Comparison of $^{18}$F-FDG PET and Bone Scintigraphy in Detection of Bone Metastases of Thyroid Cancer

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We compared the efficacies of $^{18}$F-FDG PET and $^{99m}$Tc-bone scintigraphy for the detection of bone metastases in patients with differentiated thyroid carcinoma (DTC). \textbf{Methods:} We examined 47 patients (32 women, 15 men; mean age ± SD, 57.0 ± 10.7 y) with DTC who had undergone total thyroideectomy and were hospitalized to be given $^{131}$I therapy. All patients underwent both whole-body $^{18}$F-FDG PET and $^{99m}$Tc-bone scintigraphy. The skeletal system was classified into 11 anatomic segments and assessed for the presence of bone metastases. Bone metastases were verified either when positive findings were obtained on $\geq$2 imaging modalities—$^{201}$Tl scintigraphy, $^{131}$I scintigraphy, and CT—or when MRI findings were positive if vertebral MRI was performed. \textbf{Results:} Bone metastases were confirmed in 59 of 517 (11%) segments in 18 (38%) of the 47 study patients. The sensitivities (visualization rate) for bone metastases on a segment basis using $^{18}$F-FDG PET and $^{99m}$Tc-bone scintigraphy were 50 of 59 (84.7%) and 46 of 59 (78.0%), respectively; the difference between these values was not statistically significant. There were only 2 (0.4%) false-positive cases in a total of 451 bone segments without bone metastases when examined by $^{18}$F-FDG PET, whereas 39 (8.6%) were false-positive when examined by $^{99m}$Tc-bone scintigraphy. Therefore, the specificities of $^{18}$F-FDG PET and $^{99m}$Tc-bone scintigraphy were 449 of 451 (99.6%) and 412 of 451 (91.4%), respectively; the difference between these values was statistically significant ($P < 0.001$). The overall accuracies of $^{18}$F-FDG PET and $^{99m}$Tc-bone scintigraphy were 499 of 510 (97.8%) and 458 of 510 (89.8%), respectively; the difference between these was also statistically significant ($P < 0.001$). \textbf{Conclusion:} The specificities and the overall accuracy of $^{18}$F-FDG PET for the diagnosis of bone metastases in patients with DTC are higher than those of $^{99m}$Tc-bone scintigraphy, whereas the difference in the sensitivities of both modalities is not statistically significant. In comparison with $^{99m}$Tc-bone scintigraphy, $^{18}$F-FDG PET is superior because of its lower incidence of false-positive results in the detection of bone metastases of DTC.

\textbf{Key Words:} bone metastases; differentiated thyroid carcinoma; $^{99m}$Tc-bone scintigraphy; $^{18}$F-FDG PET


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\textbf{S}keletal imaging by $^{18}$F-FDG PET has been shown to be useful in the detection of bone metastases of breast ($1-6$), lung ($1,4,7,8$), thyroid ($4$), esophageal ($4,9$), gastric ($4$), colorectal ($4$), endemic nasopharyngeal ($10$), renal cell ($11$), prostate ($1$), ovarian ($4$), and testicular ($4$) carcinomas. In most of these studies, $^{18}$F-FDG PET was proven to be superior to conventional scintigraphic imaging using $^{99m}$Tc-labeled phosphate compounds ($^{99m}$Tc-methylene diphosphonate [$^{99m}$Tc-MDP] or $^{99m}$Tc-hydroxymethylene diphosphonate [$^{99m}$Tc-HMDP]). For the detection and evaluation of bone metastases of various kinds of carcinomas, $^{99m}$Tc-bone scintigraphy has been used widely because of its overall high sensitivity and the easy evaluation of the entire skeleton ($12$). However, $^{99m}$Tc-bone scintigraphy leads often to false-positive lesions and, consequently, its specificity is reduced, because degenerative or inflammatory foci will be often confused with metastatic diseases.

