

ORIGINAL ARTICLE

## Accuracy of 18F-FDG PET/CT for primary tumor visualization and staging in T1 breast cancer

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### Abstract

**Background.** The aim of this study was to assess the accuracy of 18F-FDG PET/CT in T1 breast cancer regarding visualization of the primary tumor and the detection of locoregional and distant metastases. **Methods.** Sixty-two women with invasive T1 breast cancer underwent a PET/CT. Image acquisition of the thorax was done in prone position with hanging breasts, followed by whole-body scanning in supine position. Primary tumor FDG uptake was evaluated and compared with clinical and histopathological characteristics. Presence of locoregional and distant metastases was assessed and compared with conventional imaging procedures. **Results.** The primary tumor was visible with PET/CT in 54 (87%) of 62 patients, increasing from 59% (10/17) in tumors  $\leq 10$  mm to 98% (44/45) in tumors over 10 mm. All triple negative and HER2-positive tumors and 40/48 (83%) ER-positive/HER2-negative tumors were visualized. Sensitivity and specificity of PET/CT in the detection of axillary metastases were 73% and 100%, respectively. PET/CT depicted periclavicular nodes in two patients. Of 12 distant lesions, one was confirmed to be a lung metastasis, three were false positive, and eight were new primary proliferative lesions. **Conclusion.** Using optimal imaging acquisition, the majority of T1 breast carcinomas can be visualized with PET/CT. Specificity in the detection of axillary metastases is excellent, but sensitivity appears to be limited. Additional whole body imaging has a low yield in this specific patient group.

Imaging with 18F-fluorodeoxyglucose (FDG) positron emission tomography (PET), with or without concomitant computed tomography (CT), is based on the principle of elevated glucose metabolism in malignant tumors [1]. In current practice its use in breast cancer patients is recommended only for the detection of local recurrence or distant metastases in suspected patients [2,3]. The value of FDG PET/CT as a staging procedure in primary breast cancer or for monitoring the response to neoadjuvant chemotherapy (NAC) is not completely established, but promising results have been reported [4–6]. Since most research on PET/CT is conducted in large and/or locally advanced breast cancer, its value in small, node-negative breast cancer remains relatively unclear.

Use of PET/CT for the detection of the primary tumor is currently not advised, mainly because of

the low sensitivity in small carcinomas. Due to the partial volume effect and limited resolution, sensitivities of 25–63% in T1a-b ( $\leq 10$  mm) and 80–94% in T1c (11–20 mm) tumors have been reported [7–10]. The value of PET and PET/CT in the detection of axillary metastases has been evaluated more extensively. Several studies showed excellent positive predictive value, but also showed a poor sensitivity and negative predictive value, recommending the use of a sentinel lymph node biopsy (SLNB) in case of absence of PET-positive axillary nodes [11,12]. Research on the value of PET/CT in the detection of extra-axillary lymph nodes is limited, especially in early stage breast cancer [4,8,13,14]. Finally, PET/CT has been shown to be superior to conventional imaging techniques in the detection of distant metastases in patients with

stage II–III breast cancer and is associated with a low false positive rate [4,5]. Its accuracy in early stage breast cancer is unknown [4,8,10,15].

Published papers reporting on the use of FDG PET/CT in T1 tumors comprise small and/or heterogeneous groups of patients [7,10]. Furthermore, the majority of studies evaluate the use of PET without concomitant CT, which usually yields a lower spatial resolution and does not offer the use of CT for anatomical localization and attenuation correction [7,8,12]. The introduction of the time-of-flight technology has further increased the image quality of FDG PET/CT [16]. In addition, PET image acquisition can be adapted to the specific situation of the breasts and regional nodes using optimal positioning and image reconstruction [17]. The purpose of our study was to assess the accuracy of FDG PET/CT in T1 breast cancer patients regarding the visualization of the primary tumor and the detection of locoregional and distant metastases.

### Patients and methods

In our institute, a tertiary cancer referral center, an FDG PET/CT is performed in patients with invasive T1 breast cancer in the context of two distinct, prospective trials. All T1 breast cancers undergoing a PET/CT between March 2008 and December 2011 were included in this analysis. The institutional review board approved both trials and informed consent was obtained from all patients.

