FDG PET in breast cancer

高雄榮民總醫院核醫部

胡瑨 醫師

Outline

- FDG PET and PET/CT
- Diagnosis of primary breast tumors
- Breast cancer staging and restaging
- Monitoring response to therapy

FDG PET and PET/CT

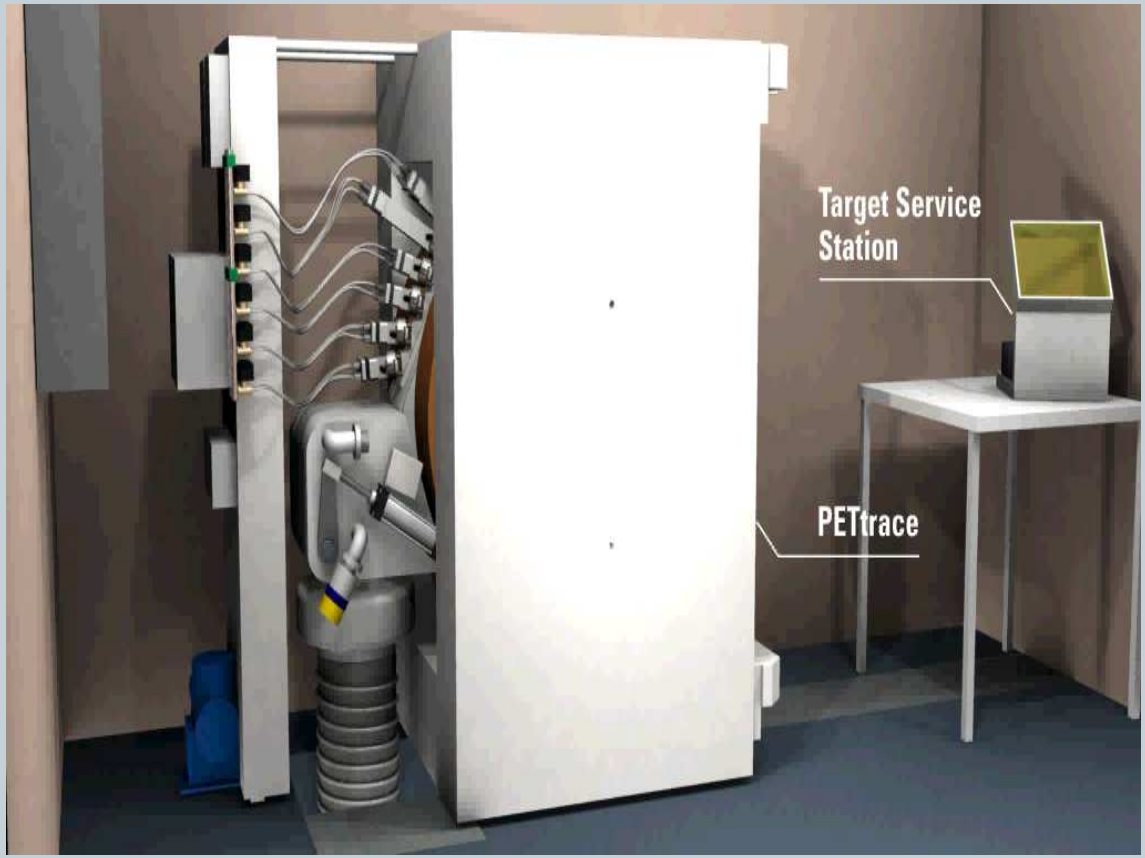
TABLE 12.1. ISOTOPES FOR POSITRON EMISSION TOMOGRAPHY

Isotope	$t_{1/2}$	Positron end point (MeV)	Effective range FWHM[a] (mm)	Means of production
C-11	20.3 min	0.97	2.06	Cyclotron
N-13	10.0 min	1.19	3[c]	Cyclotron
O-15	124.0 sec	1.7	4.5[c]	Cyclotron
F-18	110.0 min	0.635	1.4[c]	Cyclotron
Rb-82[b]	75.0 sec	3.15	13.8	Sr-82 generator
Ga-68	68.3 min	1.88	5.4	Ge-68 generator
Br-75	1.6 hr	1.7, 1.1, 0.65		Cyclotron

[a]FWHM = full width at half-maximum.
[b]The lower of the two radioactive isomers of Rb-82.
[c]Interpolated values.

FDG PET and PET/CT

- cyclotron



FDG PET and PET/CT

Positron-Emitting Radiochemicals

Physiologic alteration	Tracer(s)
Increased glucose utilization	FDG, ^{11}C-glucose
Increased amino acid transport/ protein synthesis	^{11}C-methionine, ^{11}C-ACHC, ^{11}C-tyrosine
Increased DNA synthesis	^{11}C-thymidine, ^{18}F-fluorodeoxyuridine
Tumor hypoxia	^{18}F-fluoromisonidazole
Increased estrogen receptor expression	^{18}F-β-estradiol
Increased blood flow	^{15}O-H_2O, ^{62}Cu-PTSM
Increased antigen or receptor density	^{18}F-labeled anti-tumor monoclonal antibodies
Increased retention of chemotherapeutic agents	5-^{18}F-fluorouracil, ^{11}C-daunorubicin

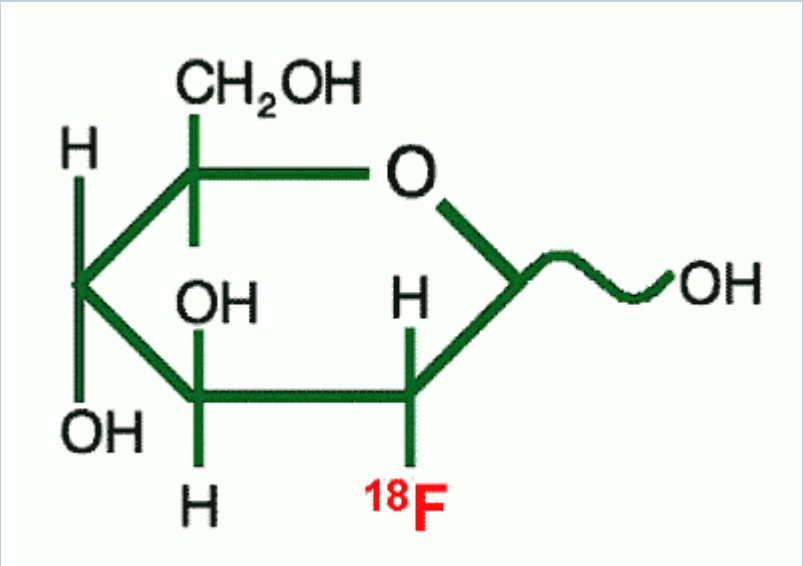
FDG PET and PET/CT

Table 1.3 Potential radiopharmaceuticals for clinical PET

Radiopharmaceutical	Application
[^{11}C]Flumazenil	Localization of epileptic foci
[^{18}F]Fluoromisonidazole	Hypoxic tumour cells, ischaemically compromised myocardium
[^{11}C]Acetate	Cardiac oxidative metabolism
[^{11}C]Palmitate	Cardiac fatty acid metabolism
[^{13}N]Glutamate	Tumour metabolism
[^{18}F]Fluorodopa	Dopamine synthesis
[^{11}C]Aminoisobutyric acid (AIB)	Tumour amino acid uptake
[^{11}C]Aminocyclopentanecarboxylic acid (ACPC)	Tumour amino acid uptake
[^{18}F]Uracil (FU)	Evaluation of response to chemotherapy
[^{11}C]Thymidine	Tumour cellular proliferation rate
[^{68}Ga]EDTA	Blood–brain barrier permeability
[^{62}Cu]PTSM	Blood flow
[^{11}C]Tyrosine	Tumour metabolism

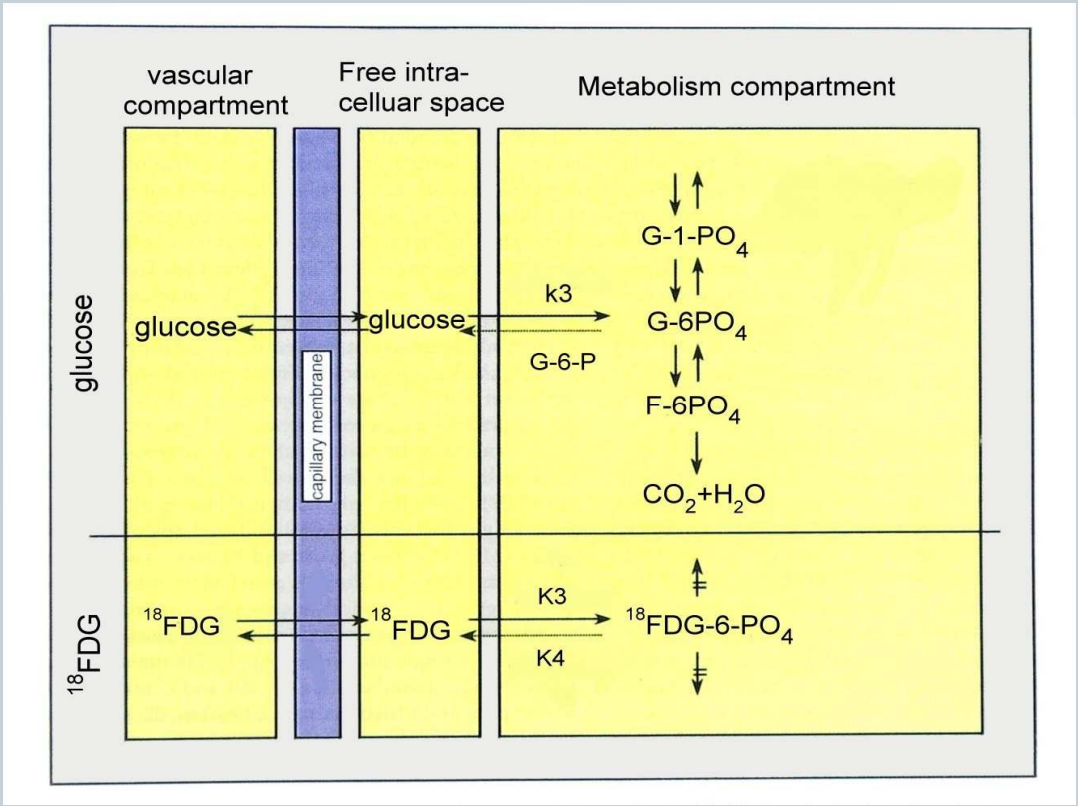
FDG PET and PET/CT

2-[^{18}F]-2-deoxy-D-glucose

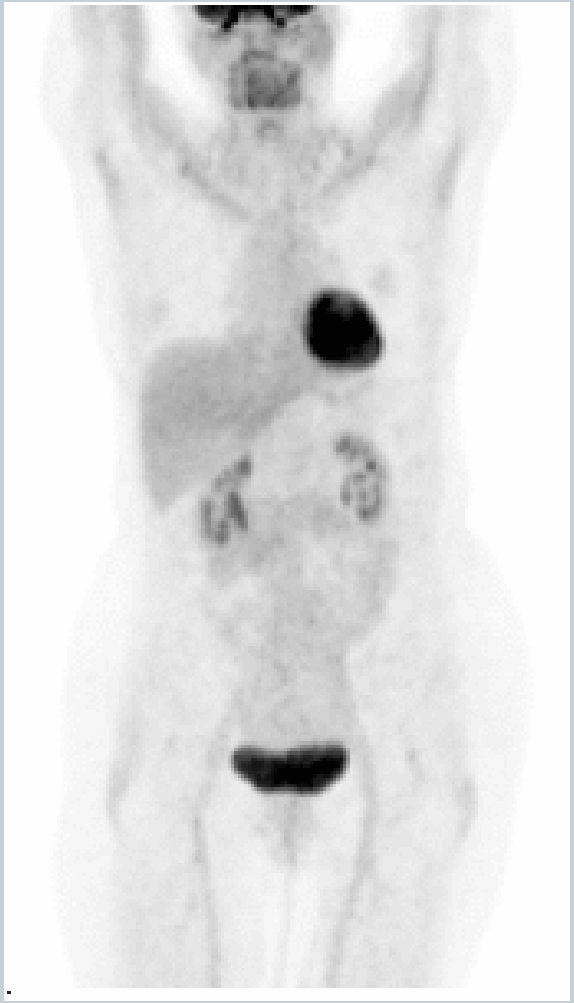


FDG PET and PET/CT

- Three compartment model



FDG PET and PET/CT



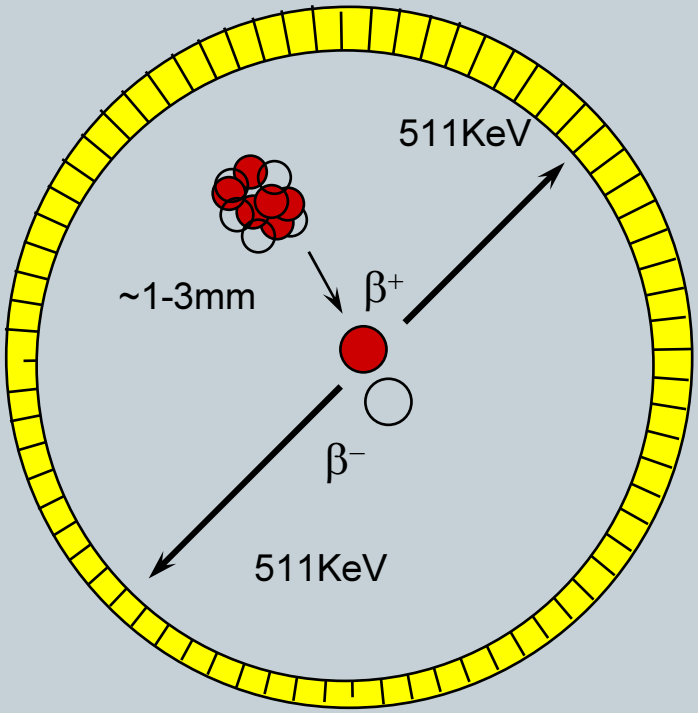
- **Physiologic FDG uptake**
  all viable tissues

- **Pathologic FDG uptake**
  benign or malignant tumor
  activated PMNs or macrophages

- Standard uptake value (SUV)

$$SUV = \frac{\text{Decay-corrected dose / cm}^3\text{ tumor}}{\text{Injected dose / Patient Wt (gm)}}$$

FDG PET and PET/CT

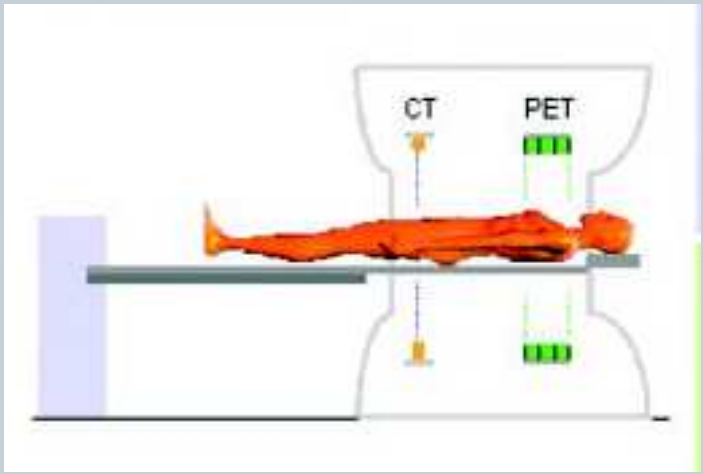


Positron Annihilation

FDG PET and PET/CT

spatial resolution = 0.5 cm

partial volume effect in <1 cm lesion



Anatomic correlation

Attenuation correction

FDG PET and PET/CT

Precautions

NPO >4 hours, blood sugar <180 mg/dl

pregnancy (x)

breast feeding 6 hours later

輻射工作人員
職業曝露劑量
（50mSv）

50

PET/CT正子造影檢查
（32mSv）

20

15

腸胃道透視攝影（4mSv）

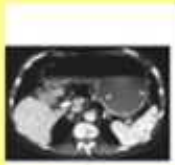
10

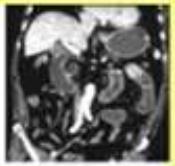
天然輻射背景值（2.4mSv）

4

放射治療
單一部位
（60,000mSv）

腹部多層面電腦斷層
(MSCT)檢查（15mSv）





2.4

核醫檢查
（0.3~10mSv）

MSCT冠狀動脈
血管攝影檢查（12mSv）

0.3

胸部X光檢查
（0.3mSv）

單位：mSv（毫西弗）

由國際輻射單位與度量委員會(ICRU)制定，人體接受輻射之等效劑量單位

Diagnosis of primary breast tumors

- **Early detection** is the most effective strategy for reducing mortality from breast cancer

- anatomic imaging

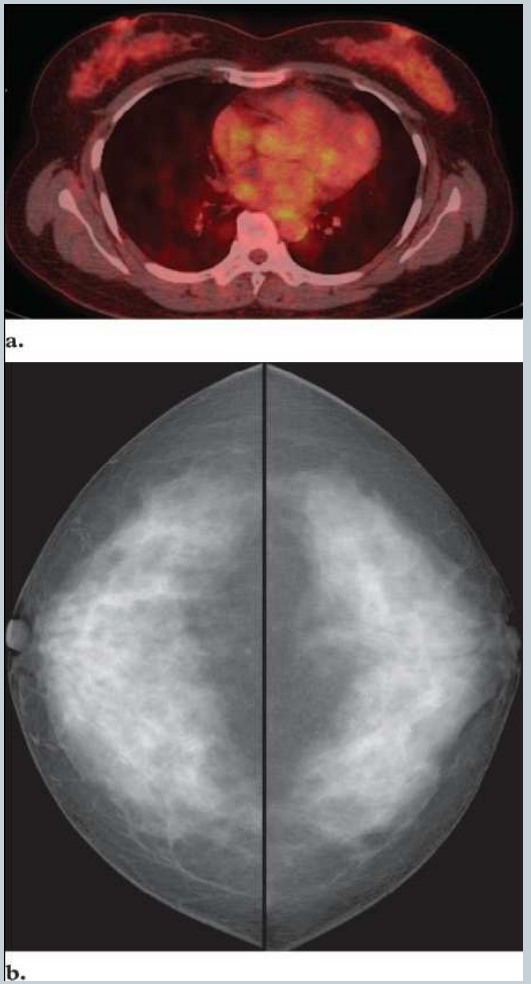
  mammography, sonography, MRI

- functional imaging ?

  FDG PET or PET/CT

Diagnosis of primary breast tumors

- physiologic FDG uptake
  - tissue density
  - hormone status
  - lactating
- pathologic FDG uptake
  - benign or malignant tumor
  - inflammation or infection



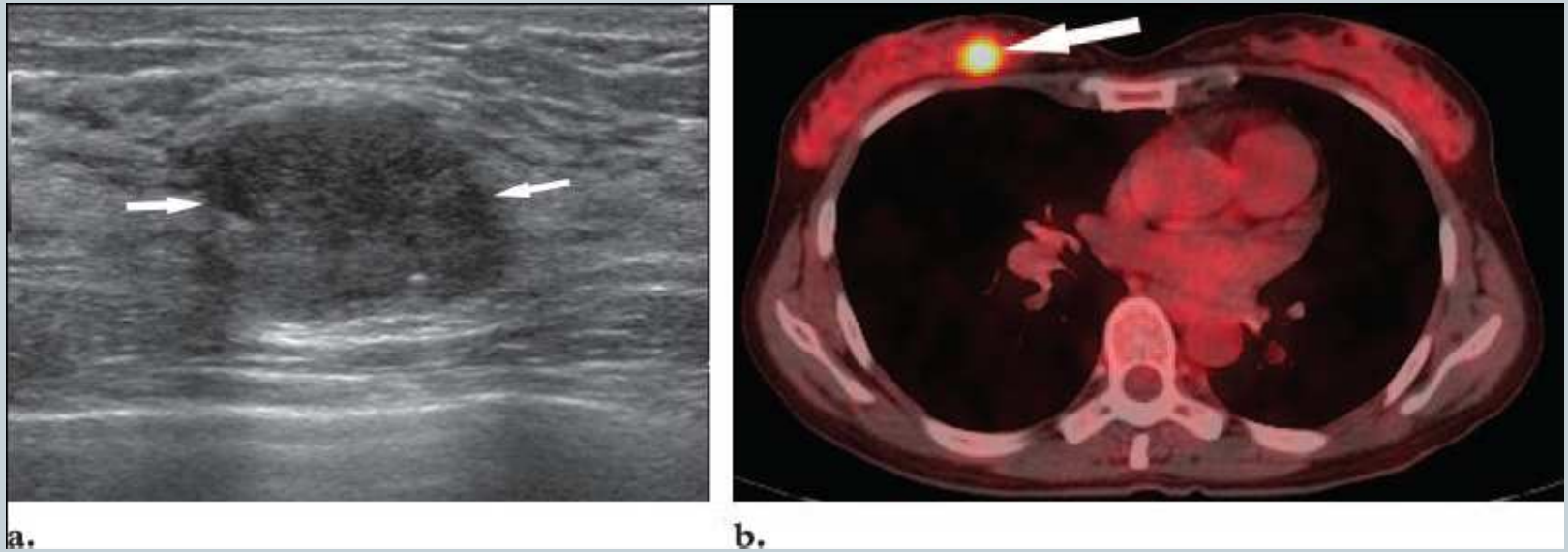
Diagnosis of primary breast tumors

- SUV ≥2.5

- False negative
  1. cancer <1 cm
  2. low-grade less-aggressive cancer
     carcinoma in situ, lobular carcinoma, tubular carcinoma
  3. diffuse growth pattern

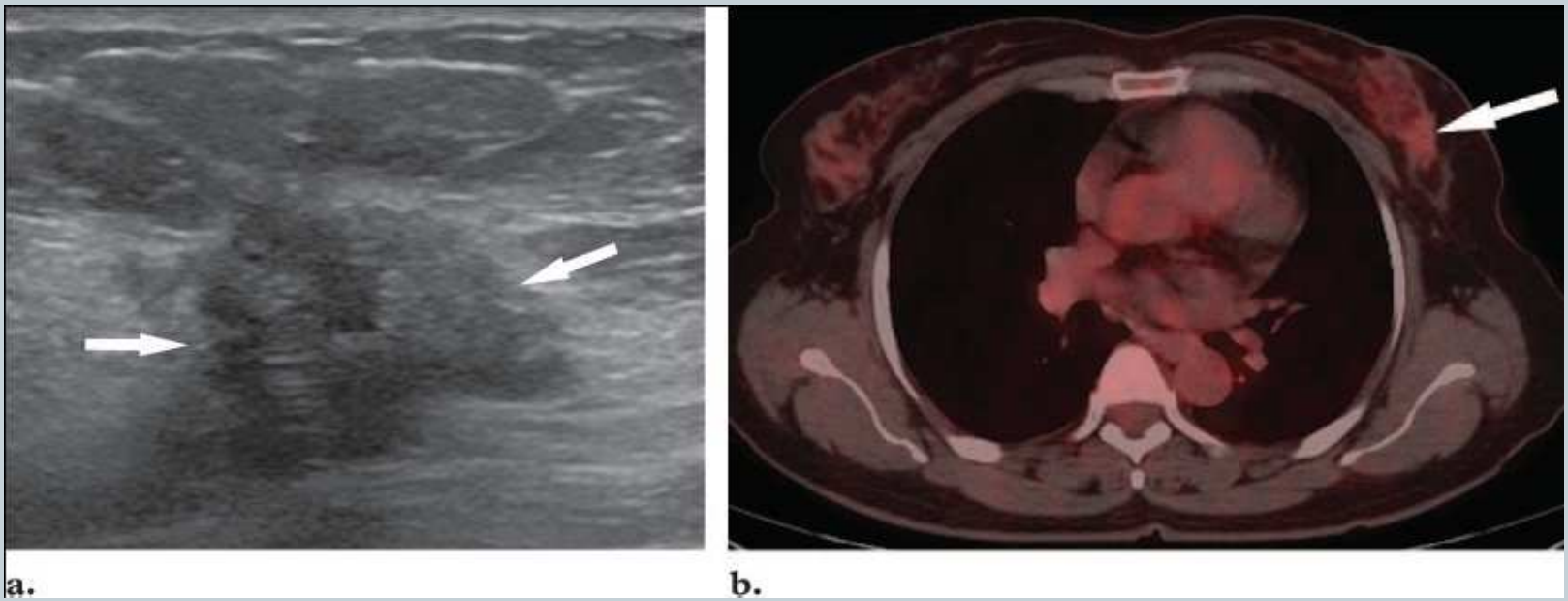
- False positive
  1. acute or chronic infection
  2. post operative healing process, granulation tissue
  3. post radiation inflammation
  4. fibrocystic change, atypical ductal hyperplasia, ductal ectasia
  5. fibroadenoma, intraductal papilloma
  6. phyllodes tumor

Diagnosis of primary breast tumors



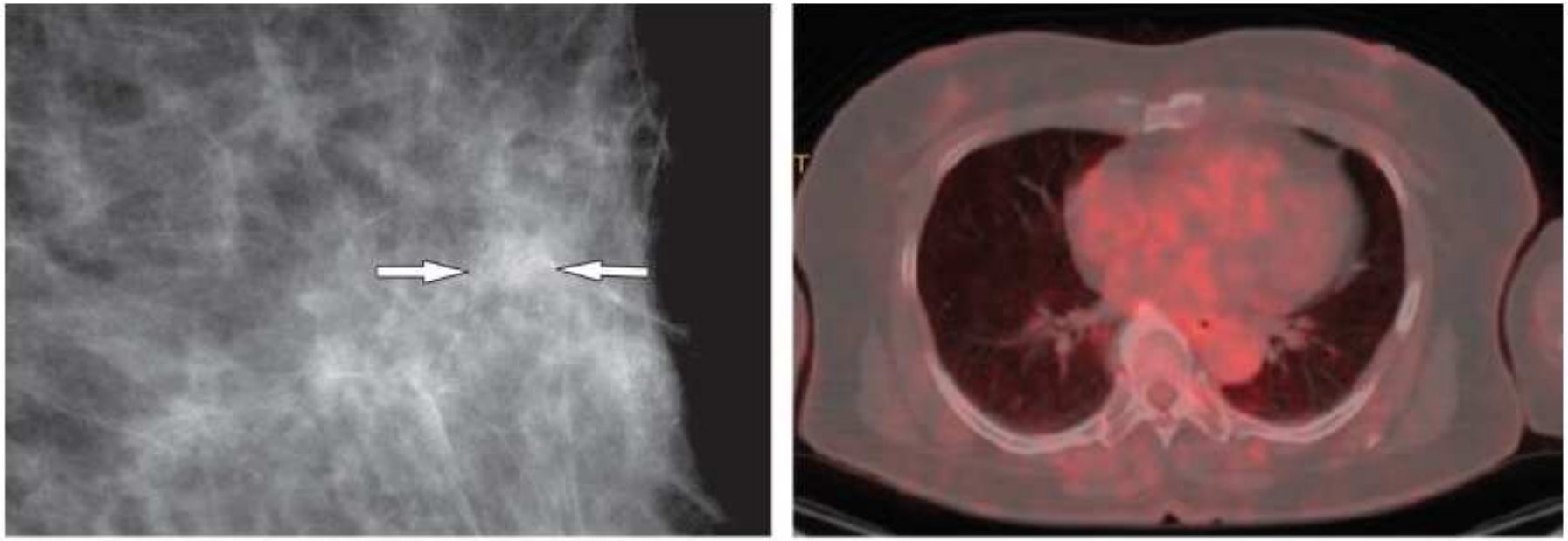
Invasive ductal carcinoma in a 42-year-old woman. **(a)** US image shows a lobular hypoechoic mass (arrows) in the right breast. The mass was diagnosed as carcinoma on the basis of pathologic analysis of a specimen from US-guided biopsy. PET/CT was performed for pretreatment staging **(b)** Axial PET/CT image shows markedly increased FDG uptake (maximum SUV, 8.9) indicative of hypermetabolism in the lesion (arrow).

