of AB-BNCT in December 2024.

**Methods:** All compassionate uses of AB-BNCT have been approved by the IRB of TVGH and the TFDA. The inclusion criteria required that no known effective conventional treatment was available for the disease and that the condition posed a threat to life or vital functions. Most patient had 18F-Fluciclovine(Axumin) PET before AB-BNCT. The neutron irradiation fee and medication fee of [10B]-L-4-boronophenylalanine (L-BPA) was provided by Heron Neutron Medical Corp for free.

**Results:** As of March 2025, we have performed compassionate AB-BNCT on 18 patients with various recurrent malignancies, including meningeal solitary fibrous tumor, atypical meningioma, diffuse midline glioma (DMG, previously known as diffuse intrinsic pontine glioma, DIPG), anaplastic oligodendroglioma, lung squamous cell carcinoma with chest wall invasion, orbital chondrosarcoma, clival chordoma, breast cancer with chest wall recurrence, soft tissue sarcoma, osteosarcoma, head and neck cancer, recurrent glioma, and melanoma. Although the median follow-up is less than two months, complete responses have been observed in patients with recurrent lung and breast cancers. Additionally, the outcome in a patient with recurrent DMG is especially encouraging, with a 25% reduction in tumor diameter and improved activity levels.

**Conclusion:** Preliminary outcomes from the compassionate use of AB-BNCT in Taiwan have indicated a favorable safety profile and promising efficacy. Given that diffuse midline glioma (DMG) is a fatal disease with a median survival of approximately 10 months, we plan to launch a formal clinical trial to further evaluate its potential.

# Neutron Capture Enhanced Particle Therapy (NCEPT): Current development, feasibility assessment, and future perspective

# 中子捕獲增強粒子治療（NCEPT）：現況發展、可行性評估與未來展望

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Neutron Capture Enhanced Particle Therapy (NCEPT) represents an innovative strategy that integrates neutron capture effects with charged particle therapy (protons, helium, and carbon ions). This concept aims to harness thermal neutrons generated during particle beam irradiation, enabling interactions with tumor-selective neutron capture agents (NCAs) such as $^{10}B$ and $^{157}Gd$, to deliver additional localized high-LET radiation.

In this presentation, three representative publications (Howell et al., 2018; Chacon et al., 2022; Howell et al., 2024) - covering theoretical proposals, detection methodology, and biological validation - are reviewed.

Furthermore, preliminary Monte Carlo-based feasibility assessments conducted by our research group using PHITS simulations are presented, focusing on neutron field distributions and dose contributions under clinical conditions. These early findings revealed differences from previously published results, highlighting the need for continued investigation, refinement of modeling parameters, and collaborative verification. Rather than drawing definitive conclusions, this presentation aims to foster discussion on the current state of evidence, practical challenges, and future directions for multi-institutional studies and advanced NCA development, ultimately contributing to a clearer understanding of NCEPT's realistic clinical potential.