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^{124}I-BPA MicroPET images in C57BL/6 mouse bearing B16-F10 melanoma

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1. Introduction

Boron Neutron Capture therapy(BNCT) uses a thermal or epithermal neutron source to bombard ^{10}B atoms inside a cancer tissue and this produces short-range alpha particles via a nuclear reaction that are able to kill tumor cells effectively [1]. Preclinical and clinical trials have been conducted in the USA, Europe and Japan using ^{10}B containing compounds such as BPA or BSH [2-4]. This success will mainly depend on a differential uptake of ^{10}B-BPA between a tumor and normal tissue. According to Soloway et al. (1998) [5], a tumor-to-normal tissue uptake ratio (T/N) of 3:1 is desirable. However, it is difficult to directly measure ^{10}B levels at the time of BNCT. Many researchers used radioactive analogs of ^{10}B ([^{18}F]-FBPA) as a probe to analyze its kinetics in vivo using PET [6, 7]. However, the production of ^{18}F-BPA is more difficult than that of ^{124}I-BPA and its half-life is too short.

In an earlier study, we obtained different individual images of C57BL/6 mice bearing melanoma on the thigh by a small animal PET scanner(microPET) using ^{124}I-BPA instead of ^{18}F-BPA on 1, 3 and 24 hr after an ^{124}I-BPA injection and calculated the boron contents by the radioactivity in the tumor and the blood. In this study, the aim of our study is to obtain an image of a C57BL/6 mouse bearing melanoma by a small animal PET according to the time(2 and 24hr) after an injection of a radiolabeled boron compound in order to obtain the changeable images by the injection time in the same individual.

2. Material and results

2.1 Animals

Male C57BL/6 mouse (6-7 week old, 22-25g) from Semdaco experimental animal center was used. The animal was housed in a cage with food and water ad libitum and maintained in a 12-h light/dark cycle throughout the experiment.

2.2 Cell culture and skin cancer induction

B16-F10 melanoma cells were maintained and propagated in Dulbecco's modified Eagle's medium (DMEM) containing 10% fetal bovine serum, 100 units/ml penicllin and 100 ug/ml streptomycin. Growing B16-F10 melanoma cells in culture flasks were suspended at a density of about 1 x 10^5 cells. The mice were implanted with 200 ul of cell suspension in the left thigh. MicroPET scanning was performed on the 20th day after a tumor implantation. ^{124}I-BPA was prepared from the cyclotron room in KCCH. Tumor-bearing mouse was anesthetized and injected with 10 ul of ^{124}I-BPA (240 uCi) through a lateral tail vein. PET images of the B16-F10 melanoma-bearing mouse was obtained by the animal microPET at 2 and 24 hr after the ^{124}I-BPA injection.

3. Result and discussion

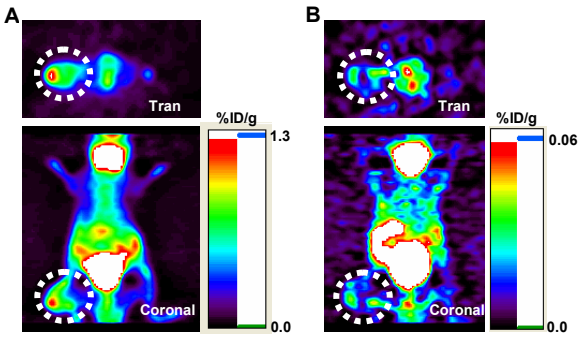

Fig. 1. ^{124}I- Boronophenylalanine(BPA) microPET images in B16-F10 melanoma tumor bearing mice. MicroPET images were acquired at 2 (A) and 24 hr(B) post injection by MicroPET R4 (Concorde system).