Diagnosis of primary breast tumors



Invasive lobular carcinoma in a 50-year-old woman. **(a)** US image shows an irregular hypoechoic mass (arrows) in the left breast. After a US-guided biopsy, the mass was diagnosed as carcinoma. PET/CT was performed for pretreatment staging. **(b)** Axial PET/CT image shows slight FDG uptake (maximum SUV, 2.0) in the mass (arrow), a finding characteristic of invasive lobular carcinoma; an invasive ductal carcinoma would have shown more marked uptake.

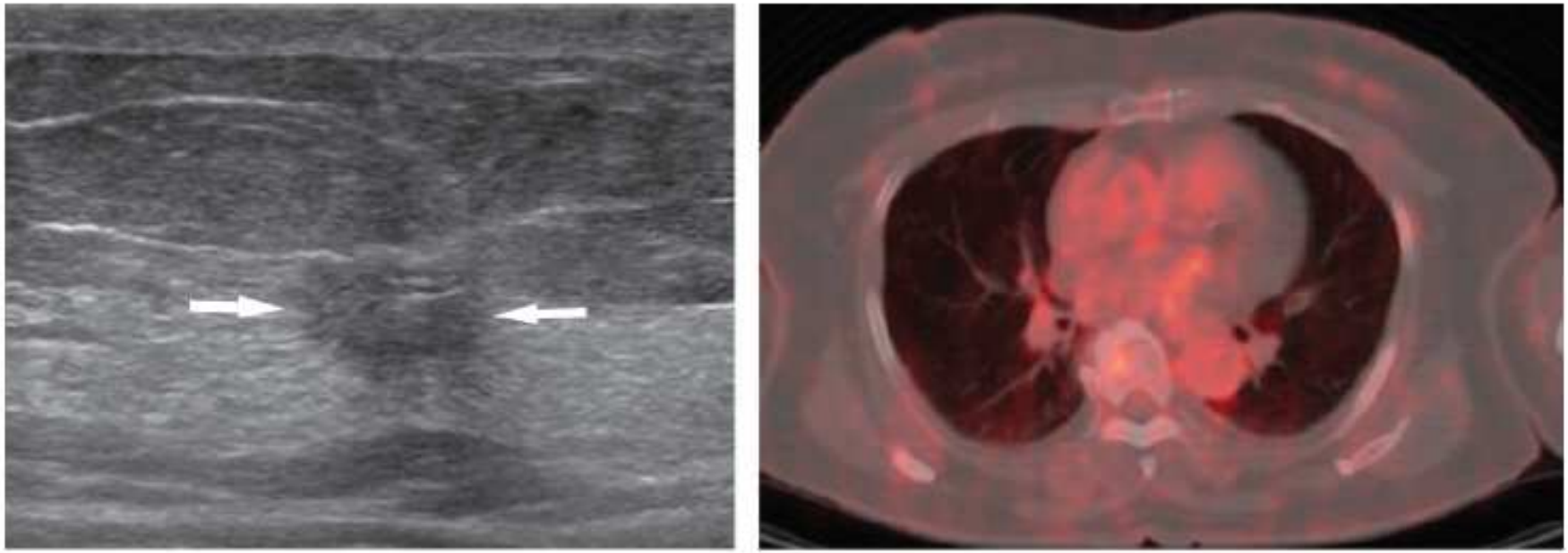
Diagnosis of primary breast tumors



a. b.

Figure 14. False-negative finding at PET/CT during staging of ovarian cancer in a 56-year-old woman. **(a)** Mammogram of the left breast, obtained before the administration of hormonal therapy, shows a cluster of pleomorphic and amorphous microcalcifications (arrows). The pathologic diagnosis after a wire localization biopsy was ductal carcinoma in situ. **(b)** Axial PET/CT image shows no corresponding area of increased FDG uptake.

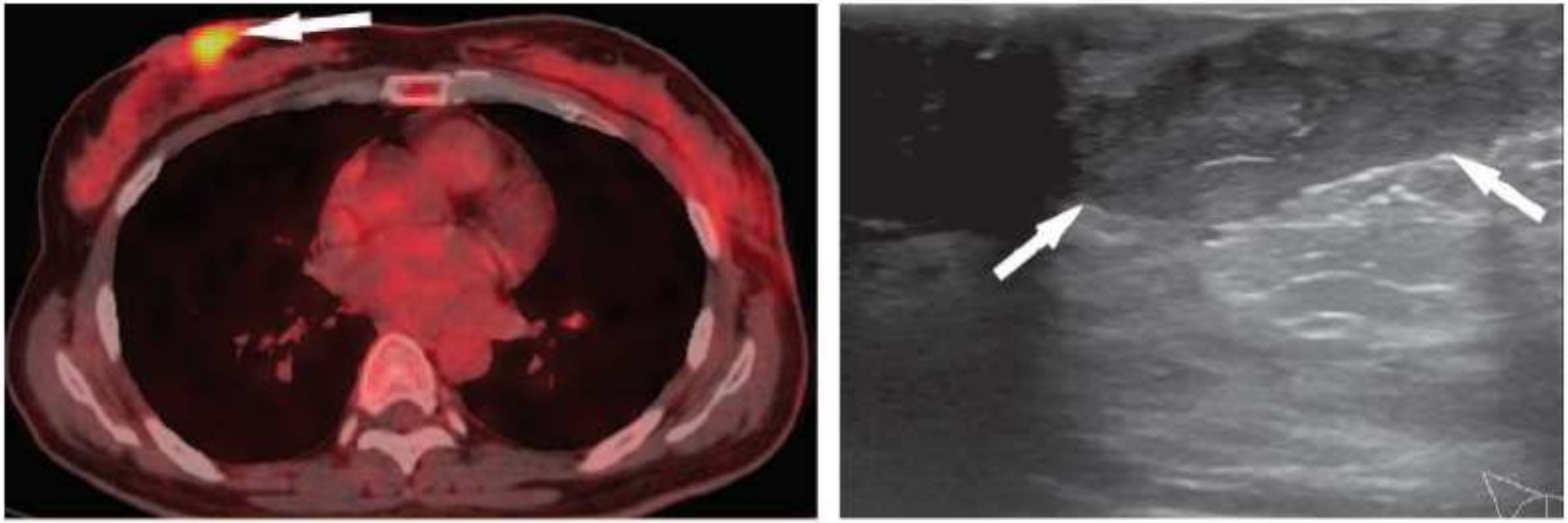
Diagnosis of primary breast tumors



a. b.

Figure 15. False-negative finding at PET/CT during restaging of ovarian cancer in a 63-year-old woman. **(a)** Image obtained at US, which was performed for evaluation of a palpable lesion in the left breast, shows an approximately 0.8-cm-diameter irregular mass (arrows) in the right breast. The diagnosis of the right breast lesion, based on pathologic analysis after a US-guided biopsy, was tubular carcinoma. **(b)** Axial PET/CT image shows no hypermetabolic lesion.

Diagnosis of primary breast tumors



a. b.

Figure 12. False-positive finding at PET/CT during preoperative staging of rectal cancer in a 47-year-old woman. **(a)** Axial PET/CT image shows a hypermetabolic (maximum SUV, 5.7) lesion (arrow) in the right breast, a finding that was believed to represent breast cancer. **(b)** Subsequent US image shows an oval circumscribed mass (arrows) in the right subareolar area. A US-guided biopsy was performed, and the mass was diagnosed on the basis of pathologic analysis as a chronic abscess.

Diagnosis of primary breast tumors

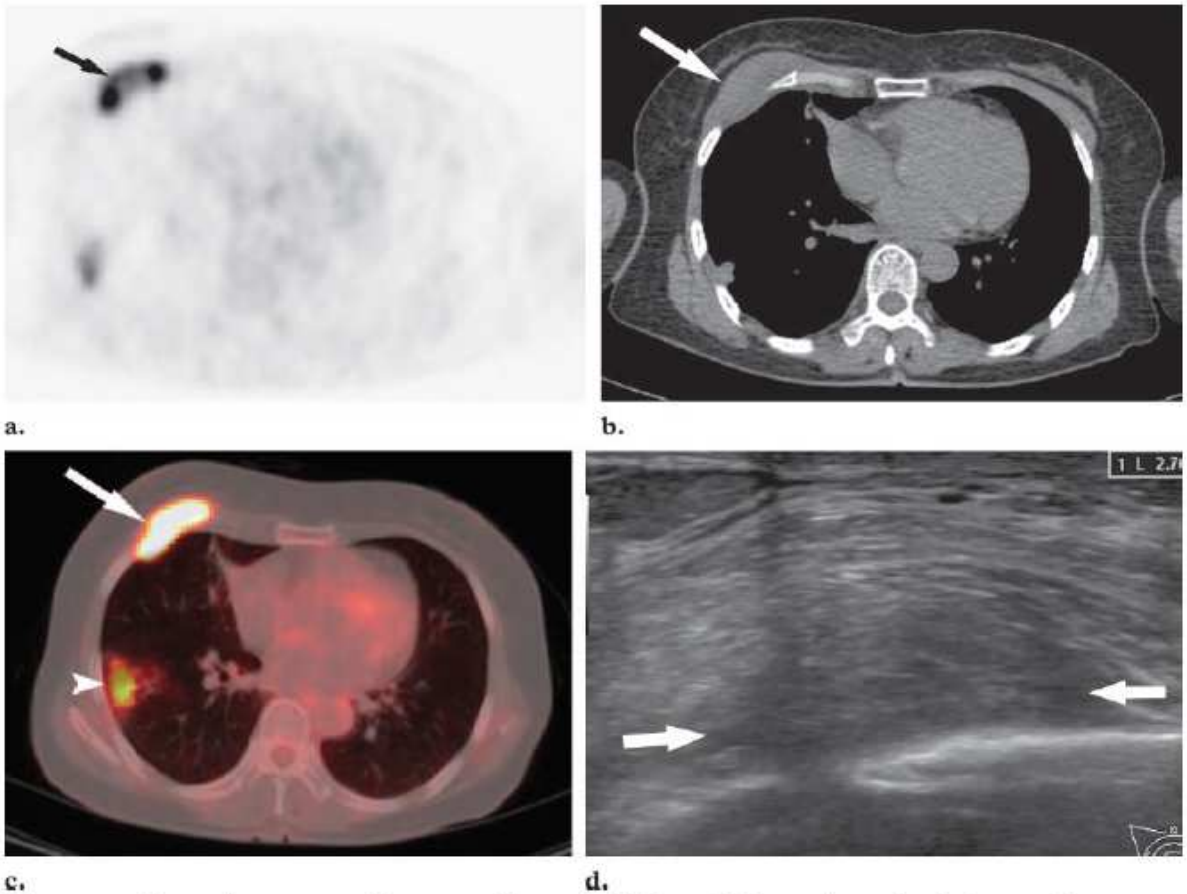
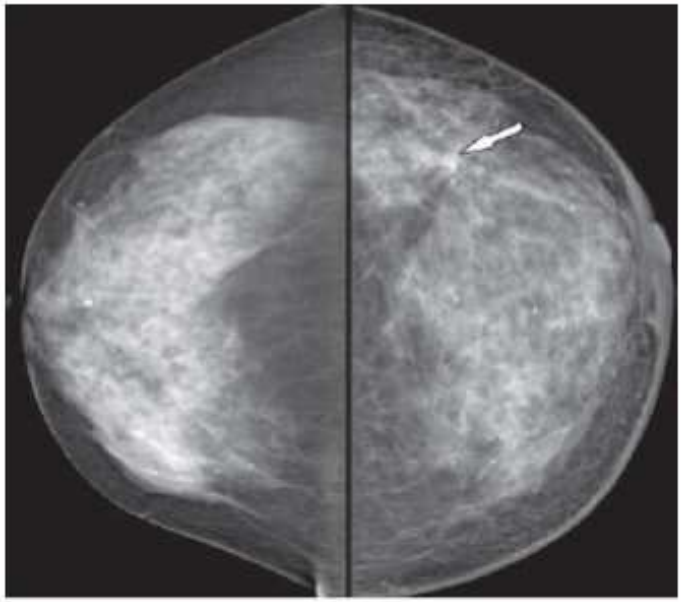
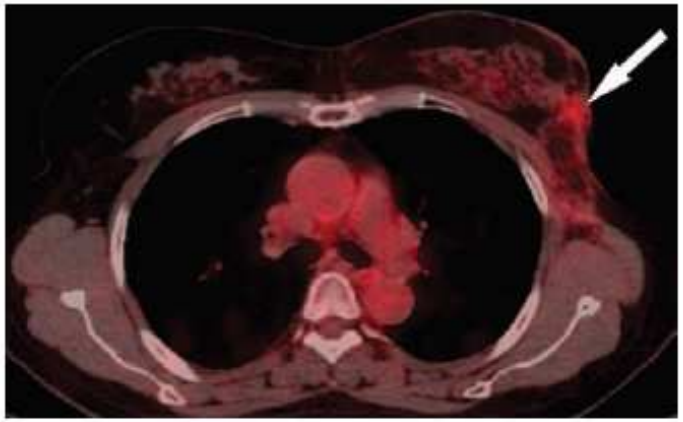


Figure 2. Abscess in a 58-year-old woman with a palpable breast lesion and a previously detected lung mass. **(a)** Axial CT attenuation–corrected PET image shows a focus of intense FDG uptake (maximum SUV, 11.5) (arrow) in the right anterior thorax. Exact localization of the area of increased uptake (confined to the breast or extending to the chest wall) was difficult on the basis of PET images. **(b)** Axial CT image shows an isoattenuating lesion (arrow) in the chest wall beneath the breast. **(c)** Axial PET/CT image shows areas of increased FDG uptake indicative of hypermetabolic lesions in the chest wall (arrow) and lung (arrowhead). **(d)** US image shows an ill-defined hypoechoic lesion (arrows) in the chest wall. At pathologic analysis, the lesion was diagnosed as a tuberculous abscess. Inflammation surrounding the abscess led to the increased FDG uptake.

Diagnosis of primary breast tumors



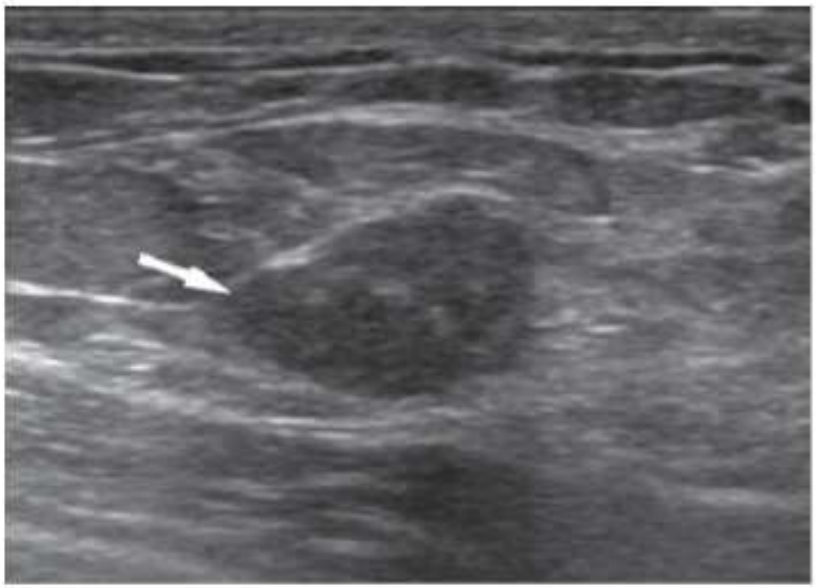
a.

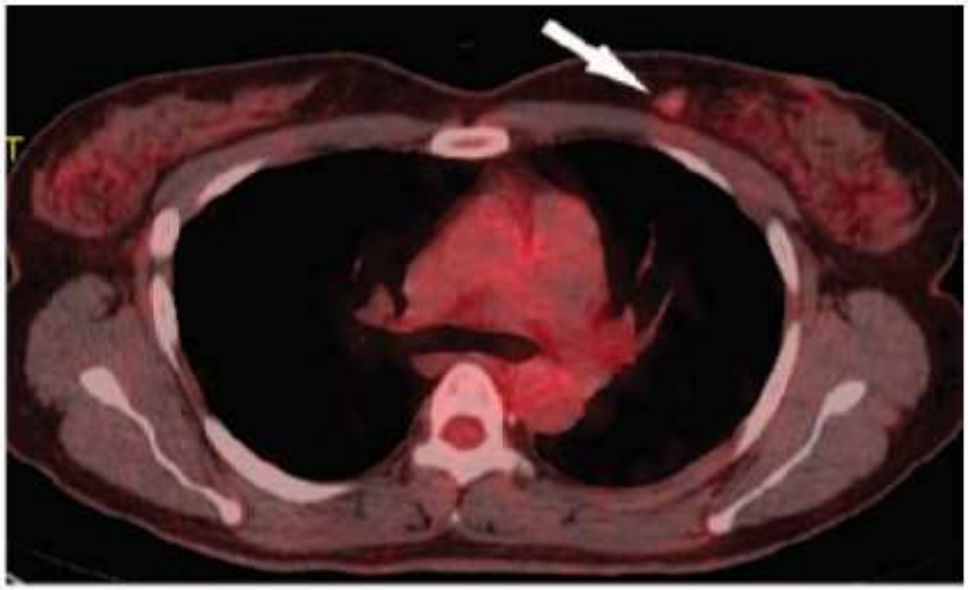


b.

Figure 13. False-positive finding at PET/CT during restaging and follow-up after breast-conserving surgery and radiation therapy for invasive ductal carcinoma in a 53-year-old woman. **(a)** Mammogram shows an area of postoperative and radiation-induced change (arrow) in the outer region of the left breast. **(b)** Axial PET/CT image shows a focus of FDG uptake (maximum SUV, 3.1) (arrow) in the upper outer region of the left breast. A US-guided biopsy was performed, and pathologic analysis showed no evidence of a recurrence.

Diagnosis of primary breast tumors

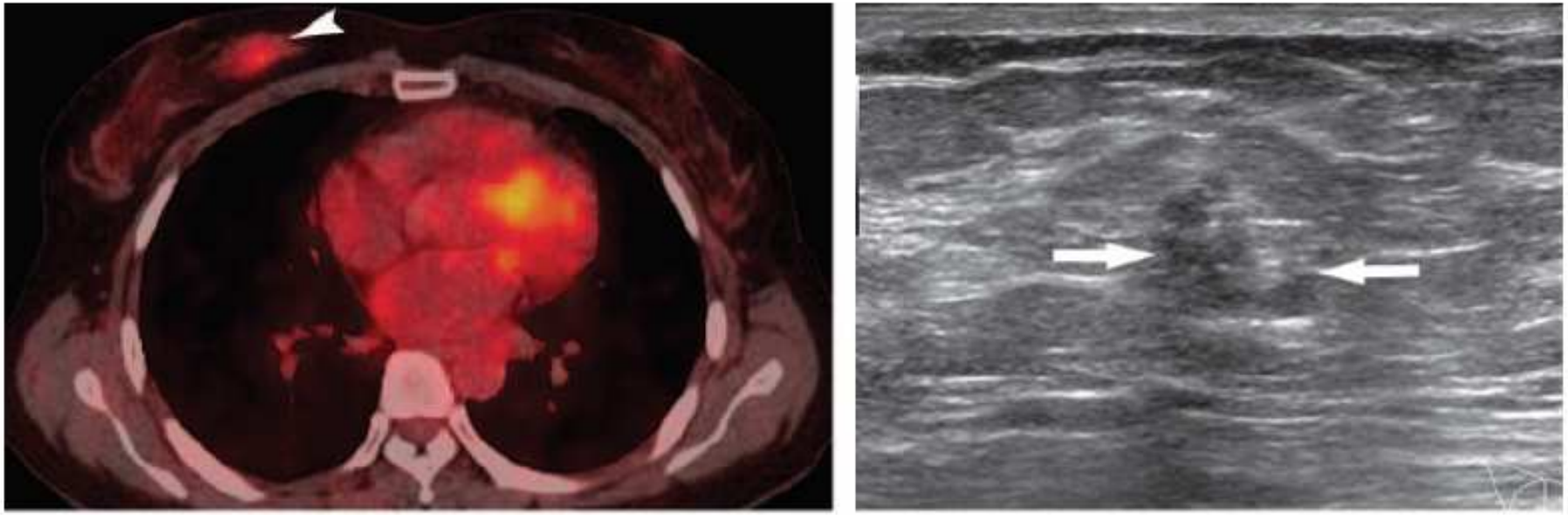




a. b.

Figure 18. Fibroadenoma in the left breast of a 43-year-old woman. **(a)** US image obtained for routine monitoring of a previously diagnosed fibroadenoma shows a well-circumscribed oval mass (arrow). **(b)** Axial PET/CT image shows no significant uptake (maximum SUV, 1.6) in the mass (arrow).

Diagnosis of primary breast tumors

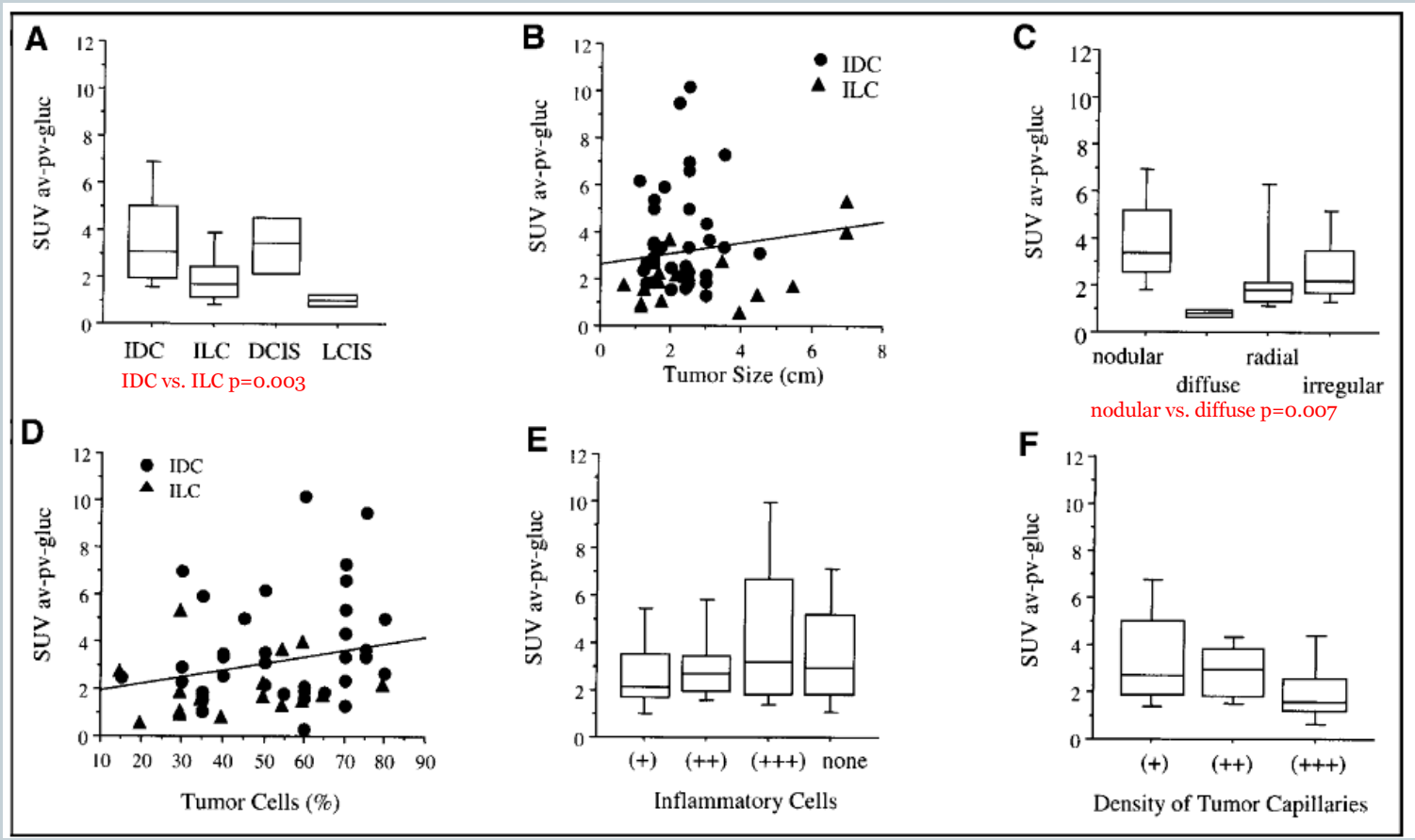


a. b.

Figure 19. False-positive finding at PET/CT in a 47-year-old woman. **(a)** Axial PET/CT image shows a hypermetabolic (maximum SUV, 3.5) lesion (arrowhead) in the right breast, a finding suggestive of breast cancer. **(b)** US image shows an irregular mass (arrows) in the upper inner area of the right breast. The diagnosis, based on pathologic analysis of an excisional biopsy specimen, was fibrocystic change with florid ductal hyperplasia, columnar cell hyperplasia, and apocrine metaplasia.

