Abstract for OIST mini symposium
"New Medical Imaging and Advanced Cancer Therapy (BNCT) Instrumentation," 14-16 May 2015

Day 2 (14 May 2015)

"BNCT as a new generation chraged particle therapy - From Reactor to Accelerator –"

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Boron Neutron Capture Therapy (BNC) has been performed since several decades. Modernization of the BNCT has been developed in 1980's where boron compound borono-phenylalanine(BPA) become available as BNCT treatment agent as well as fluorinated BPA become available for PET scan in order to evaluate the BPA accumulation before BNCT.

Moreover, the treatment planning system for BNCT enabled precise 3 dimensional dosimetry for BNCT. Before having the treatment planning system, neutron flux were measured by sporadic points with gold wires.

Recently, the movement from nuclear reactor to accelerator is paradigm shift for BNCT and it enables the in-hospital treatment.

The review of the development of BNCT will be presented in the lecture.

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"Boron-neutron capture therapy for head and neck cancer"

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We retrospectively reviewed the outcomes of boron neutron capture therapy (BNCT) in patients with recurrent or unresectable advanced head and neck cancer. Patients who were treated with BNCT for local recurrent or newly diagnosed unresectable advanced head or neck cancers between December 2001 and December 2012 were included. The clinicopathologic characteristics and clinical outcomes were retrieved from hospital records.

Boronophenylalanine was used as the boron compound. In all cases, the dose constraint was set to deliver a dose <12 Gy-eq to the skin or oral mucosa. The treatment cohort was comprised of 24 patients (recurrent tumors = 17; unresectable advanced tumors = 7), with a median follow-up of 18.5 months (range, 3–82 months). The overall response rate was 87.5% (CR/PR = 13/9) within 3 months following BNCT. The 1- and 2-year overall survival rates for recurrent and newly diagnosed advanced tumors were 47.1% and 31.4%, and 85.7% and 71.4%, respectively. The major acute grade 3 and 4 toxicity was carotid blowout syndrome (CBS), which affected 8% of the patients, and all of the patients died 1 month after bleeding. All of the patients with CBS had widespread skin invasion and recurrence close to the carotid artery after irradiation. No other major acute grade 3 or 4 toxicities occurred; all minor toxicities were manageable. These results showed that BNCT is effective in patients with recurrent and unresectable advanced head and neck cancers, and this study confirmed the feasibility of our dose-estimation method. Randomized control trials are warranted to confirm our findings.

OIST workshop

Light and Magnetic Field Activated Release of Anticancer Drugs and Use of siRNA to Inhibit EMT Cancer Program

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Controlled release of anticancer drugs in response to external stimuli is one of the holy grails of Nenomedicine. We have developed mechanized nanoparticles that respond to external stimuli such as light and magnetic field and release anticancer drugs. To achieve this, we used mesoporous silica nanoparticles (MSNs) that contain thousands of pores that can store anticancer drugs. Openings of the pores can be capped by the use of a "nanovalve" that provides an open and close function. We also developed "nanoimpeller" that is synthesized by incorporating azobenzene to the pore interior. Azobenzene can absorb energy from blue light and change conformation resulting in the generation of a movement within the pore pushing the anticancer drugs out of nanoparticles. Recently, we have developed a new generation of nanoimpeller that responds to two-photon light. As for magnetic field, we have developed nanoparticles that contain iron oxide core. Exposure to oscillating magnetic field increases temperature of the nanoparticle resulting in the opening of the pore releasing anticancer drugs. Iron oxide core also provides MRI enhancing effect.

Epithelial to mesenchymal transition (EMT) is a cancer program that is critical for metastasis, stem like property, drug resistance, proliferation and angiogenesis in a variety of cancer including breast cancer, ovarian cancer and head and neck cancer. Genes such as TWIST and SNAIL are overexpressed resulting in the conversion of epithelial cells to mesenchymal type cells that have increased drug resistance and migration/invasion. We have recently succeeded in delivering siRNA against TWIST in an animal model system causing dramatic inhibition of tumor growth and EMT inhibition in the tumor. The delivery of siRNA was accomplished by using MSNs surface coated with polyethyleneimine.

Currently, we are developing multifunctional nanoparticles that combine both of the above features; they can deliver siRNA first and then deliver anticancer drugs upon magnetic field exposure. This enables combining a variety of approaches for cancer therapy leading to the development of multi-wave therapies for cancer treatment.