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MicroPET image of radiolabeled boron compound ^{124}I-BPA in C57BL/6 mouse bearing B16-F10 melanoma

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1. Introduction

Boron Neutron Capture therapy(BNCT) uses thermal or epithermal neutron source to bombard ^{10}B atoms inside 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 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.

The aim of our study obtain to image C57BL/6 mice bearing melanoma on the thigh by a small animal PET scanner(microPET) using ^{124}I-BPA instead of ^{18}F-BPA and to calculate boron contents by the radioactivity in the tumor and the blood.

2. Material and method

2.1 Animals

Male C57BL/6 mice (6-7 week old, 22-25g) from Semdaco experimental animal center were used. The animals were housed in 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 on the left thigh. Each microPET scanning was performed on the 20th day after tumor implantation. ^{124}I-BPA was prepared from cyclotron room in KCCH. Each tumor-bearing mouse was anesthetized and injected with 10 ul of ^{124}I-BPA (240 uCi) through lateral tail vein. PET images of the mice bearing B16-F10 melanoma were obtained by the animal microPET on 1, 3 and 24 hr after ^{124}I-BPA injection. At that time, blood and tumor tissue were taken for radioactivity measurement by gamma counter.

3. Result and discussion

Figs. 1.1 and 1.2 show the microPET image of a C57BL/6 mouse bearing melanoma as a function of the time after ^{124}I-BPA injection. The tumor lesion around the left thigh is indicated by the spot through 24 hr of the experimental time showing the highest spot image on the 3 hr.

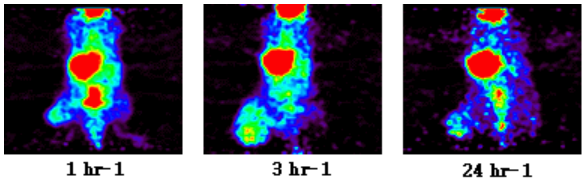

Fig.1.1. MicroPET image of a C57BL/6 mouse bearing B16-F10 melanoma on the 1, 3 and 24 hr after intravenous injection of ^{124}I-BPA.

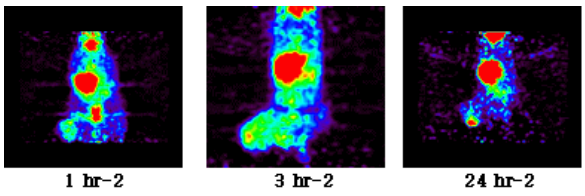

Fig.1.2. MicroPET image of a C57BL/6 mouse bearing B16-F10 melanoma on the 1, 3 and 24 hr after intravenous injection of ^{124}I-BPA.

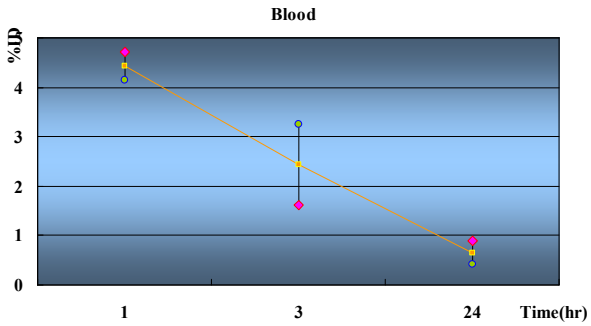

Fig.2. Time-activity curve of blood in C57BL/6 mice bearing melanoma.

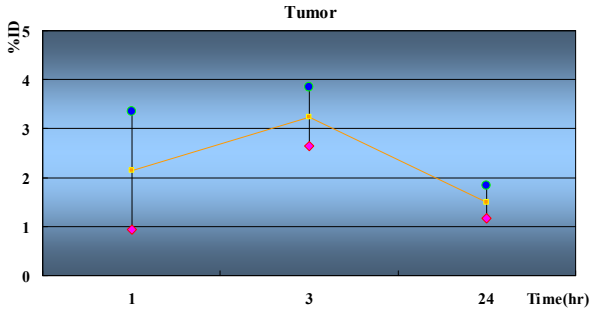

Fig.3.Time-activity curve of tumor in C57BL/6 mice bearing melanoma.

The radioactivity in the blood was decreased gradually until 24 hr as shown in Fig. 2. However, the accumulation of the radioactivity in tumor tissue was increased until 3 hr after injection and then reduced until 24 hr after injection (Fig. 3). In this study, the radioactivity of the tumor tissue approached the highest value 3 hr later after injection and so imaging findings depended on the ^{124}I-BPA postinjection. Important factors for the BNCT are the ^{10}B level or the uptake of boron compounds. Ishiwata et al. (1992) had shown that the uptake of ^{10}B-BPA was the similar to that of [^{18}F]-FBPA in terms of the pharmacokinetics. The ^{10}B-BPA per total injection dose estimated by inductively coupled plasma-atomic emission spectroscopy (ICP-AES) corresponded with almost 1:1 relative to the ^{18}F-FBPA as estimated by specific activity. We observed the concentration of the boron compound in vivo from the radioactivity of the blood and tumor tissue and the animal microPET image as well. These were shown the advantages of PET imaging as a non-invasive in vivo tool in monitoring the BPA distribution before BNCT.

4. Conclusion

The microPET image in human and animal use ^{18}F-BPA in general, however, the process of this production is very difficult and the half life of this compound is too short compared to the ^{124}I-BPA. Because of these reasons, we used an animal microPET to image ^{124}I-BPA biodistribution in C57BL/6 mice bearing B16-F10 melanoma in vivo. The image in the tumor tissue is shown the highest spot on the 3 hr after ^{124}I-BPA injection. This microPET image with the ^{124}I-BPA instead of the ^{18}F-BPA is suggested as a probe for ^{10}B-BPA in the BNCT. This preclinical study in animal will be provided an useful information for a clinical application of BNCT in the near future.

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 tumour 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.