#### *PAPBI trial*

In the ongoing PAPBI trial (Preoperative Accelerated Partial Breast Irradiation, registered with clinicaltrials.gov under number NCT01024582), women aged 60 years and over with unifocal invasive breast cancer  $\leq 30$  mm are treated with preoperative partial breast irradiation. In this trial, assessment of the primary tumor and locoregional lymph node involvement is performed with mammography and ultrasound (US), magnetic resonance imaging (MRI) is performed to confirm unifocality. A core biopsy is used for histologic characterization and immunohistochemical stainings. A pre-radiotherapy SLNB is performed for exclusion of axillary metastases. Prior to the start of radiotherapy a whole body PET/CT is performed to investigate its value for response monitoring after radiotherapy. Patients are excluded from this trial in case of extensive in situ carcinoma, multifocality, contralateral breast cancer, a tumor-positive node, or a large tumor-breast ratio hindering partial breast radiotherapy treatment. Six weeks after the end of radiotherapy breast-conserving surgery is performed.

Between October 2009 and December 2011 a total of 53 women with T1 breast cancer were eligible for the PAPBI trial. Fourteen of them were excluded from this trial before a PET/CT was performed. The remaining 39 patients (mean age 66.8 years, range 60.1–74.8) underwent PET/CT and were included in this analysis.

#### *Neoadjuvant chemotherapy*

Since January 2005 patients with T1 breast cancer and a tumor-positive locoregional node by fine needle aspiration (FNA), for whom adjuvant chemotherapy is indicated on the basis of tumor characteristics and nodal status, are offered to be treated with NAC [18]. Since March 2008 a whole body PET/CT is performed prior to the start of chemotherapy, both as a staging procedure and as a baseline procedure for response monitoring [5]. In all patients a core biopsy from the primary tumor is used to determine the histologic type and to perform immunohistochemical stainings. MRI, ultrasonography, bone scintigraphy, and chest radiography are used for assessment of the primary tumor and to determine the presence of locoregional and/or distant metastases (TNM-stage). If response monitoring during NAC with MRI is impossible (occult lesion, whole breast contrast uptake), patients are treated with primary surgery instead. Following chemotherapy, surgery of the breast and, in case of axillary lymph node macrometastases, axilla is performed.

Twenty-three T1 tumors (mean age 47.0 years, range 26.4–64.0), treated with NAC since March 2008, underwent a PET/CT and were included in this analysis.

#### *<sup>18</sup>F-FDG PET/CT*

The PET/CT was performed after a fasting period of 6 hours with a blood glucose level  $< 10$  mmol/l. A total FDG dose of 180–240 MBq was given intravenously, depending on body mass index. In patients under the age of 60, 10 mg diazepam was administered orally 10 minutes before FDG injection to reduce FDG uptake in brown fat and muscle [19]. The PET/CT scan was acquired after a resting period of  $60 \pm 10$  minutes. Using a whole body PET/CT scanner (Gemini TF, Philips, Cleveland, OH, USA), a PET scan (3.00 minutes per bed position) of the thorax was performed for locoregional assessment with the patient in prone position, with hanging breasts and the arms above the head, with image reconstruction to  $2 \times 2 \times 2$  mm voxels. This approach provides high-resolution images of the breasts and regional lymph node areas without tissue compression or breathing motion [17]. PET acquisition was preceded by a low-dose CT (40 mAs) with 2.0 mm slices. Subsequently, as

staging procedure, a standard whole body PET/CT scan (1.30 minutes per bed position and 5.0 mm CT slices) in supine position was performed from the base of the skull to the upper half of both femora.

