Time course of tumor SUV in FBPA PET of brain tumor

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Aims and objectives

Boron neutron capture therapy (BNCT) is a targeted radiotherapy technique developed to treat patients with certain malignant tumors for which there is no effective conventional treatment. It has recently attracted attention and is being increasingly applied in clinical settings. It has been tested in malignant glioma, melanoma, and head and neck cancer (1-3).

This particular radiation therapy is based on the combined use of slow neutrons and one of the two stable isotopes of boron ($^{10}$B) to destroy tumor cells via the $^{10}$B(n,$\alpha$)$^7$Li neutron capture reaction. It requires a high-intensity epithermal neutron beam and a $^{10}$B carrier that accumulates in target tumor cells. Interaction of neutrons with $^{10}$B nuclei releases ionizing particles of very short range (< 10 µm) that should kill the cell. The selectivity of the therapy is based on the fact that only tumor cells containing $^{10}$B will be destroyed, preserving normal tissues due to their low affinity for the boron drug (4).

The success of BNCT is dependent on the sufficient accumulation of $^{10}$B in cancer tissue relative to adjacent tissues, with preferably a 3- to 5-fold greater concentration in the former (5). Therefore, estimation of $^{10}$B content in tumor and normal tissue helps predict the therapeutic potential of BNCT. Since $^{10}$B accumulation varies by tumor type, and even tumors of the same grade may differ in their biochemical properties, tumor $^{10}$B concentration should be determined for each individual before performing BNCT.

The most frequently used $^{10}$B carrier compound today is 4-$^{10}$B-borono-L-phenylalanine (BPA). An $^{18}$F-labelled analog of BPA, 4-borono-2-$^{18}$F-fluoro-phenylalanine (FBPA) has been developed to predict $^{10}$B concentration in tumors (6, 7). Imahori et al. designed a method for quantitative measurement of $^{10}$B concentration using FBPA positron emission tomography (PET) (8, 9). FBPA PET is generally used to anticipate the therapeutic effects of BNCT performed using BPA (10). Since brain tumor is one of major target for BNCT, we demonstrate in this study the time course of FBPA uptake in brain tumor in order to speculate optimal timing for neutron irradiation.

Methods and materials

Subjects

Patients included in this study had histologically confirmed brain tumors, at least 1 site of measurable disease, Eastern Cooperative Oncology Group performance status (PS) of 0-1, adequate organ function (neutrophil count # 1,500/µL, platelet count # 75,000/
µL, hemoglobin concentration # 9.0 g/dL, serum bilirubin # 1.5 mg/dL, AST and ALT # 100 IU/L, serum creatinine # 1.5 mg/dL, baseline left ventricular ejection fraction (LVEF) > 60%), and were over 20 years old. The main exclusion criteria were congestive heart failure, uncontrolled angina pectoris, arrhythmia, symptomatic infectious disease, severe bleeding, pulmonary fibrosis, obstructive bowel disease or severe diarrhea, and symptomatic peripheral or cardiac effusion.

**PET/CT protocol**

The schedule of examination is shown in Figure 1. Patients were requested to fast for at least 4 hours before the scheduled FBPA injection. Dynamic PET/CT scan of 1 h from FBPA injection (ca. 4 MBq/kg) was performed in one bed position that cover tumor location, and followed by whole-body PET/CT studies of 1, 2 and 4 h after FBPA injection. For whole-body PET/CT imaging, a scout image was acquired to determine the scanning field ranging from head to pelvis, using settings of 10 mA and 120 kV. Next, whole-body 16-slice helical computed tomography (CT) and whole-body 3D PET acquisition were performed. PET images were acquired in 7-8 bed positions with 2-min acquisition per bed position, so that the imaging covered the same field as that of whole-body CT. The acquired data were reconstructed as 192 × 192 matrix images (3.65 × 3.65 mm) using a 3D ordered subsets-expectation maximization (3D OS-EM) algorithm. PET image evaluation and quantification of the standardized uptake value (SUV) were performed using AW Volume Share 4.5 software (GE Healthcare, Milwaukee, WI, USA). Regions of interest (ROIs) were delineated on the PET/CT images, and the maximum SUV in the ROI (SUVmax) was determined.

**Tumor uptake of FBPA in brain tumor**

Sequential FBPA uptakes in bain tumor after injection were evaluated using SUVmax. Tumor ROIs were defined as the areas of highest activity. SUVmax was then determined as the average tumor radioactivity divided by the injected radioactivity normalized to the body weight. PET image evaluation and quantification of SUVmax were performed using AW Volume Share 4.5 software (GE Healthcare, Milwaukee, WI, USA).

**Images for this section:**
**Fig. 1:** Schedule of FBPA PET/CT
Results

Patient Characteristics

A total of 7 patients (5 male, 2 female, age range 37-62 y, mean age 47 y) with pathologically brain tumor were enrolled in this study from May 2012 to July 2013. Patient characteristics are summarized in Table 1. Tumor histological types varied widely (3 glioblastoma, 1 anaplastic astrocytoma, 1 anaplastic oligodendroglioma, 1 astrocytoma, and 1 oligodendroglioma).

Distribution and Internal Dosimetry of FBPA

Typical body distribution and brain tumor uptake of FBPA at 1 hour after injection are shown in Figure 2A and B, respectively (Patient No. 2). The typical time versus activity curve (TAC) from sequential data of 1 h dynamic PET study and following data sets of 1, 2, and 4 hours after FBPA injection were also shown in Figure 2C.

The sequential FBPA images and TAC revealed that in many cases, the accumulation of FBPA in the tumor changed in a time-dependent manner individually (Figure 3). The shapes of TAC in glioblastoma (Patient No. 3, 4 and 5) were also different with each other. This findings suggest that FBPA accumulation varies by not only the tumor histology but also by the time-point from the injection.

Images for this section:
# Patient Characteristics

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<th>WHO grade</th>
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</table>


**Table 1: Summary of Patient Characteristics**

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A

B

C

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**Fig. 2:** Typical images and TAC of FBPA-PET/CT A: maximum intensity projection image of FBPA-PET. B: axial PET/CT fusion image. C: TAC of FBPA in brain tumor.

**Fig. 3:** TAC of 7 brain tumor cases. The accumulation of FBPA in brain tumor changed in a time-dependent manner. The shapes of TAC were different with each other, even within the glioblastoma cases (Patient No. 3, 4 and 5).
Conclusion

Our findings that the accumulation of FBPA in brain tumor changed in a time-dependent manner may suggest that optimal timing for neutron irradiation could be different in each case. For treatment planning of BNCT, the evaluation of time-dependent accumulation of boron carrier in each case might be important. The major limitations of the present study were the small patient population and limited histological variety. Further research using a larger number of participants, with selection of particular histological diagnostic criteria, is thus called for.

Personal information

References