Differentiated thyroid carcinoma ([DTC] papillary and follicular) is characterized by good prognosis in comparison with carcinomas of other organs. The 10-y survival rate of DTC is $>$80% because of treatments such as total thyroideectomy and ablation of remnants with radioiodine ($13$). However, metastases of thyroid carcinoma develop in $7\%–23\%$ of patients; the distant metastases occur commonly in the lungs, bones, and brain, and bones are the second common site of metastases from thyroid carcinoma ($14$).

Several earlier reports showed that $^{18}$F-FDG PET is highly sensitive in detecting DTC and is particularly useful for the evaluation of patients with negative radioactive iodine scintigraphy and elevated thyroglobulin levels ($15–20$). For the detection of bone metastases of thyroid
carcinoma, 99mTc-bone scintigraphy has been also used widely. However, to our knowledge, there have been no systematic comparative studies on the efficacies of 18F-FDG PET and 99mTc-bone scintigraphy in the detection of bone metastases of DTC. The purpose of this study was to compare 18F-FDG PET and 99mTc-bone scintigraphy in the detection of bone metastases of DTC.

MATERIALS AND METHODS

Subjects
All procedures followed the clinical guidelines of Nagoya University Hospital and were approved by the International Review Board. Written consent was obtained after a complete description of the study was given to all patients and their relatives. Forty-seven patients (32 women, 15 men; mean age 57.0 ± 10.7 y), who had DTC and had undergone total thyroidectomy, were selected for the present study. All patients were hospitalized to be given 131I therapy for ablation of remnants and underwent both whole-body 18F-FDG PET and 99mTc-bone scintigraphy to detect bone metastases. 18F-FDG PET and 99mTc-bone scintigraphy were performed from 3 to 30 d before the radioiodine therapy, and the interval between 18F-FDG PET and 99mTc-bone scintigraphy was, at most, 1 mo. At the start of the study, 25 (53%) of the 47 study patients had metastases to the cervical lymph nodes and 20 (43%) had distant metastases in the lungs and mediastinal or supraclavicular lymph nodes.

Histopathologic Type
Fifteen (32%) and 29 (62%) of the 47 study patients had follicular and papillary carcinomas, respectively. In the other 3 (6.4%) patients, the histopathologic type was unknown, but they were diagnosed as having DTC by clinical and radiologic follow-up.

Bone Scintigraphy
99mTc-Bone scintigraphy was performed 3 h after intravenous injection of 555 MBq 99mTc-HMDP (Nihon Medi-Physics, Ltd.) or 740 MBq 99mTc-MDP (Daichi Radioisotope Laboratories, Ltd.). Anterior and posterior whole-body planar images were obtained with high-resolution collimation on a dual-head γ-camera (E.CAM; Toshiba Corp.). At least 2 experienced radiologists interpreted the planar images visually.

PET Procedure
The patients fasted for at least 6 h before PET. Scanning was performed using 18F-FDG and a Headtome-V PET scanner (Shimadzu). 18F-FDG (296 MBq) was injected intravenously 40 min before imaging. Whole-body emission/transmission images were obtained simultaneously. At least 2 experienced radiologists interpreted the coronal and axial images visually.

Data Analysis
The presence of bone metastases was assessed in 11 bone segments: cervical, thoracic, and lumbar spines, sacrum with coccyx, right and left pelves, sternum, right and left scapulae with clavicles, and right and left ribs. At least 2 experienced radiologists diagnosed bone metastases using 201Tl scintigraphy, 131I scintigraphy, CT, plain film radiography, or MR images. The presence of bone metastases was verified by the following definitions. First, the positive findings for bone metastases must be obtained in >2 imaging modalities—201Tl scintigraphy, 131I scintigraphy, CT, plain film radiography, or MR images. The presence of bone metastases was verified by the following definitions. First, the positive findings for bone metastases must be obtained in >2 imaging modalities—201Tl scintigraphy, 131I scintigraphy, CT, plain film radiography, or MR images. The presence of bone metastases was verified by the following definitions. First, the positive findings for bone metastases must be obtained in >2 imaging modalities—201Tl scintigraphy, 131I scintigraphy, CT, plain film radiography, or MR images.

