Comparison between positron emission tomography using 2-[fluorine-18]fluoro-2-deoxy-D-glucose, conventional imaging and computed tomography for staging of breast cancer

S. Mahner, S. Schirrmacher, W. Brenner, L. Jenicke, C. R. Habermann, N. Avril & J. Dose-Schwarz

1Department of Gynecologic Oncology; 2Department of Nuclear Medicine; 3Department of Diagnostic and Interventional Radiology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany

Background: The presence, extent and localization of distant metastases are key prognostic factors in breast cancer patients and play a central role in therapeutic decision making. The aim of this study was to compare the diagnostic performance of positron emission tomography using 2-[fluorine-18]fluoro-2-deoxy-D-glucose (FDG–PET) with that of computed tomography (CT) and conventional imaging including chest radiography, abdominal ultrasound and bone scintigraphy.

Patients and methods: A total of 119 consecutive patients with newly diagnosed locally advanced disease (n = 69) or previous history of breast cancer (n = 50) who had clinical suspicion of metastatic disease underwent FDG–PET, CT and conventional imaging procedures. Imaging results were retrospectively compared with histopathology and clinical follow-up which served as a reference standard.

Results: FDG–PET detected distant metastases with a sensitivity of 87% and a specificity of 83%. In contrast, the sensitivity and specificity of combined conventional imaging procedures were 43% and 98%, respectively. CT revealed a sensitivity of 83% and a specificity of 85%.

Conclusions: In breast cancer, FDG–PET is superior to conventional imaging procedures for detection of distant metastases. Although FDG–PET and CT provided similar diagnostic accuracy, the information was often found to be complementary. With increasing availability of FDG–PET/CT, prospective studies are needed to determine whether it could potentially replace the array of conventional imaging procedures used today.

Key words: breast cancer, CT, FDG–PET, imaging, metastasis, staging

introduction

Breast cancer is the leading cause of cancer and the second leading cause of cancer death in women in Western countries with a lifetime risk of ~10% [1]. The presence of distant metastasis is a key prognostic factor since women with localized disease have a 5-year relative survival rate of ~80% compared with 25% for women with metastatic disease [2]. Disease localized to the breast and to locoregional lymph nodes is generally treated with surgery, adjuvant chemotherapy and endocrine therapy. In contrast, palliative treatment of metastatic disease consists of less aggressive regimens. In addition, there is now a growing array of cytostatic, endocrine and targeted treatment options available which could potentially improve survival, making early detection of metastasis increasingly important [3, 4].

To detect distant metastases, physical examination, chest radiography, abdominal ultrasound and bone scintigraphy with the addition of plain bone radiographs if necessary are carried out as the standard of care in many centers. Additional imaging procedures to assess suspicious findings include computed tomography (CT) and magnetic resonance imaging (MRI). However, conventional imaging procedures often do not reliably characterize the extent of disease since it is difficult to identify small tumors on the basis of morphological criteria and to distinguish potential abnormalities from benign findings.

Positron emission tomography using 2-[fluorine-18]fluoro-2-deoxy-D-glucose (FDG–PET) visualizes the increased glucose consumption of the malignant tissue in various types of tumors [5]. The functional–metabolic information derived...
from FDG–PET generally provides high accuracy for detecting cancer deposits and for differentiating benign from malignant tissue [6]. FDG–PET is being used with great success, e.g. in the staging of lung cancer, colorectal cancer and melanoma, and recent consensus papers recommend its use for various types of lymphoma [7]. In breast cancer, FDG–PET has been studied for the detection of primary tumors as well as lymph nodes and distant metastases [8–11]. However, literature regarding the diagnostic performance of FDG–PET for staging of breast cancer compared with conventional imaging and CT is limited and inconclusive.

The aim of this study was to compare the diagnostic performance of FDG–PET with that of conventional imaging, including chest radiography, abdominal ultrasound and bone scintigraphy, and with contrast-enhanced CT.