Diagnosis of primary breast tumors

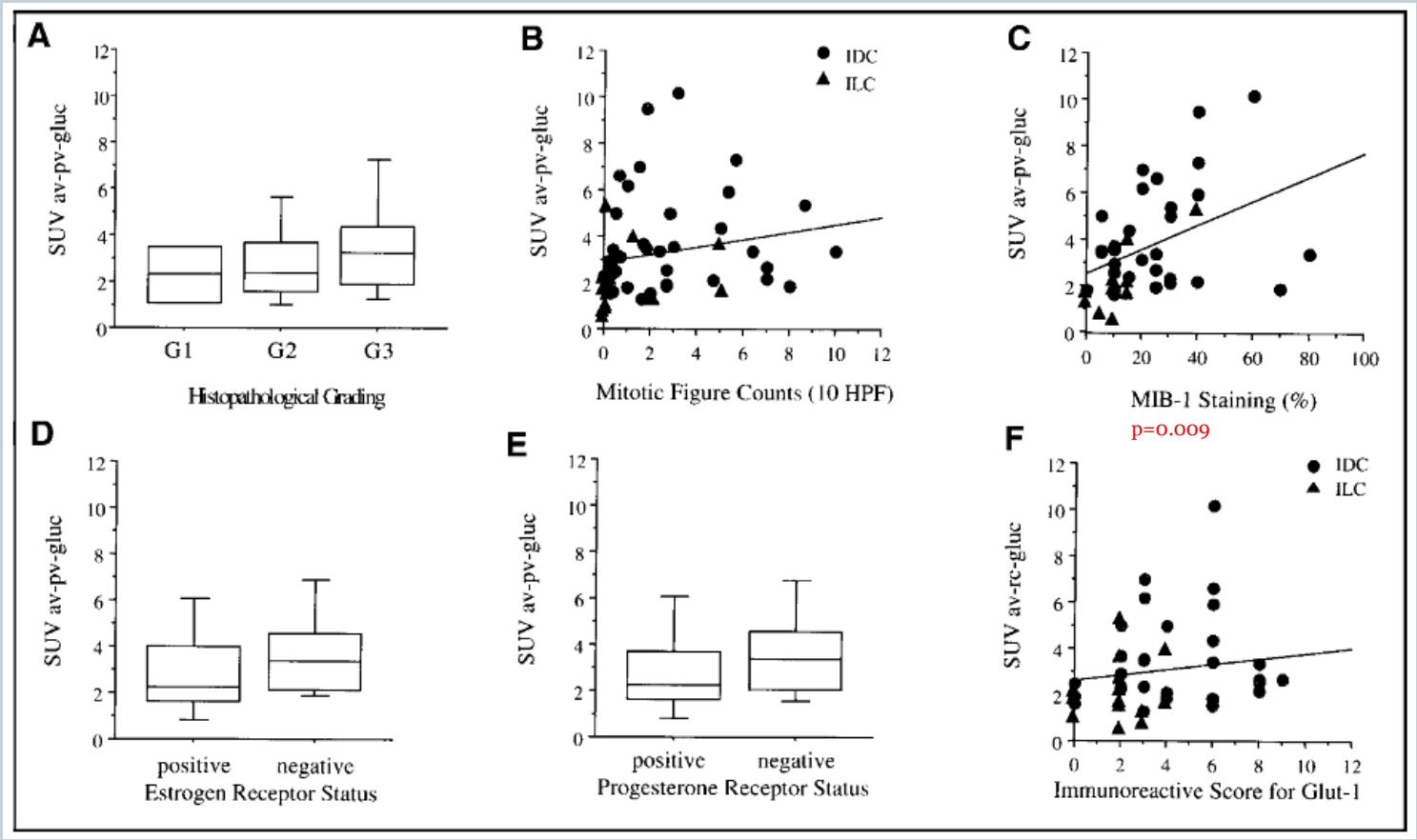
- Cancer types *vs* FDG uptake



Glucose Metabolism of Breast Cancer Assessed by 18F FDG PET Histologic and Immunohistochemical Tissue Analysis
J Nucl Med 2001; 42:9–16

Diagnosis of primary breast tumors

- Cancer types *vs* FDG uptake



Glucose Metabolism of Breast Cancer Assessed by 18F FDG PET Histologic and Immunohistochemical Tissue Analysis
J Nucl Med 2001; 42:9–16

Diagnosis of primary breast tumors

- Cancer types *vs* FDG uptake

Table 2. Showing significant factors predicting FN results

Factors	Category	*n*	FN	TP	*p*-value
Tumor size	Tumor size	73	12.14 ± 13.26	20.94 ± 11.80	0.003
Tumor grade	High		07	22	
	Moderate	85	16	13	0.001
	Low		13	02	
	In situ		08	04	

n – Number of patients.

Table 3. Showing multivariate logistic regression analysis

Factors	Category	Regression coefficient (β)	Odds ratio (OR)	95% CI of OR	*p*-value
Tumor size	>10 mm[a]				
	≤ 10 mm	2.09	8.09	(3.38, 31.52)	0.001
Tumor grade	High[a]				
	Low	2.82	16.76	(2.87, 57.65)	0.002
	Moderate	1.82	6.26	(1.74, 22.18)	0.005
	Constant	−0.092			0.874

Clinicopathologic factors associated with false negative FDG–PET in primary breast
Breast Cancer Research and Treatment (2006) 98: 267–274

Diagnosis of primary breast tumors

- Cancer types *vs* FDG uptake

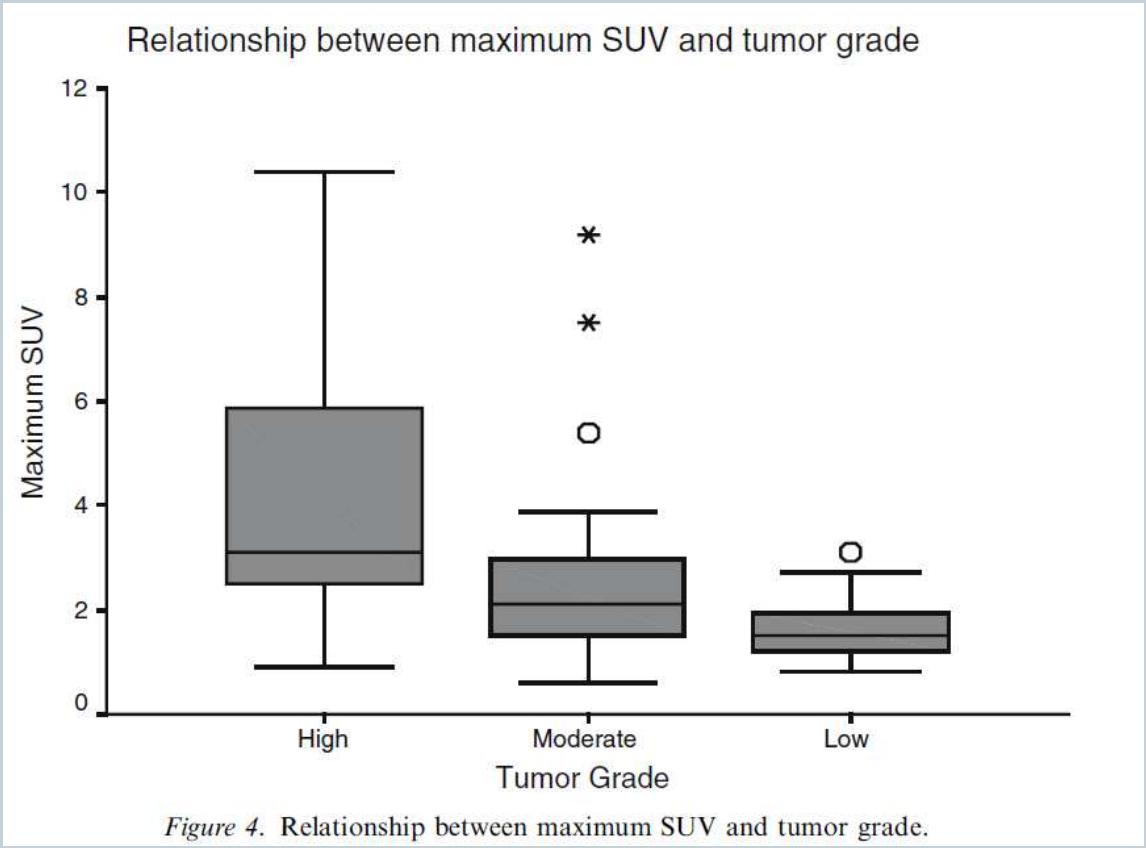


Figure 4. Relationship between maximum SUV and tumor grade.

Clinicopathologic factors associated with false negative FDG–PET in primary breast
Breast Cancer Research and Treatment (2006) 98: 267–274

Diagnosis of primary breast tumors

- **Dual-time-point**

  lesion detectability

TABLE 1

SUVmax Measurements and Changes over Time in Normal Breast, Invasive Cancer, Noninvasive Cancer, and T/B Ratios

Histopathology	SUVmax1	SUVmax2	Δ%SUVmax	Δ% in ratio 1 and ratio 2 (T/B ratio)
Group A (n = 82)	3.9 ± 3.7	4.3 ± 4.0	8.3 ± 11.5	22.0 ± 26.8
Group B (n = 24)	2.0 ± 0.6	2.1 ± 0.6	3.4 ± 13.0	15.7 ± 18.6
Group C (n = 120)	1.2 ± 0.3	1.1 ± 0.2	−10.0 ± 10.8	

Group A = invasive cancer; group B = noninvasive cancer; group C = contralateral breast; ratio 1 = T/B ratios of SUVmax at first time point; ratio 2 = T/B ratios of SUVmax at second time point; Δ% = percent change.

Data are presented as mean ± SD.

Dual Time Point ^{18}F-FDG PET Imaging Detects Breast Cancer with High Sensitivity and Correlates Well with Histologic Subtypes

J Nucl Med 2006; 47:1440–1446

Diagnosis of primary breast tumors

- **Dual-time-point**

  lesion detectability

TABLE 2
SUVmax Measurements and Changes over Time in Invasive Cancers According to Subtypes

Group A (n = 82)	SUVmax1	SUVmax2	Δ% SUVmax
Invasive ductal (n = 66)	4.3 ± 3.9*	4.7 ± 4.3*	8.1 ± 10.6*
Invasive lobular (n = 7)	2.7 ± 1.8*	3.1 ± 2.3*	10.5 ± 14.0*
Invasive mixed (n = 7)	2.0 ± 0.9*	2.2 ± 1.1*	9.3 ± 14.6*
Medullary (n = 1)	7.2	8.6	19.4
Mucinous (n = 1)	1.0	1.0	0

*Data are presented as mean ± SD.
Group A = invasive cancers; Δ% = percent change.

Diagnosis of primary breast tumors

- **Dual-time-point**

  lesion detectability

TABLE 3

SUVmax Measurements and Changes over Time According to Tumor Size in Invasive Cancers with Increase in T/B Ratios

Group A (n = 82)	SUVmax1	SUVmax2	Δ%SUVmax	Δ% in ratio 1 and ratio 2 (T/B ratio)
Tumors >10 mm (n = 57)	4.8 ± 4.1	5.3 ± 4.4	8.6 ± 12.2	23.1 ± 28.5
Tumors 4–10 mm (n = 25)	1.9 ± 0.8	2.0 ± 0.7	6.5 ± 9.9	18.8 ± 23.5

Group A = invasive cancer; ratio 1 = T/B ratios of SUVmax at first time point; ratio 2 = T/B ratios of SUVmax at second time point; Δ% = percent change.

Data are presented as mean ± SD.

	Invasive cancer >10 mm	Invasive cancer 4-10 mm	Noninvasive cancer
Single-time	91%	57%	25%
Dual-time	90%	83%	77%

Dual Time Point ^{18}F-FDG PET Imaging Detects Breast Cancer with High Sensitivity and Correlates Well with Histologic Subtypes

J Nucl Med 2006; 47:1440–1446

Diagnosis of primary breast tumors

- **Dual-time-point**

  malignant lesion

TABLE 1

Single- and Dual-Time-Point Imaging SUVs in Patients with Malignant Lesions

Sample	Average SUV at time: 1	Average SUV at time: 2	% Change in average SUV	Histopathologic findings	Tumor grade	Size (cm)
1	1.2	1.4	16.7	IDC	Low	0.2
2	1.5	1.7	13.3	IDC	High	1.5
3	0.7	0.7	0	IDC + ILC	Moderate	3.5
4	0.6	0.7	16.7	IDC	Not known	1.0
5	1.1	0.9	−18.2	IDC	Moderate	0.2
6	3.0	3.3	10.0	IDC	High	2.0
7	2.1	2.3	9.5	IDC	Moderate	2.4
8	2.1	2.2	4.8	IDC + ILC	Low	4.0
9	1.4	1.6	14.3	IDC	Moderate	0.5
10	1.9	2.3	21.1	IDC	High	Not known
11	1.8	1.9	5.6	ILC + IDC	Moderate	1.5
12	0.8	0.9	12.5	IDC	Low	Not known
13	7.4	9.1	23.0	IDC	High	Not known
14	2.3	2.5	8.7	IDC	Moderate	2.9
15	1.8	2.0	11.1	IDC	Moderate	1.9
16	0.9	0.9	0	IDC	Moderate	1.6
17	2.0	2.3	15.0	IDC	Low	3.5
18	2.7	3.5	29.6	IDC + ILC	High	2.4
19	0.6	0.8	33.3	IDC	Low	1.6
20	11.7	15.7	34.2	IDC	High	2.6
21	0.7	0.8	14.3	IDC	Low	1.4
22	2.9	3.2	10.3	IDC	Moderate	2.1
23	15.3	20.0	30.7	IDC	High	2.8
24	5.7	5.9	3.5	IDC	High	1.9
25	0.7	0.7	0	IDC + ILC	Low	0.3
26	6.0	6.9	15.0	Medullary carcinoma	High	1.8
27	5.2	5.8	11.5	IDC	Moderate	2.5
28	2.2	2.4	9.1	IDC	High	2.2
29	1.5	1.7	13.3	IDC	Moderate	1.2
30	0.4	0.4	0	IDC	Moderate	0.4
31	2.5	2.6	4.0	IDC	High	0.5
32	2.5	2.7	8.0	IDC	Low	Not known
33	1.7	1.9	11.8	IDC + ILC	Low	Not known
34	1.4	1.7	21.4	IDC	Moderate	0.9
35	0.8	1.0	25	IDC	High	Not known
36	2.7	3.6	33.3	IDC	Moderate	1.0
37	6.2	7.7	24.2	IDC	Moderate	4.0
38	3.0	3.2	6.7	IDC	Moderate	Not known
39	3.3	3.0	−9.1	Adenocarcinoma	Not known	Not known
Mean	2.88	3.38	12.7			
SD	3.04	3.98	11.4			

IDC = invasive ductal carcinoma; ILC = invasive lobular carcinoma.

Potential of Dual-Time-Point Imaging to Improve Breast Cancer Diagnosis with 18F-FDG PET
J Nucl Med 2005; 46:1819–1824

Diagnosis of primary breast tumors

- **Dual-time-point**

  benign lesion

TABLE 2

Single- and Dual-Time-Point Imaging SUVs in Patients with Postbiopsy Inflammation

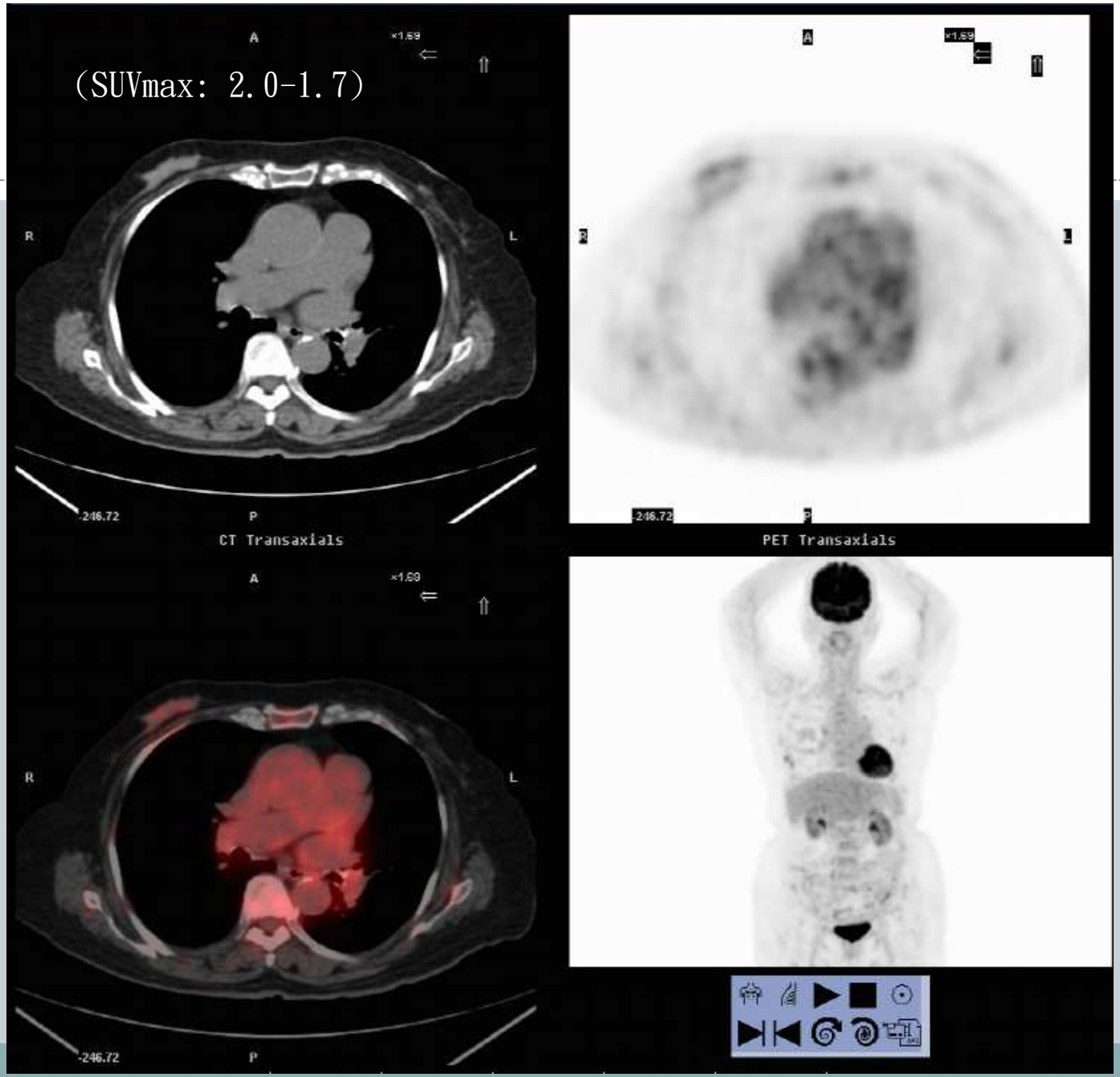
Sample	Average SUV at time: 1	Average SUV at time: 2	% Change in average SUV	Histopathologic findings
1	1.7	1.4	−0.176	No tumor, Bx Rx +
2	1.1	0.8	−0.273	Benign, Bx Rx +
3	1.5	1.9	0.267	No tumor, Bx Rx +, Ch Inf
4	1.3	1.1	−0.154	No tumor, Bx Rx +
5	1.0	0.7	−0.300	No tumor
6	1.3	1.2	−0.077	No tumor, Bx Rx +
7	1.0	0.8	−0.200	No tumor, Bx Rx +
8	1.0	1.1	0.100	Bx Rx +, proliferative fibroblasts
9	1.6	1.6	0	No tumor, Bx Rx +
10	1.5	1.3	−0.133	No tumor, Bx Rx +
11	1.0	0.8	−0.200	No tumor, Bx Rx +
12	0.8	0.6	−0.250	No tumor, Bx Rx +
13	1.4	1.3	−0.071	No tumor, Bx Rx +
14	1.5	1.4	−0.067	Benign, Bx Rx +
15	2.0	1.9	−0.050	No tumor, Bx Rx +
16	1.5	1.5	0	No tumor, Bx Rx +
17	1.5	1.7	0.133	Bx Rx, foreign-body giant-cell reaction
18	0.5	0.3	−0.400	No tumor, Bx Rx +
Mean	1.29	1.19	−0.103	
SD	0.36	0.45	0.166	

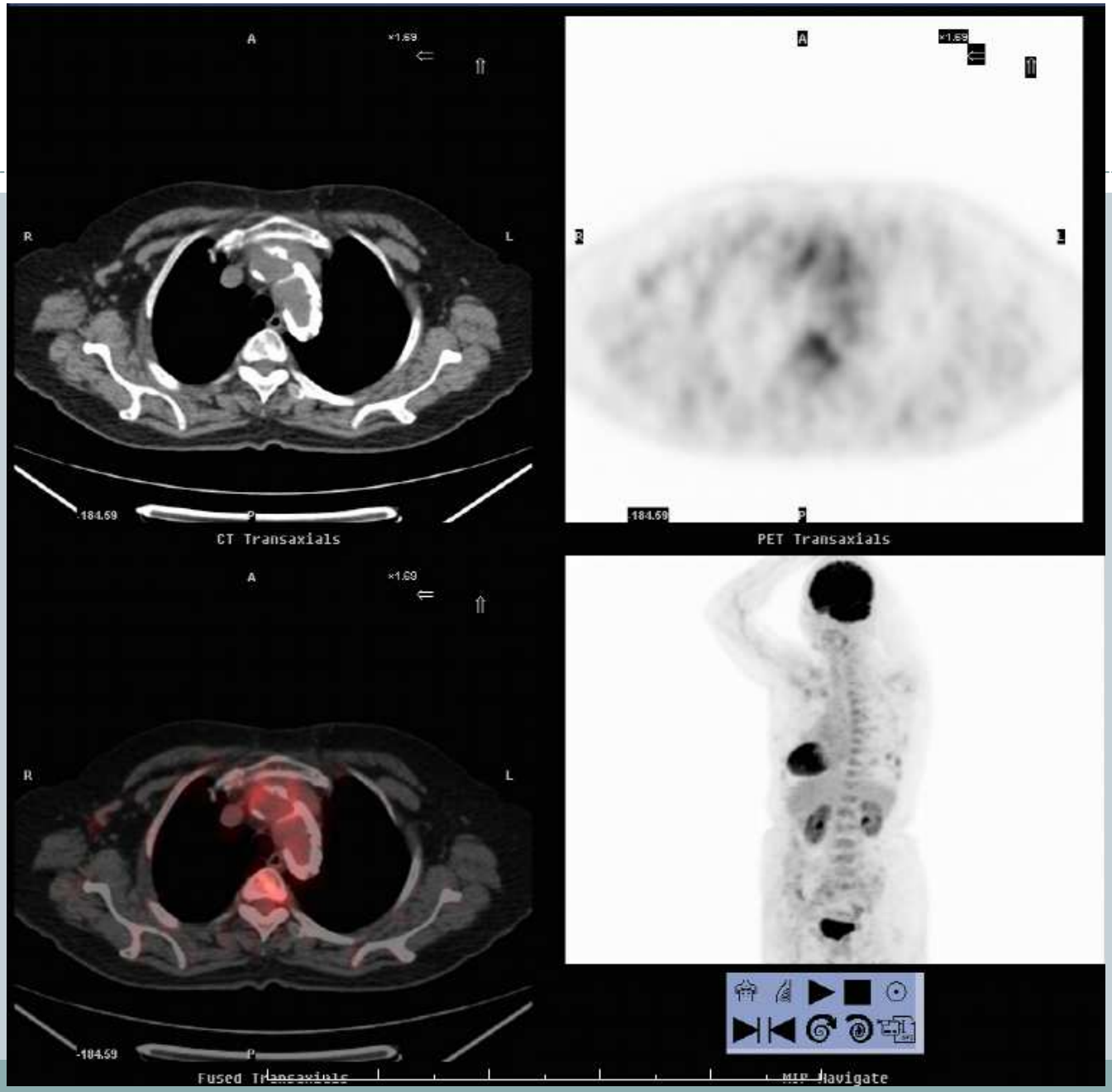
Bx Rx = biopsy reaction; Ch Inf = chronic inflammation.

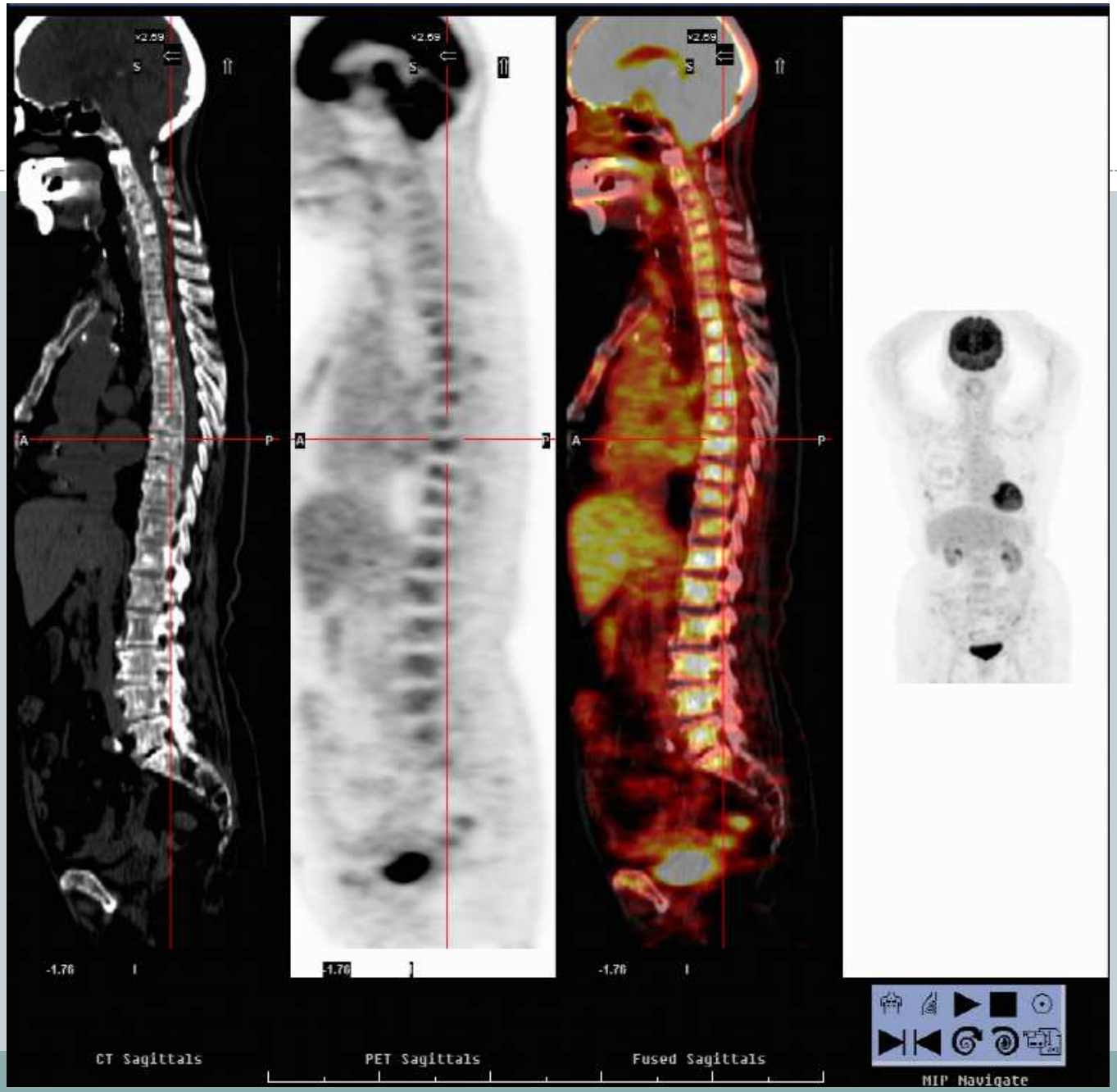
Potential of Dual-Time-Point Imaging to Improve Breast Cancer Diagnosis with 18F-FDG PET
J Nucl Med 2005; 46:1819–1824

Case

- 12203199
- 71 y/o female had right breast mass, suspected malignancy


(SUVmax: 2.0-1.7)
CT Transaxials
PET Transaxials


A
×1.69
R
L
-184.59
P
CT Transaxials
A
×1.69
P
L
184.69
P
PET Transaxials
A
×1.69
R
L
-184.59
P
Fused Transaxials
MIP Navigate


CT Sagittals
PET Sagittals
Fused Sagittals
MIP Navigate

Diagnosis of primary breast tumors

- Hayato Kaidaa et al:

  Improved breast cancer detection of **prone** breast FDG-PET in 118 patients

  total 114 cancer

  94 by supine PET, additional 10 by prone PET

Results Sensitivity, specificity, positive predictive value, NPV, and accuracy of whole-body PET images were 83, 50, 97, 17, and 80%, and of prone breast PET images they were 95, 50, 96, 43, and 93%. Ten of 114 breast cancerous lesions (8.8%) were detected on prone breast PET images alone.