### Table 1

<table>
<thead>
<tr>
<th>Bone segment</th>
<th>Bone segments with metastases (no.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervical spine</td>
<td>3</td>
</tr>
<tr>
<td>Thoracic spine</td>
<td>9</td>
</tr>
<tr>
<td>Lumbar spine</td>
<td>11</td>
</tr>
<tr>
<td>Sacrum with coccyx</td>
<td>7</td>
</tr>
<tr>
<td>R pelvis</td>
<td>8</td>
</tr>
<tr>
<td>L pelvis</td>
<td>8</td>
</tr>
<tr>
<td>R scapula and clavicle</td>
<td>4</td>
</tr>
<tr>
<td>L scapula and clavicle</td>
<td>1</td>
</tr>
<tr>
<td>Sternum</td>
<td>0</td>
</tr>
<tr>
<td>R ribs</td>
<td>3</td>
</tr>
<tr>
<td>L ribs</td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td>59</td>
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### Table 2

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Positive</th>
<th>Negative</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male* (no.)</td>
<td>4 (27)</td>
<td>11 (73)</td>
<td>15 (100)</td>
</tr>
<tr>
<td>Female* (no.)</td>
<td>14 (44)</td>
<td>18 (56)</td>
<td>32 (100)</td>
</tr>
<tr>
<td>Average age¹ (y)</td>
<td>58.0 ± 12.4</td>
<td>56.4 ± 9.7</td>
<td>57.0 ± 10.7</td>
</tr>
<tr>
<td>Follicular carcinoma* (no.)</td>
<td>13 (87)</td>
<td>2 (13)</td>
<td>15 (100)</td>
</tr>
<tr>
<td>Papillary carcinoma* (no.)</td>
<td>3 (10)</td>
<td>26 (90)</td>
<td>29 (100)</td>
</tr>
<tr>
<td>Unclear (no.)</td>
<td>2</td>
<td>1</td>
<td>3</td>
</tr>
</tbody>
</table>

*Values in parentheses are percentages.
¹Mean ± SD.

### Table 3

<table>
<thead>
<tr>
<th>Parameter</th>
<th>18F-FDG PET</th>
<th>99mTc-Bone scintigraphy</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity (%)</td>
<td>50/59 (84.7)</td>
<td>46/59 (78.0)</td>
<td>0.45*</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>449/451 (98.9)</td>
<td>412/451 (91.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Accuracy (%)</td>
<td>449/510 (87.8)</td>
<td>458/510 (88.8)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Not significant.
TABLE 4

<table>
<thead>
<tr>
<th>Detectability</th>
<th>Metastases</th>
<th>Total lesions (no.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>18F-FDG PET</td>
<td>Positive</td>
<td>Negative</td>
</tr>
<tr>
<td>99mTc-Bone scintigraphy</td>
<td>Positive</td>
<td>Negative</td>
</tr>
<tr>
<td>Type of lesion</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Osteoblastic lesion (no.)</td>
<td>40</td>
<td>8</td>
</tr>
<tr>
<td>Osteolytic lesion (no.)</td>
<td>2</td>
<td>0</td>
</tr>
</tbody>
</table>

Five metastatic lesions could not be classified because the images on CT scan were unclear.

