Uptakes of FDG and FBPA in malignant tumors by PET/CT

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Purpose

Boron Neutron Capture Therapy (BNCT) is an anticancer treatment with alpha and Li particles produced by $^{10}\text{B}(n, #)^7\text{Li}$ reaction in tumors. For BNCT, $^{10}\text{B}$-boronophenylalanine (BPA) has been used as a boron delivery agent to tumor cell, and evaluation of BPA levels in the tumor is essential for patient selection and neutron dosimetry. To evaluate BPA levels by positron emission tomography (PET), $^{18}\text{F}$-fluoroboronophenylalanine (FBPA), an analogue of BPA, has been developed and synthesized from 1991. However, FBPA-PET study is not suitable for screening use because of the limitations of FBPA-synthesis from $^{18}\text{F}_2$ gas, such as low radio-yielding, low specific activity, and high cost. In this study, we demonstrated the correlation between $^{18}\text{F}$-fluorodeoxyglucose (FDG) and FBPA uptakes in patient with various malignant tumors to consider whether FDG-PET can be used as a screening for BNCT-applicable patients.
Methods and Materials

This study was conducted according to a protocol approved by the institutional review board and independent ethics committee, and informed consent was obtained from all patients for the use of blood samples, biopsy samples, and the analysis of clinical information. Patients were recruited and entered into the PET protocol study after written informed consent was obtained. Both whole-body FDG-PET/CT and FBPA-PET/CT were conducted within 2 weeks in our hospital.

Patient Eligibility Criteria

Eligible patients had histologically proven malignant tumor, and at least 1 site of measurable disease, age # 20 years and # 75 years, Eastern Cooperative Oncology Group performance status (PS) of 0-1, and adequate organ function. 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, symptomatic peripheral or cardiac effusion, and symptomatic brain metastasis.

Synthesis of FDG and FBPA

The synthesis of FDG was conducted using a automated synthesizer (F200, Sumitomo Heavy Industries, Ltd), and the quality of FDG were checked by automated analyzer (Q200, Sumitomo Heavy Industries, Ltd).

The procedures for FBPA preparation were described in elsewhere with modification (1). In brief, $^{18}$F$_2$ gas generated using a cyclotron was reacted with L-3-(p-boronophenyl)alanine. The crude reaction mixture was purified by preparative chromatography (Delta Pak, ø25 mm × 100 mm, Waters, Inc.). The purified FBPA solution was checked using radio high-performance liquid chromatography, and then filtered through a Millipore filter, MILLEX-GS 0.22 µm (Waters, Inc.), and was tested for pH, sterility, and pyrogenic properties. The final product after quality control had a specific activity of 25 GBq/mol and a radiochemical purity of >99%. Quality control of the products and the FBPA-PET/CT study were subject to the guidelines of the PET Committee in National Cancer Center Hospital, Tokyo, Japan.

Imaging protocols of FDG and FBPA PET/CT

Both whole-body PET/CT images of FDG and FBPA were acquired 60 min after injection of the radioactivity (4 MBq/kg of FDG, or FBPA) with Discovery 600 (GE Healthcare, Milwaukee, WI, USA). The acquired data were reconstructed in 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 were performed using AW Volume Share 4.5 software (GE Healthcare, Milwaukee, WI, USA). Maximum of standardized
uptake value (SUV) and tumor versus normal tissue uptake ratio (TNR) were calculated and compared between FDG and FBPA PET/CT.

**Internal dosimetry for FBPA**

To evaluate internal dosimetry for FBPA, sequential whole-body PET/CT were also conducted additionally at 2, and 4 h after the injection of FBPA. The internal radiation dose was calculated based on radioactivity data from blood, urinary excretion, and normal tissues of the heart, liver, spleen, kidneys, and other parts of the body at each time point using OLINDA/EXM software(2).
Results

Patient characteristics

Between March 2012 and June 2012, 10 patients were enrolled in the current study. Patient characteristics are presented in Table 1. Median age of the patients was 53. The histological type of the tumors ranged widely, but it included 2 cases of squamous cell carcinoma. Among the 10 cases, 4 recurrent tumor after treatment were included. All of targeted lesions were detected by both FDG and FBPA PET/CT studies. No infusion-related reactions or adverse events were observed during the study.