### *Image reading*

A panel of at least three nuclear medicine specialists evaluated the images together, using orthogonal multiplanar reconstruction and simultaneous display of PET, CT, and fused PET/CT images. They were blinded for other diagnostic procedures; the only information provided was that invasive breast cancer had been found, that the PET/CT was performed because of inclusion in a trial, and whether an SLNB had been performed prior to the scan. Consensus had to be reached before conclusions were drawn. First, FDG uptake was qualitatively assessed using a four-degree scoring system [14]: (0) similar to surrounding tissue or lymph nodes, (1) slightly more than in surrounding structures, (2) moderately intense, and (3) very intense. Lesions with degree 2 or degree 3 uptake were considered suspect for primary tumor or metastasis. In lesions of 1 cm or less, a degree 1 uptake was also considered as probably malignant. Degree 2 or 3 FDG uptake was considered sufficient for response monitoring with PET/CT. All FDG-avid lesions were measured using maximum standardized uptake values (SUV<sub>max</sub>) using a 3D automated region of interest (ROI) based on region-growing procedures. In case of a low tumor-to-background ratio, rendering an automated ROI generation unreliable, the SUV was derived from a manually drawn 3D volume of interest.

### *Data analysis*

Due to pretreatment with radio- or chemotherapy, tumor size (T-stage) and histopathological findings were determined with MRI and core biopsies, respectively. Axillary findings on PET/CT were compared with histopathology (US/FNA or SLNB); extra-axillary and distant lesions as detected with PET/CT were compared with histopathology and additional imaging (US and/or SLNB for locoregional metastases in all patients; bone scintigraphy, chest radiography, and ultrasound of the liver for distant metastases in patients treated with NAC). Differences in likelihood of visualization of the primary tumor between different subgroups were calculated using Fisher's Exact (two groups), Pearson  $\chi^2$  (three or more nominal groups), and Linear-by-linear Association tests (three or more ordered groups). Differences in SUV<sub>max</sub> of the primary tumor between different subgroups were calculated using Wilcoxon rank sum (two groups), Kruskal-Wallis (three or more nominal groups), and Linear-by-Linear Association tests

(three or more ordered groups). Qualitative axillary and extra-axillary lymph node uptake was compared with histopathology. Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of PET/CT in the detection of axillary metastases were calculated. Suspect distant lesions outside the breast and locoregional lymph nodes were compared with conventional staging techniques, targeted imaging procedures, and, preferably, histopathological verification.

## **Results**

Of 76 patients with a T1 tumor eligible for inclusion in one of the trials after March 2008, 14 were excluded before a PET/CT was performed. The remaining 62 patients who underwent a PET/CT were included in this analysis. Figure 1 depicts a flowchart on eligibility and exclusion. Table I shows baseline characteristics of included patients, demonstrating that patients treated with NAC were more often younger, node-positive, and having triple negative and grade 3 tumors.

### *Primary tumor*

PET/CT depicted the primary tumor in 54 (87%) of 62 patients (score 1, 2, or 3). Two T1a tumors (of 4 and 5 mm) could not be visualized with PET/CT. The majority (10/15, 67%) of T1b tumors (6–10 mm) showed increased FDG uptake and in T1c tumors (11–20 mm) nearly all tumors were visualized (44/45, 98%). The smallest size of tumor that was visualized was 8 mm. All triple negative (7/7) and human epidermal growth factor receptor 2 (HER2)-positive (7/7) tumors were visualized with PET/CT, as compared with 40 of 48 (83%) estrogen receptor (ER)-positive/HER2-negative tumors.

Tumor FDG uptake was sufficient for response monitoring in 4 (27%) of 15 T1b tumors and 40 (89%) of 45 T1c tumors. Although the primary tumor could be visualized in 80% (28/35) of N0-patients, baseline FDG uptake was sufficient for response monitoring in 57% (20/35) of them; in node-positive disease 96% (26/27) of tumors was visualized and baseline FDG uptake was sufficient for response monitoring in 89% (24/27).

Since multifocality was one of the exclusion criteria for the PAPBI trial, neither MRI nor PET/CT depicted multifocality in this cohort. In the group treated with NAC multifocality was seen on both MRI and PET/CT in three (13%) of 23 patients. In one patient MRI depicted multifocality, which was not seen on PET/CT. In another patient multifocality was visualized with PET/CT, but not with MRI. In both patients multifocality was proven with histopathology.

