Early Prediction of Response to Chemotherapy in Metastatic Breast Cancer Using Sequential ^{18}F-FDG PET

Joerg Dose Schwarz, MD[1]; Michael Bader, MD[1]; Lars Jenicke, MD[2]; Gabriele Hemminger, MD[1]; Fritz Jänicke, MD[1]; and Norbert Avril, MD[3]

[1]*Department of Gynecology, University Hospital Hamburg-Eppendorf, Hamburg, Germany;* [2]*Department of Nuclear Medicine, University Hospital Hamburg-Eppendorf, Hamburg, Germany; and* [3]*Division of Nuclear Medicine, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania*

Chemotherapy is currently the treatment of choice for patients with high-risk metastatic breast cancer. Clinical response is determined after several cycles of chemotherapy by changes in tumor size as assessed by conventional imaging procedures including CT, MRI, plain film radiography, or ultrasound. The aim of this study was to evaluate the use of sequential ^{18}F-FDG PET to predict response after the first and second cycles of standardized chemotherapy for metastatic breast cancer. **Methods:** Eleven patients with 26 metastatic lesions underwent 31 ^{18}F-FDG PET examinations (240–400 MBq of ^{18}F-FDG; 10-min 2-dimensional emission and transmission scans). Clinical response, as assessed by conventional imaging after completion of chemotherapy, served as the reference. ^{18}F-FDG PET images after the first and second cycles of chemotherapy were analyzed semiquantitatively for each metastatic lesion using standardized uptake values (SUVs) normalized to patients' blood glucose levels. In addition, whole-body ^{18}F-FDG PET images were viewed for overall changes in the ^{18}F-FDG uptake pattern of metastatic lesions within individual patients and compared with conventional imaging results after the third and sixth cycles of chemotherapy. **Results:** After completion of chemotherapy, 17 metastatic lesions responded, as assessed by conventional imaging procedures. In those lesions, SUV decreased to 72% ± 21% after the first cycle and 54% ± 16% after the second cycle, when compared with the baseline PET scan. In contrast, ^{18}F-FDG uptake in lesions not responding to chemotherapy (n = 9) declined only to 94% ± 19% after the first cycle and 79% ± 9% after the second cycle. The differences between responding and nonresponding lesions were statistically significant after the first (P = 0.02) and second (P = 0.003) cycles. Visual analysis of ^{18}F-FDG PET images correctly predicted the response in all patients as early as after the first cycle of chemotherapy. As assessed by ^{18}F-FDG PET, the overall survival in nonresponders (n = 5) was 8.8 mo, compared with 19.2 mo in responders (n = 6). **Conclusion:** In patients with metastatic breast cancer, sequential ^{18}F-FDG PET allowed prediction of response to treatment after the first cycle of chemotherapy. The use of ^{18}F-FDG PET as a surrogate endpoint for monitoring therapy response offers improved patient care by individualizing treatment and avoiding ineffective chemotherapy.

Key Words: ^{18}F-FDG; PET; metastases; breast cancer; prediction of response to therapy

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The treatment of breast cancer patients who have metastatic disease aims to improve survival and quality of life since the disease is generally not curable (*1*). It is therefore essential to identify patients who do not respond to chemotherapy early in the course of treatment to avoid ineffective therapies and unnecessary side effects such as nausea, vomiting, alopecia, and hematologic toxicity with the risk of subsequent (life-threatening) infections, neurotoxicity (e.g., taxanes), or cardiotoxicity (e.g., anthracyclines). Anatomic imaging procedures including ultrasound, plain film radiography, CT, and MRI are commonly used to follow the size of metastases over time and to determine the degree of response (*2*). Frequently, several cycles of chemotherapy are necessary to significantly change tumor size and, therefore, current anatomic imaging modalities do not reliably predict therapy response early in the course of treatment (*3–7*).