Improved breast cancer detection of prone breast FDG-PET in 118 patients
Nuclear Medicine Communications 2008, 29:885–893

Diagnosis of primary breast tumors

Table 2 The characteristic performance of 10 cases detected by prone breast image alone

	Clinical staging	US (mm)	SUV max	Pathological staging	Histopathological findings
1	TisN0M0	18.6 × 10.0	1.3	T1N0M0	Papilotubular carcinoma
2	T1N0M0	9.6 × 6.0	1.4	T1N0M0	Papilotubular carcinoma
3	TisN0M0	9.6 × 3.3	1.2	T1N0M0	Papilotubular carcinoma
4	T2N0M0	14.0 × 9.0	2.4	T2N0M0	Papilotubular carcinoma
5	T1N0M0	11.5 × 6.7	1.1	T1N0M0	Papilotubular carcinoma
6	T2N0M0	22.0 × 9.0	1.1	T2N1M0	Invasive lobular carcinoma
7	T1N0M0	8.1 × 8.7	2.5	T1N0M0	Schirrous carcinoma
8	T1N0M0	11.3 × 13.8	1.3	T1N0M0	Invasive lobular carcinoma
9	T1N0M0	15.0 × 15.0	1.0	T1N0M0	Papilotubular carcinoma
10	T0N0M0	Not detected	1.8	T2N0M0	Papilotubular carcinoma

SUV max, maximum standardized uptake value; Tis, carcinoma *in situ*; US, ultrasound.

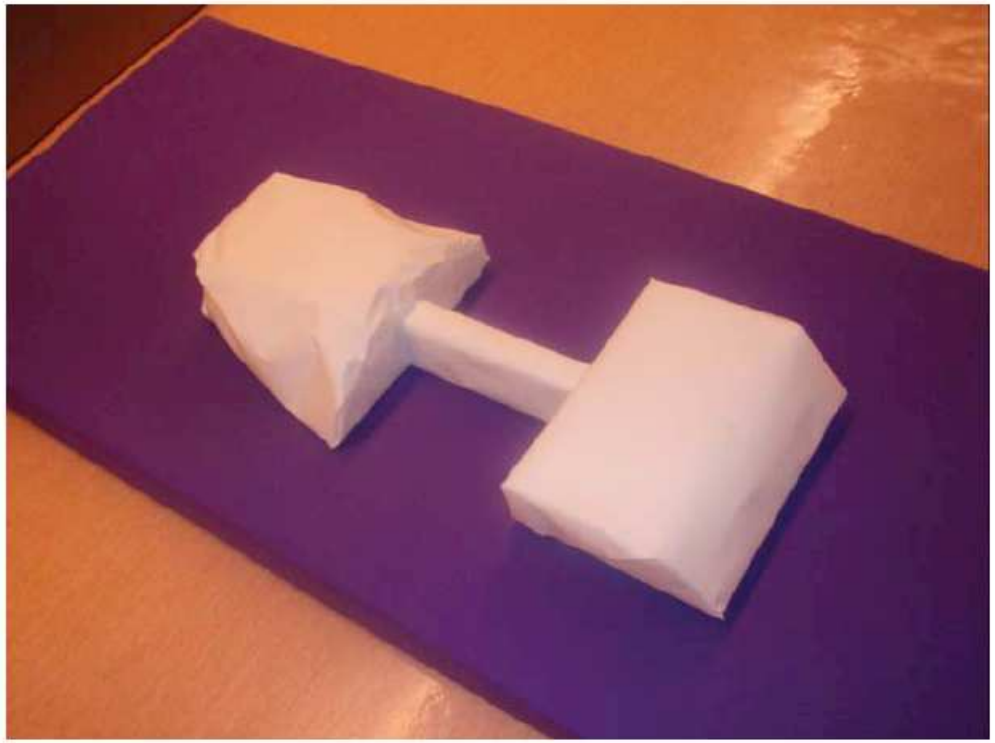
Table 1 The characteristics of 118 patients with 122 lesions

	Lesions (n=122)
Breast cancer	114
Clinical stage	
Stage 0	16
I	35
IIA	44
IIB	16
IIIA	1
IIIB	1
IIIC	1
IV	0
Surgical methods	
Conservative surgery	36
Modified radical mastectomy	72
Simple mastectomy	3
Tumor resection	3
Histopathological findings	
Papilotubular carcinoma	71
Schirrous carcinoma	21
Noninvasive ductal carcinoma	12
Mucinous carcinoma	5
Invasive lobular carcinoma	5
Pathological T stage	
Tis	8
T1	45
T2	52
T3	8
T4	1
Benign tumor	8
Histopathological findings	
Fibroadenoma	2
Intraductal papiloma	1
Adenosis	1
Others	4

Others, others were diagnosed as benign by biopsy; Tis, carcinoma *in situ*; however, the histopathological findings were not identified. These four cases were followed up for 2 years, however, malignant findings were not detected.

Improved breast cancer detection of prone breast FDG-PET in 118 patients
Nuclear Medicine Communications 2008, 29:885–893

Diagnosis of primary breast tumors

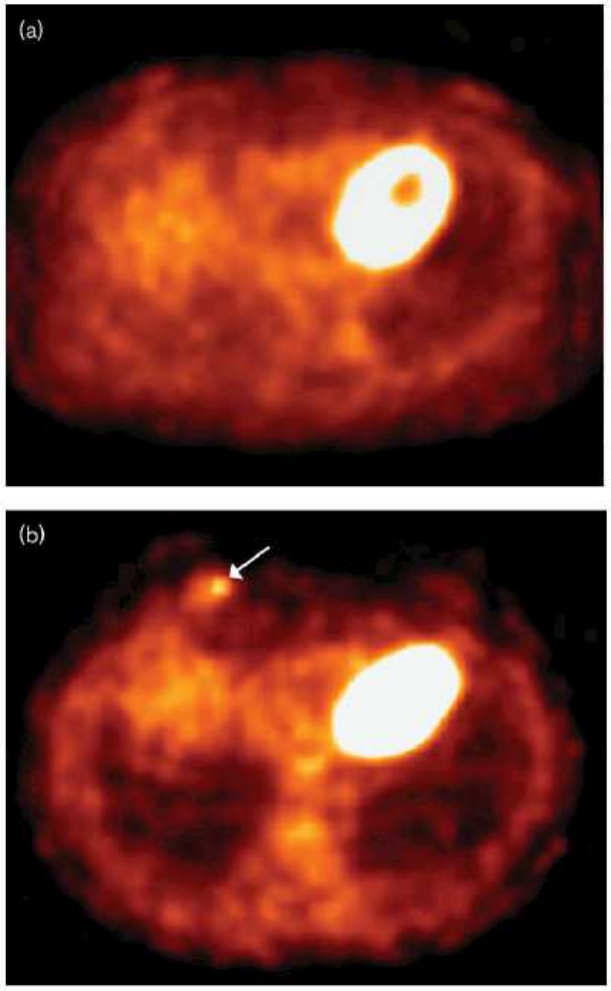


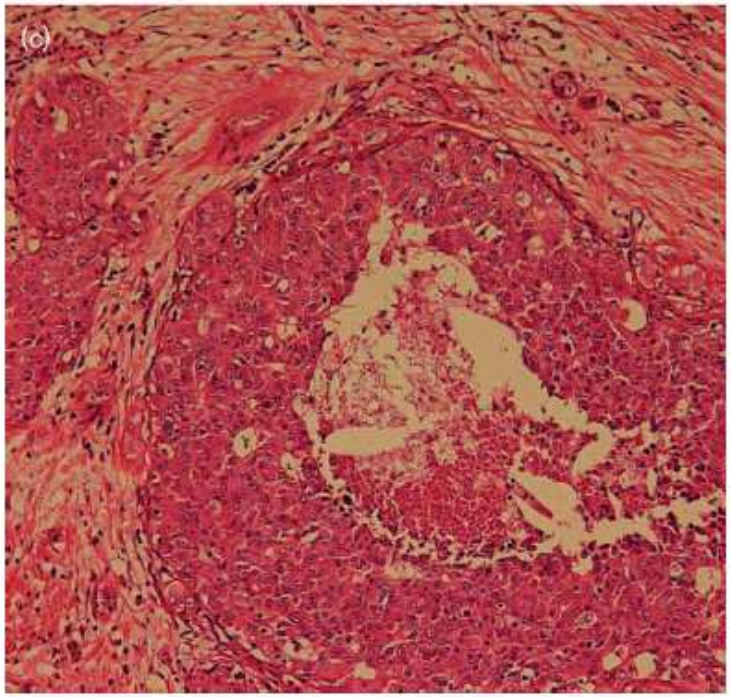
This figure shows our breast-positioning device. The patients were in the prone position with their arms at their sides. For positioning, a foam cushion on the scanner table was adapted with a hole that allows the breasts to be unconstrained.

Improved breast cancer detection of prone breast FDG-PET in 118 patients
Nuclear Medicine Communications 2008, 29:885–893

Diagnosis of primary breast tumors

Diagnosis of primary breast tumors

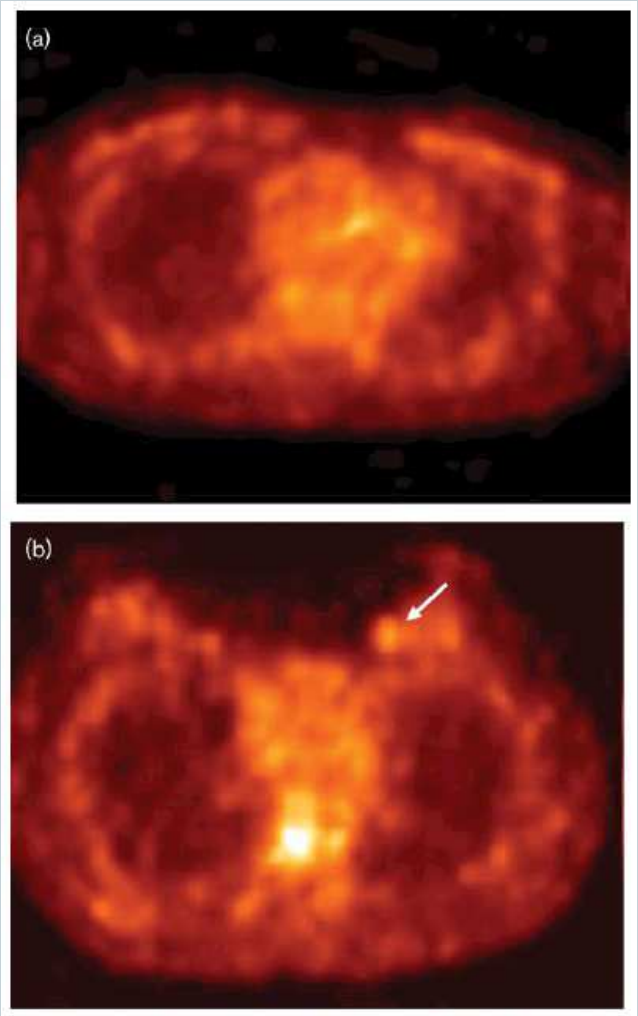


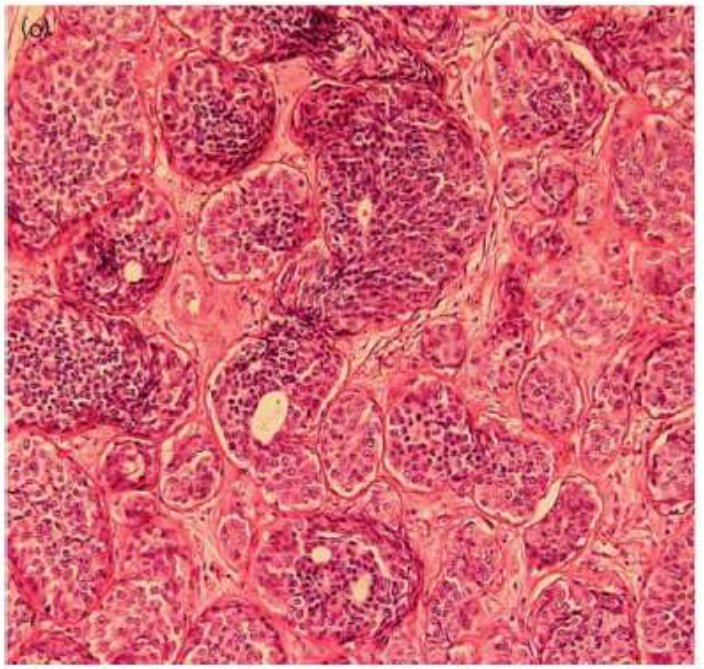


False-negative breast cancer in the whole-body PET image but a true positive in the prone breast PET image of a 56-year-old woman with breast cancer stage I. (a) ^{18}F-FDG avid lesions were not detected on the axial image of the whole-body PET image. (b) ^{18}F-FDG was accumulated in the right mammary gland on the axial image of the prone breast PET image (FDG-SUV max 1.2) (arrow). (c) The postoperative microscopic findings show papilotubular carcinoma (hematoxylin and eosin × 200). ^{18}F-FDG, fluorine-18 fluorodeoxyglucose; max, maximum; SUV, standardized uptake value.

Improved breast cancer detection of prone breast FDG-PET in 118 patients
Nuclear Medicine Communications 2008, 29:885–893

Diagnosis of primary breast tumors





False-negative breast cancer in the whole-body PET image but a true positive in the prone breast PET image in a 49-year-old woman with breast cancer stage 0. (a) ^{18}F-FDG avid lesions were not seen on the axial image of the whole-body PET image. (b) ^{18}F-FDG was accumulated in the left mammary gland on the axial image of the prone breast PET image (FDG-SUV max 1.8) (arrow). (c) The postoperative microscopic findings show papilotubular carcinoma (hematoxylin and eosin × 200). ^{18}F-FDG, fluorine-18-fluorodeoxyglucose; max, maximum; SUV, standardized uptake value.

Improved breast cancer detection of prone breast FDG-PET in 118 patients
Nuclear Medicine Communications 2008, 29:885–893

Diagnosis of primary breast tumors

- Dual-time-point + prone PET/CT *vs* Dynamic MRI

TABLE 2: MRI and Early and Late PET Results in 35 Malignant and Benign Lesions with a Diameter > 10 mm

Performance	MRI	Early PET	Late PET
Accuracy (%)	97 (91–100)	77 (63–92)	89 (78–100)
Sensitivity (%)	100 (87–100)	75 (56–88)	88 (70–96)
Specificity (%)	67 (13–98)	100 (31–100)	100 (31–100)

Note—Data in parentheses are 95% CIs. PET was performed with patient in prone position.

TABLE 3: MRI and Early and Late PET Results in 20 Malignant and Benign Lesions with a Diameter < 10 mm

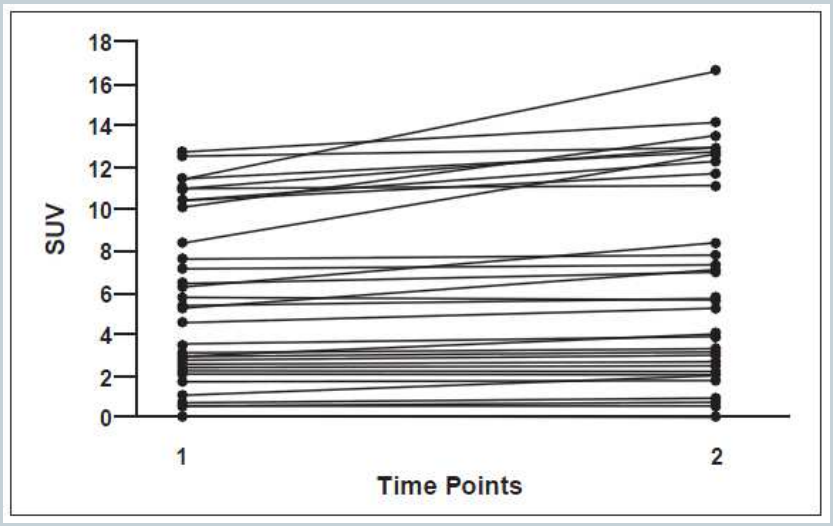
Performance	MRI	Early PET	Late PET
Accuracy (%)	90 (76–100)	55 (32–78)	75 (55–95)
Sensitivity (%)	92 (62–100)	31 (10–61)	62 (32–85)
Specificity (%)	86 (42–100)	100 (56–100)	100 (56–100)

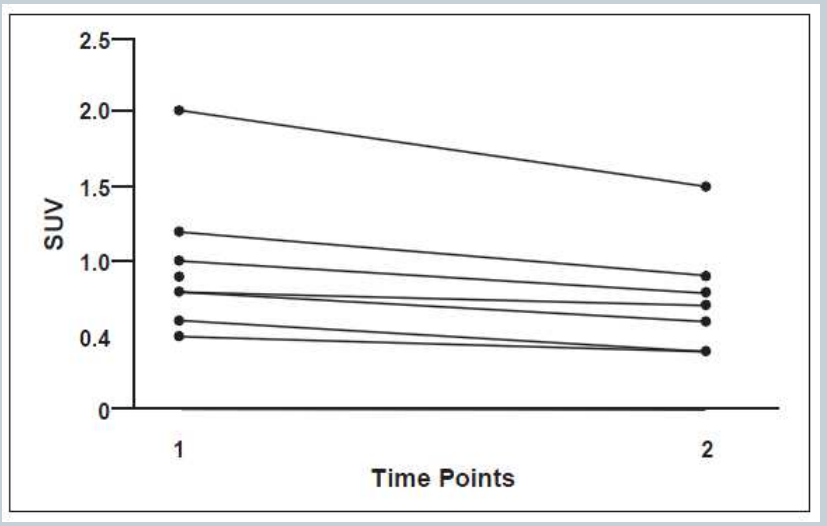
Note—Data in parentheses are 95% CIs. PET was performed with patient in prone position.

Dual-Time-Point 18F-FDG PET/CT Versus Dynamic Breast MRI of Suspicious Breast Lesions
AJR 2008; 191:1323–1330

Diagnosis of primary breast tumors

- Malignancy *vs* Benign tumor



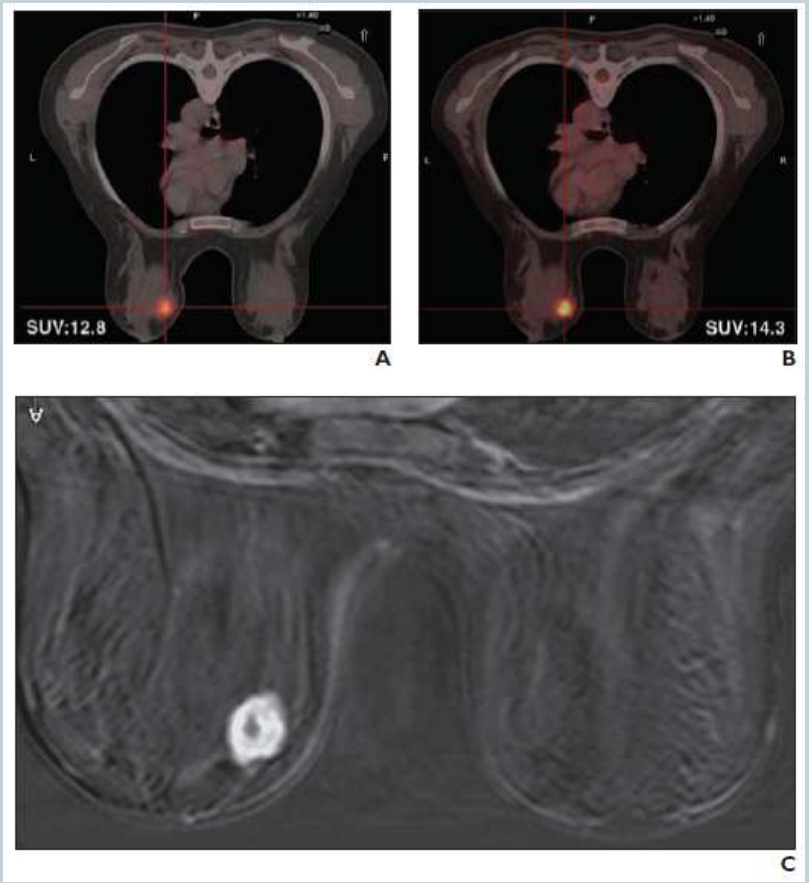


SUVmax ≥2.5 *or* ΔSUVmax>0

Dual-Time-Point 18F-FDG PET/CT Versus Dynamic Breast MRI of Suspicious Breast Lesions
AJR 2008; 191:1323–1330

Diagnosis of primary breast tumors

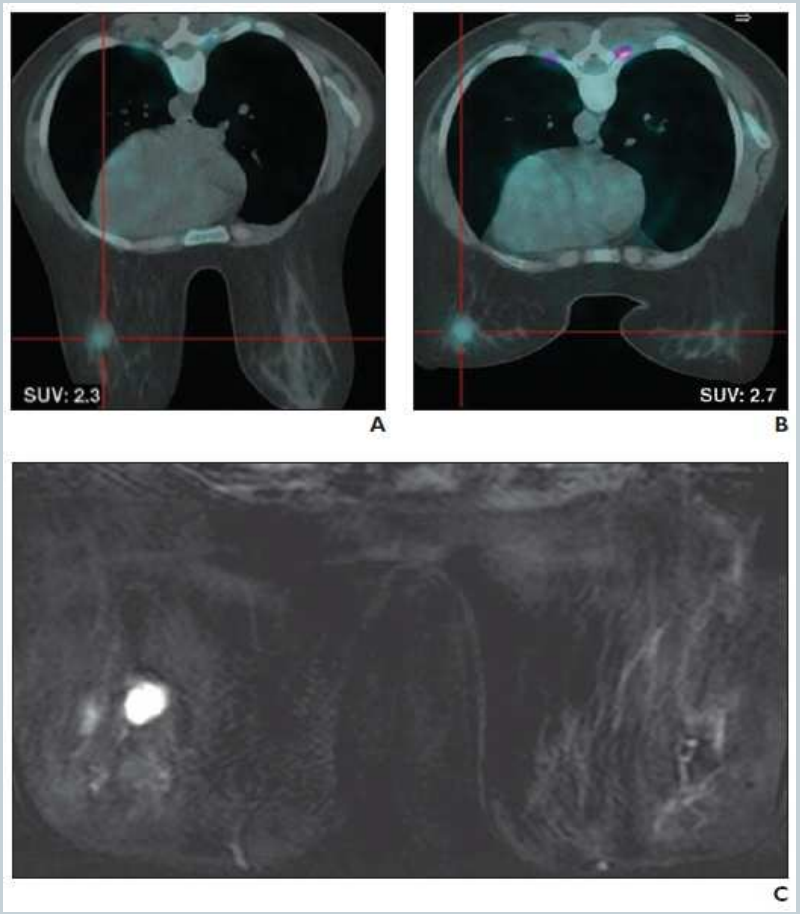
- Invasive ductal carcinoma



Dual-Time-Point 18F-FDG PET/CT Versus Dynamic Breast MRI of Suspicious Breast Lesions
AJR 2008; 191:1323–1330