**patients and methods**

**patients**

Patients with a history of breast cancer or newly diagnosed locally advanced disease were referred for FDG–PET imaging at the University Medical Center Hamburg-Eppendorf when suspected of having distant metastases. Thus, a total of 119 consecutive breast cancer patients who underwent whole-body FDG–PET as well as conventional imaging procedures as part of their diagnostic work-up before initiation of therapy were studied between August 1996 and April 2004 and retrospectively analyzed. A subset of 61 patients also underwent contrast-enhanced CT. Detailed patient characteristics are listed in Table 1. All patients gave written informed consent to review their medical records according to our investigational review board and ethics committee guidelines.

Table 1. Patient characteristics

<table>
<thead>
<tr>
<th>No. of patients (n)</th>
<th>119</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>54.5</td>
</tr>
<tr>
<td>Range</td>
<td>28–89</td>
</tr>
<tr>
<td>Menopausal status</td>
<td></td>
</tr>
<tr>
<td>Premenopausal</td>
<td>34</td>
</tr>
<tr>
<td>Perimenopausal</td>
<td>2</td>
</tr>
<tr>
<td>Postmenopausal</td>
<td>78</td>
</tr>
<tr>
<td>Unknown</td>
<td>5</td>
</tr>
<tr>
<td>Evaluation at primary diagnosis</td>
<td>69</td>
</tr>
<tr>
<td>Evaluation during follow-up</td>
<td>50</td>
</tr>
<tr>
<td>Histology</td>
<td></td>
</tr>
<tr>
<td>Invasive ductal carcinoma</td>
<td>58</td>
</tr>
<tr>
<td>Invasive lobular carcinoma</td>
<td>17</td>
</tr>
<tr>
<td>Inflammatory carcinoma</td>
<td>12</td>
</tr>
<tr>
<td>Undifferentiated carcinoma</td>
<td>7</td>
</tr>
<tr>
<td>Invasive, NOS</td>
<td>24</td>
</tr>
<tr>
<td>Estrogen receptor status</td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>80</td>
</tr>
<tr>
<td>Negative</td>
<td>32</td>
</tr>
<tr>
<td>Unknown</td>
<td>7</td>
</tr>
<tr>
<td>Progesterone receptor status</td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>79</td>
</tr>
<tr>
<td>Negative</td>
<td>31</td>
</tr>
<tr>
<td>Unknown</td>
<td>9</td>
</tr>
</tbody>
</table>

NOS, not otherwise specified.

**imaging procedures**

Conventional imaging consisted of chest radiography, ultrasound of the abdomen and axillae and bone scintigraphy as well as plain-film X-ray of the bones if necessary. In addition, contrast-enhanced CT was carried out as clinically indicated. All imaging studies were retrospectively reviewed by a single experienced radiologist and two nuclear medicine physicians with many years of experience in reading PET scans, blinded to the results of other imaging studies, patient names and medical history. The presence and localization of metastases was recorded on case report forms. Findings were classified as ‘positive’, ‘equivocal’ or ‘negative’ for metastasis. In case of different lesion classifications by the two nuclear medicine physicians, the images were re-read in a joint session by both physicians to reach consensus statement. For final analysis, only positive findings were considered to represent metastatic disease, whereas equivocal and negative findings were classified as ‘no metastasis’. For abdominal ultrasound, the written report was reviewed since only a limited number of images were archived. Results were analyzed on a patient basis.

Before FDG–PET imaging all patients fasted for at least 6 h. Serum glucose was obtained and PET was rescheduled if glucose levels were >130 mg/dl. In patients with initial diagnosis of breast cancer, PET was acquired in prone position with the breasts hanging freely in a gap of the scanner couch. All other subjects were imaged in supine position for patient comfort. Images were acquired in two-dimensional mode using an ECAT EXACT 47/921 scanner (Siemens, Inc., Knoxville, TN). After i.v. administration of 350–400 MBq of FDG, 10-min emission scans of the breasts and the axillary regions were started at 40 and 50 min, respectively. Subsequently, transmission scans were obtained using 68Ge rod sources for 10 min per field of view. Additional emission scans were carried out in whole-body technique from top of the skull to midthigh with 7-min emission scans per bed position of 15.2 cm field of view. Images were reconstructed by filtered back-projection using a Hanning filter with a cutoff frequency of 0.4 of the Nyquist frequency. Scans were reconstructed in axial, coronal and sagittal views and used in addition to maximum-intensity projections for visual image interpretation. Increased FDG uptake not corresponding to physiological uptake patterns was recorded as negative for metastases.

