Abstracts (in order of talks)

"Solid Li target production techniques at OIST" – Yasuo Higashi, Engineering Section, OIST

TBA

"Multifunctional Mesoporous Silica Nanoparticles for Boron Neutron Capture Therapy" – Vincent Jallet, Sugawara Unit (Drug Delivery), OIST

The Boron Neutron Capture Therapy (BNCT) is an innovative therapy against cancer involving the capture of neutrons by boron atoms, producing highly cytotoxic particles (⍰-rays and ⍰-particles). Our research unit is dedicated to the development of Drug Delivery System for the delivery of boron atoms inside cancer cells. This therapy is highly promising but efficient systems to specifically deliver boron atoms inside cancer cells still have to be developed. To address this problem, herein we describe an innovative Drug Delivery System for BNCT based on nanomaterials with cell-penetrating peptides grafted on their surface.

The research project developed at OIST aims to go beyond academic research by developing efficient and patentable drug delivery systems for BNCT. Thus, the use of mesoporous silica nanoparticles (MSNs) as robust drug delivery nanovectors and of sodium borocaptate as boron sources play a critical role in the design of this drug delivery system. The PEGylation of the silica nanoparticles enhances their stability and their stealth towards the immune system while the grafting of targeting ligands enables the nanoparticles to specifically target cancer cells.

Cellular uptake of PEGylated fluorescent MSNs bearing cell penetrating peptides (CPPs) was measured in vitro using cultured cell lines (normal breast MCF10A, triple-negative breast cancer MDA-MB-231, chondrocytes T/C-28a2, chondrosarcoma CH-2879), by flow cytometry and fluorescence microscopy. Within 3 hours, nanoparticle uptake was observed without toxicity. MSNs were functionalized with folic acid or specific cell penetrating peptides CPPs (BR2, PRWAVSP, Bac, L-R8, D-R8, PLGLAG). Functionalization with CPPs improved cell penetration in cancer cells, suggesting that functionalized MSNs might serve as boron-delivery vectors for BNCT.

"Multifunctional Complex Nanocomposites for BNCT" – Shubhra Quazi, Sugawara Unit (Drug Delivery), OIST

In this study, we have prepared a complex polymer nanocomposite drug delivery system that can be targeted to specific cancer site to co-deliver Boron and anticancer drug. Nanoparticles (NPs) are prepared using multiple emulsion solvent evaporation method. To prevent quick clearance of the NPs from the bloodstream by macrophages, PEG (Polyethylene glycol) polymer was used to coat the surface of the nanoparticles. To achieve dual targeting capability of our system, magnetic NPs have been incorporated inside the polymer nanoparticles and cell penetrating peptide (CPP) will be incorporated on their surface. Our prepared NPs are easily attracted to external magnet showing good magnetic property for targeted drug deliver. Multiple emulsion method allows easy and higher incorporation of boron from over single or double emulsion method. Presence of boron was analyzed using ICP-MS method. Presence of anticancer drug was confirmed by observing supernatant. Cellular uptake of our FITC containing NPs by HeLa cells was observed and confirmed by fluorescent imaging. In vitro and in vivo therapeutic effects of our NPs are yet to be investigated.

"Development of DoPECT, OIST Gantry and ASICs" - Tadashi Orita, Sugawara Unit (Imaging), OIST

My main research topics for two years in OIST are development of Double Photon Emission Computed Tomography (DoPECT) and super high-resolution Single Photon Emission Computed Tomography (SPECT) called as OIST-Gantry, two ASICs that one is for pixel type CdTe detector and another is for MPPC detectors of Time-of-Flight (ToF) Positron Emission Tomography.

- DoPECT

It consisted of two Compton cameras developed by ISAS/JAXA group for astrophysics and detected two cascade photons, specified the source position with the image reconstruction.

- OIST-Gantry

It consisted of high resolution CdTe dectectors and multi-pinhole collimators. It is for ~100um space resolution enables to visualize in-vivo micron environments in the tumor of a mouse. It is under construction. With the prototype, we conducted the principle verification.