Diagnosis of primary breast tumors

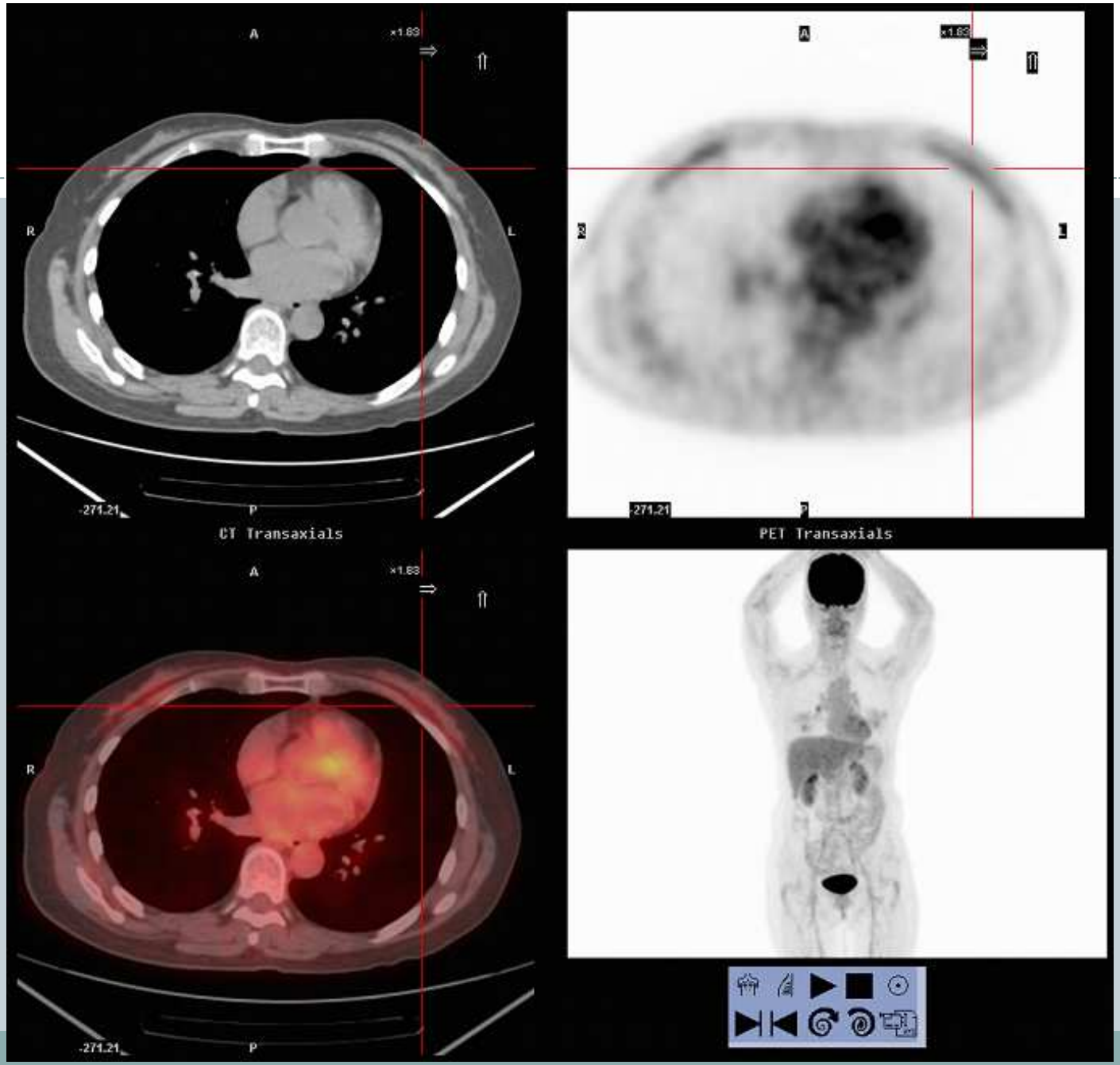
- Invasive lobular carcinoma

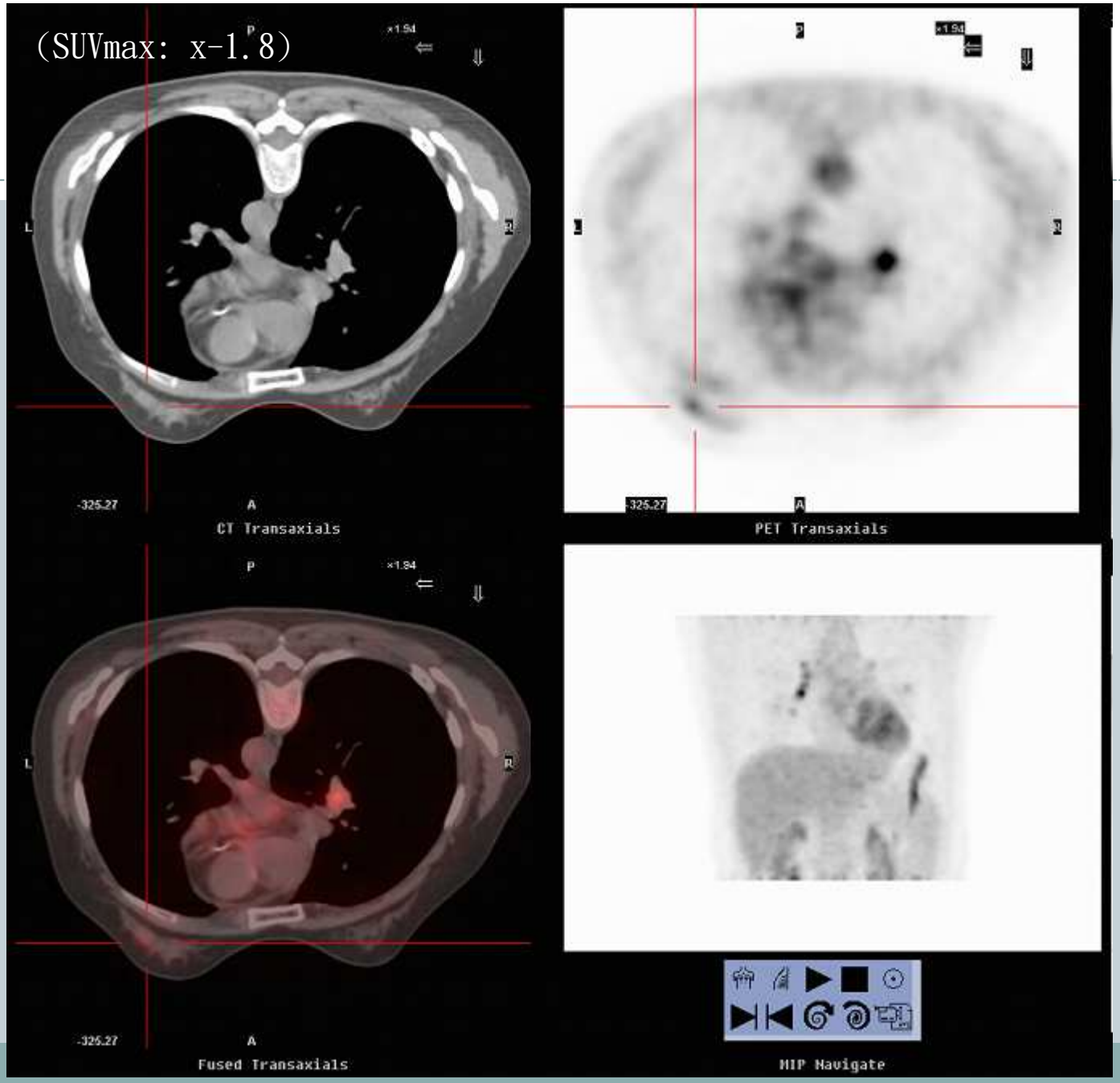


Dual-Time-Point 18F-FDG PET/CT Versus Dynamic Breast MRI of Suspicious Breast Lesions
AJR 2008; 191:1323–1330

case

- 10499408
- 54 y/o female is for physical check-up
- intraductal carcinoma of left breast


A
×1.83
R
L
-271.21
P
CT Transaxials
A
×1.83
R
L
-271.21
P
A
×1.83
-271.21
P
PET Transaxials


(SUVmax: x-1.8)
CT Transaxials
PET Transaxials
Fused Transaxials
MIP Navigate

Diagnosis of primary breast tumors

- FDG PEM

Figure 1. PET mammography system and mammography gantry. Film holder has been rotated to the right side to make room for lower detector (arrow). Upper detector (arrowhead) is positioned above compression paddle, which compresses the breast against the lower detector. (Reprinted, with permission, from reference 17.)

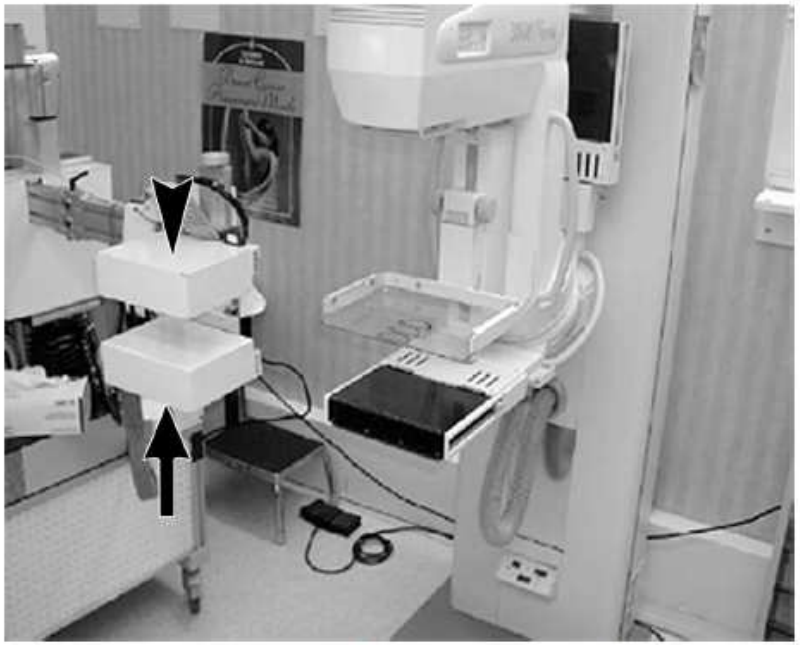


Figure 2. PET mammography detector interfacing with mammography gantry. Upper detector (arrowhead) can be moved vertically toward or away from lower detector (arrow). In addition, the entire detector assembly can be pivoted, allowing acquisition of oblique views. Finally, the entire gantry can be moved up and down by using a motorized control to adjust to the height of each patient (Reprinted, with permission, from reference 17.)

Diagnosis of primary breast tumors

- FDG PEM

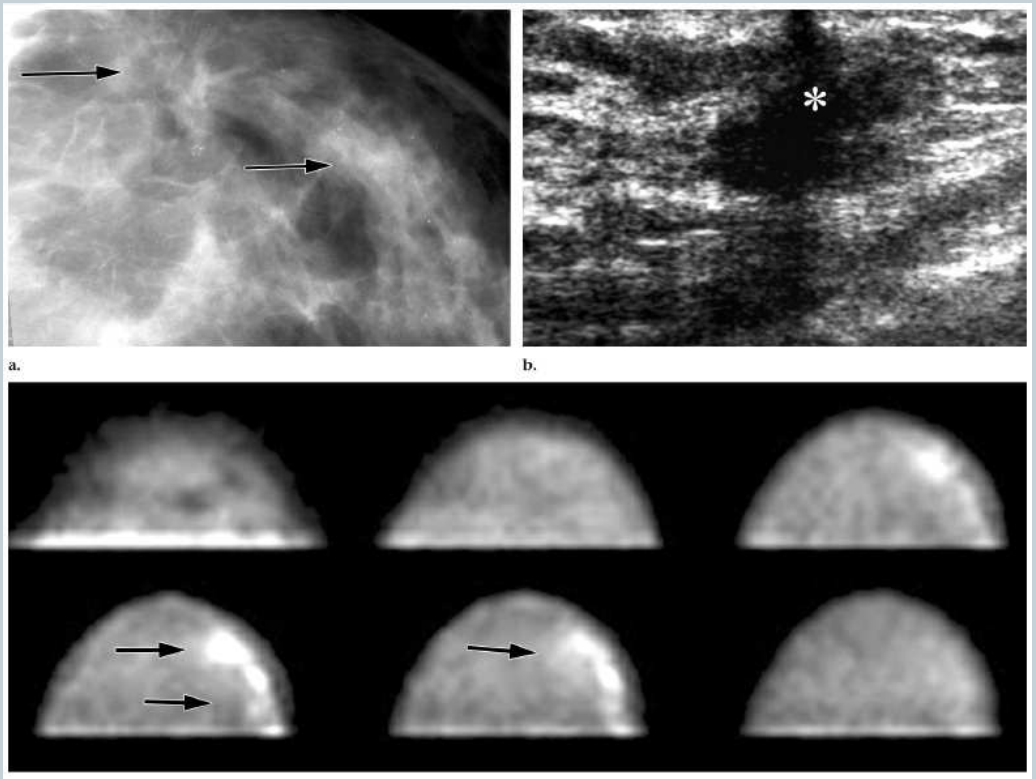
Table 1
Summary of the Results of Published FDG PEM Studies

Authors and Year of Study	No. of Patients	Average Lesion Size (cm)*	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Murthy et al 2000	18	NA	50	100	100	67
Levine et al 2003	14	2.0 (1.0–5.5)	86	91	86	91
Rosen et al 2005	23	2.1 (0.4–4.6)	86	33†	90	25†
Tafra et al 2005	44 + 10	2.2‡ (0.1–10.0)	88	NA	NA	45
Berg et al 2006	92	2.1‡ (0.3–10.0)	90	86	88	88
Rosen et al 2006	50	1.4 (0.8–4.0)	87	70	71	86

Note.—NA = not available, NPV = negative predictive value, PPV = positive predictive value.
*Numbers in parentheses are ranges.
†Only two of 23 were true negative, according to Breast Imaging Reporting and Data System criterion 5 only.
‡Median size, invasive lesions only.

Diagnosis of primary breast tumors

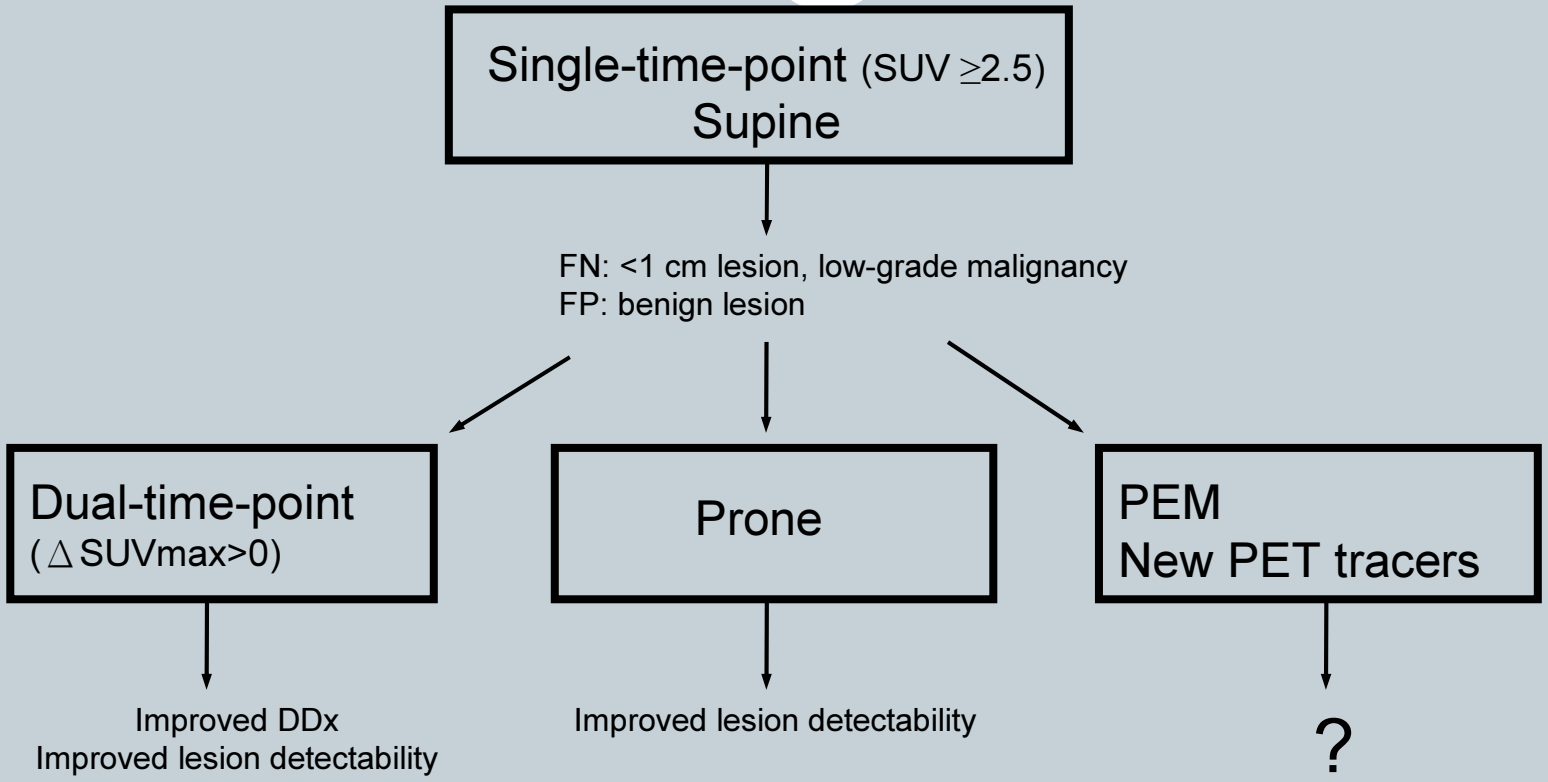
- FDG PEM



a. b. c.

Figure 4. Images of a 38-year-old woman with T1cN1M0 breast carcinoma in the right breast. **(a)** Spot-compression magnification conventional mammogram demonstrates architectural distortion and segmentally distributed microcalcifications (arrows). **(b)** US scan demonstrates an irregular 1.4-cm mass (*). **(c)** Transverse PET mammography image demonstrates segmental increased FDG activity (arrows) that mirrors the mammographic abnormality. Histologic examination demonstrated a 1.6-cm invasive adenocarcinoma with extensive ductal carcinoma in situ.

Diagnosis of primary breast tumors



Breast cancer staging (AJCC 7th edition)

Table 1

American Joint Committee on Cancer (AJCC)
TNM Staging System For Breast Cancer

Primary Tumor (T)

Definitions for classifying the primary tumor (T) are the same for clinical and for pathologic classification. If the measurement is made by the physical examination, the examiner will use the major headings (T1, T2, or T3). If other measurements, such as mammographic or pathologic measurements, are used, the subsets of T1 can be used. Tumors should be measured to the nearest 0.1 cm increment.

TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ
Tis (DCIS)	Ductal carcinoma in situ
Tis (LCIS)	Lobular carcinoma in situ
Tis (Paget's)	Paget's disease of the nipple with no tumor

Note: Paget's disease associated with a tumor is classified according to the size of the tumor.

T1		Tumor 2 cm or less in greatest dimension
	T1mic	Microinvasion 0.1 cm or less in greatest dimension
	T1a	Tumor more than 0.1 cm but not more than 0.5 cm in greatest dimension
	T1b	Tumor more than 0.5 cm but not more than 1 cm in greatest dimension
	T1c	Tumor more than 1 cm but not more than 2 cm in greatest dimension
T2		Tumor more than 2 cm but not more than 5 cm in greatest dimension
T3		Tumor more than 5 cm in greatest dimension
T4		Tumor of any size with direct extension to (a) chest wall or (b) skin, only as described below
	T4a	Extension to chest wall, not including pectoralis muscle
	T4b	Edema (including peau d'orange) or ulceration of the skin of the breast, or satellite skin nodules confined to the same breast
	T4c	Both T4a and T4b
	T4d	Inflammatory carcinoma

Regional Lymph Nodes (N)

Clinical

NX		Regional lymph nodes cannot be assessed (e.g., previously removed)
N0		No regional lymph node metastasis
N1		Metastasis to movable ipsilateral axillary lymph node(s)
N2		Metastases in ipsilateral axillary lymph nodes fixed or matted, or in *clinically apparent** ipsilateral internal mammary nodes in the *absence* of clinically evident axillary lymph node metastasis
	N2a	Metastases in ipsilateral axillary lymph nodes fixed to one another (matted) or to other structures
	N2b	Metastasis only in *clinically apparent** ipsilateral internal mammary nodes and in the *absence* of clinically evident axillary lymph node metastasis
N3		Metastasis in ipsilateral infraclavicular lymph node(s) with or without axillary lymph node involvement, or in *clinically apparent** ipsilateral internal mammary lymph node(s) and in the *presence* of clinically evident axillary lymph node metastasis; or metastasis in ipsilateral supraclavicular lymph node(s) with or without axillary or internal mammary lymph node involvement
	N3a	Metastasis in ipsilateral infraclavicular lymph node(s)
	N3b	Metastasis in ipsilateral internal mammary lymph node(s) and axillary lymph node(s)
	N3c	Metastasis in ipsilateral supraclavicular lymph node(s)

**Clinically apparent* is defined as detected by imaging studies (excluding lymphoscintigraphy) or by clinical examination or grossly visible pathologically.

Staging continued on next page (ST-2)

Breast cancer staging (AJCC 7th edition)

Table 1 (continued)

Pathologic (pN)*

pNX	Regional lymph nodes cannot be assessed (e.g., previously removed, or not removed for pathologic study)
pN0	No regional lymph node metastasis histologically, no additional examination for isolated tumor cells (ITC)

Note: Isolated tumor cells (ITC) are defined as single tumor cells or small cell clusters not greater than 0.2 mm, usually detected only by immonohistochemical (IHC) or molecular methods but which may be verified on H&E stains. ITCs do not usually show evidence of malignant activity e.g., proliferation or stromal reaction.

pN0(i-)	No regional lymph node metastasis histologically, negative IHC
pN0(i+)	No regional lymph node metastasis histologically, positive IHC, no IHC cluster greater than 0.2 mm
pN0(mol-)	No regional lymph node metastasis histologically, negative molecular findings (RT-PCR)[b]
pN0(mol+)	No regional lymph node metastasis histologically, positive molecular findings (RT-PCR)[b]

*Classification is based on axillary lymph node dissection with or without sentinel lymph node dissection. Classification based solely on sentinel lymph node dissection without subsequent axillary node dissection is designated (sn) for "sentinel node," e.g., pN0(i+) (sn).

[b] RT-PCR: reverse transcriptase/polymerase chain reaction.

pN1	Metastasis in 1 to 3 axillary lymph nodes, and/or in internal mammary nodes with microscopic disease detected by sentinel lymph node dissection but not *clinically apparent***
pN1mi	Micrometastasis (greater than 0.2 mm, none greater than 2.0 mm)
pN1a	Metastasis in 1 to 3 axillary lymph nodes
pN1b	Metastasis in internal mammary nodes with microscopic disease detected by sentinel lymph node dissection but not *clinically apparent***
pN1c	Metastasis in 1 to 3 axillary lymph nodes and in internal mammary nodes with microscopic disease detected by sentinel lymph node dissection but not *clinically apparent*.** (If associated with greater than 3 positive axillary lymph nodes, the internal mammary nodes are classified as pN3b to reflect increased tumor burden)
pN2	Metastasis in 4 to 9 axillary lymph nodes, or in *clinically apparent** internal mammary lymph nodes in the *absence* of axillary lymph node metastasis
pN2a	Metastasis in 4 to 9 axillary lymph nodes (at least one tumor deposit greater than 2.0 mm)
pN2b	Metastasis in *clinically apparent** internal mammary lymph nodes in the *absence* of axillary lymph node metastasis
pN3	Metastasis in 10 or more axillary lymph nodes, or in infraclavicular lymph nodes, or in *clinically apparent** ipsilateral internal mammary lymph nodes in the *presence* of 1 or more positive axillary lymph nodes; or in more than 3 axillary lymph nodes with clinically negative microscopic metastasis in internal mammary lymph nodes; or in ipsilateral supraclavicular lymph nodes
pN3a	Metastasis in 10 or more axillary lymph nodes (at least one tumor deposit greater than 2.0 mm), or metastasis to the infraclavicular lymph nodes
pN3b	Metastasis in *clinically apparent** ipsilateral internal mammary lymph nodes in the *presence* of 1 or more positive axillary lymph nodes; or in more than 3 axillary lymph nodes and in internal mammary lymph nodes with microscopic disease detected by sentinel lymph node dissection but not *clinically apparent***
pN3c	Metastasis in ipsilateral supraclavicular lymph nodes

* *Clinically apparent* is defined as detected by imaging studies (excluding lymphoscintigraphy) or by clinical examination.

** *Not clinically apparent* is defined as not detected by imaging studies (excluding lymphoscintigraphy) or by clinical examination.

Staging continued on next page (ST-3)

Breast cancer staging (AJCC 7th edition)

Table 1 (continued)

Distant Metastasis (M)

MX	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis

STAGE GROUPING

Stage 0	Tis	N0	M0	**Stage IIIB**	T4	N0	M0
Stage I	T1*	N0	M0		T4	N1	M0
Stage IIA	T0	N1	M0		T4	N2	M0
	T1*	N1	M0	**Stage IIIC**	Any T	N3	M0
	T2	N0	M0	**Stage IV**	Any T	Any N	M1
Stage IIB	T2	N1	M0				
	T3	N0	M0				
Stage IIIA	T0	N2	M0				
	T1*	N2	M0				
	T2	N2	M0				
	T3	N1	M0				
	T3	N2	M0				

* T1 includes T1mic

Note: Stage designation may be changed if post-surgical imaging studies reveal the presence of distant metastases, provided that the studies are carried out within 4 months of diagnosis in the absence of disease progression and provided that the patient has not received neoadjuvant therapy.

HISTOPATHOLOGIC TYPE

The histopathologic types are the following:

In situ Carcinomas

NOS (not otherwise specified)
Intraductal
Paget's disease and intraductal

Invasive Carcinomas

NOS
Ductal
Inflammatory
Medullary, NOS
Medullary with lymphoid stroma
Mucinous
Papillary (predominantly micropapillary pattern)
Tubular
Lobular
Paget's disease and infiltrating
Undifferentiated
Squamous cell
Adenoid cystic
Secretory
Cribriform

HISTOPATHOLOGIC GRADE (G)

All invasive breast carcinomas with the exception of medullary carcinoma should be graded. The Nottingham combined histologic grade (Elston-Ellis modification of Scarff-Bloom-Richardson grading system) is recommended.[1,2] The grade for a tumor is determined by assessing morphologic features (tubule formation, nuclear pleomorphism, and mitotic count), assigning a value of 1 (favorable) to 3 (unfavorable) for each feature, and adding together the scores for all three categories. A combined score of 3-5 points is grade 1; a combined score of 6-7 points is grade 2; a combined score of 8-9 points is grade 3.

[1] Elston CW, Ellis IO. Pathological prognostic factors in breast cancer. I. The value of histologic grade in breast cancer: experience from a large study with long-term follow-up. Histopathology 1991;19:403-410.

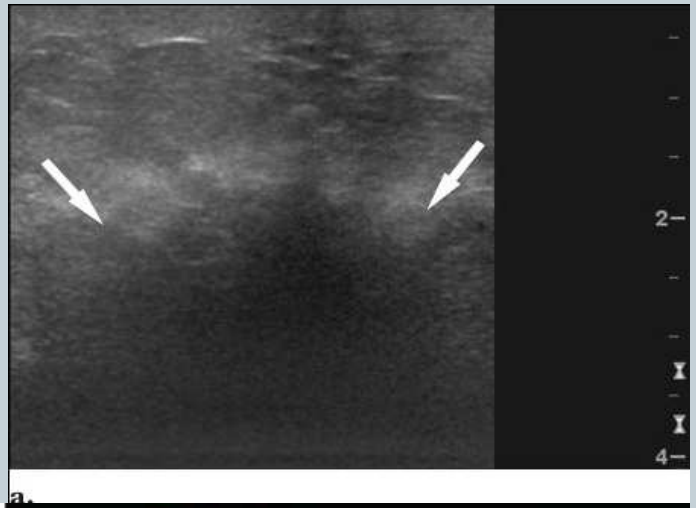
[2] Fitzgibbons PL, Page DL, Weaver D et al. Prognostic factors in breast cancer. College of American Pathologists consensus statement 1999. Arch Pathol Lab Med 2000;124:966-978.