RESULTS

Eighteen (38%) of the 47 study patients were finally diagnosed to have bone metastases, and 59 bone segments were confirmed to have at least 1 metastatic lesion according to the definitions of this study. The distribution of metastases in the examined bone segments is given in Table 1. The difference in the patient populations (sex, age, and histopathologic type) between bone metastases-positive and -negative groups is shown in Table 2. The presence of bone...
metastases was 4 of 15 (27%) in the male group and 14 of 32 (44%) in the female group; the difference between these groups was not statistically significant ($P = 0.34$). There was no difference in the average age of patients between the bone metastases-positive and -negative groups. Thirteen (87%) of 15 patients with follicular carcinoma had bone metastases, whereas only 3 (19%) of 29 patients with papillary carcinoma had bone metastases; the difference between these values was statistically significant ($P < 0.001$).

As indicated in Table 3, 50 (84.7%) of the 59 bone segments with metastases were detected by $^{18}$F-FDG PET, and 46 (78.0%) of the 59 bone segments were detected by $^{99m}$Tc-bone scintigraphy. However, the difference in the sensitivity between $^{18}$F-FDG PET and $^{99m}$Tc-bone scintigraphy was not statistically significant ($P = 0.45$).

As also shown in Table 3, there were only 2 (0.4%) false-positive cases in the 451 bone segments that were confirmed to have no bone metastases when examined by $^{18}$F-FDG PET, whereas 39 (8.6%) of the 451 bone segments were false-positive when examined by $^{99m}$Tc-bone scintigraphy. Therefore, the specificity of $^{18}$F-FDG PET in diagnosing the bone metastases of DTC (449/451, 99.6%) was higher than that of $^{99m}$Tc-bone scintigraphy (412/451, 91.4%); the difference between these values was statistically significant ($P < 0.001$). The overall accuracy of $^{18}$F-FDG PET (499/510, 97.8%) was also higher than that of $^{99m}$Tc-bone scintigraphy (458/510, 89.8%); the difference between these values was statistically significant ($P < 0.001$) (Table 3).

Sixty-seven metastatic lesions were detected in the 59 affected bone segments. Among them, 52 (78%) were classified into the osteolytic, 7 (10%) into the osteoblastic, and 3 (4.5%) into the mixed-type lesions on the basis of the CT images. Five (7.5%) lesions could not be classified because of their unclear CT images. The detectability of $^{18}$F-FDG PET and $^{99m}$Tc-bone scintigraphy for these metastatic bone lesions is shown in Table 4. Of the 52 osteolytic metastatic lesions, 48 (92%) and 42 (81%) lesions were detected by $^{18}$F-FDG PET and $^{99m}$Tc-bone scintigraphy, respectively; the difference between these values was not statistically significant ($P = 0.15$). Of the 7 osteoblastic lesions, 4 and 5 lesions were detected by $^{18}$F-FDG PET and $^{99m}$Tc-bone scintigraphy, respectively.

The exemplary images of bone metastases of DTC by $^{18}$F-FDG PET, $^{99m}$Tc-bone scintigraphy, and the other radiologic methods in 3 patients are shown in Figures 1, 2, and 3.