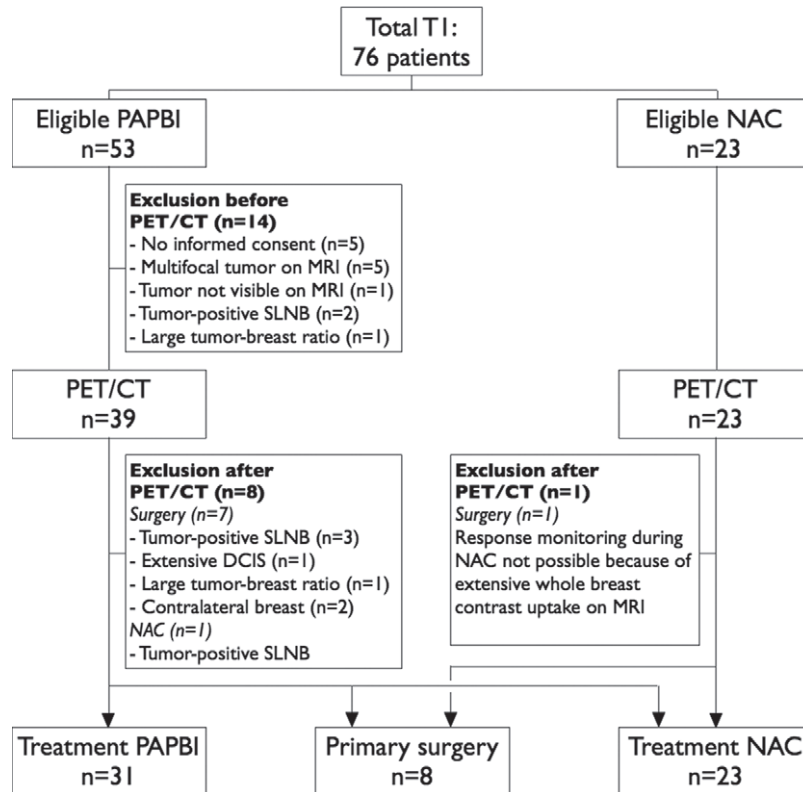


Figure 1. Flow chart of 76 eligible patients, reasons for exclusion from both trials (before and after PET/CT), and final treatment. DCIS, ductal carcinoma in situ; MRI, magnetic resonance imaging; NAC, neoadjuvant chemotherapy; PAPBI, preoperative accelerated partial breast irradiation; SLNB, sentinel lymph node biopsy.

All eight patients treated with primary surgery were found to have unifocal breast cancers.

SUVmax in T1 breast cancer, calculated in case of increased FDG uptake (score 1, 2, or 3), was significantly higher in tumors over 10 mm, in node-positive patients, and in patients with a higher stage (Table II). Invasive ductal carcinoma showed higher SUVmax as compared with other histologic subtypes ( $p = 0.040$ ). When subdividing tumors according to the three clinical subtypes, triple negative tumors showed highest SUVmax and ER-positive/HER2-negative tumors showed lowest SUVmax ( $p = 0.009$ ). Further, SUVmax was higher in tumors with a high proliferation (Ki-67 staining) in comparison with tumors with a low proliferation index ( $p = 0.035$ ). When subdividing tumors according to grade, highest SUVmax was seen in grade 3 tumors and lowest SUVmax was seen in grade 1 tumors ( $p < 0.001$ ). Since tumors treated with NAC were more likely to be node-positive, triple negative, and grade 3 (Table I), highest SUVmax was seen in this group as compared with both other treatment groups ( $p = 0.013$ ).

#### Axillary and extra-axillary lymph nodes

Axillary lymph node involvement could not be assessed with PET/CT in 18 (29%) patients because of a SLNB

procedure prior to the scan (all in the PAPBI group). PET/CT showed intense axillary uptake (score 2 or 3) in 19 patients, faint uptake (score 1) in two, and no increased uptake in 23 patients. When considering intense FDG uptake as suspect for axillary metastasis, sensitivity, specificity, positive predictive value, and negative predictive value of PET/CT were 73% (19/26), 100% (18/18), 100% (19/19), and 72% (18/25), respectively (Supplementary Table I, to be found online at <http://informahealthcare.com/doi/abs/10.3109/0284186X.2013.783714>). In two (3%) patients an FDG-avid node was seen in the periclavicular region, which was detected with US and FNA as well.

