

Preclinical Application of a Boron Neutron Capture Therapy(BNCT) by using Hanaro

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1. Introduction

Boron Neutron Capture Therapy (BNCT) is based on the nuclear reaction that occurs between the boron-10 and thermal neutrons and is tumor-cells targeted radiography that significantly increases the therapeutic ratio relative to conventional radiotherapies [1-3]. The Ministry of Science and Technology in Korea has funded the clinical application of BNCT since July 1997. Korea Atomic Energy Research Institute in Daejeon houses the BNCT operation room and the setup for an analytical laboratory of a Prompt Gamma Neutron Activation Analysis (PGNAA) in the Hanaro reactor which is the only research reactor in Korea. Also Korea Institute Radiological and Medical Sciences (KIRAMS) in Seoul with similar funding has performed boron neutron capture therapy research for a clinical application.

2. Material and results

2.1 Port and flux

The port for the BNCT, which is one of the 7 ports of the Hanaro reactor, was operated at 24 MW and it produce thermal neutron. The flux was 2×10^9 (n/cm³) on phantom surface and the contaminated gamma dose rate was 7.6 Gy/hour on phantom surface.

- **Thermal neutron flux** (24MW, without LN₂ cooling)
 $\Phi_{th} = 8.34 \times 10^8$ n/cm²-s, In Air
 $\Phi_{th} = 1.77 \times 10^9$ n/cm²-s, In Phantom Surface
 Cd ratio : ~100
- **Photon dose rate in tissue** (24MW, without LN₂ cooling)
 (dD_γ/dt) = 7.6 Gy/h, In phantom surface

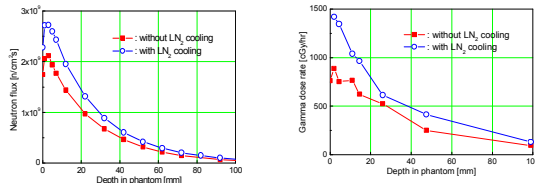


Fig.1. Characteristics of neutron flux.

2.2 PGNAA facility and its accuracy

A device for prompt gamma neutron activation analysis became available from 2002 for boron analysis in Boron Neutron Capture Therapy(BNCT). PGNAA

facility uses the polychromatic diffraction beam and the sensitivity of an analysis is 1000-2200 cps/mg. To test the accuracy, standard samples with known concentrations of boron were measured and the data from the PGNAA was approximately the same as the standard data.

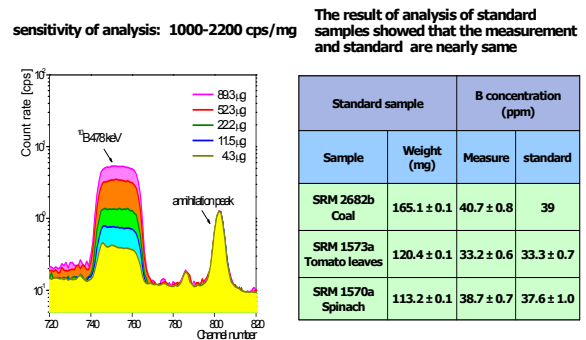


Fig.2. Capability of detection for connection of boron in PGNAA

2.3 Imaging technique and TN ratio in patients

To establish the ratio of boronophenylalanine (BPA) between normal tissue and a tumor (TN ratio), we developed the I-123 tagging BPA SPECT and F-18 tagging BPA PET image(Fig 3). Clinical application was implemented and showed the TN ratio was 3.15 ± 0.77 for an anaplastic glioma patient on the brain SPECT.

I-123 tagging BPA bio-distribution in clinical trial

tumor : normal tissue uptake ratio = 3.15 ± 0.77 (1 hrs brain SPECT),
 4.53 ± 2.02 (24 hrs brain SPECT), (p=0.17)

•Brain SPECT

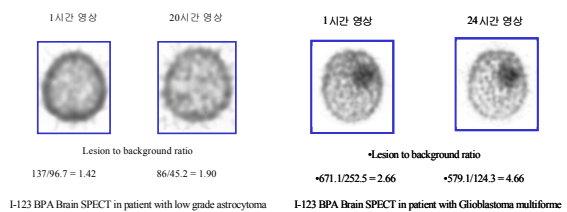


Fig.3. I-123 tagging BPA SPECT

2.4 Preclinical application

We have performed simulations for a clinical application by using three cats. Under an endotracheal anesthesia, the brain of the cat was exposed to an irradiation and two gold wires were located on the

central and peripheral of the exposure area. After being infused with the BPA-fructose complex through a vein, a cat's blood was sampled. The blood sample was transferred to the PGNAA facility for an assay of the BPA concentration. The irradiation field was established as a 4 cm diameter circle and protected with lithium carbonate. The normal brain tissue was expected to receive a total of a 12 Gy equivalent dose at a 2 cm depth. After the operation, we nursed the cat for 1 month to establish the safety of the operation. All of the experimental cats survived the operation and then they were sacrificed to detect the pathological change of their brain.

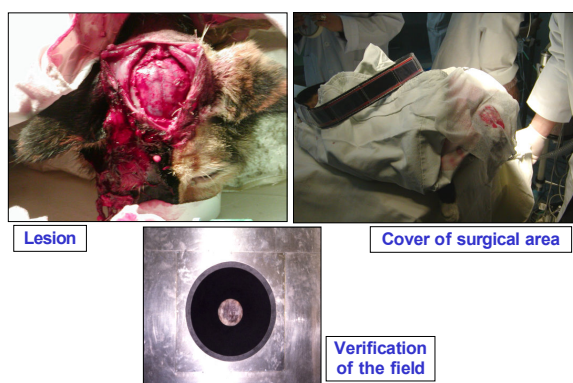


Fig.4. Preclinical application by using a cat

3. Conclusion

For a clinical application, a facility and preclinical simulation were performed and prepared well. For a national approval of the first clinical application of the BNCT, our protocol documentation has already been submitted and we have been evaluated by Korea FDA.

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