P217 / #615
EVALUATION OF THE EFFICACY AND SAFETY OF NOVEL BORON AGENTS USING PHENYLBORONIC ACID-CONTAINING SUPRAMOLECULES.

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Boron neutron capture therapy (BNCT), which uses neutron irradiation to accumulate boron (^{10}B) in cancer cells, has recently begun to be used as a fifth cancer treatment method. BNCT uses nuclear reactions between accumulated ^{10}B and thermal neutrons, and is characterized by selective destruction of only cancer cells. Boronophenylalanine (BPA), a boron compound currently in clinical use, shows therapeutic efficacy, but has some problems such as rapid cell excretion. On the other hand, FPBA-PRX, a novel boron compound, has a supramolecular structure and shows an accumulation mechanism that targets sialic acid differently from BPA, suggesting that it may be able to solve the problems of BPA. The aim of this study is to verify the kinetics, efficacy, and safety of the novel boron compound FPBA-PRX and to demonstrate the potential of FPBA-PRX as a BNCT drug. cytotoxicity evaluation using the ATP assay showed that a high concentration of more than 12.5 mg/ml continuous treatment for more than 12 hours confirmed significant cytotoxicity. In vivo toxicity study, no significant weight loss, appearance abnormalities or blood cell changes were observed in the group treated with 2000 mg/kg of FPBA-PRX. Blood and tumor concentrations were evaluated using ICP-AES after administration of FPBA-PRX, FPBA, and BPA-f (BPA fructose complex) to tumor-bearing mice of Colon26 cells overexpressing sialic acid. FPBA-PRX and FPBA were administered 18 h, and BPA-f was administered 2 h prior to measurement, with a unified ^{10}B concentration of 35 ppm (BPA-f was an additional 1440 ppm). FPBA-PRX showed significantly higher boron concentrations in blood and tumors than FPBA and comparable to the BPA-f group. Tumor-bearing mice were prepared under the same conditions as above and irradiated with neutrons after drug administration to examine the anti-tumor effect. The tumor size of the mice was measured for about one month after irradiation, and the anti-tumor effect was confirmed by drawing a tumor growth curve. As a result, FPBA-PRX showed a more significant antitumor effect than FPBA, although it was not as strong as BPA-f. These results suggest that FPBA-PRX may allow safe and effective BNCT to be performed at lower boron concentrations.

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P218 / #797
PATIENTS SEEKING BORON NEUTRON CAPTURE THERAPY IN SINGAPORE OVER THE PAST 12 YEARS: VALUABLE LESSONS LEARNT ALONG THIS JOURNEY

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Boron Neutron Capture Therapy (BNCT) has been shown to be a effective treatment in patients who have exhausted standard cancer therapy. While BNCT facilities are not available in every corner of the world, such patients who will benefit from it exists in every country around the globe. Singapore is no exception. This presentation will highlight the ups and downs of helping patients in Singapore who were seeking BNCT, over a period of 12 years. As more patients seek out BNCT that is not available in their own country, it is hoped that the lessons we have shared will be useful for other countries in helping these patients, both through medical tourism as well as though the arduous tasks of setting up a BNCT facility locally.

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P219 / #908
ADVANCEMENTS IN NCEPT: ANIMAL STUDY OUTCOMES AND TECHNOLOGICAL DEVELOPMENTS TOWARD CLINICAL APPLICATION

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Background and aims: Neutron Capture Enhanced Particle Therapy (NCEPT) represents a promising advancement in cancer treatment, utilising neutron capture agents (NCAs) to enhance therapeutic efficacy of proton/heavy ion radiation. This work focuses on animal experiments and concurrent technological developments aimed at translating NCEPT into clinical practice.

Methods: Animal studies were conducted to assess the therapeutic impact of NCEPT. Baseline dose response of U87MG xenograft Balb/c nu/nu mice to 12C and 4He ion radiation was evaluated at

HIMAC (February 2021, January 2022). NCEPT dose-response experiments with 10B-BPA as the NCA and using the same animal model were conducted in two campaigns in 2023. 200 mice were irradiated with helium or carbon ions across four dose levels (0 Gy, 5 Gy, 10 Gy, and 15 Gy, n = 6 mice/ion/dose); tumour growth was measured at different time points. In parallel, a scintillator-based detector for measurement of photon spectrum changes due to neutron capture was developed and evaluated in simulations and experiments with boron-loaded PMMA targets irradiated by helium/carbon ion beams.