#### Distant lesions

Twelve lesions outside the affected breast and ipsilateral locoregional nodes were detected in 10 (16%) of 62 patients (Supplementary Table II, to be found online at <http://informahealthcare.com/doi/abs/10.3109/0284186X.2013.783714>). Suspect lesions in the contralateral breast were detected in three patients, being false positive in one patient, in situ carcinoma in the second patient, and small invasive ductal carcinoma in the third patient. An axillary node with FDG uptake in the contralateral axilla could not be confirmed to harbor tumor cells. In

Table I. Baseline characteristics of 62 included patients, subdivided by final treatment group.

	PAPBI n = 31	Surgery n = 8	NAC n = 23
Age			
Mean $\pm$ SD	66.6 $\pm$ 4.5	65.1 $\pm$ 8.6	47.9 $\pm$ 12.4
Range	60–75	45–74	26–67
T-stage			
1a (2–5 mm)	2 (6%)	0	0
1b (6–10 mm)	10 (32%)	2 (25%)	3 (13%)
1c (11–20 mm)	19 (61%)	6 (75%)	20 (87%)
N-stage			
0	31	4 (50%)	0
1	0	4 (50%)	21 (91%)
3	0	0	2 (9%)
Histology			
IDC	30 (97%)	6 (75%)	22 (96%)
ILC	0	1 (13%)	0
Other	1 (3%)	1 (13%)	1 (4%)
Clinical subtype			
ER+/HER2–	29 (94%)	7 (88%)	12 (52%)
TN	1 (3%)	1 (13%)	5 (22%)
HER2+	1 (3%)	0	6 (26%)
Ki-67			
< 15%	24 (77%)	5 (63%)	11 (48%)
$\geq$ 15%	7 (23%)	3 (38%)	9 (39%)
Unknown			3 (13%)
Grade			
1	16 (52%)	1 (13%)	4 (17%)
2	15 (48%)	6 (75%)	8 (35%)
3	0	1 (13%)	8 (35%)
Unknown			3 (13%)

ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; NAC, neoadjuvant chemotherapy; N-stage, locoregional lymph node stage; PAPBI, preoperative accelerated partial breast irradiation; SD, standard deviation; TN, triple negative; T-stage, tumor stage.

four patients FDG uptake was seen in the thyroid gland, being suspect for malignancy in one of them. Additional imaging procedures and histopathological examination showed benign proliferative lesions in all four patients. In one patient from the NAC group a suspect lesion in the lung was visualized with PET/CT. High-resolution diagnostic CT was suspect for metastasis as well and the radiotherapy treatment was changed accordingly. PET/CT detected FDG-avid lesions outside the thorax in three patients. In one patient it was compatible with a small, benign polyp in the colon and further investigations were omitted. A colonoscopy confirmed the presence of a villous adenoma in two patients. In total, FDG-avid distant lesions corresponded with one metastasis, two new primary malignancies in the contralateral breast, three false positive findings, two premalignant lesions, and four benign proliferative lesions. Images of primary tumor, locoregional nodes, and distant lesions as obtained with PET/CT are presented in Figure 2.

## Discussion

This study demonstrates that the majority of T1 breast carcinomas show increased FDG uptake and can be visualized with PET/CT using state-of-the-art imaging protocols. Response monitoring during radio- or chemotherapy is possible in most of them. Tumors with prognostically unfavorable characteristics (node-positive, triple negative, grade 3, high proliferation index) were more likely to be eligible for response monitoring and had a higher SUVmax. As expected in early breast cancer, not many distant metastases were detected. Distant lesions detected with PET/CT were located in the thorax area in particular. In accordance with previous research, sensitivity of PET/CT in the detection of axillary metastases was suboptimal, but specificity and positive predictive value were excellent.