Chest radiography was carried out in two projections at maximal inspiration with a Flat Panel Detector (Thoravision; Philips Medical Systems, Eindhoven, The Netherlands). Standardized 125-kV plate current was used for posterior–anterior and lateral exposures. Plate voltage was automatically adjusted resulting in 1.3–2.1 mAs in posterior–anterior view and 3.6–6.1 mAs in lateral view.

Abdominal ultrasound was carried out using a 3.5-MHz probe. Standardized examinations focused on the liver were carried out using subcostal oblique views, paramedian vertical views and extended intercostal views during maximal inspiration.

Possible axillary lymph node involvement was evaluated using a 7.5-MHz probe. A lymph node was considered to be involved by tumor if there was abnormal nodal architecture. Additionally, extracapsular spread, represented by an irregular margin of a lymph node, was recorded as positive for malignant involvement.

CT scans were carried out using a four-row detector system (Volume Zoom; Siemens Medical Solutions, Erlangen, Germany). The field of view was adjusted in every patient for optimal evaluation. For examination of the chest, slice collimation was 4 × 2.5 mm with a rotation time of 0.5 s. The standard tube voltage was 120 kV with 90 mAs. Patients received 90 cc of nonionic intravenous contrast material (Solustrast 300; Bayer-Healthcare, Berlin, Germany) 50 s before the scan. Images were reconstructed with a 5-mm slice thickness and analyzed in soft tissue and lung window. For abdominal CT, the tube voltage was 120 kV with...
low-energy high-resolution collimators (ECAM; Siemens Medical
matrix, filtered back-projection for image reconstruction) of the respective
imaging (64 views, 20-s acquisition time, each view applying a 128
256
equivocal findings, either planar spot views (10 min acquisition time,
a total of 116 patients underwent conventional imaging within
chest, 40 patients had CT of the abdomen and 29 patients
had chest radiography, 100 patients had abdominal ultrasound,
95 patients had bone metastases and 21 patients (18%) had metastatic
disease along the chest wall.
A double-head gamma camera (ECAM; Siemens Medical Solutions)
with low-energy high-resolution collimators was used applying a scan
speed of 10 cm/min and a matrix of 256 × 1024 pixels. In case of
equivocal findings, either planar spot views (10 min acquisition time,
256 × 256 matrix) or single photon emission computed tomography
imaging (64 views, 20-s acquisition time, each view applying a 128 × 128
matrix, filtered back-projection for image reconstruction) of the respective
bony location was carried out using a double-head gamma camera with
low-energy high-resolution collimators (ECAM; Siemens Medical
Solutions). If no definite assessment of bone metastases could be achieved
by bone scanning, MRI was carried out in addition to reach a final
statement on bone metastases.

reference standard
Histopathology and clinical follow-up as well as imaging follow-up
studies except FDG–PET served as the reference standard to define
whether or not distant metastases were present.

statistical analysis
Sensitivity, specificity, accuracy and positive and negative predictive values
were calculated for various patient subgroups for FDG–PET, CT and
conventional imaging procedures by using SPSS software Version 13
(SPSS Inc., Chicago, IL).