PET using ^{18}F-FDG allows assessment of the metabolic activity of cancer tissue and has been shown to be better than conventional imaging for staging and restaging various types of cancer, including breast cancer (*8,9*). PET allows accurate quantification of ^{18}F-FDG uptake in tissue, and previous studies have demonstrated that standardized uptake values (SUVs) provide highly reproducible parameters of tumor glucose use (*10,11*). Several groups have studied the relationship between changes in tumor glucose metabolism and response to treatment in breast cancer (*12–17*). However, most of these studies used sequential ^{18}F-FDG PET in patients with locally advanced breast cancer and histopathology after primary (neoadjuvant) chemotherapy served as a reference to assess tumor response. In 1993,

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For correspondence or reprints contact: Joerg Dose Schwarz, MD, Department of Gynecology, University Hospital Hamburg-Eppendorf, Martinistrasse 52, D-20246 Hamburg, Germany.

E-mail: dose@uke.uni-hamburg.de

Wahl et al. (*12*) reported 11 women with newly diagnosed locally advanced primary breast cancer undergoing chemohormonotherapy and sequential ^{18}F-FDG PET. The ^{18}F-FDG uptake in 8 patients with partial or complete pathologic responses decreased promptly with treatment, whereas the tumor diameter did not significantly decrease. In contrast, 3 patients with nonresponding tumors did not show a significant decrease in ^{18}F-FDG uptake. So far, there has been little information available on the utility of ^{18}F-FDG PET for predicting response early in the course of chemotherapy in metastatic breast cancer.

The aim of this study was to prospectively evaluate the use of sequential ^{18}F-FDG PET in standardized first-line chemotherapy of metastatic breast cancer to predict treatment response early in the course of therapy. Semiquantitative ^{18}F-FDG PET images after the first and second cycles of chemotherapy were compared with baseline images to determine changes in ^{18}F-FDG uptake in metastatic tumor lesions. In addition, whole-body ^{18}F-FDG PET images were viewed for overall changes in the ^{18}F-FDG uptake pattern of metastatic lesions within individual patients, and the metabolic response was compared with response on conventional imaging after the third and sixth cycles of chemotherapy. Changes in the pattern of ^{18}F-FDG uptake in metastatic lesions were also compared with overall survival. Clinical response determined by conventional anatomic imaging after completion of chemotherapy served as a reference. The hypothesis was that changes in ^{18}F-FDG uptake early in the course of treatment allow prediction of the effectiveness of chemotherapy.

MATERIALS AND METHODS

Patients

Patients with the diagnosis of metastatic breast cancer who were participating in a phase III chemotherapy trial were offered enrollment in this prospective evaluation of sequential ^{18}F-FDG PET. The purpose of the chemotherapy trial was to compare standard chemotherapy using epirubicin/cyclophosphamide with epirubicin/paclitaxel. Inclusion criteria for sequential ^{18}F-FDG PET were the diagnosis of metastatic breast cancer, at least 1 measurable metastatic lesion seen on conventional anatomic imaging, and an age of 18–70 y. Exclusion criteria were pregnancy, breast feeding, and diabetes mellitus. Between February 1997 and February 2000, 11 patients were enrolled to undergo sequential ^{18}F-FDG PET for monitoring of treatment response. All patients were treated at the Department of Obstetrics and Gynecology of the University Hospital Hamburg-Eppendorf, Germany (patient characteristics are shown in Table 1). All patients were followed up either until death or until April 2004. The Committee for Human Research at the University Hospital Hamburg-Eppendorf approved the study protocol. A physician explained the details of the study to the patients, and all consented in writing to participate.

Chemotherapy

The patients were treated with chemotherapy according to a phase III study protocol with epirubicin/cyclophosphamide versus epirubicin/paclitaxel. Chemotherapy was repeated every 3 wk. Nine patients received epirubicin/paclitaxel (60/175 mg/m^2 of body surface), and 2 patients received epirubicin/cyclophosphamide (60/600 mg/m^2 of body surface). Chemotherapy was discontinued in patients who showed progressive disease on conventional imaging, and they subsequently were excluded from further participation in the study. Patients with no change, partial remission, or complete remission received additional cycles of chemotherapy up to a maximum of 10 cycles.