Use of PET/CT for detection of the primary tumor is currently not recommended, mainly because of the supposedly low sensitivity in small carcinomas. In other studies sensitivities of 25–63% in T1a-b and 80–94% in T1c have been reported [7–10]. However, most studies have used PET only and are not directly comparable with current generation imaging equipment [7,8]. In the current study we showed that 67% of T1b and 98% of T1c tumors could be visualized with PET/CT. In this study the two tumors smaller than 5 mm (T1a) were not visualized. All triple negative and HER2-positive tumors could be visualized, as compared with 83% of ER-positive/HER2-negative tumors. Currently, several dedicated high-resolution breast PETs have become available (either with compression of the breast or using hanging breast technique) and their use is increasingly investigated [20–22]. They could offer more accurate molecular imaging of breast tumors as compared with conventional PET/CT, especially in small tumors, and might be a valuable addition to conventional imaging modalities.

Several studies have shown that breast cancer with aggressive characteristics shows a higher degree of FDG uptake [23,24]. Our study shows similar results, with higher FDG uptake and SUVmax in larger tumors, node-positive patients, patients with a higher stage, in triple negative tumors, and in tumors with a high grade or proliferation index as assessed with Ki-67 stainings.

The value of response monitoring of breast cancer with PET/CT during NAC is currently being investigated [6]. Results are promising, but patient groups are relatively small and recommendations for the use of PET/CT cannot be made. While radiotherapy is given postoperatively in most cases, there are no data, to our knowledge, concerning response monitoring following neoadjuvant radiotherapy as was done for part of our patients treated in the PAPBI

Table II. Visualization of the primary tumor, possibility of response monitoring, and SUVmax for different subgroups of 62 patients.

		Total	Tumor visible (score 1-2-3)	p-value	Response monitoring possible (score 2-3)	p-value	SUVmax Median (IQR) (score 1-2-3)	p-value
T-stage	1a (2–5 mm)	2	0	<0.001	0	<0.001		0.001
	1b (6–10 mm)	15	10 (67%)		4 (27%)		2.2 (1.2)	
	1c (11–20 mm)	45	44 (98%)		40 (89%)		3.9 (3.7)	
N-stage	0	35	28 (80%)	0.091	20 (57%)	0.012	3.0 (2.4)	0.001
	1	25	24 (96%)		22 (88%)		3.7 (4.5)	
	3	2	2 (100%)		2 (100%)		18.4 (24.2)	
Stage	1a	35	28 (80%)	0.068	20 (57%)	0.009	3.0 (2.4)	<0.001
	1b	2	2 (100%)		2 (100%)		3.4 (0)	
	2a	23	22 (96%)		20 (87%)		4.1 (5.0)	
	3c	2	2 (100%)		2 (100%)		18.4 (24.2)	
Histology	IDC	58	50 (86%)	0.729	42 (72%)	0.282	3.5 (3.9)	0.04
	ILC	1	1 (100%)		1 (100%)		2.7	
	Other	3	3 (100%)		1 (33%)		2 (2.7)	
Subtype	ER+/HER2–	48	40 (83%)	0.262	31 (65%)	0.103	3.2 (1.9)	0.009
	TN	7	7 (100%)		7 (100%)		7.7 (3.7)	
	HER2+	7	7 (100%)		6 (86%)		4.4 (4.2)	
Ki-67	< 15%	40	33 (83%)	0.416	25 (63%)	0.037	3.0 (2.2)	0.035
	≥ 15%	19	18 (95%)		17 (89%)		5.0 (4.6)	
	Unknown	3						
Grade	1	21	16 (76%)	0.063	9 (43%)	<0.001	2.7 (1.4)	<0.001
	2	29	26 (90%)		25 (86%)		3.4 (2.8)	
	3	9	9 (100%)		9 (100%)		7.7 (5.8)	
	Unknown	3						
Treatment	PAPBI	31	24 (77%)	0.05	17 (55%)	0.014	3.0 (1.9)	0.013
	Surgery	8	7 (88%)		6 (75%)		3.4 (3.3)	
	NAC	23	23 (100%)		21 (91%)		4.4 (5.5)	
Total		62	54 (87%)		44 (71%)		3.4 (3.7)	

ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; IQR, interquartile range; NAC, neoadjuvant chemotherapy; N-stage, locoregional lymph node stage; PAPBI, preoperative accelerated partial breast irradiation; SUVmax, maximum standardized uptake value; TN, triple negative; T-stage, tumor stage.

trial. This study shows that response monitoring is possible in the majority of T1 breast cancer patients.