results
A total of 119 patients were included in this study. Sixty-nine
patients with newly diagnosed breast cancer and 50 patients
with previous history of breast cancer underwent FDG–PET for
staging. Patient characteristics are listed in Table 1.
Follow-up ranged from 1 to 62 months (mean 11 months).
Seventy-one patients (69 patients with newly diagnosed breast
cancer and 2 patients with recurrent disease) underwent
surgery or biopsy for histopathological evaluation. The location
of metastases was as follows: 21 patients (18%) had pulmonary
metastases, 17 patients (14%) had liver metastases, 32 (27%)
had bone metastases and 21 patients (18%) had metastatic
disease along the chest wall.
All 119 patients underwent FDG–PET imaging, 106 patients
had chest radiography, 100 patients had abdominal ultrasound,
95 patients had bone scintigraphy, 49 patients had CT of the chest,
40 patients had CT of the abdomen and 29 patients
underwent plain-film radiography of bones. On a patient basis,
a total of 116 patients underwent conventional imaging within
a time interval of 20 ± 30 days between FDG–PET and
conventional imaging. A total of 61 patients underwent CT
imaging within a time interval of 13 ± 7 days between
FDG–PET and CT imaging.
FDG–PET was positive in 70 cases and negative in 49 cases.
There were 62 true-positive and 40 true-negative cases,
resulting in a sensitivity of 87% and a specificity of 83%.
Conventional imaging procedures were true positive in 22 cases
and true negative in 64 cases with an overall sensitivity
of 43% and a specificity of 98%. CT was true positive in
40 cases and true negative in 11 cases, resulting in a sensitivity
and specificity of 83% and 85%, respectively. Detailed results
are presented in Table 2.
In addition, a separate analysis for patients with newly
diagnosed locally advanced breast cancer (n = 69) and
patients with previous history of breast cancer (n = 50) was
Carried out. For newly diagnosed breast cancer, FDG–PET had
a sensitivity of 93% and a specificity of 85%, compared with
a sensitivity of 83% and a specificity of 78% at suspected
recurrence. Conventional imaging procedures had a sensitivity
of 39% and a specificity of 98% at primary diagnosis, while
the sensitivity and specificity for recurrent disease were
46% and 100%, respectively. The sensitivity of CT in patients
with newly diagnosed disease was 89% with a corresponding
specificity of 89%; in patients with history of breast cancer,
the sensitivity was 80% with a specificity of 75%.
We also analyzed the diagnostic performance of the different
imaging procedures with respect to metastatic sites. These
results are shown in Table 3. In the group of patients who
underwent CT scanning as part of their diagnostic work-up,
a direct comparison between CT and FDG–PET was carried
out as shown in Table 4. Results did not differ substantially
from the overall diagnostic performance listed in Table 3.
In 19 of 69 patients with locally advanced primary breast
cancer, distant metastases were found: 7 patients had
pulmonary metastases, 5 patients had liver metastases and
11 had bone metastases. Conventional imaging detected distant
metastases in 8 of 19 patients (42%), FDG–PET detected
metastatic disease in 18 of 19 patients (95%). In one patient,
lobe and bone metastases were detected by CT scan and bone
scintigraphy but have been missed by FDG–PET. CT was
carried out in a subset of nine patients with locally advanced
primary breast cancer. In these patients CT detected all distant
metastases (100%).

Table 2. Detection of metastatic disease with conventional imaging
procedures (X-ray, abdominal ultrasound and bone scintigraphy),
contrast-enhanced computed tomography (CT) and positron emission
tomography using 18F-fluorodeoxyglucose (FDG–PET)

<table>
<thead>
<tr>
<th></th>
<th>Conventional imaging procedures (n = 116)</th>
<th>CT (n = 61)</th>
<th>FDG–PET (n = 119)</th>
</tr>
</thead>
<tbody>
<tr>
<td>True positive (n)</td>
<td>22</td>
<td>40</td>
<td>62</td>
</tr>
<tr>
<td>True negative (n)</td>
<td>64</td>
<td>11</td>
<td>40</td>
</tr>
<tr>
<td>False positive (n)</td>
<td>1</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>False negative (n)</td>
<td>29</td>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td>Sensitivity (%)</td>
<td>43</td>
<td>83</td>
<td>87</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>98</td>
<td>85</td>
<td>83</td>
</tr>
<tr>
<td>Positive predictive value (%)</td>
<td>96</td>
<td>95</td>
<td>89</td>
</tr>
<tr>
<td>Negative predictive value (%)</td>
<td>69</td>
<td>58</td>
<td>82</td>
</tr>
<tr>
<td>Accuracy (%)</td>
<td>74</td>
<td>84</td>
<td>86</td>
</tr>
</tbody>
</table>
Table 3. Diagnostic performance of all imaging procedures with respect to anatomical locations