Diagnostic Procedures

Patients underwent conventional imaging, including ultrasound, plain film radiography, contrast-enhanced CT, and MRI, depending on the localization of the metastatic lesions. The imaging procedures were performed according to routine clinical practice. Ultrasound was performed by an experienced radiologist, plain film radiographs were obtained in at least 2 projections, and contrast-enhanced CT or MRI was performed if no contraindications were present. A total of 26 separate metastases had been identified before the patients were enrolled in sequential ^{18}F-FDG PET. The imaging procedures were repeated after 3 cycles of

TABLE 1
Characteristics of the 11 Patients

Patient no.	Age (y)	Initial staging (TNM classification)	Histology	Estrogen receptor status	Progesterone receptor status	Prior adjuvant therapy
1	34	pT2 pN0 G3	Ductal	Negative	Positive	CMF
2	53	pT2 pN1 G2	Lobular	NA	NA	EC, tamoxifen
3	55	pT4 pNx G3	Ductal	Positive	Positive	None
4	60	pT4 pNx G3	Ductal	Positive	Positive	None
5	58	pT2 pN1 G3	Ductal	Negative	Negative	CMF
6	44	pT3 pN0 Gx	Ductal	Negative	Negative	CMF
7	68	pT1 pN0 G2	Ductal	Negative	Positive	Tamoxifen
8	49	pT2 pN0 G3	Ductal	Negative	Negative	None
9	41	pT2 pN0 G3	Ductal	Positive	Positive	CMF, tamoxifen
10	45	pT2 pN1 G3	Ductal	Positive	Negative	None
11	30	pT2 pN0 G3	Ductal	Positive	Positive	CMF, tamoxifen

CMF = cyclophosphamide, methotrexate, and fluorouracil; NA = not applicable; EC = epirubicin/cyclophosphamide.

chemotherapy (9 wk), 6 cycles of chemotherapy (18 wk), and 9 cycles of chemotherapy (27 wk).

Classification of Response Seen on Conventional Imaging

Response to treatment was classified according to the criteria of the World Health Organization (*2*): Complete response was determined as resolution of metastatic lesions; partial response, as a reduction in size (product of the 2 largest perpendicular dimensions) of more than 50%; no change, as a reduction of less than 50% or an increase of less than 25%; and progressive disease, as an increase (product of the 2 largest perpendicular dimensions) of more than 25%. For conventional imaging, patients with no change or with partial or complete response were classified as responders to chemotherapy and patients with progressive disease were classified as nonresponders to chemotherapy.

^{18}F-FDG PET Imaging

^{18}F-FDG PET was performed at baseline before chemotherapy, after the first cycle (3 wk) of chemotherapy, and after the second cycle (6 wk) of chemotherapy. Eleven patients underwent a total of 31 ^{18}F-FDG PET examinations; 2 patients did not undergo a third ^{18}F-FDG PET examination after the second cycle (6 wk) of chemotherapy. A whole-body PET scanner (ECAT EXACT 47/921; CTI Siemens, Inc.) was used, and patients fasted for at least 6 h before undergoing PET. The serum glucose level was measured before the intravenous administration of 240–400 MBq (approximately 10 mCi) of ^{18}F-FDG. The blood glucose level in all patients was less than 150 mg/dL. All patients lay supine during the study, after being comfortably positioned on the scanner table with both arms at their sides. Emission scans (2-dimensional) were started 60 min after intravenous administration of ^{18}F-FDG, with 10 min allowed per bed position. Depending on the location of metastases, emission scans of 1–4 bed positions were acquired, followed by transmission scanning for attenuation correction. Additionally, whole-body emission scans from the base of the skull to the groin were obtained without attenuation correction. Emission data corrected for random events, dead time, and attenuation were reconstructed with filtered backprojection (Hanning filter with cutoff frequency of 0.4 cycles per bin). The image pixel counts were calibrated to activity concentration (Bq/mL) and were decay corrected using the time of tracer injection as a reference. For visual analysis, PET images were printed on transparency films (Helios 810; Sterling Diagnostic Imaging) using a linear gray scale with the highest activity displayed in black. Standard documentation on film included 20 transverse slices with a slice thickness of 13.5 mm, 20 coronal slices with a slice thickness of 13.5 mm, and maximum-intensity projections in anterior, left lateral, right anterior oblique, and left anterior oblique views. In addition, a monitor was used with full control over the display.