The value of PET/CT for the assessment of axillary lymph node involvement in early breast cancer has been investigated earlier. Sensitivity was suboptimal (37–95%), but specificity was consistently high (84–100%) [11,12]. These findings have been confirmed in a subgroup in this study, showing a suboptimal sensitivity, but excellent positive predictive value, confirming that an immediate axillary dissection instead of SLNB is reasonable in case of an FDG-avid axillary node. However, SLNB remains mandatory in axillae with no or slightly increased FDG uptake.

The application of PET and PET/CT for the detection of distant metastases has been studied extensively, mainly in locally advanced breast cancer [4,5,13,25]. Although a PET/CT is currently not recommended as a staging procedure in breast cancer patients, it has been shown to outperform conventional imaging procedures, and several studies suggest that PET/CT should be incorporated in the standard diagnostic work-up before start of NAC.

Use of PET/CT as a staging procedure in early breast cancer is investigated less frequently and its yield seems lower in this subgroup, predominantly because of the lower incidence of metastases [4,8,10,15]. The results from the current study confirm the low yield of PET/CT as a staging device in early breast cancer. PET/CT depicted a lung metastasis in one patient. Three suspect FDG-avid lesions were found to be false positive and both lesions in the contralateral breast, suspect for new primary malignancy, were detected with US and/or MRI as well. Most distant lesions were found to be new primary proliferative disorders, both benign and malignant. Of 12 distant lesions, three were located outside the thorax, all being coincidental findings not influencing patient’s breast cancer care.

A few limitations of this study should be mentioned. First, this is a selected group of T1 tumors. We have included patients who were treated according to one of two prospective trials: either patients aged 60 years and over treated with preoperative partial breast irradiation or patients with a cytology-proven locoregional metastasis treated with NAC. Further, our group consisted of two distinct patient