<table>
<thead>
<tr>
<th>Site</th>
<th>Imaging procedure</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung</td>
<td>X-ray</td>
<td>28</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>CT</td>
<td>65</td>
<td>97</td>
</tr>
<tr>
<td></td>
<td>FDG–PET</td>
<td>76</td>
<td>94</td>
</tr>
<tr>
<td>Liver</td>
<td>Ultrasound</td>
<td>100</td>
<td>96</td>
</tr>
<tr>
<td></td>
<td>CT</td>
<td>67</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>FDG–PET</td>
<td>75</td>
<td>94</td>
</tr>
<tr>
<td>Bone</td>
<td>Sцинтigraphy</td>
<td>67</td>
<td>99</td>
</tr>
<tr>
<td></td>
<td>X-ray</td>
<td>29</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>CT</td>
<td>67</td>
<td>95</td>
</tr>
<tr>
<td></td>
<td>FDG–PET</td>
<td>76</td>
<td>92</td>
</tr>
<tr>
<td>Axillary lymph nodes</td>
<td>Ultrasound</td>
<td>88</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>CT</td>
<td>88</td>
<td>97</td>
</tr>
<tr>
<td></td>
<td>FDG–PET</td>
<td>94</td>
<td>97</td>
</tr>
<tr>
<td>Supraclavicular lymph nodes</td>
<td>Ultrasound</td>
<td>88</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>CT</td>
<td>49</td>
<td>90</td>
</tr>
<tr>
<td></td>
<td>FDG–PET</td>
<td>84</td>
<td>97</td>
</tr>
<tr>
<td>Mediastinal lymph nodes</td>
<td>X-ray</td>
<td>65</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>CT</td>
<td>50</td>
<td>94</td>
</tr>
<tr>
<td></td>
<td>FDG–PET</td>
<td>96</td>
<td>96</td>
</tr>
<tr>
<td>Chest wall</td>
<td>CT</td>
<td>67</td>
<td>97</td>
</tr>
<tr>
<td></td>
<td>FDG–PET</td>
<td>86</td>
<td>99</td>
</tr>
</tbody>
</table>

CT, contrast-enhanced computed tomography; FDG–PET, positron emission tomography using 2-[fluorine-18]fluoro-2-deoxy-D-glucose.

Table 4. Diagnostic performance of CT and FDG–PET with respect to anatomical locations in patients who underwent both imaging modalities

<table>
<thead>
<tr>
<th>Site</th>
<th>Imaging procedure</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung (n = 49)</td>
<td>CT</td>
<td>65</td>
<td>97</td>
</tr>
<tr>
<td></td>
<td>FDG–PET</td>
<td>76</td>
<td>94</td>
</tr>
<tr>
<td>Liver (n = 40)</td>
<td>CT</td>
<td>92</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>FDG–PET</td>
<td>75</td>
<td>100</td>
</tr>
<tr>
<td>Bone (n = 34)</td>
<td>CT</td>
<td>67</td>
<td>95</td>
</tr>
<tr>
<td></td>
<td>FDG–PET</td>
<td>92</td>
<td>86</td>
</tr>
<tr>
<td>Axillary lymph nodes (n = 46)</td>
<td>CT</td>
<td>53</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>FDG–PET</td>
<td>94</td>
<td>100</td>
</tr>
<tr>
<td>Supraclavicular lymph nodes (n = 49)</td>
<td>CT</td>
<td>40</td>
<td>97</td>
</tr>
<tr>
<td></td>
<td>FDG–PET</td>
<td>80</td>
<td>95</td>
</tr>
<tr>
<td>Mediastinal lymph nodes (n = 50)</td>
<td>CT</td>
<td>31</td>
<td>94</td>
</tr>
<tr>
<td></td>
<td>FDG–PET</td>
<td>94</td>
<td>94</td>
</tr>
</tbody>
</table>

CT, contrast-enhanced computed tomography; FDG–PET, positron emission tomography using 2-[fluorine-18]fluoro-2-deoxy-D-glucose.