Results: Baseline experiments showed expected dose-response relationships, with tumour response and measured neutron fluence informing the NCEPT study protocol. NCEPT experiments demonstrated significant tumour volume reductions (33%/46% for helium/carbon ion irradiation, respectively) and delays in tumour growth relative to baseline. The prototype detector measured increases in the area of the 478 keV peak by 26%/45% for helium/carbon beams, respectively, compared to simulation-based values of 57%/45%. >65% of these photons originated from 10B captures in the detector's PCB, highlighting the need for neutron shielding and boron-free materials in detector construction. The linear increase in neutron capture photons at 10B concentrations up to 20000 ppm, with potential for detection down to 100 ppm using temporal windowing, paves the way for a SPECT-like neutron capture imaging system, crucial for NCEPT quality assurance.

Conclusion: The combined animal study outcomes and technological advancements underscore the potential of NCEPT as a highly effective cancer therapy. The progress in dosimetry and imaging techniques mark significant steps toward the clinical translation of NCEPT, promising improved patient outcomes in cancer treatment.

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P220 / #623
DEVELOPMENT OF ACCELERATOR-BASED BORON NEUTRON CAPTURE THERAPY AT TAIWAN

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Boron neutron capture therapy (BNCT), a cell-level targeted heavy-ion particle therapy has shown its efficacy in recurrent head-and-neck cancer through clinical trial using the reactor-based epithermal neutron beam at Tsing Hua Open-pool Reactor (THOR). With the hope to realize this treatment in-hospital, Heron Neutron Medical Corporation has been working on the design and installation for an accelerator-based boron neutron capture therapy (AB-BNCT) facility at Taiwan. The site selection was done on August 2019. The location is nearby the China Medical University hospital at Zhubei. The AB-BNCT system has two beamlines and two irradiation rooms for an optimal use 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 site construction began in November 2021. The floor area is 35 m by 35 m, an underground two-story-high building. 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. During Phase I of system commissioning, the focus was on testing of the proton beam. This includes beam diagnosis, measurement of beam current and energy, monitoring of beam profiles, integration of cooling system, safety interlock system, and treatment control system. The system shows good proton beam stability under the anticipated clinical situation. Phase II will commence with focus on neutron beam generation, including installation of target system, neutron beam monitoring system, and characterization.of neutron beam. Heron also involves in the development of boron drug BPA and diagnostic boron drug ^{18}FBPA. Together with the ability of target design, beam shaping assembly design and shielding design, Heron is aiming on being a total solution provider for AB-BNCT.

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P221 / #161
INFLUENCE OF ULTRA-HIGH DOSE RATE (FLASH) IRRADIATION WITH CARBON ION ON INTESTINAL DAMAGE IN MICE

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Background and aims: Ultra-high dose rate (FLASH) irradiation has been attracting a huge interest with its ability to spare normal tissues. While several hypotheses for its mechanism have been discussed, experimental data are still limited especially for heavy ion irradiation. This study aimed to investigate the effect of the FLASH irradiation on intestinal damage in mice with carbon-ion beams. Early results from the evaluation of mouse survival after FLASH irradiation are presented.

Methods: Scanning irradiation port of HIMAC was used for the FLASH irradiation. A beam monitor was replaced by a parallel plate ionization chamber which has a gap distance of 4 mm. To reduce the recombination effect, applied voltage was increased to 2500 V. Dose was calibrated by the PTW PinPoint chamber (type 31023) with applied voltage of 400 V which is higher than nominal value to reduce the recombination effect. With the equipment, 30 female mice (C3H/He) were exposed to the entrance part of a 400-MeV/u carbon-ion beam delivered at a ultra-high dose rate (~95 Gy/s). Field size was 2×2 cm^2. Various dose levels (12-18 Gy) were used, and three mice were assigned for each dose level. For the comparison, 18 mice were exposed to the same beam delivered at a conventional dose rate (~0.3 Gy/s).

Results: At 15 days post irradiation, no clear difference was observed between FLASH and conventional dose-rate group, and survival rate decreased at around 14 Gy for both groups. For 13, 14, and 15 Gy with FLASH, the number of survived mice were 3/3, 1/3, and 0/3, respectively. The number for conventional dose-rate groups were 3/3, 2/3, and 0/3, respectively. No mice survived after 15 Gy and higher dose irradiations irrespective of the dose rate. Survived mice are already showing the recovery from weight loss.