HISTOLOGIC GRADE (NOTTINGHAM COMBINED HISTOLOGIC GRADE IS RECOMMENDED)

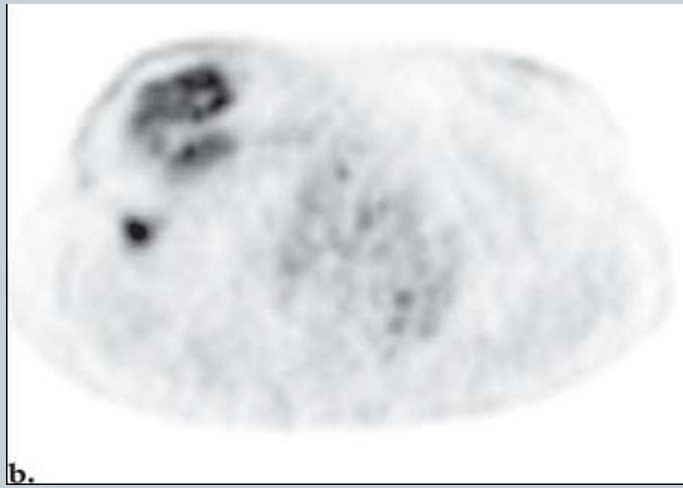
GX	Grade cannot be assessed
G1	Low combined histologic grade (favorable)
G2	Intermediate combined histologic grade (moderately favorable)
G3	High combined histologic grade (unfavorable)

Breast cancer T staging

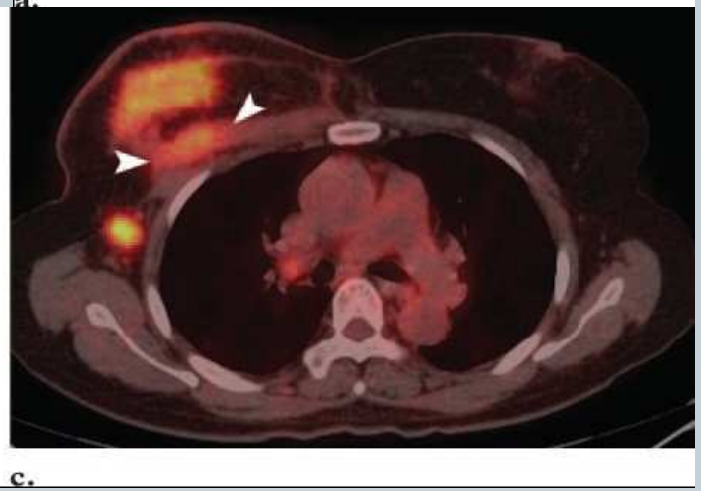
1. tumor size ?
2. local invasion



a.



b.



c.

Breast cancer N staging

- Axillary nodal status is important for treatment planning and prognosis, even microscopic metastasis

- There is currently no clinical role for routine FDG PET axillary staging in early stage breast cancer, because of low sensitivity for axillary nodal metastasis (can not replace sentinel LN sampling).

- Because of high specificity for axillary metastasis, there may be a clinical role for preoperative FDG PET in locally advanced breast cancer, which helps accurately determine the extent of nodal metastasis (especially extra-axillary LNs).

Breast cancer N staging

- early studies *vs* prospective multicenter trial

Table 2
Results of Early Studies of FDG PET in Axillary Nodal Staging versus Results of a Multicenter Trial

Authors and Year of Study	No. of Patients	Sensitivity (%)	Specificity (%)
Utech et al 1996	124	100	75
Avril et al 1996	51	79	96
Adler et al 1997	52	95	66
Smith et al 1998	50	90	97
Crippa et al 1998	68	85	91
Wahl et al 2004	308	61	80

Note.—Results of the early studies suggested high sensitivity and high specificity for nodal disease; these were not found in the 2004 multicenter trial, which evaluated 360 women with newly diagnosed breast carcinoma (axillae were assessed in only 308 patients). In the later trial, almost 50% of the women had small T1 breast cancers, whereas the earlier trials were biased toward larger primary lesions.

Breast cancer N staging

Table 1. Largest Prospective Series of Axillary Nodal Staging with Positron Emission Tomography Using ^{18}F-fluorodeoxyglucose in Breast Cancer

Series	Number of Patients	Sensitivity	Specificity
Tse[13]	10	57 (4/7)	100 (3/3)
Adler 1997[14]	52	95 (19/20)	66 (21/32)
Utech[42]	122	100 (44/44)	75 (60/80)
Avril[43] overall	51	79 (19/24)	96 (26/27)
T1 tumors	18	33 (2/6)	100 (12/12)
>T1 tumors	23	94 (17/18)	100 (5/5)
Crippa[26]	72	85 (23/27)	91 (41/45)
Smith[44]	50	90 (19/21)	97 (28/29)
Greco[45]	167	94 (68/72)	86 (82/95)
Schirrmeister[84]	113	79 (27/34)	92 (73/79)
Wahl[46]	308	61	80

Numbers in parentheses are patient numbers used to derive sensitivity and specificity values.

Breast cancer N staging

- early-stage breast cancer

  FDG PET *vs* sentinel LN biopsy

Table 3
Results of Studies of FDG PET in Staging Axillary Nodal Disease

Authors and Year of Study	No. of Patients	Sensitivity (%)	Specificity (%)
van der Hoeven et al 2002	80	25	97
Keleman et al 2003	15	20	94
Barranger et al 2003	32	20	100
Wahl et al 2004	308	61	80
Zornoza et al 2004	200	84	98
Fehr et al 2004	30	20	93
Lovrics et al 2004	98	40	97
Kumar et al 2006	80	44	95
Gil-Rendo et al 2006	275	84	98
Chung et al 2006	54	60	100

Note.—Recent studies demonstrate a consistently high specificity for axillary nodal metastases but lower sensitivity compared with that of sentinel lymph node biopsy. FDG PET is not sufficient for exclusion of axillary metastases, which requires histologic evaluation.

Breast cancer N staging

- early-stage breast cancer

  FDG PET *vs* sentinel LN biopsy

Table 3
Results of Studies of FDG PET in Staging Axillary Nodal Disease

Authors and Year of Study	No. of Patients	Sensitivity (%)	Specificity (%)
van der Hoeven et al 2002	80	25	97
Keleman et al 2003	15	20	94
Barranger et al 2003	32	20	100
Wahl et al 2004	308	61	80
Zornoza et al 2004	200	84	98
Fehr et al 2004	30	20	93
Lovrics et al 2004	98	40	97
Kumar et al 2006	80	44	95
Gil-Rendo et al 2006	275	84	98
Chung et al 2006	54	60	100

Note.—Recent studies demonstrate a consistently high specificity for axillary nodal metastases but lower sensitivity compared with that of sentinel lymph node biopsy. FDG PET is not sufficient for exclusion of axillary metastases, which requires histologic evaluation.

Breast cancer N staging

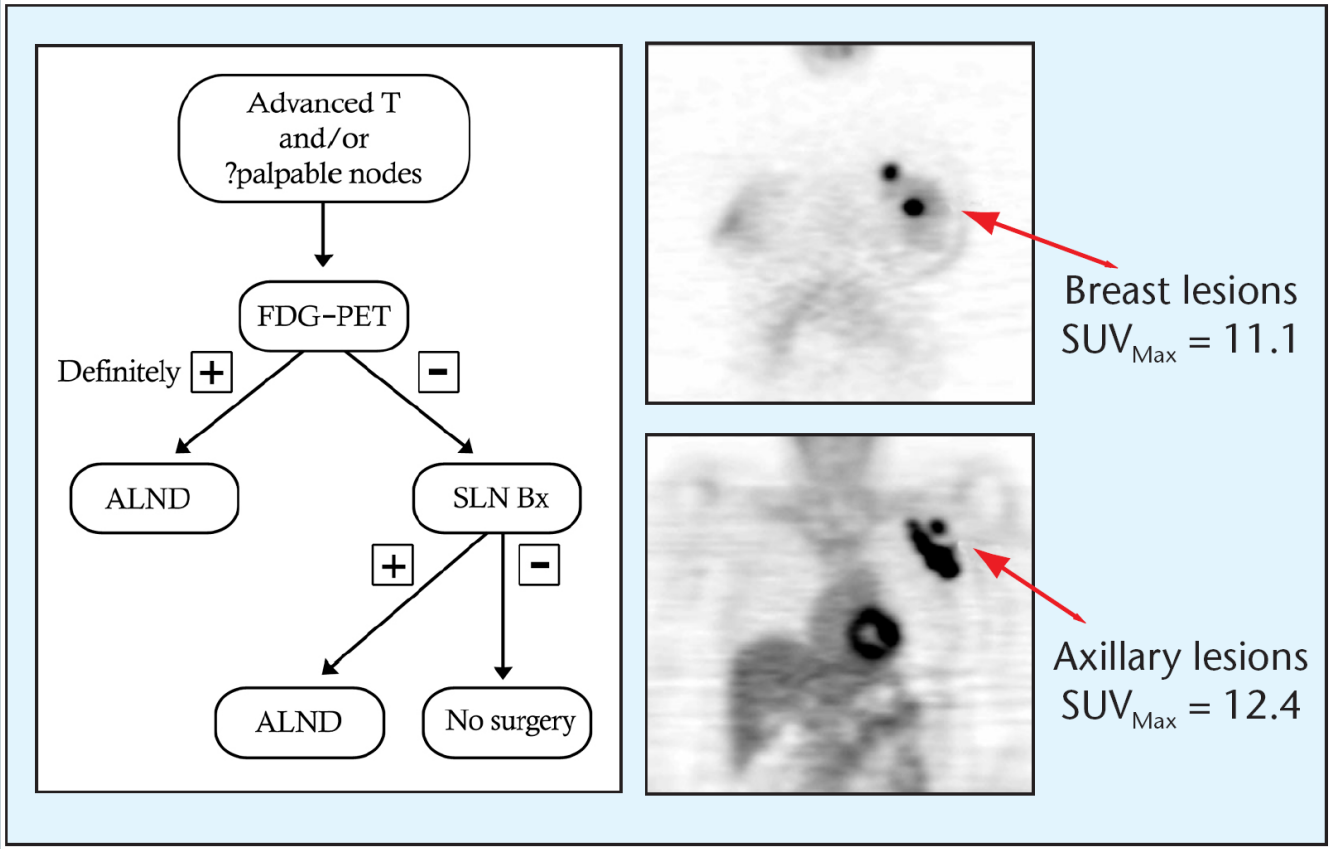
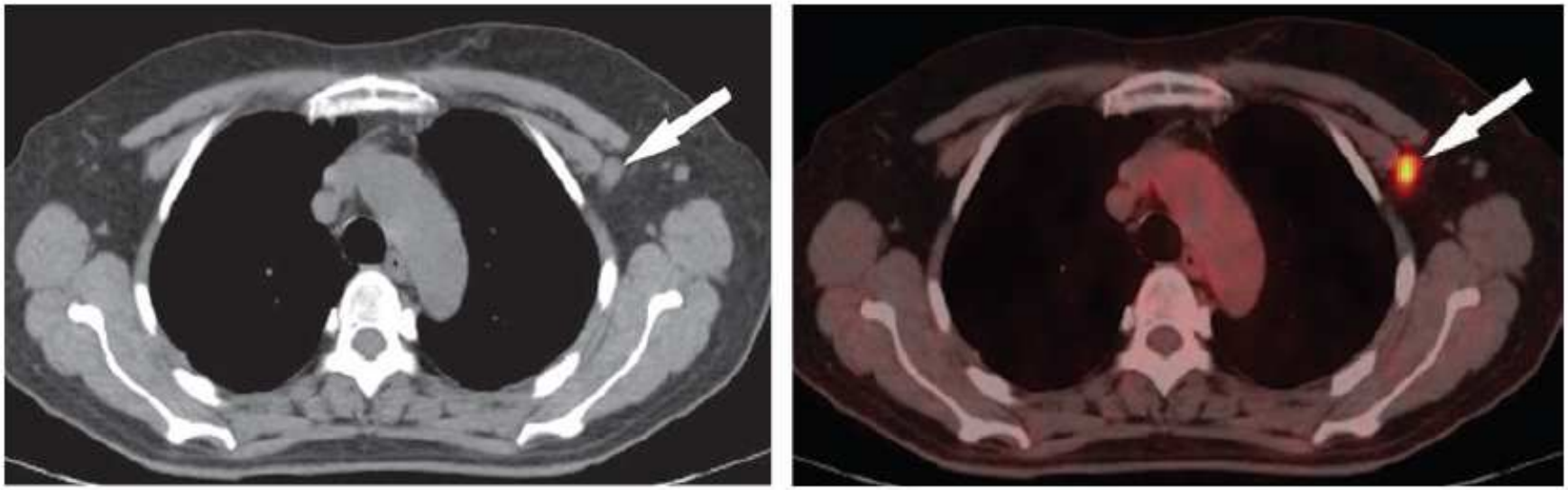


Figure 2. A potential algorithm that may be cost effective in patients with more advanced T-stage primary tumors or with questionably palpable nodes.

Breast cancer N staging



a. b.

Figure 6. Local metastasis at PET/CT performed for pretreatment staging of invasive ductal carcinoma in a 65-year-old woman. **(a)** Axial CT image shows an enlarged lymph node (arrow) in the left axillary area, a finding that was not considered to represent metastasis. **(b)** Axial PET/CT image shows high FDG uptake (maximum SUV, 4.2) in the lymph node (arrow), a finding suggestive of metastasis. Metastasis was confirmed at pathologic analysis.

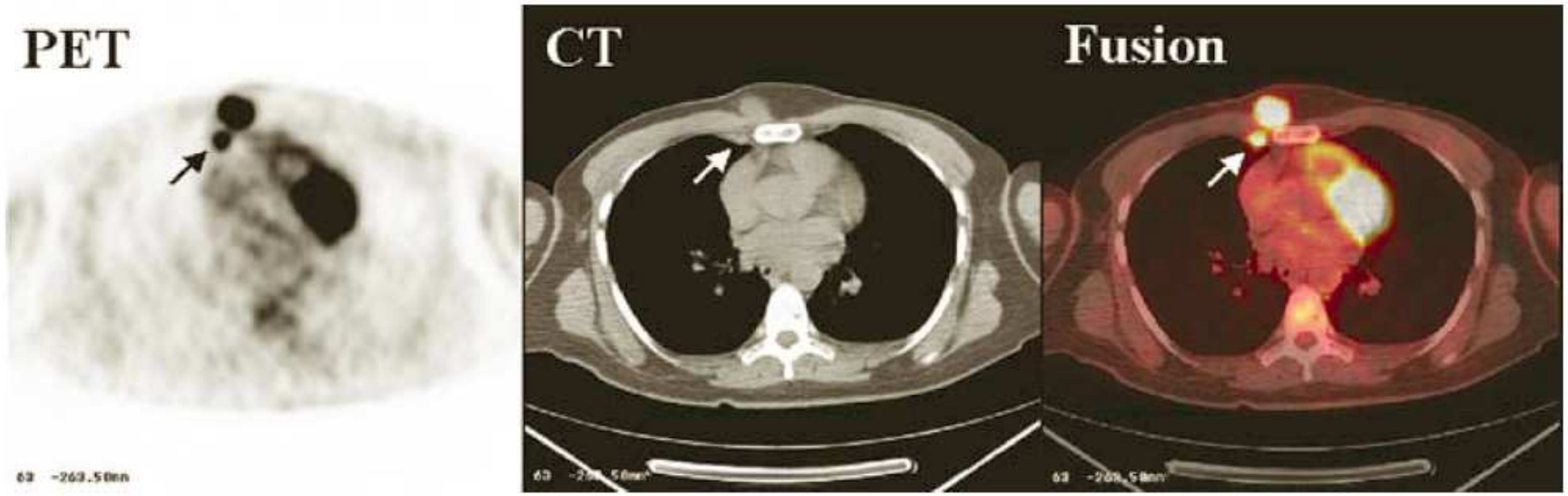
Breast cancer N staging

- IM nodes

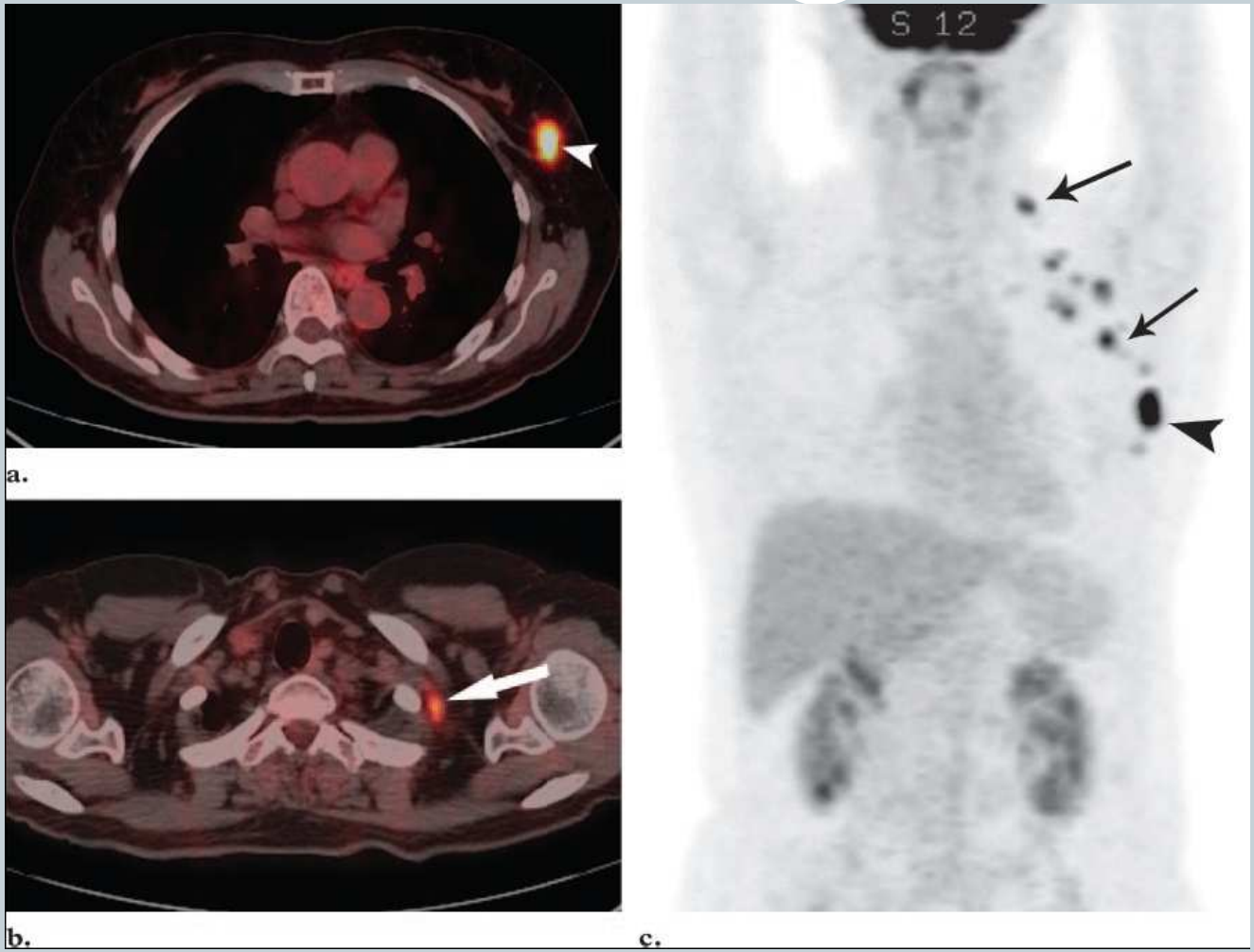
Table 4
Results of Studies of FDG PET of the IM Nodes

Authors and Year of Study	No. of Patients	Patients with Positive IM Nodes (%)	Comments
Bernstein et al 2000	15	20	Medial T2 tumors, 2 of 3 cases were biopsy proved
Danforth et al 2002	46	25	Stage II–IV disease
Bellon et al 2004	28	25	LABC
Zornoza et al 2004	200	8	High-risk axillae
Gil-Rendo et al 2006	275	8	High-risk axillae

Breast cancer N staging



Breast cancer N staging



Metastatic & recurrent disease

- The most important advantage of FDG PET/CT compared with other imaging modalities is detection of unsuspected metastasis during a single whole body examination, especially in advanced stage breast cancer.

- equivocal or suspicious findings on conventional imaging.

- Guide treatment planning

Metastatic & recurrent disease

Table 5
Results of Studies of FDG PET and PET/CT in Systemic Disease Staging and Restaging of Recurrent Breast Cancer

Authors and Year of Study	No. of Patients	Sensitivity (%)	Specificity (%)	Comments*
Moon et al 1998	57	93	79	False-negative lesions in bone
Schirrmeister et al 2001	117	93	75	. . .
Eubank et al 2001	73	85	90	IM or mediastinal nodes
Kanel et al 2004	60	89	84	Suspected recurrence
Vranjesevic et al 2002	61	. . .	. . .	59% NPV, 85% PPV, FDG uptake was prognostic
Tran et al 2005	141	. . .	. . .	Worse prognosis for inner quadrant tumors with extraaxillary findings
Fueger et al 2005	58	. . .	. . .	90% accuracy for PET/CT
Tatsumi et al 2006	75	. . .	. . .	86% accuracy for PET/CT, 77% accuracy for CT alone

*NPV = negative predictive value, PPV = positive predictive value.

Metastatic & recurrent disease

Table 3. True positive (TPR) and false positive rate (FPR) of studies evaluating FDG PET for the diagnosis of recurrent and metastatic breast cancer (January 1995–June 2004): patient-based data

Author	Year	*n* (patients)	TPR (%) (sensitivity)	FPR (%) (1 − specificity)
Bender et al. [8]	1997	75	80.0	3.6
Moon et al. [40]	1998	57	93.1	21.4
Smith et al. [10]	1998	50	90.5	3.4
Hathaway et al. [41]	1999	10	100.0	0.0
Rostom et al. [42]	1999	74	85.7	0.0
Hubner et al. [31]	2000	64	85.7	27.3
Lonneux et al. [28]	2000	39	93.9	50.0
Kim et al. [43]	2001	27	94.1	20.0
Ohta et al. [11]	2001	51	77.8	2.4
Dose et al. [12]	2002	50	86.2	9.5
Liu et al. [27]	2002	30	96.4	100.0
Suarez et al. [44]	2002	38	92.3	25.0
Goerres et al. [30]	2003	32	100.0	27.8
Gallowitsch et al. [29]	2003	62	97.0	17.9
Kamel et al. [45]	2003	60	94.3	8.0
Van der Hoeven et al. [26]	2004	48	55.6	18.9

Metastatic & recurrent disease

Table 5. True positive (TPR) and false positive rate (FPR) of studies evaluating FDG-PET for the diagnosis of recurrent and metastatic breast cancer (January 1995–June 2004): Lesion-based data

Author	Year	*n* (lesions)	TPR (%) (sensitivity)	FPR(%)(1 – specificity)
Bender et al. [8]	1997	80	85.4	20.5
Moon et al. [40]	1998	375	91.7	3.6
Kim et al. [43]	2001	61	95.8	15.4
Gallowitsch et al. [29]	2003	135	56.5	11.1
Kamel et al. [45]	2003	118	96.6	16.7
Lin et al. [46]	2003	117	85.2	5.6
Yang et al. [47]	2002	127	95.2	9.1

Metastatic & recurrent disease

- Bony metastasis

most common site of distant metastasis (90%)
most common initial distant metastasis

osteoblastic, osteolytic, mixed, or early marrow metastasis

Metastatic & recurrent disease

	Sensitivity	Specificity	Accuracy
Bone scintigraphy	78.2 (43/55)	82.4 (28/34)	79.8 (71/89)
FDG-PET	80.0 (44/55)	88.2 (30/34)	83.1 (74/89)

The test showed no significant differences

Table 2. The visualisation rates of bone scintigraphy and FDG-PET for the different CT types of bone metastases

CT type	Bone scintigraphy	FDG-PET	*p* value
Blastic (18)	100.0 (18/18)	55.6 (10/18)	$p<0.0781$
Lytic (10)	70.0 (7/10)	100.0 (10/10)	NS
Mixed (19)	84.2 (16/19)	94.7 (18/19)	NS
Invisible (8)	25.0 (2/8)	87.5 (7/8)	$p<0.0313$