**DISCUSSION**

The incidence of bone metastases in the patients examined in this study (38% on a patient basis) seems to be unusually high. We believe that this finding is due to the fact that the patient group contained a large proportion of high-risk patients who showed extrathyroidal extension of the disease or distant metastases.
Earlier studies of bone metastases in patients with breast carcinoma showed that $^{18}$F-FDG PET had a similar sensitivity and a higher specificity in detecting bone metastases in comparison with conventional bone scintigraphy (1–3,24)—however, there were conflicting reports, which showed that $^{18}$F-FDG PET was less sensitive than conventional $^{99m}$Tc-bone scintigraphy (25,26). The results indicating that $^{18}$F-FDG PET and $^{99m}$Tc-bone scintigraphy had a similar sensitivity for the detection of bone metastases but that $^{18}$F-FDG PET was more specific than $^{99m}$Tc-bone scintigraphy were also obtained in patients with lung carcinoma (1,27,28). Furthermore, many comparative studies showed different results with regard to the sensitivity and specificity of $^{18}$F-FDG PET and conventional $^{99m}$Tc-bone scintigraphy for the detection of bone metastases of various kinds of carcinoma. $^{18}$F-FDG PET was more sensitive and specific than $^{99m}$Tc-bone scintigraphy for the detection of bone metastases in patients with renal cell carcinoma (11) and esophageal carcinoma (9). $^{18}$F-FDG PET also revealed more bone metastatic lesions than did $^{99m}$Tc-bone scintigraphy, independent of the type of carcinoma or the location of bone metastases (4). A recent report indicated that $^{18}$F-FDG PET was more sensitive than $^{99m}$Tc-bone scintigraphy for the detection of bone metastases in patients with endemic nasopharyngeal carcinoma (10). According to Fogelman et al. (29), the efficacy of $^{18}$F-FDG PET for the detection
of bone metastases in patients with prostate carcinoma has not yet been conclusive. Thus, so far, there is no definite consensus as to the detection of $^{18}$F-FDG PET for bone metastases in comparison with $^{99m}$Tc-bone scintigraphy in various kinds of carcinomas. However, the present study definitely showed that the specificity and the accuracy of $^{18}$F-FDG PET for the diagnosis of bone metastases in patients with DTC are higher than those of $^{99m}$Tc-bone scintigraphy.

In this study, we assessed whole planar images in $^{99m}$Tc-bone scintigraphy in place of SPECT bone imaging. The most conspicuous observation of our results is that there were only 0.4% false-positive cases in 451 bone segments—which were confirmed to be no bone metastases when examined by $^{18}$F-FDG PET—whereas 8.6% were false-positive when examined by $^{99m}$Tc-bone scintigraphy. Even if we use SPECT bone imaging for $^{99m}$Tc-bone scintigraphy, it is difficult to imagine that the false-positive cases will be largely decreased.

On the basis of the CT images, bone metastases are classified into the osteoblastic, osteolytic, mixed, and invisible types. Nakai et al. studied bone metastases from breast carcinoma and reported that the sensitivity of $^{99m}$Tc-bone scintigraphy/$^{18}$F-FDG PET was 100%/55.6% for the blastic type, 70.0%/100% for the lytic type, 84.2%/94.7% for the mixed type, and 25.0%/87.5% for the invisible type (5). The sensitivity of $^{99m}$Tc-bone scintigraphy for the blastic type and $^{18}$F-FDG PET for the invisible type were significantly higher. On the basis of these results, they concluded that $^{18}$F-FDG PET has limitations in depicting metastases of the osteoblastic type, although it is useful for detection of bone metastases from breast carcinoma (5). In a study with bone metastases from breast carcinoma, Abe et al. reported that $^{18}$F-FDG PET was superior to $^{99m}$Tc-bone scintigraphy in detection of osteolytic lesions (92% vs. 73%) but was inferior in the detection of osteoblastic lesions (74% vs. 95%); they concluded that $^{18}$F-FDG PET should play a complementary role in detecting bone metastases with $^{99m}$Tc-bone scintigraphy (6). In the present study, the sensitivities of $^{18}$F-FDG PET and $^{99m}$Tc-bone scintigraphy for the detection of both the osteolytic and the osteoblastic lesions were not largely different (Table 4). However, we cannot conclude that the detectability of $^{18}$F-FDG PET for the osteoblastic metastatic lesions of DTC is almost the same as $^{99m}$Tc-bone scintigraphy because the number of the osteoblastic lesions examined in this study was too small. Elucidation of this problem must await further investigation.

**CONCLUSION**

On the basis of our results, we conclude that the specificity and the overall accuracy of $^{18}$F-FDG PET for the diagnosis of bone metastases in patients with DTC are higher than those of $^{99m}$Tc-bone scintigraphy and that $^{18}$F-FDG PET is superior to $^{99m}$Tc-bone scintigraphy because of its lower incidence of false-positive results in the detection of bone metastases of DTC.

**REFERENCES**


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