discussion

FDG–PET offers important diagnostic information on the presence of distant metastases in breast cancer patients. In our study, 119 patients underwent FDG–PET imaging, representing one of the largest cohorts comparing FDG–PET with conventional imaging and CT. FDG–PET detected metastatic disease with a sensitivity, specificity and accuracy of 87%, 83% and 86%, respectively. In contrast, the sensitivity of combined conventional imaging procedures including chest radiography, abdominal ultrasound and bone scintigraphy was only 43% with a corresponding specificity of 98%. CT yielded a sensitivity, specificity and accuracy of 83%, 85% and 84%, respectively. The diagnostic performance of FDG–PET in our study is in line with previous reports which found a sensitivity ranging from 84% to 93% for detection of distant metastases [12–17]. False-positive findings were mostly attributed to muscle and bowel uptake and inflammatory lesions, resulting in a specificity ranging from 55% to 86% [13]. A meta-analysis of 18 studies on FDG–PET for the evaluation of breast cancer recurrence and metastases reported a sensitivity of 92.7% and a specificity of 81.6% [18].

We carried out a detailed analysis for different metastatic locations.

The liver is the main site of visceral breast cancer metastases; however, only little information is available regarding the detection of liver metastases with FDG–PET. Bender et al. [19] reported two cases with liver metastases in a series of 37 patients. In colorectal cancer, FDG–PET provided an overall sensitivity of >90% compared with the sensitivity of CT, which ranged from 74% to 85% [20, 21]. In our series, the sensitivity was 67% for ultrasound, 76% for FDG–PET and 92% for CT, with a high corresponding specificity for all modalities of 96%, 99% and 100%, respectively. Evaluation of the liver by FDG–PET is slightly hampered by increased background activity of normal liver tissue. Therefore, small metastases as well as lesions with low metabolic activity can potentially be missed. In addition, there might be a selection bias in our study as 100 of 119 patients who underwent FDG–PET underwent ultrasound of the liver but only 40 had a three-phase contrast-enhanced CT scan. Generally, liver metastases from breast cancer are readily identified in the porto-venous phase on CT, although hypervascular lesions can potentially be missed. While ultrasound of the liver is considered an appropriate test, its limitations are mainly due to operator variability, body habitus, patient compliance and the evaluation of the subcostal area. In addition, small lesions within a fatty liver are difficult to depict.

Pleural and lung metastases are usually seen in more advanced stages of disease. In a small series of 23 symptomatic patients with advanced breast cancer, published by Wolfort et al. [22], FDG–PET detected pulmonary metastases in five of six patients. In our study, FDG–PET detected lung metastasis with a sensitivity of 75% compared with 65% for CT. The specificity was 94% and 97% for FDG–PET and CT, respectively. Plain chest radiography revealed a poor sensitivity of only 28%. The advantage of CT is the ability to detect small lung metastases before they become apparent on plain chest radiography and in locations which are difficult to evaluate on chest radiography. We found CT scans often to be complementary to FDG–PET because CT identified small metastases of only a few millimeters in size, which are usually too small to be seen by FDG–PET. The increased metabolic activity, however, allowed for improved characterization of lung abnormalities classified as equivocal on CT.

In breast cancer, axillary lymph node involvement is an important prognostic factor and strongly affects the choice of
adjuvant therapy. According to a survey on several recent studies, FDG–PET provides an overall sensitivity of 88% and specificity of 92% [23]. This is in line with our results, revealing a sensitivity of 86% and a specificity of 97% (Table 3). In a large prospective study, Wahl et al. [24] suggested that FDG–PET may fail to detect axillary lymph node metastases if there is a small number of lymph nodes and if the lymph nodes are small (i.e. <3–5 mm). FDG–PET is, however, highly predictive for nodal involvement when multiple foci of intense FDG uptake are present. Since mainly patients with advanced-stage primary breast cancer were included in our study, one could expect a high rate of axillary lymph node metastases. Of note, CT detected axillary lymph node metastases with a sensitivity of only 53%. Similar results were found for detection of supraclavicular lymph node metastases (Table 3).