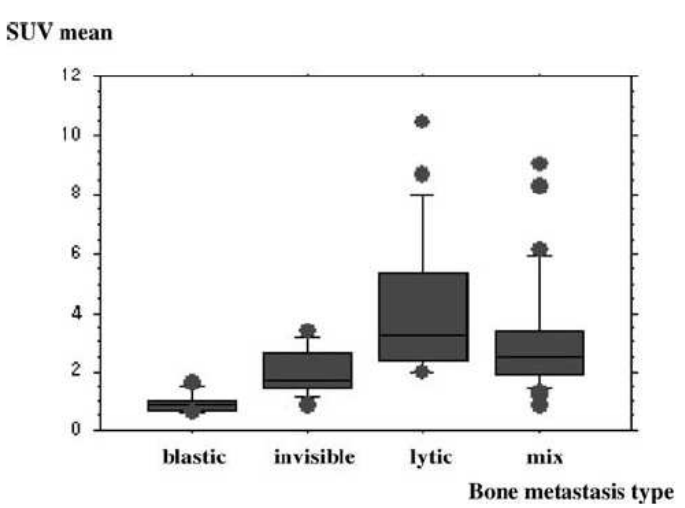
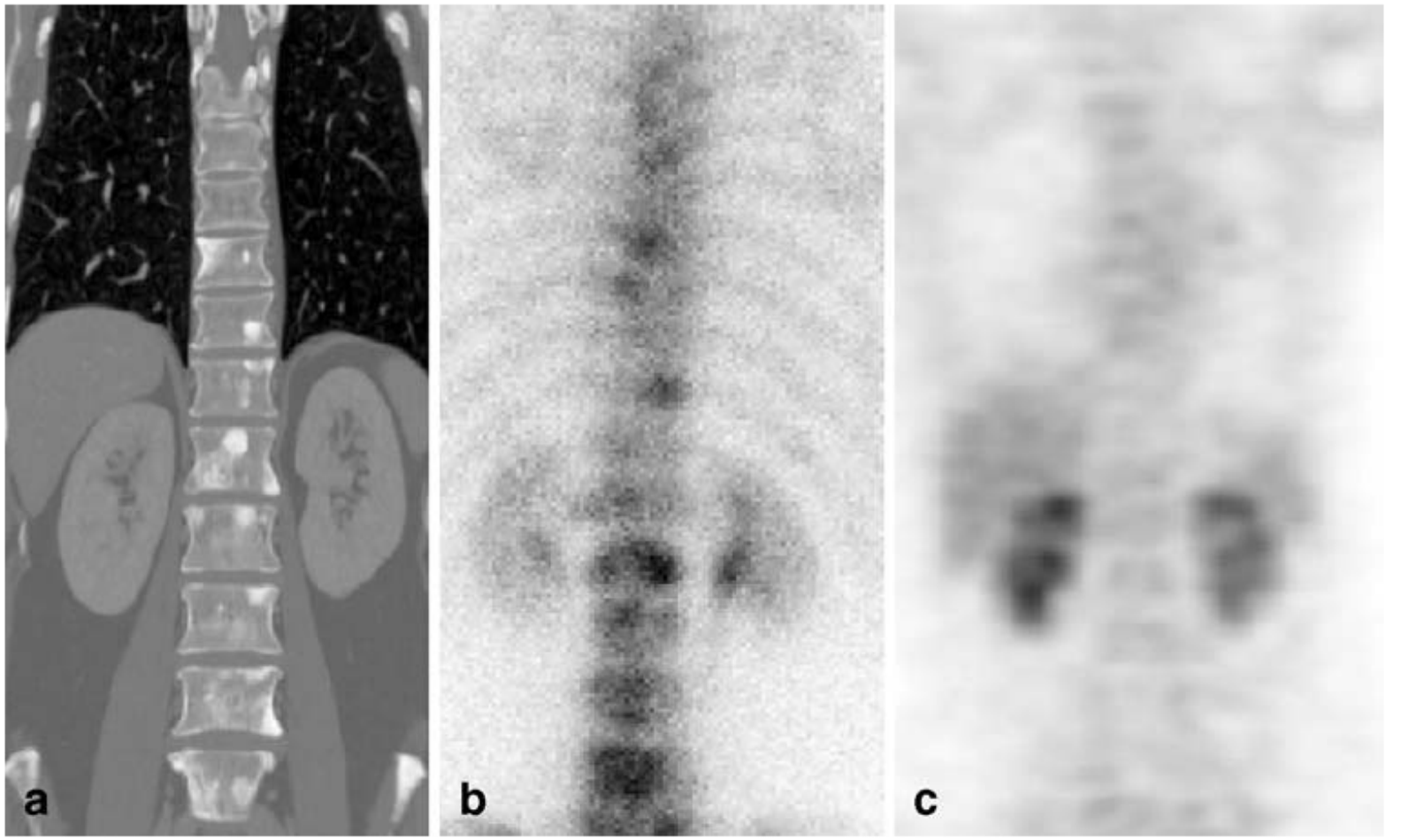


Fig. 5. Box-whisker graph of SUV_{mean} values of the different types of bone metastases

Pitfalls of FDG-PET for the diagnosis of osteoblastic bone metastases in patients with breast cancer
Eur J Nucl Med Mol Imaging (2005) 32:1253–1258

Metastatic & recurrent disease



Pitfalls of FDG-PET for the diagnosis of osteoblastic bone metastases in patients with breast cancer
Eur J Nucl Med Mol Imaging (2005) 32:1253–1258

Metastatic & recurrent disease

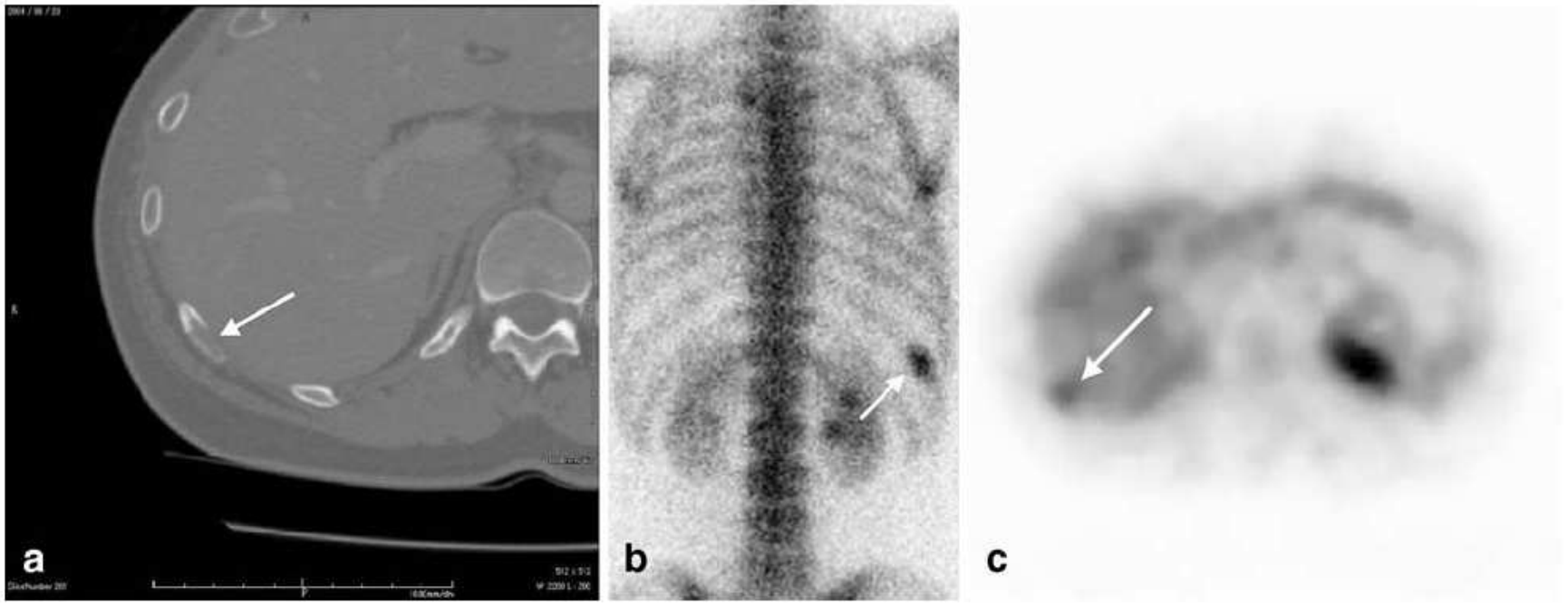


Fig. 2. **a** Axial CT image of a lytic-type metastasis in a 75-year-old man with breast carcinoma. A lytic metastasis is visible in the right 10th rib (*arrow*).**b** Posterior bone scintigram. The 10th rib contains a lytic metastasis in the form of a hot lesion (*arrow*), highly suggestive of a metastasis. **c** Axial FDG-PET image. Uptake was observed in the lytic metastasis to the 10th rib (*arrow*)

Pitfalls of FDG-PET for the diagnosis of osteoblastic bone metastases in patients with breast cancer
Eur J Nucl Med Mol Imaging (2005) 32:1253–1258

Metastatic & recurrent disease

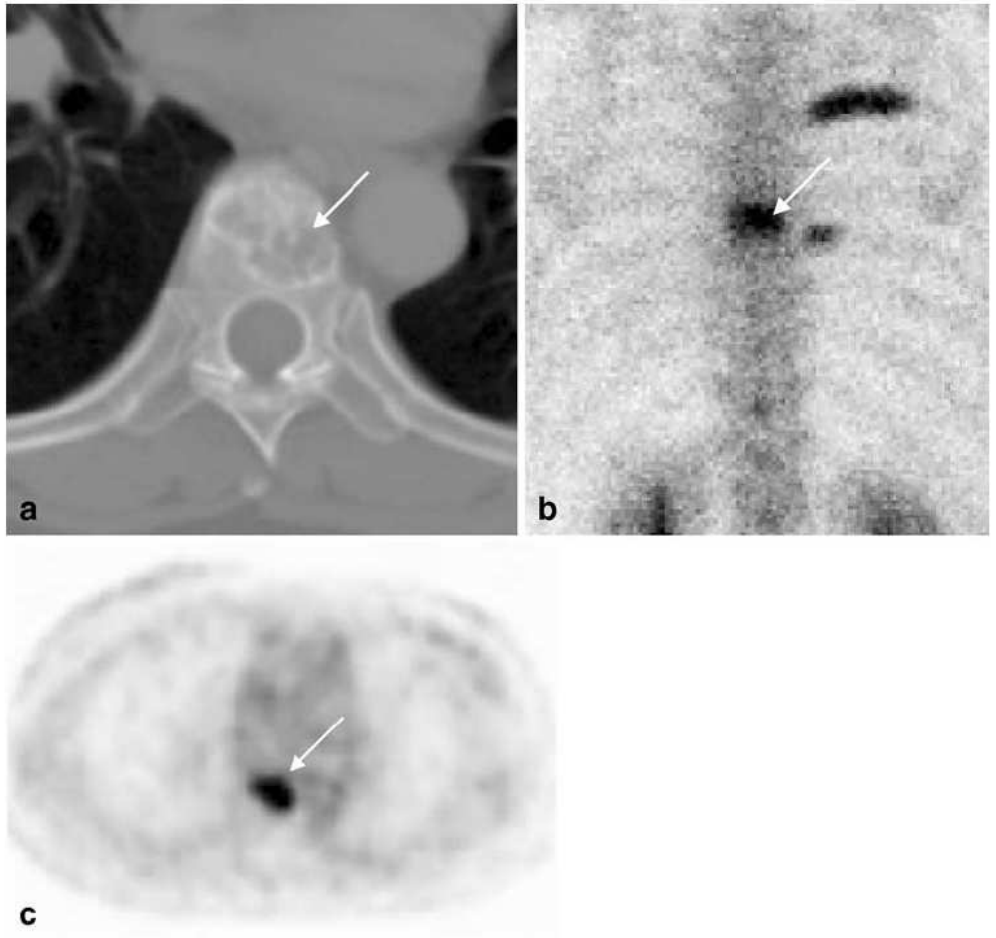
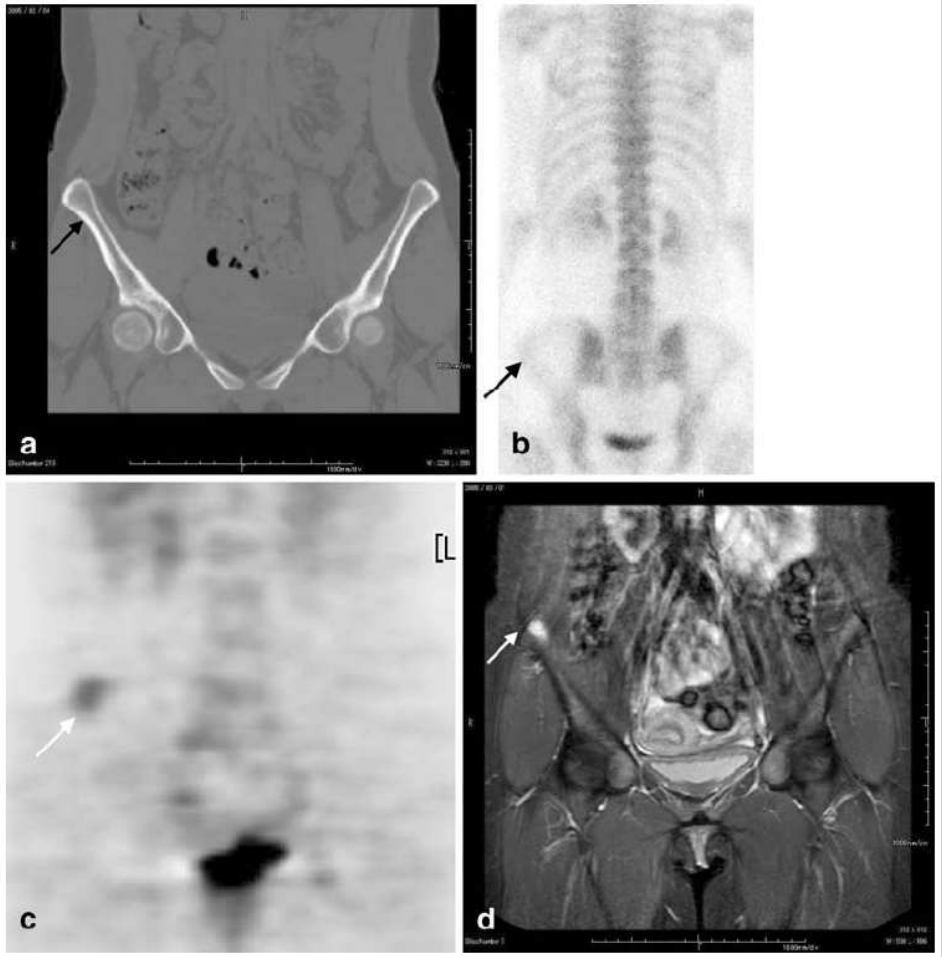


Fig. 3. a Axial CT image of a mixed-type metastasis in a 49-year-old woman after surgery for breast cancer. A mixed blastic-lytic metastasis is seen in the vertebral body of T7 (*arrow*). **b** Posterior whole-body bone scintigram. High uptake is seen in the vertebral body of T7 (*arrow*). Multiple bone metastases were suspected because of the presence of uptake in the right 5th and 8th ribs, suggestive of metastases. **c** Axial FDG-PET image. FDG-PET showed high uptake in T7 (*arrow*), corresponding to the uptake on bone scintigraphy

Pitfalls of FDG-PET for the diagnosis of osteoblastic bone metastases in patients with breast cancer
Eur J Nucl Med Mol Imaging (2005) 32:1253–1258

Metastatic & recurrent disease

Fig. 4. a Coronal CT image of an invisible metastasis in a 55-year-old woman after surgery for breast cancer. The metastasis should be present at the site indicated by the *arrow*, but could not be clearly seen. **b** Posterior bone scintigrams. Uptake in the ilium bone metastasis is unclear (*arrow*). **c** Coronal FDG-PET image. Uptake was seen in the ilium (*arrow*). This metastasis had a SUV_{mean} of 2.9. **d** Gadolinium-enhanced MR image with coronal fat suppression. Enhanced signal intensity is seen in the ilium (*arrow*), suggesting a bone metastasis. The lesion grew larger during follow-up, suggesting bone metastases clinically



Pitfalls of FDG-PET for the diagnosis of osteoblastic bone metastases in patients with breast cancer
Eur J Nucl Med Mol Imaging (2005) 32:1253–1258

Metastatic & recurrent disease

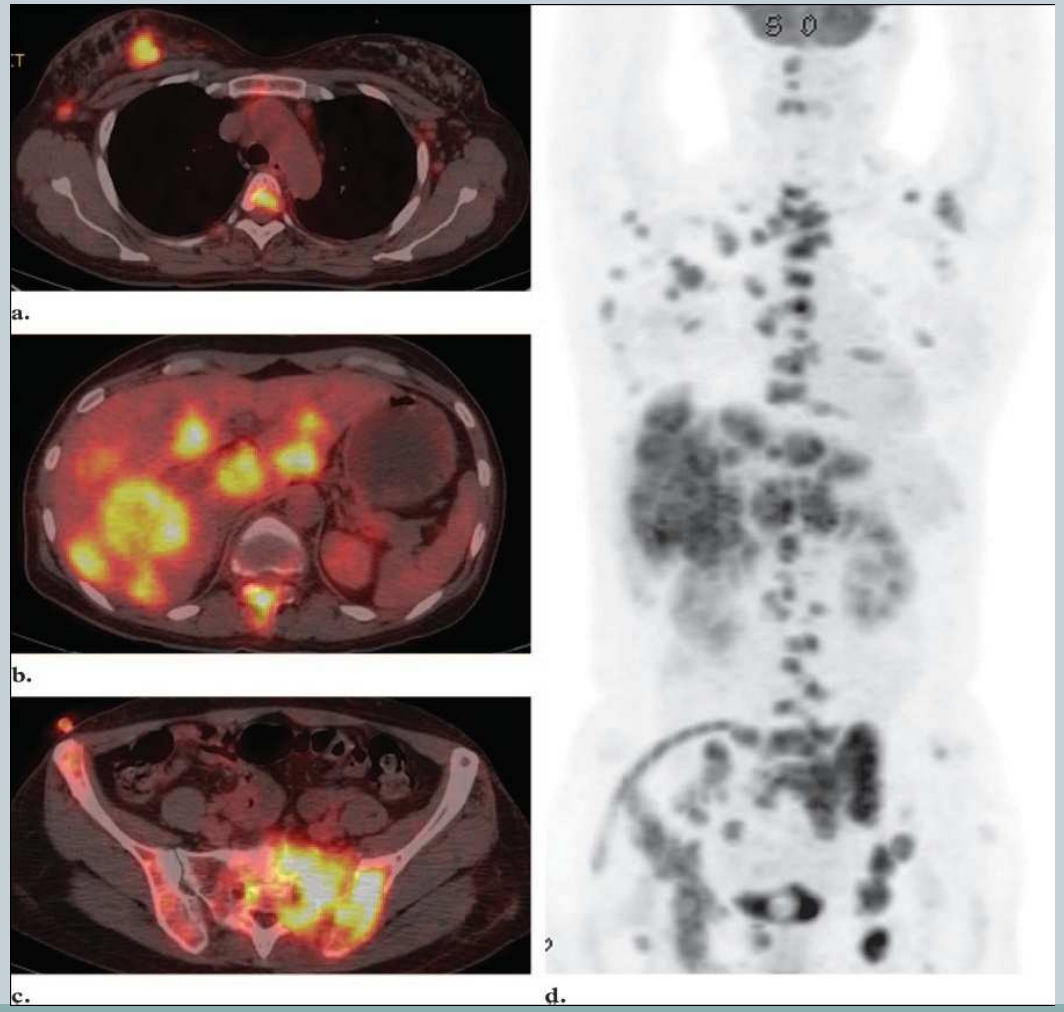


Table 5. PET/CT and CT findings in the regions with suspected malignancies

	Proof	No.	PET/CT		CT		
			Finding	No.	Positive	Equivocal	Negative
Breast	Malignant	9	Positive	7	5	2	0
			Negative	2	0	0	2
	Benign	3	Positive	2	1	1	0
			Equivocal	1	0	0	1
Chest wall	Malignant	2	Positive	2	2	0	0
Subtotal: breast and chest wall	Malignant	11	Positive	9	7	2	0
			Negative	2	0	0	2
	Benign	3	Positive	2	1	1	0
			Equivocal	1	0	0	1
Axillary LN	Malignant	10	Positive	9	7	2	0
			Negative	1	0	0	1
Internal mammary LN	Malignant	4	Positive	3	0	1	2
			Negative	1	0	0	1
Mediastinal or hilar LN	Malignant	10	Positive	9	5	2	2
			Negative	1	1	0	0
	Benign	1	Equivocal	1	0	0	1
Clavicular LN	Malignant	4	Positive	4	2	1	1
	Benign	1	Negative	1	0	1	0
Subtotal: LN regions	Malignant	28	Positive	25	14	6	5
			Negative	3	1	0	2
	Benign	2	Equivocal	1	0	0	1
			Negative	1	0	1	0

Lung	Malignant	10	Positive	8	8	0	0
			Negative	2	2	0	0
	Benign	4	Equivocal	1	0	1	0
			Negative	3	0	3	0
Liver	Malignant	4	Positive	3	3	0	0
			Negative	1	0	1	0
	Benign	1	Equivocal	1	0	1	0
Bone	Malignant	11	Positive	11	8	0	3
	Benign	2	Positive	2	2	0	0
Others[a]	Malignant	5	Positive	4	3	0	1
			Negative	1	1	0	0
	Benign	1	Positive	1	1	0	0
Subtotal: other regions	Malignant	30	Positive	26	22	0	4
			Negative	4	3	1	0
	Benign	8	Positive	3	3	0	0
			Equivocal	2	0	2	0
			Negative	3	0	3	0
Total	Malignant	69	Positive	60	43	8	9
			Negative	9	4	1	4
	Benign	13	Positive	5	4	1	0
			Equivocal	4	0	2	2
			Negative	4	0	4	0

Positive: definitely positive finding; negative: definitely negative finding

LN Lymph node

[a]Brain, thyroid (2 incl. 1 benign), adrenal gland, uterine (negative PET/CT), and abdominal LN

Metastatic & recurrent disease

- Asymptomatic treated breast cancer, elevated tumor markers, FDG PET/CT has 85% sensitivity for diagnosing recurrence, and affect clinical management in 51% of patients.

TABLE 4
Comparison of Contrast-enhanced CT and PET/CT Performance in 37 Patients With Suspected Breast Cancer Recurrence

	CT	PET/CT
TP, n	14	17
TN, n	8	13
FP, n	9	4
FN, n	6	3
Sensitivity, %	70	85
Specificity, %	47	76
Accuracy, %	59	81
PPV, %	56	81
NPV, %	57	81

TP indicates true positive; TN, true negative; FP, false positive; FN, false negative; PPV, positive predictive value; NPV, negative predictive value.

The role of FDG-PET/CT in suspected recurrence of breast cancer
cancer 2006; 107(11):2545-2551

Metastatic & recurrent disease

- In setting of locoregional recurrence, FDG PET affects treatment in up to 44% of patients.

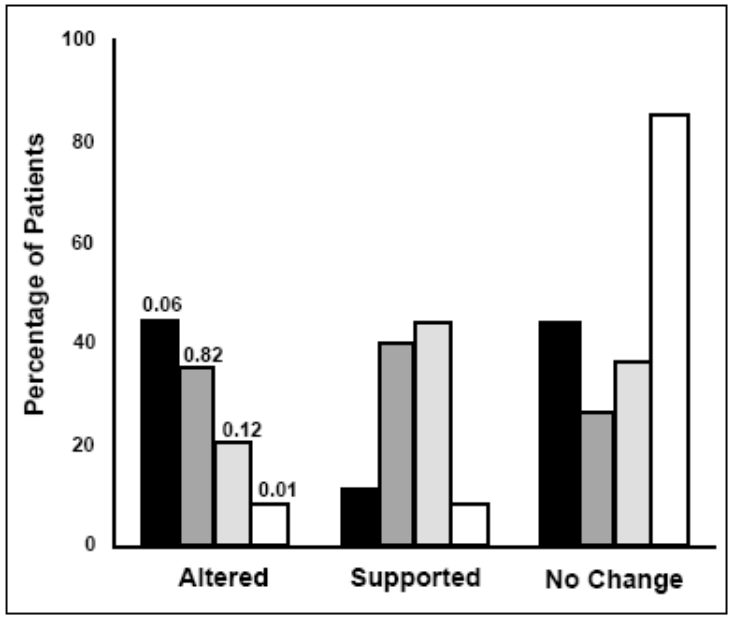


Fig. 1.—Bar graph illustrates impact of FDG PET on therapeutic plan by category of referral in 125 patients with advanced breast cancer. Black bars represent patients with locoregional disease, dark gray bars represent patients being evaluated for response to therapy, light gray bars represent patients with equivocal findings on conventional imaging, and white bars represent patients with known metastases being evaluated for extent of disease. Above each category, *p* values from chi-square analysis of impact of FDG PET on alteration of management plan for each referral category are presented.

Impact of FDG PET on defining the extent of disease and on the treatment of patients with recurrent or metastatic breast cancer
AJR 2004; 183(2):479-486

Metastatic & recurrent disease

- In setting of locoregional recurrence, FDG PET affects treatment in up to 44% of patients.

TABLE 1 Alteration of Therapeutic Plan Based on FDG PET Findings in 40 Patients, by Category of Referral

Change in Plan	Response to Treatment (*n* = 43)	Locoregional Disease (*n* = 39)	Equivocal Findings[a] (*n* = 25)	Evaluate Extent of Known Metastases (*n* = 13)	Increase in Tumor Markers (*n* = 5)	Total (*n* = 125)
Intermodality						
From surgery to systemic treatment	2	11	0	0	1	14
From radiation to systemic treatment	0	2	1	0	0	3
From treatment to no treatment	2	0	0	0	0	2
From no treatment to surgery	0	0	1	0	0	1
From systemic treatment to radiation and chemotherapy	0	0	1	0	0	1
From no treatment to chemotherapy	1	0	0	0	0	1
From systemic treatment to surgery and radiation	1	0	0	0	0	1
Intramodality						
Systemic treatment	8	2	2	0	2	14
Radiation plan	0	2	0	1	0	3
Total changed	14 (33)	17 (44)	5 (20)	1 (8)	3 (60)	40 (32)

Note.—Numbers in parentheses are percentages. See Figure 1 for *p* values from chi-square analysis of the four largest referral categories.

[a]On conventional imaging.