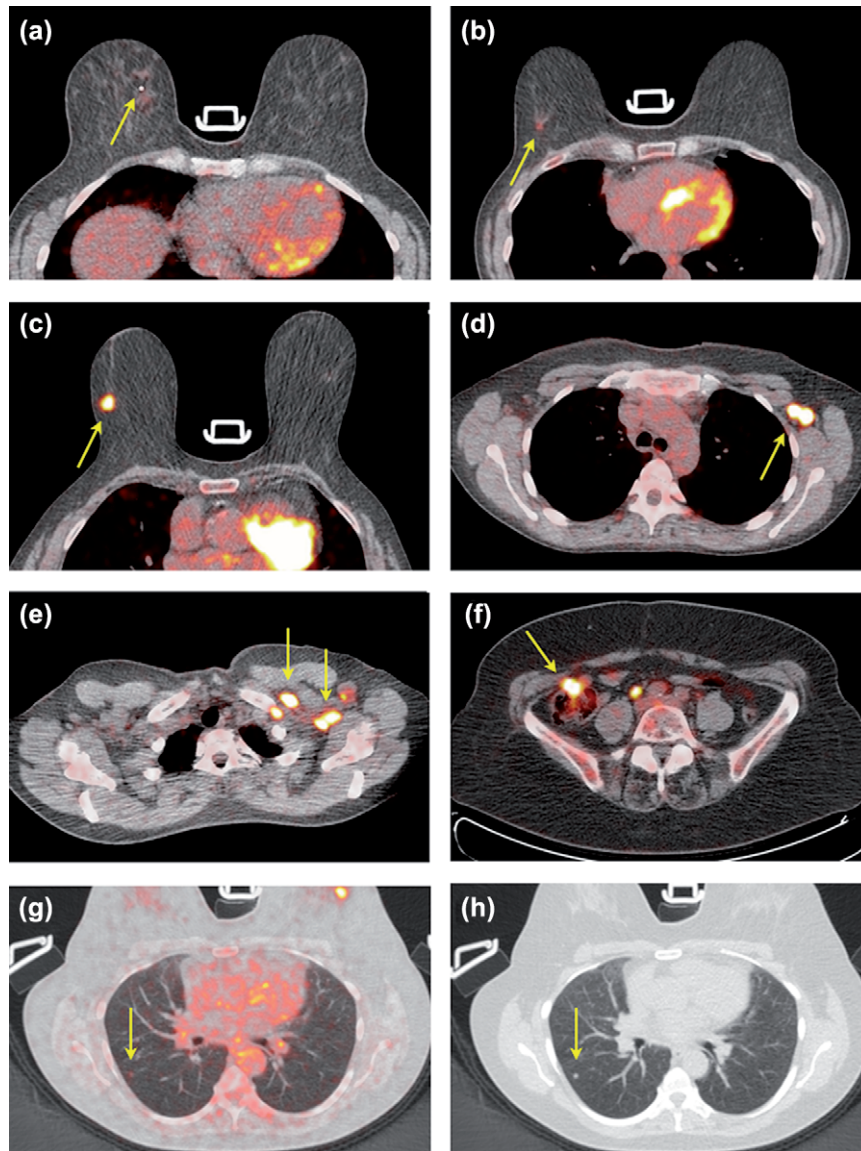


Figure 2. Fused PET/CT images (a-g) and low-dose CT images (h) of different patients with T1 breast cancer, showing a primary tumor without FDG uptake in the right breast (a), a tumor with questionable FDG uptake in the right breast (b), a tumor with intense FDG uptake in the right breast (c), two intense FDG-avid lymph nodes in the left axilla (d), multiple FDG-avid lymph nodes in the left periclavicular region (e), an intense lesion in the ascending colon (f), and an FDG-avid metastasis in the right lung (g, h).

populations, possibly confounding our results. Second, axillary evaluation was possible in a subgroup of patients only (SLNB prior to PET/CT in 29% of patients). However, the primary goal of this study was to assess accuracy of PET/CT for primary tumor visualization and (distant) staging. Also, our analysis is in accordance with previously published studies on axillary evaluation with FDG PET/CT. Finally, we used MRI as a reference for tumor size and core biopsies as a reference for histopathology and immunohistochemistry, since the surgical specimen was no longer the reference standard due to pretreatment with radio- or chemotherapy.

In our opinion, PET/CT in T1N0 and T1N1 breast cancer should be used for research purposes

only. Although the primary tumor is visualized with PET/CT in the majority of T1 breast cancer patients, its value for response monitoring is still being investigated; standard use for staging is not recommended because of the suboptimal sensitivity regarding the axilla and low yield regarding distant metastases. The added radiation dose and high costs further limit its use as a standard staging procedure. If, based on study protocols, a PET/CT is performed in T1 breast cancer, scanning of the thorax or the use of a dedicated breast PET could be sufficient.

In summary, this study shows that the majority of T1 breast carcinomas can be visualized with FDG PET/CT. Response monitoring to radiotherapy or chemotherapy with PET/CT could be performed in

most T1 tumors. The excellent positive predictive value for axillary staging, as mentioned in previous research, was confirmed in this study, allowing immediate axillary dissection instead of SLNB in case of FDG-avid axillary nodes. However, sensitivity was low, requiring an SLNB in case of absence of FDG-avid nodes. Distant staging can be done relatively reliably, but the yield in T1 tumors is low.

**Declaration of interest:** The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

Part of this study was performed within the framework of CTMM, the Center for Translational and Molecular Medicine ([www.ctmm.nl](http://www.ctmm.nl)), project Breast Care (grant 03O-104). The PAPBI trial is part of a project supported by a grant from the Dutch Cancer Society (Grant NKI 2009-4389), extended to F. van der Leij and P.H.M. Elkhuisen.

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## Supplementary material available online

Supplementary Table I and II.