Visual analysis and quantification of FDG and FBPA imaging

The SUV of FBPA in tumor ranged 1.8 to 11.1 (average, 4.6 ± 3.2), whereas that of FDG ranged 2.1 to 12.4 (average, 7.4 ± 3.9). In all cases, the SUV of FDG in tumor was higher than that of FBPA. The normal organs of brain, heart, liver and spleen showed higher accumulations of FDG than those of FBPA. A typical example of the differences between FDG and FBPA uptakes in tumor or normal organs is shown in Fig.1 (Case 1). Sequential PET/CT images of 1, 2 and 4 h after FBPA injection revealed that the accumulation of FBPA in the tumor decreased by time dependent manner (Fig.2). Between FDG and FBPA, SUV in the tumor and TNR showed acceptable correlation (Fig3, 4). Internal dosimetry of FBPA was calculated to be $1.2 \times 10^{-2}$ mSv/MBq, whereas that of FDG was reported to be $1.9 \times 10^{-2}$ mSv/MBq.
### Table 1. Patient characteristics

<table>
<thead>
<tr>
<th>No.</th>
<th>Age/Sex</th>
<th>Histology</th>
<th>SUV of FDG</th>
<th>SUV of FBPA</th>
<th>TNR of FBPA</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>76 /M</td>
<td>Gingiva ca. (SqCC), s/p ope, rec.</td>
<td>7.9</td>
<td>3.9</td>
<td>2.6</td>
</tr>
<tr>
<td>2</td>
<td>56 /M</td>
<td>Leiomyosarcoma</td>
<td>4.2</td>
<td>1.8</td>
<td>1.1</td>
</tr>
<tr>
<td>3</td>
<td>76 /M</td>
<td>Angiosarcoma, rec.</td>
<td>2.6</td>
<td>1.6</td>
<td>1.2</td>
</tr>
<tr>
<td>4</td>
<td>75 /M</td>
<td>Nasopharyngeal ca. (SqCC), s/p CRT.</td>
<td>11.8</td>
<td>7.1</td>
<td>3.9</td>
</tr>
<tr>
<td>5</td>
<td>57 /F</td>
<td>Malignant mesothelioma, s/p ope, rec.</td>
<td>5.7</td>
<td>3.7</td>
<td>1.7</td>
</tr>
<tr>
<td>6</td>
<td>63 /M</td>
<td>Adenoid cystic carcinoma</td>
<td>2.1</td>
<td>2.0</td>
<td>1.4</td>
</tr>
<tr>
<td>7</td>
<td>62 /M</td>
<td>Oligodendroglioma</td>
<td>7.2</td>
<td>3.1</td>
<td>3.0</td>
</tr>
<tr>
<td>8</td>
<td>65 /F</td>
<td>Malignant melanoma</td>
<td>12.4</td>
<td>11.1</td>
<td>9.2</td>
</tr>
<tr>
<td>9</td>
<td>70 /F</td>
<td>Thyroid ca.</td>
<td>7.7</td>
<td>2.3</td>
<td>1.2</td>
</tr>
<tr>
<td>10</td>
<td>51 /F</td>
<td>Astrocytoma</td>
<td>9.8</td>
<td>5.6</td>
<td>5.5</td>
</tr>
</tbody>
</table>

M, Male; F, Female; s/p ope, status of post-operation; rec, recurrent tumor; SqCC, squamous cell carcinoma; CRT, chemoradiation therapy.

Table 1

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Fig. 1: Case 1 76 M Gingiva ca.( SqCC), status of post-operation, neck LN recurrence. PET/CT images of 60 min after injection of FDG or FBPA. A, maximum intensity projection images; B, PET/CT fusion images at the site of tumor.

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<table>
<thead>
<tr>
<th>FDG</th>
<th>F-BPA</th>
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<tbody>
<tr>
<td><img src="image1.png" alt="Image" /></td>
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<td><img src="image3.png" alt="Image" /></td>
<td><img src="image4.png" alt="Image" /></td>
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</tbody>
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**Fig. 2:** Case 4 76 M Nasopharyngeal ca.(SqCC), status of post-CRT, recurrence.

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Fig. 3

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Fig. 4

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Conclusion

The accumulation of FBPA in tumor was correlated with that of FDG. Internal dosimetry of FBPA was less than that of FDG. FDG-PET study could be an acceptable screening exam for further study of FBPA-PET/CT towards BNCT.
References


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