PET Image Analysis

The region-of-interest technique was used for quantification of ^{18}F-FDG uptake in metastatic lesions. Circular regions of interest were placed manually over each lesion by 1 observer. The maximum activity values within the regions of interest were normalized to injected activity and patient body weight and were corrected for variation in blood glucose levels at the time of tracer injection by normalizing to a level of 100 mg/100 mL (SUVs) (*18*).

An experienced nuclear medicine physician unaware of the patient's history, clinical findings, and conventional imaging results interpreted the whole-body PET images visually. Response was classified according to the following criteria: Complete response was defined as resolution of abnormal ^{18}F-FDG uptake in metastatic lesions; partial response, as a reduction in the intensity of uptake or in the number of metastatic lesions with increased uptake; no change, as no change in the number of metastatic lesions and in the intensity of uptake in metastatic lesions; and progressive disease, as an increase in the intensity of uptake or in the number of metastatic lesions. Patients with ^{18}F-FDG PET scans showing partial or complete response were classified as responders to chemotherapy, and patients with scans showing no change or progressive disease were classified as nonresponders.

Statistical Analysis

The Mann–Whitney *U* test was used to compare SUVs between responding and nonresponding metastases at a 5% level of significance.

RESULTS

Conventional Imaging

Conventional imaging was repeated after the third, sixth, and ninth cycles of chemotherapy and compared with the pretreatment findings. Table 2 shows the treatment response for individual metastases after the third and sixth cycles of chemotherapy. Two of 11 patients had a mixed response, with metastases classified as no change and partial response. After the third cycle of chemotherapy, 9 patients were classified as responders (1, complete response; 5, partial response; and 3, no change) and 2 patients as nonresponders (progressive disease). In accord with the protocol of the chemotherapy trial, the 2 patients who did not respond were excluded from further participation in the study. The findings on conventional imaging changed after the sixth cycle of chemotherapy; only 6 patients were classified as responders and another 3 patients as nonresponders (Table 3). A patient with a lung metastasis (patient 8) initially responded after the third cycle (partial response), but the metastasis progressed in size after the sixth cycle of chemotherapy (progressive disease). There was no change between the sixth and ninth cycles of chemotherapy, and responders who continued to receive chemotherapy were still classified as responders after the ninth cycle of chemotherapy. In summary, 6 of 11 patients were classified as responders and 5 patients as nonresponders on the basis of conventional imaging results after completion of chemotherapy, which determined the gold standard for this study. Therefore, conventional imaging after the third cycle of chemotherapy misclassified 3 patients (27%) as responders (Table 3).

PET Quantitative Image Analysis (Lesion Based)

Conventional imaging before initiation of chemotherapy identified a total of 26 separate metastases of which 17 metastatic lesions responded after completion of chemotherapy. In those lesions, SUVs decreased to 72% ± 21% after the first cycle and to 54% ± 16% after the second cycle, when compared with the baseline PET scan. In contrast, ^{18}F-FDG uptake in lesions not responding to chemotherapy ($n = 9$) declined only to 94% ± 19% after the first cycle and

TABLE 2
Treatment Response for Individual Metastases

Patient no.	Treatment	Location of metastases	Conventional imaging after. . .	
			Third cycle of chemotherapy	Sixth cycle of chemotherapy
1	8 × ET	Lung	PR	PR
		Lymph node, mediastinum	PR	PR
2	10 × ET	Liver segment 4	NC	NC
		Liver segment 7	PR	PR
		Thoracic spine	PR	PR
3	10 × EC	Breast	PR	CR
		Liver	PR	CR
4	6 × ET	Liver segment 3	NC	PD
		Liver segment 5	NC	PD
		Thoracic spine	NC	PD
5	5 × ET	Lymph node	CR	CR
		Thoracic spine	PR	CR
		Lumbar spine	PR	CR
6	10 × ET	Breast	NC	PR
		Lymph node	NC	PR
7	4 × ET	Lymph node	NC	PD
		Liver	NC	PD
8	6 × ET	Lung	PR	PD
9	10 × ET	Lung	CR	CR
		Lymph node	CR	CR
10	3 × EC	Liver	PD	—
11	3 × ET	Lymph node	PD	—
		Lung	PD	—

ET = epirubicin/taxol; PR = partial response; NC = no change; EC = epirubicin/cyclophosphamide; CR = complete response; PD = progressive disease.

to 79% ± 9% after the second cycle (Fig. 1). The differences between responders and nonresponders were statistically significant after the first ($P = 0.02$) and second ($P = 0.003$) cycles.