- ASIC for fine pitch pixel CdTe detector

Based on the past design, we designed and fabricated 28 by 28 pixel type ASIC whose pixel size is 250 um by 250 um with TSMC 0.35-um process. It can work either in both of peak-hold mode or sample-hold mode and performs parallel AD conversion. We tested circuit performance and confirmed that its ENC was 40 electrons and its INL was about 1%. CdTe pixel detector with a pixel size of 250 um by 250 um and a matrix of 28 by 28 pixels will plan to be assembled to examine the detector performance as a whole.

- ASIC for ToF PET

We developed the current mode ToT ASIC for a MPPC module which consists of a current buffer, a threshold current DAC and a current comparator. Its timing resolution was less than 50 ps (FWHM) in the case that the fired cell number is over 1500. And its power consumption per channel is about 2.0mW. We confirmed that this ASIC could distinguish a 511keV peak in measured spectra with 22Na. The coincidence timing resolution was 200 ps (FWHM).

"Blistering of copper and copper-tantalum materials under 2 MeV proton irradiation" - Alex Badrutdinov, Engineering Section, OIST

In an accelerator-based BNCT setup, a neutron flux of optimal properties can be obtained by nuclear reaction of protons with lithium. For a solid lithium target, one potential problem is blistering of the substrate material under proton irradiation, which may result in degradation of the neutron flux properties. In this study we evaluate performance of several candidate materials for a lithium target substrate, including copper of different grades, and several copper-tantalum compounds, under 2 MeV proton beam. At a value of fluence, practical for BNCT application, copper tends to develop blisters, although the blistering threshold and blister size depend on the copper grade significantly. In contrast, copper-tantalum compounds do not develop blistering, suggesting that they may have better performance as a lithium target substrate.

"Monte Carlo simulation for Li target activation" – Yasuo Higashi on behalf of Shin'ichiro Takeda, Sugawara Unit (Imaging), OIST

TBA

"Proton irradiation test schedule at BINP and actual Li target design for the therapy" - Yasuo Higashi, Engineering Section, OIST

TBA

"In-situ observation of blistering on the Cu samples, irradiated by 2 MeV energy protons" – Evgeniia Sokolova, BINP

A vacuum-insulated tandem accelerator was used to observe in situ blistering during 2-MeV proton irradiation of copper of different purity to a fluence of up to 6 1019 cm–2. Samples were placed on the proton beam path and forced to cool. The surface state of the samples was observed using a CCD camera with a remote microscope. Thermistors, a pyrometer, and an infrared camera were applied to measure the temperature of the samples during irradiation. After irradiation, the samples were analyzed on an X-ray diffractometer, laser and electron microscopes. The report describes the experiment, presents the results obtained and notes their relevance and significance in the development of a lithium target for an accelerator-based neutron source, for use in boron neutron capture therapy of cancer.

"In-situ observation of blistering on the Ta samples, irradiated by 2 MeV energy protons" – Iaroslav Kolesnikov, BINP

A vacuum-insulated tandem accelerator was used to observe in situ blistering during 2-MeV proton irradiation of tantalum, and tantalum-copper compound to a fluence of up to 6.7 1020 cm–2. Samples were placed on the proton beam path and forced to cool. The surface state of the samples was observed using a CCD camera with a remote microscope. Thermistors, a pyrometer, and an infrared camera were applied to measure the temperature of the samples during irradiation. After irradiation, the samples were analyzed on an X-ray diffractometer, laser and electron microscopes. The report describes the experiment, presents the results obtained and notes their relevance and significance in the development of a lithium target for an accelerator-based neutron source, for use in boron neutron capture therapy of cancer.

"Detection of increasing Ta-surface temperature after long-term proton irradiation" – Alexandr Makarov, BINP