Fig. 1 shows the microPET images of the C57BL/6 mouse bearing melanoma model as a function of the time after the ^{124}I-BPA injection. The tumor lesion around the left thigh is indicated by showing the highest spot image at 2 hr compared to the spot image at 24 hr. From this study using one animal, the imaging of a tumor tissue approached the highest value after the 2 hr injection and the imaging findings depends on the ^{124}I-BPA postinjection. Important factor for BNCT is the ^{10}B level or the uptake of boron compounds in a cancer tissue. Ishiwata et al. (1992) had shown that the uptake of ^{10}B-BPA was similar to that of [^{18}F]-FBPA in terms of the pharmacokinetics. The ^{10}B-BPA per total injection dose estimated by an inductively coupled plasma-atomic emission spectroscopy (ICP-AES) corresponded to almost 1:1 relative to the ^{18}F-FBPA as estimated by the specific activity. In an earlier study, we estimated the imaging of the cancer from a microPET scanner(Fig. 2) and also the concentration of the boron

compounds in vivo from the radioactivity of blood or a tumor tissue. We have already obtained the images from each mice and the image from one mouse this time by showing the highest spot image between 2 and 3 hrs after ^{124}I-BPA. These results show the advantages of a PET imaging as a non-invasive in vivo tool on monitoring a cancer and BPA distribution before a BNCT.

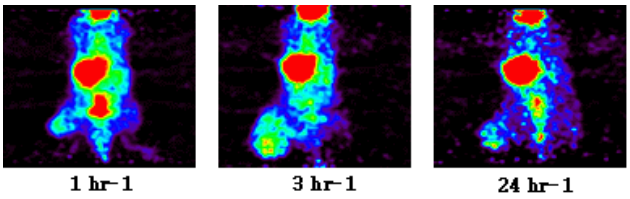

Fig. 2. MicroPET image of a C57BL/6 mouse bearing B16-F10 melanoma on the 1, 3 and 24hr after intravenous injection of ^{124}I-BPA.

4. Conclusion

The microPET imaging process for humans and animals uses ^{18}F-BPA in general, however, the process of this production is very difficult and the half life of this compound is too short when compared to the ^{124}I-BPA. For these reasons, we used an animal microPET to image an ^{124}I-BPA biodistribution in B16-F10 melanoma-bearing C57BL/6 mice in vivo. The image in the tumor tissue showed the highest spot at 2 hr after the ^{124}I-BPA injection. This microPET imaging with the ^{124}I-BPA instead of the ^{18}F-BPA can be used as a probe for ^{10}B-BPA in a BNCT. This preclinical study can provide useful information for a future clinical application of BNCT.

REFERENCES

[1] D.N. Slatkin, A history of boron neutron capture therapy of brain tumors: postulation of a brain radiation dose tolerance limit. Brain, 114, pp. 1609-1629, 1991.
[2] H. Hatanake, H., Nakagawa, Y., Clinical results of long surviving brain tumor patients who underwent boron neutron capture therapy, Inst. J. Radiat. Oncol. Biol. Phys., 28, pp. 1061-1066, 1994.
[3] K. Hideghety, W. Sauerwein, K. Haselsberger, et al., Postoperative treament of glioblastoma with BNCT at the Petten irradiation facility, Strahlenther Onkol. 175(suppl 2), pp. 111-114, 1999.
[4] A.Z. Diaz, Assessment of the results from the phase I/II boron neutron capture therapy trials at the brookhaven national laboratory from a clinician's point of view, J. Neuro-oncol., 62, pp. 101-109, 2003.
[5] A.H. Soloway, W. Rkarks, B.A. Barnum et al., The chemistry of neutron capture therapy, Chem. Rev., 98, pp. 1515-1562, 1998.
[6] K. Ishiwata, M. Shiono, K. Kubota, et al., A unique in vivo assessment of 4-[^{10}B]borono-L-phenylalanine in tumor tissues for boron neutron capture therapy of malignant melanomas using positron emission tomography and 4-borono-2[^{18}F]fluoro-L-Phenylalanine, Melanoma Res., 2, pp. 171-179, 1992.
[7] Y. Imahori, S. Ueda, Y. Ohmori, et al., Positron emission tomography-based boron neutron capture therapy using boronophenylalanine for high-grade gliomas: Part I. Clin. Cancer Res., 4, pp. 1825-1832, 1998.