PET Visual Image Analysis (Patient Based)

Whole-body ^{18}F-FDG PET images obtained after the first ($n = 11$) and second ($n = 9$) cycles of chemotherapy were viewed and compared with the baseline ^{18}F-FDG PET im-

TABLE 3
Treatment Response Seen on ^{18}F-FDG PET After First Cycle of Chemotherapy and on Conventional Imaging After Third and Sixth Cycles of Chemotherapy

Patient no.	^{18}F-FDG PET	Conventional imaging after. . .		Overall survival* (mo)
		Third cycle of chemotherapy	Sixth cycle of chemotherapy	
Responders				19.2 ± 13.6
1	PR	PR	PR	
2	PR	PR	PR	
9	PR	CR	CR	
3	PR	PR	CR	
5	PR	PR	CR	
6	PR	NC	PR	
Nonresponders				8.8 ± 6.7
4	PD	NC	PD	
7	PD	NC	PD	
11	PD	PD	NA	
8	NC	PR	PD	
10	NC	PD	NA	

*No significant difference between patients responding to chemotherapy and patients not responding to chemotherapy.
PR = partial response; CR = complete response; NC = no change; PD = progressive disease; NA = not applicable (chemotherapy was discontinued because conventional imaging showed progressive disease after third cycle of chemotherapy).

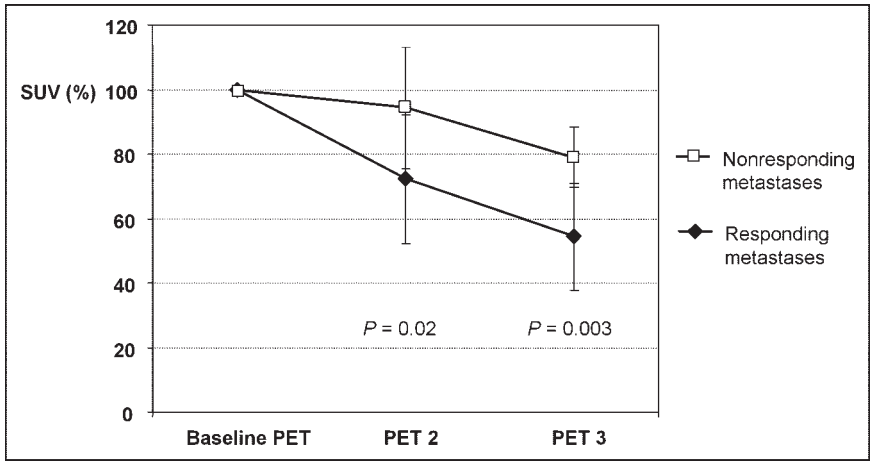

FIGURE 1. Changes in SUV in responding and nonresponding metastases.

age. After the first cycle of chemotherapy, 6 patients were classified as metabolic responders and 5 patients as nonresponders by ^{18}F-FDG PET. These classifications did not change after the second cycle of chemotherapy. ^{18}F-FDG PET correctly predicted the response in all patients as early as after the first cycle of chemotherapy. Compared with conventional imaging procedures obtained after the third cycle of chemotherapy, ^{18}F-FDG PET was superior specifically in the identification of nonresponders. In the present study, ^{18}F-FDG PET identified 2 nonresponding patients 3 wk (1 cycle of chemotherapy) and 3 nonresponding patients 12 wk (4 cycles of chemotherapy) before progression was detected on conventional imaging. Use of a PET-based strategy could have avoided 14 cycles of chemotherapy in 5 patients, and these patients could have received earlier second-line chemotherapy. ^{18}F-FDG PET also correctly classified 3 patients who had no change on conventional imaging after the third cycle of chemotherapy; 1 turned out to be a responder and 2, nonresponders.