Present work is devoted to an important and previously unexplored problem – the lifetime of a lithium neutron producing target under conditions of daily operation at a high power proton beam. The conducted experiments showed that one of the promising options for realizing a thin, long-living and blistering-free lithium target is the multilayer Li-Ta-Cu-Water structure with layer thicknesses of 100 μm - 100 μm - 3 mm - 3 mm respectively. In this work endurance tests of such a Ta-Cu-Water structure (specially prepared by OIST team) without lithium under a proton beam with 2 MeV energy and 1 kW/cm2 power density were carried out. Multilayer structure was irradiated during 11 days by protons with an average current of 0.5 mA to a total fluence of 22.8 mA·h (6.7·1020 cm-2). As a result, the surface of the tantalum layer was visibly modified: the polished tantalum became matted. We assume that this phenomenon is associated with the formation of tantalum hydrides, since the average H:Ta mole ratio in the 100 μm thick tantalum layer could reach 1:1. It was also found that during the tests, the average surface temperature (measured by infrared pyrometer) of the tantalum layer was continuously increasing from an initial 165 °C to 208 °C, which can also be explained by reduced thermal conductivity of the tantalum hydrides formed. The obtained result is important for the lifetime of the target, since the temperature of the target should not exceed 180 °C in order to avoid melting of the lithium layer on its surface. The work describes the experimental setup, presents and discusses the results of the tests and proposes a plan for further research on the development of a neutron producing target with a long service life.

"Determination of ion beam parameters on the vacuum insulation tandem accelerator" – Ivan Shchudlo, BINP

In Budker Institute of Nuclear Physics an accelerator based neutron source for boron-neutron capture therapy was created. A proton beam with energy of 2 MeV and current of up to 5 mA is obtained. To further magnification of the parameters of facility, studies of transporting negative hydrogen ions in a low-energy path have been carried out. Using a wire scanner, the effect of a space charge depending of the residual gas pressure was studied. The phase portrait of the beam in the radial and azimuth directions was measured, the influence of aberrations of focusing magnetic lenses limiting the efficiency of further beam transportation was observed. The report discusses ways to modernize the low-energy channel to increase the proton beam current, reliability and stability of the accelerator.

"Development and implementation of the automation system for BNCT" – Alexey Koshkarev, BINP

The source of epithermal neutrons, designed for Boron Neutron Capture Therapy (BNCT) of cancer in oncology clinic, was proposed and developed in Budker Institute of Nuclear Physics. This method of treatment is effective against several currently incurable radioresistant tumors, such as brain glioblastoma and melanoma metastases. The neutron source includes an accelerator-tandem with vacuum insulation, lithium neutron generating target and neutron beam shaping assembly. Current accelerator produces a stationary 5 mA proton beam with 2 MeV energy. For clinical use, the current should be increased to 10 mA, energy up to 2.3 MeV. One of the most important stages in the development of facilities – is to automate and connect all control units together. To achieve this goal, the automation system for BNCT accelerator have been created. The specific feature of the accelerator is its frequent modernization and introduction of diagnostics of different types. For stable operation of the accelerator, it is necessary to create a flexible and scalable automation system that allows to control the preparation of the accelerator for operation, carry out experiments and turn off the accelerator after operation with minimal operator involvement. Created system will increase stability of the proton beam and, as a result, the neutron yield, that is needed to heal people.

"Lithium targets for BNCT developed at BINP" – Sergey Taskaev, BINP

The concept of the optimal target for BNCT is presented. The design of the target used during the last 10 years to generate neutrons, the design of the target from tantalum tubes and the newest design of the target, supposed to be made in the current half year, are described and discussed.

"Determination of the sensitivity of LBO chamber for the real time monitoring of the epithermal neutron flux" – Masaharu Hoshi, Hiroshima University

TBA

"Next-Generation Accelerator BNCT System with Near Threshold Neutrons of 7Li(p,n)7Be using Liquid Lithium Target" – Tooru Kobayashi, K2BNCT Science & Engineering Laboratory Co. Ltd.

The neutron irradiation system (NIS) for boron-neutron capture therapy (BNCT) should supply low-energy neutron irradiation field less than several tens of keVs and also have enough neutron intensity and temporal stability. When the accelerator BNCT-NIS is used for practical implementation, the technical main issues are the heat removal of 30-80 kW and for the radiation damage at the neutron producing target. High reliability of neutron producing target supported by the safety, stability, security of the system, is required as a clinical implementation. The liquid lithium target has been known having a good stability and long life because of no radiation damage. The 7Li(p,n)7Be near threshold reaction combined with a liquid lithium target has an advantage for the on line dose monitoring system such as PG-SPECT system during clinical BNCT. A stable liquid lithium jet flow was established at January 2012 for the neutron producing target of BNCT. The combination of a liquid lithium target and a stable and high current proton accelerator such as an electric statistic type is considered as a promising candidate for next generation BNCT NIS.

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