CT is currently the primary modality for evaluation of mediastinal lymph nodes. CT, however, relies on size criteria and might therefore miss tumor involvement in nonenlarged lymph nodes. Previous studies have shown the superiority of FDG–PET over CT for the detection of mediastinal and internal mammary lymph node metastases [25–27], with sensitivity and specificity of FDG–PET of 85% and 90%, respectively. In a retrospective analysis, Eubank et al. [26, 27] compared FDG–PET with CT in 73 recurrent or metastatic breast cancer patients. In 33 patients who underwent follow-up CT or biopsy, FDG–PET revealed a detection rate of 85% compared with 54% for CT. In our study, the sensitivity and specificity was 96% for FDG–PET while CT had a sensitivity of only 31% with a specificity of 94%. It is important to note that a sophisticated PET imaging approach was used in patients with newly diagnosed breast cancer with dedicated imaging of breasts and axilla before whole-body imaging.

The skeleton is the most common site of distant metastases in breast cancer patients, and bone scintigraphy is widely accepted for detection of bone metastases. Additional imaging procedures, however, are often necessary to determine whether scintigraphic abnormalities are benign or malignant. In recent studies, FDG–PET identified bone metastases with a similar sensitivity as bone scintigraphy but with a higher specificity [28, 29]. A retrospective analysis of 62 patients revealed a sensitivity of 92% for both modalities with a specificity of 92% for FDG–PET and 80% for bone scintigraphy [30]. Interestingly, FDG–PET was more sensitive in the detection of osteolytic metastases or lesions predominantly involving the bone marrow [31, 32]. In our study, FDG–PET had a sensitivity of 87% compared with 67% for bone scintigraphy with specificities of 92% and 99%, respectively (Table 3). Plain X-ray used as an adjunct for evaluation of equivocal scintigraphy results showed a sensitivity of 57% compared with 67% for CT. A recent study suggested that combined FDG–PET/CT might be superior to bone scintigraphy in the detection of bone metastases [33]. Prospective trials are, however, still necessary to elucidate whether or not bone scintigraphy can be replaced by FDG–PET.

The use of FDG–PET as a single whole-body imaging procedure instead of multiple modalities is intriguing. FDG–PET, however, lacks precise anatomical localization and morphological characterization of metastases which could be overcome by using combined PET/CT scanners. Indirect evidence from our results which often revealed complimentary findings of FDG–PET and CT as well as recently published comparative studies indicate the need to evaluate a potential consolidation of imaging studies by FDG–PET/CT [14, 19, 34–38]. FDG–PET/CT could potentially change the diagnostic algorithms used in breast cancer patients today.

Limitations of our study are its retrospective nature and the fact that not every imaging modality was carried out in all patients. Inclusion of patients with inconclusive findings on conventional imaging may have contributed to a referral bias in favor of FDG–PET. PET technology has improved over recent years, and the latest generation of PET/CT scanners provides a higher sensitivity and spatial resolution as well as additional morphological information for FDG–PET interpretation which may result in a higher sensitivity and specificity than those found in our study. For ethical reasons, histopathologic confirmation of imaging results could not be obtained in all patients. Nevertheless, uneventful follow-up in patients with suspicious FDG uptake indicates that subsequent confirmation might still be necessary. The inclusion of patients with advanced-stage primary tumors and with suspected metastatic disease might be a strength of this study, since patients with a relatively high pretest likelihood will most likely benefit from FDG–PET imaging.

**Conclusion**

FDG–PET was considerably superior to conventional imaging for detection of distant breast cancer metastases while the overall diagnostic performance of FDG–PET was comparable with that of contrast-enhanced CT. FDG–PET had clinically relevant advantages in the detection of lymph node metastases particularly if the nodes were not enlarged. FDG–PET also identified bone metastases with higher accuracy compared with bone scintigraphy. On the other hand, CT had distinct advantages in the identification of both small lung and liver metastases. Thus, combined FDG–PET/CT could potentially replace the array of conventional imaging procedures and detect distant metastases in breast cancer patients with sufficient accuracy. Therefore, prospective studies on new FDG–PET/CT-based imaging algorithms in breast cancer patients are highly desirable.

**Funding**

University Medical Center Hamburg-Eppendorf.

**References**