Patient Follow-up and Survival

Mean follow-up was 14.5 mo (range, 2–39 mo). During this time, 10 patients died and mean overall survival was 14.5 ± 3.6 mo. The overall survival in nonresponders identified by ^{18}F-FDG PET after the first cycle of chemotherapy was 8.8 ± 6.7 mo, compared with 19.2 ± 13.6 mo in responders (not significant).

DISCUSSION

This study demonstrated that in patients with metastatic breast cancer, sequential ^{18}F-FDG PET allowed prediction of response early in the course of chemotherapy. Changes in tumor ^{18}F-FDG SUVs were statistically significantly different between responding and nonresponding metastatic lesions after the first ($P = 0.02$) and second ($P = 0.003$) cycles of chemotherapy. Most studies that addressed the role of sequential ^{18}F-FDG PET for predicting response to chemotherapy included patients with locally advanced breast cancer before surgery (*15–17*). Schelling et al. (*16*) compared changes in ^{18}F-FDG uptake with pathologic response using distinct histopathologic criteria, namely minimal residual disease and gross residual disease. By a threshold defined as a decrease of >55% compared with baseline, all responders were correctly identified after the first cycle of chemotherapy. The accuracy of predicting histopathologic response was 88% and 91% after the first and second cycles of therapy, respectively. In another study, 30 patients with locally advanced breast cancer received 8 doses of primary chemotherapy (*15*). The mean reduction in ^{18}F-FDG uptake after the first cycle of chemotherapy was significantly higher in responding than in nonresponding tumors. Little information is available on the clinical utility of sequential ^{18}F-FDG PET in patients with metastatic breast cancer. Jansson et al. (*13*) studied 16 patients with advanced breast cancer who underwent polychemotherapy and found decreased ^{18}F-FDG uptake 6–13 d after the first cycle of chemotherapy in 8 of 12 patients who had responded to chemotherapy. Stafford et al. recently reported a close correlation between changes in ^{18}F-FDG uptake and the overall clinical assessment of response in 24 breast cancer patients with bone metastases (*19*). However, more information is needed on how these findings and the ^{18}F-FDG PET results from the neoadjuvant treatment discussed above could potentially be used in the clinical setting to predict response to chemotherapy in metastatic breast cancer.

Our study confirms previous reports on the predictive information of early changes in glucose metabolism after initiation of chemotherapy (*5,7,15,17*). When compared with the baseline ^{18}F-FDG PET scan, the SUV in responding metastatic lesions decreased to 72% ± 21% after the first cycle of chemotherapy and to 54% ± 16% after the second cycle. In contrast, ^{18}F-FDG uptake in metastases not responding to chemotherapy declined only to 94% ± 19% after the first cycle and 79% ± 9% after the second cycle. Gennari et al. also found a rapid and significant decrease in tumor glucose metabolism after the first cycle of chemotherapy in 6 of 9 responders and no significant decrease in nonresponders (*20*). Modern treatment regimens in meta-

static breast cancer are developing toward being tailored to the needs of each patient. Response to therapy in solid tumors is currently assessed by measuring the change in tumor size (*2*)—a method that often is not accurate early in the course of chemotherapy. It is becoming increasingly important to identify response to therapy as early as possible so that ineffective therapies can be discontinued. Particularly, early identification of nonresponders is crucial to avoid ineffective treatment, unnecessary side effects, and costs (*16*). Patients not responding to continued chemotherapy experience a decreased quality of life and are detained from potentially more effective treatments. Dissolution and shrinkage of a tumor is the final step in a complex cascade of cellular and subcellular alterations after chemotherapy. Therefore, changes in the cellular energy metabolism assessed by ^{18}F-FDG PET are more likely to predict response than are changes in tumor size (*3,5–7*).

In this series, whole-body ^{18}F-FDG PET correctly predicted the response in all patients as early as after the first cycle (3 wk) of chemotherapy. Conventional imaging performed after the third cycle (9 wk) of chemotherapy misclassified 3 patients (27%) falsely as responders and was less accurate than ^{18}F-FDG PET. Chemotherapy is usually ineffective and discontinued in patients with progressive disease (*21*). A specific dilemma is presented by no change on conventional imaging, specifically in the first assessment after 3 cycles of chemotherapy. Chemotherapy is frequently continued in these patients since they might still respond later in the course of treatment. In our study, 3 patients who had no change on conventional imaging after the third cycle of chemotherapy had been correctly classified by ^{18}F-FDG PET after the first cycle of chemotherapy. A specific strength of ^{18}F-FDG PET is the identification of nonresponders, who are characterized by virtually no change in ^{18}F-FDG uptake after initiation of chemotherapy. The overall survival in the 5 patients who did not respond, according to ^{18}F-FDG PET, was 8.8 ± 6.7 mo, compared with 19.2 ± 13.6 mo in responding patients. ^{18}F-FDG PET identified 2 nonresponders 3 wk (1 cycle of chemotherapy) and 3 nonresponders 12 wk (4 cycles of chemotherapy) before progression was detected on conventional imaging. Use of a PET-based strategy could have avoided 14 cycles of chemotherapy in these 5 patients, and they could have received earlier second-line chemotherapy. In our study, 2 of 11 patients had a mixed response. An advantage of ^{18}F-FDG PET is that it can more easily identify a mixed response than can conventional imaging, which frequently is used to assess 1 "leading lesion" for changes in size. Another advantage of ^{18}F-FDG PET is the ability to monitor lesions in soft tissue, lymph nodes, liver, lungs, and bone in 1 imaging procedure that might be more cost effective than various imaging modalities currently used.

Our study had several limitations. Because of the small number of patients studied, a quantitative (SUV) analysis on a patient basis was not possible. The statistical analysis of changes in ^{18}F-FDG uptake in individual metastases was based on the assumption that they are independent, which might not be true in metastases within the same patient. On the other hand, our results were consistent with previous findings for locally advanced breast cancer and other tumor types (*5,7,12,15–17*). An important advantage of the study design was that all patients underwent standardized chemotherapy and that follow-up information was available for a mean of 14.5 mo.

In the present study, ^{18}F-FDG PET was not used to change patient management; nevertheless, the question arises of how to use ^{18}F-FDG PET in the clinical setting. In the United States, health insurers reimburse the cost of ^{18}F-FDG PET as an adjunct to standard imaging for monitoring treatment response in women with locally advanced, metastatic breast cancer when a change in therapy is anticipated. However, specific criteria to determine response by ^{18}F-FDG PET have yet to be established. If semiquantitative analysis is used, close monitoring of all factors that affect SUV measurements is crucial, such as the amount of activity injected, the uptake time before imaging, and the scanner cross calibration (*18*). The threshold for differentiating between responders and nonresponders on the basis of changes in ^{18}F-FDG uptake is critical. Chemotherapy should not be discontinued in responders, even at the cost of not identifying all nonresponders. Weber et al. recently proposed that metabolic response be defined as an SUV decrease larger than 2 times the SD (20%) of spontaneous changes in ^{18}F-FDG uptake (*5,11*). In the present study, a decrease in ^{18}F-FDG SUV of more than 20%, compared with baseline, after the first cycle of chemotherapy correctly identified 5 (71.2%) of 7 nonresponding and 12 (85.7%) of 14 responding lesions. The proposed approach is supported by a recent study on non–small cell lung cancer in which this criterion was prospectively applied to 57 patients with advanced disease and only 1 of 27 metabolic nonresponders achieved a partial response after completion of chemotherapy, resulting in a negative predictive value of 96% (*5*). However, this promising strategy needs to be validated in a separate prospective study for patients with metastatic breast cancer.

CONCLUSION

In patients with metastatic breast cancer, the effectiveness of chemotherapy can be evaluated earlier with ^{18}F-FDG PET than with conventional imaging. Sequential ^{18}F-FDG PET performed at baseline and after initiation of treatment allowed prediction of response as early as after the first cycle of chemotherapy. Furthermore, ^{18}F-FDG PET allows monitoring of multiple metastases using a single functional imaging procedure. The use of a 20% decrease in SUV after the first cycle of chemotherapy as a threshold for identifying nonresponders needs further evaluation in a larger prospective study. The use of ^{18}F-FDG PET findings as a surrogate endpoint for predicting therapy response offers improved

patient care by individualizing treatment and avoiding ineffective chemotherapy.

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