Impact of FDG PET on defining the extent of disease and on the treatment of patients with recurrent or metastatic breast cancer
AJR 2004; 183(2):479-486

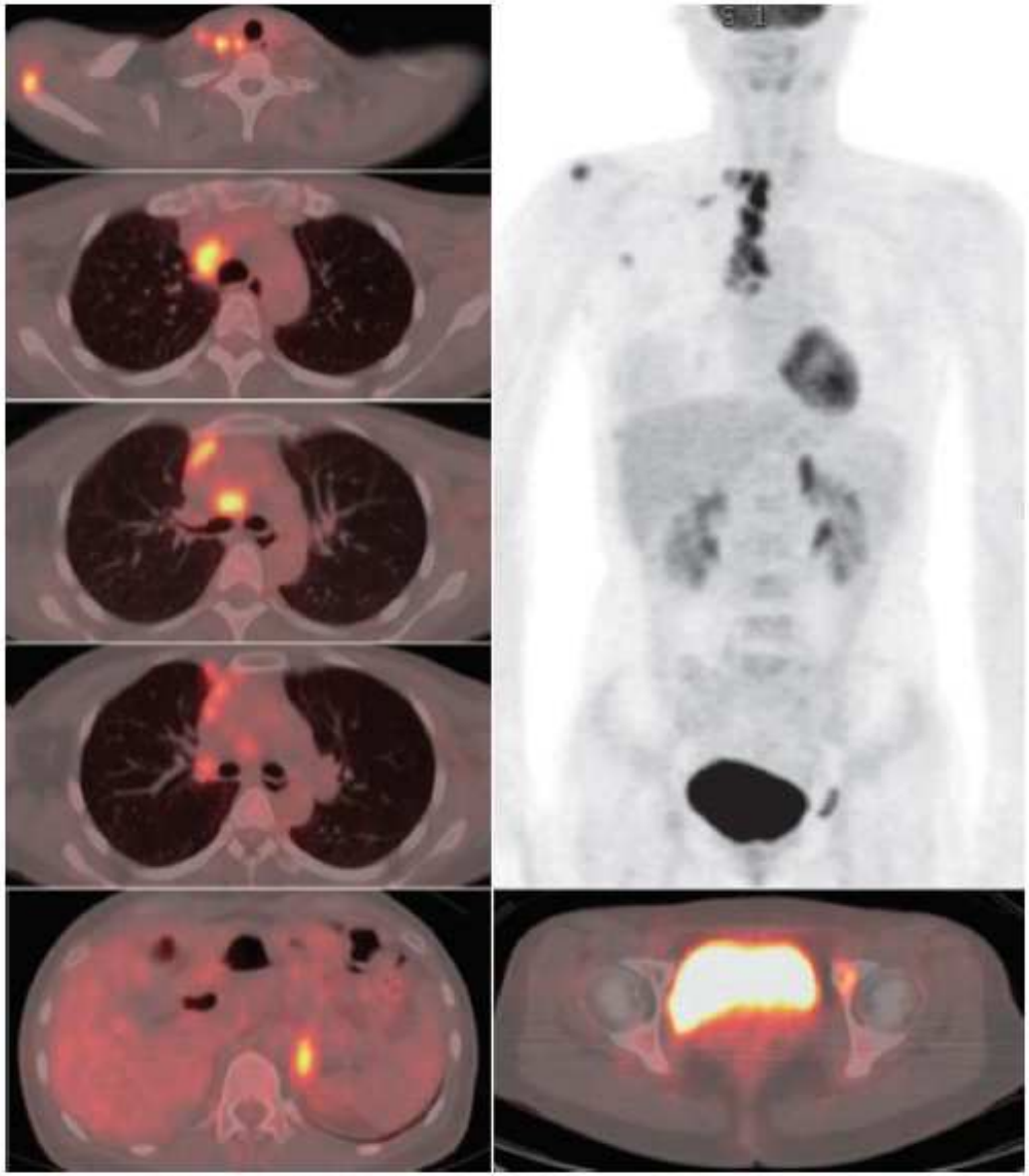
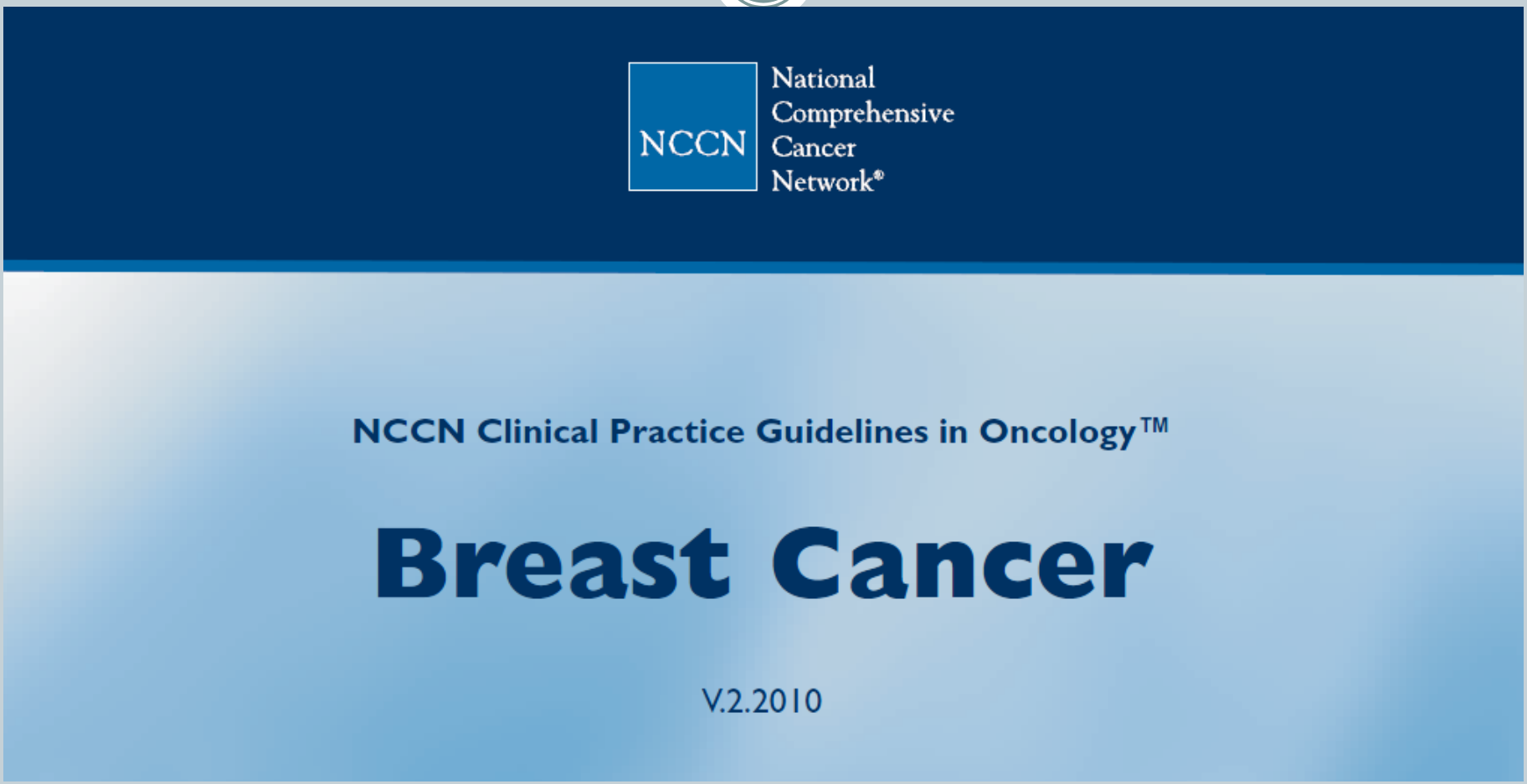
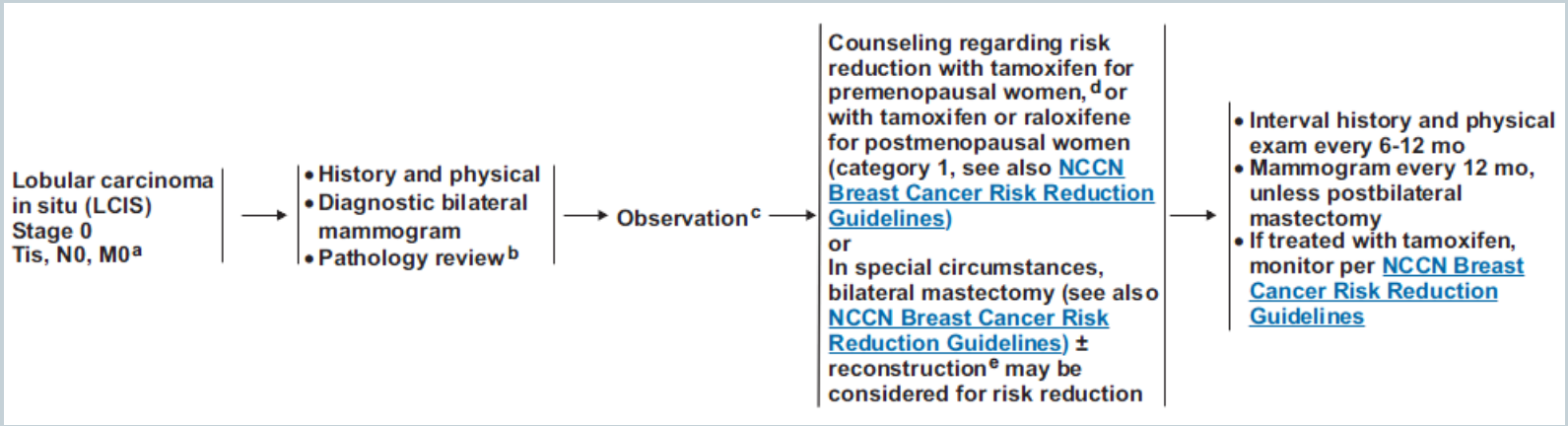


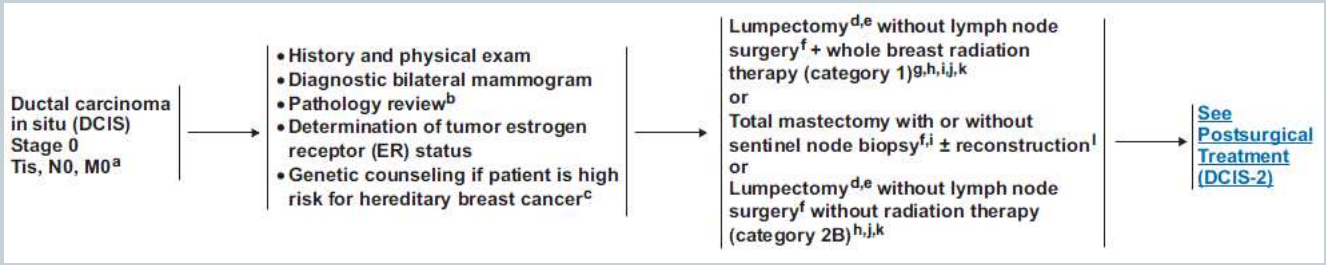
Figure 11. Extensive metastatic disease at PET/CT in a 38-year-old woman with elevated blood serum levels of tumor markers after a left total mastectomy for invasive ductal carcinoma. Axial fused PET/CT images at progressively lower levels (left and bottom) show multiple areas of increased FDG uptake. Maximum intensity projection reconstruction of CT attenuation–corrected PET image data (right) shows multiple metastases in the right lower internal jugular, right supraclavicular, paratracheal, internal mammary, and tracheobronchial lymph nodes; the left adrenal gland; and the left pubic bone and right acromion.

Breast cancer staging (NCCN)



Breast cancer staging (NCCN)





Breast cancer staging (NCCN)

NCCN® Practice Guidelines in Oncology – V.2.2010

Invasive Breast Cancer

Guidelines Index
Breast Cancer TOC
Staging, Discussion, References

CLINICAL STAGE

Stage I
T1, N0, M0
or
Stage IIA
T0, N1, M0
T1, N1, M0
T2, N0, M0
or
Stage IIB
T2, N1, M0
T3, N0, M0
or
T3, N1, M0

→

WORKUP

General workup including:
- History and physical exam
- CBC, platelets
- Liver function tests and alkaline phosphatase
- Diagnostic bilateral mammogram, ultrasound as necessary
- Pathology review[a]
- Determination of tumor estrogen/progesterone receptor (ER/PR) status and HER2 status[b]
- Genetic counseling if patient is high risk for hereditary breast cancer[c]

Optional studies for breast imaging:
- Breast MRI[d]

If clinical stage IIIA (T3, N1, M0) consider:
- Bone scan (category 2B)
- Abdominal ± pelvis CT or US or MRI
- Chest imaging

Additional studies as directed by symptoms:[e]
- Bone scan indicated if localized bone pain or elevated alkaline phosphatase
- Abdominal ± pelvis CT or US or MRI if elevated alkaline phosphatase, abnormal liver function tests, abdominal symptoms, abnormal physical examination of the abdomen or pelvis
- Chest imaging (if pulmonary symptoms are present)

→ See Locoregional Treatment (BINV-2)

[a] The panel endorses the College of American Pathology Protocol for pathology reporting for all invasive and non-invasive carcinomas of the breast. http://www.cap.org.
[b] See Principles of HER2 Testing (BINV-A).
[c] See NCCN Genetics/Familial High-Risk Assessment: Breast and Ovarian Guidelines.
[d] See Principles of Dedicated Breast MRI Testing (BINV-B).
[e] The use of PET or PET/CT scanning is not indicated in the staging of clinical stage I, II, or operable III breast cancer.

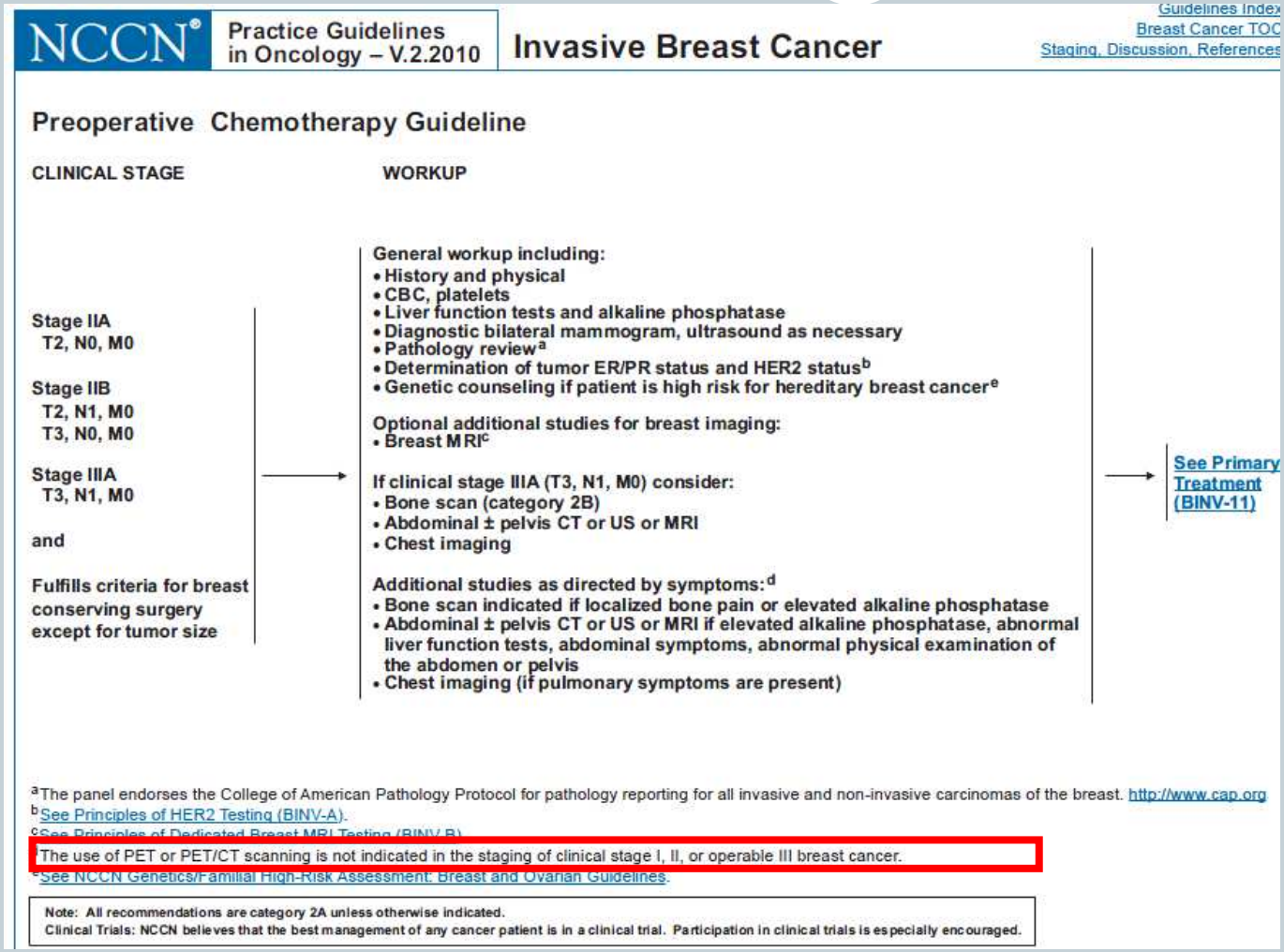
Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

Breast cancer staging (NCCN)

- The use of PET or PET/CT scanning is not indicated in the staging of clinical stage I, II or operable III breast cancer

1. High false-negative rate in <1 cm tumor or low-grade tumor
2. Low sensitivity in detection of axillary nodal metastasis
3. Low pretest probability of distant metastasis, resulting in high false-positive scans

Breast cancer staging (NCCN)



NCCN® Practice Guidelines in Oncology – V.2.2010

Invasive Breast Cancer

Guidelines Index
Breast Cancer TOC
Staging, Discussion, References

Preoperative Chemotherapy Guideline

CLINICAL STAGE

Stage IIA
T2, N0, M0

Stage IIB
T2, N1, M0
T3, N0, M0

Stage IIIA
T3, N1, M0

and

Fulfills criteria for breast conserving surgery except for tumor size

WORKUP

General workup including:
- History and physical
- CBC, platelets
- Liver function tests and alkaline phosphatase
- Diagnostic bilateral mammogram, ultrasound as necessary
- Pathology review[a]
- Determination of tumor ER/PR status and HER2 status[b]
- Genetic counseling if patient is high risk for hereditary breast cancer[e]

Optional additional studies for breast imaging:
- Breast MRI[c]

If clinical stage IIIA (T3, N1, M0) consider:
- Bone scan (category 2B)
- Abdominal ± pelvis CT or US or MRI
- Chest imaging

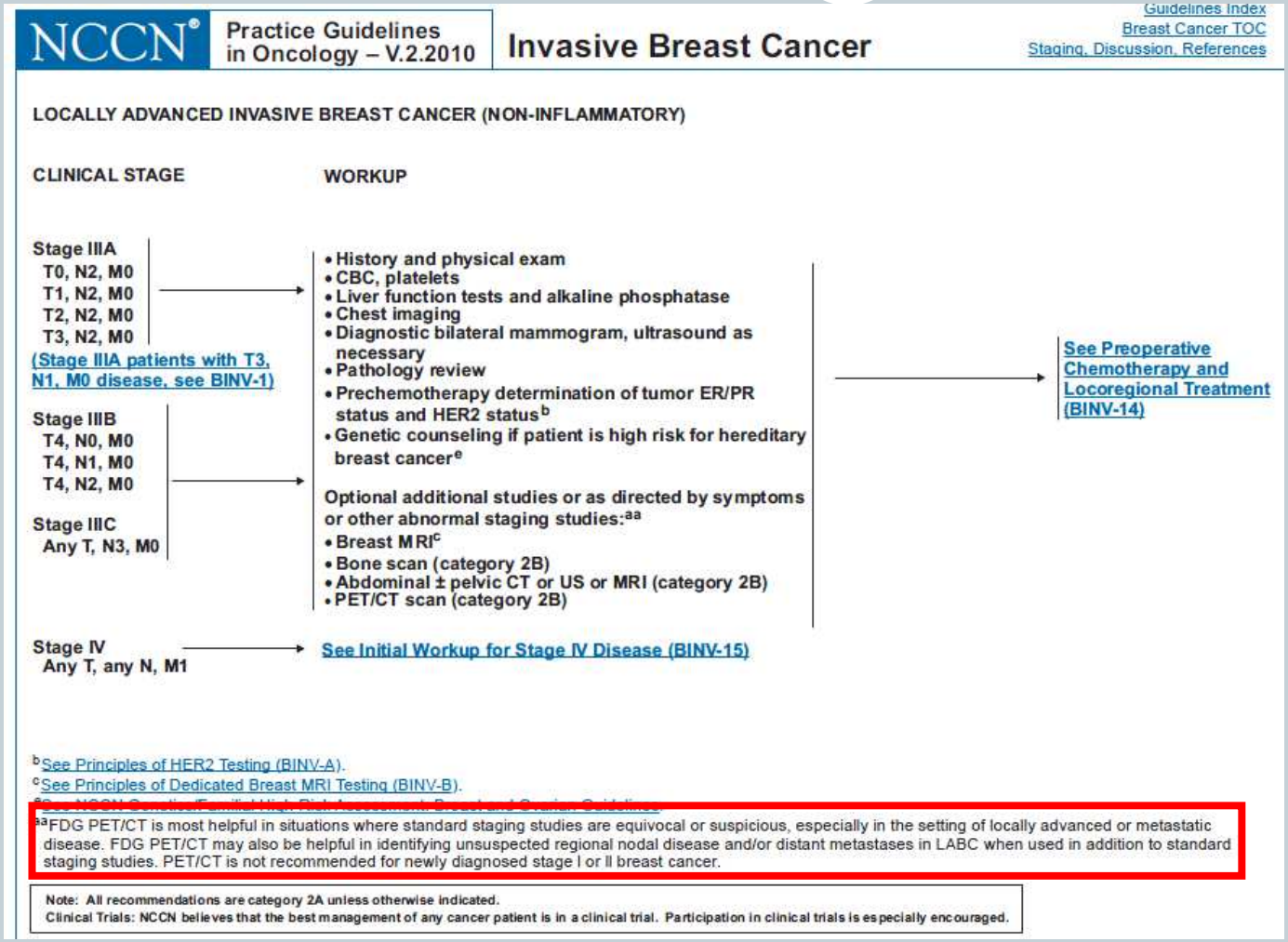
Additional studies as directed by symptoms:[d]
- Bone scan indicated if localized bone pain or elevated alkaline phosphatase
- Abdominal ± pelvis CT or US or MRI if elevated alkaline phosphatase, abnormal liver function tests, abdominal symptoms, abnormal physical examination of the abdomen or pelvis
- Chest imaging (if pulmonary symptoms are present)

→ See Primary Treatment (BINV-11)

[a] The panel endorses the College of American Pathology Protocol for pathology reporting for all invasive and non-invasive carcinomas of the breast. http://www.cap.org
[b] See Principles of HER2 Testing (BINV-A).
[c] See Principles of Dedicated Breast MRI Testing (BINV-B)
[d] The use of PET or PET/CT scanning is not indicated in the staging of clinical stage I, II, or operable III breast cancer.
[e] See NCCN Genetics/Familial High-Risk Assessment: Breast and Ovarian Guidelines.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

Breast cancer staging (NCCN)



NCCN® Practice Guidelines in Oncology – V.2.2010

Invasive Breast Cancer

Guidelines Index
Breast Cancer TOC
Staging, Discussion, References

LOCALLY ADVANCED INVASIVE BREAST CANCER (NON-INFLAMMATORY)

CLINICAL STAGE	WORKUP
Stage IIIA T0, N2, M0 T1, N2, M0 T2, N2, M0 T3, N2, M0 (Stage IIIA patients with T3, N1, M0 disease, see BINV-1)	• History and physical exam • CBC, platelets • Liver function tests and alkaline phosphatase • Chest imaging • Diagnostic bilateral mammogram, ultrasound as necessary • Pathology review • Prechemotherapy determination of tumor ER/PR status and HER2 status[b] • Genetic counseling if patient is high risk for hereditary breast cancer[e] Optional additional studies or as directed by symptoms or other abnormal staging studies:[aa] • Breast MRI[c] • Bone scan (category 2B) • Abdominal ± pelvic CT or US or MRI (category 2B) • PET/CT scan (category 2B)
Stage IIIB T4, N0, M0 T4, N1, M0 T4, N2, M0 Stage IIIC Any T, N3, M0	
Stage IV Any T, any N, M1	See Initial Workup for Stage IV Disease (BINV-15)

→ See Preoperative Chemotherapy and Locoregional Treatment (BINV-14)

[b] See Principles of HER2 Testing (BINV-A).
[c] See Principles of Dedicated Breast MRI Testing (BINV-B).
[aa] FDG PET/CT is most helpful in situations where standard staging studies are equivocal or suspicious, especially in the setting of locally advanced or metastatic disease. FDG PET/CT may also be helpful in identifying unsuspected regional nodal disease and/or distant metastases in LABC when used in addition to standard staging studies. PET/CT is not recommended for newly diagnosed stage I or II breast cancer.

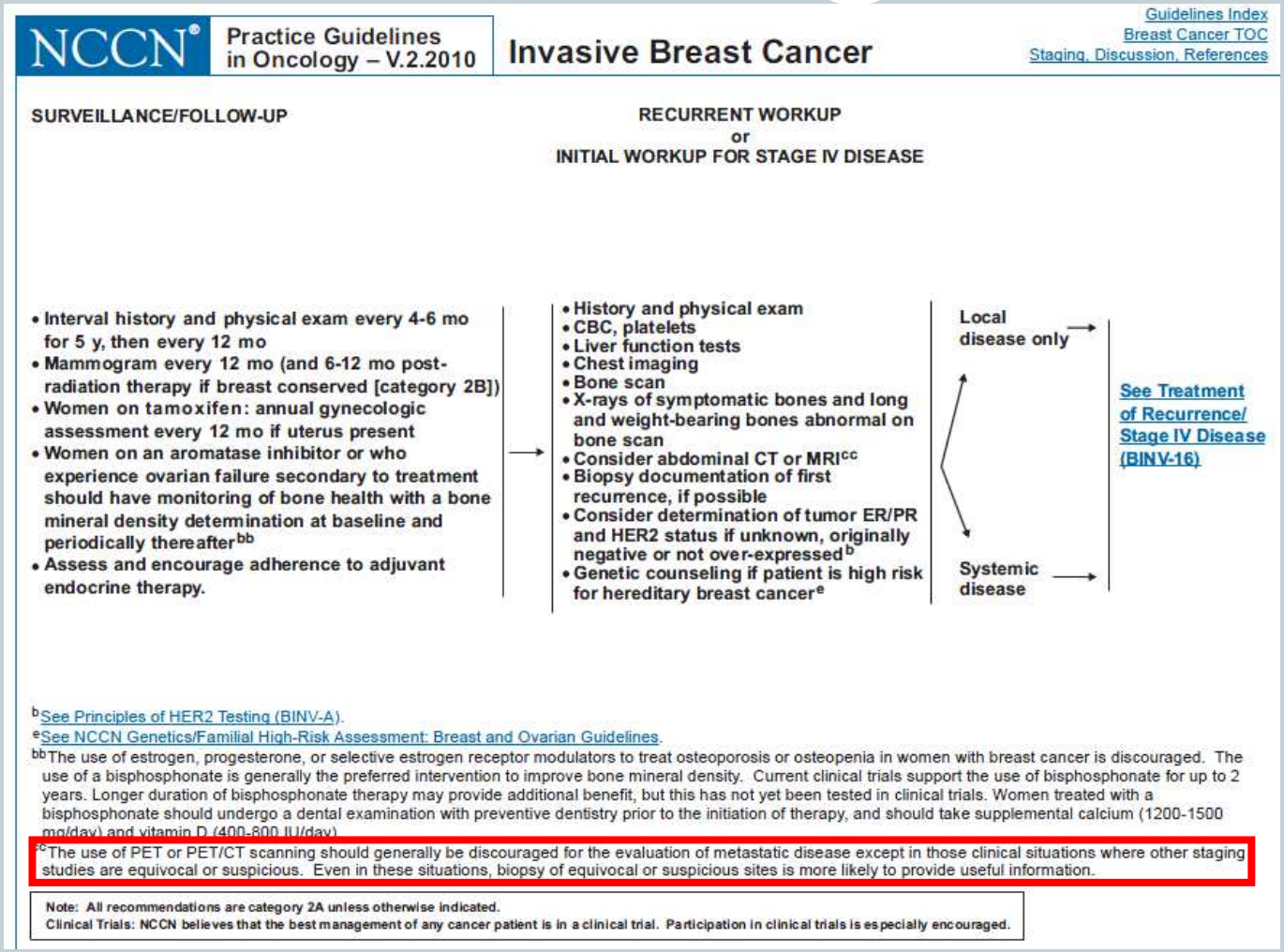
Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

Breast cancer staging (NCCN)

- PET or PET/CT is an optional additional study in locally advanced breast cancer

1. most useful when standard imaging studies have equivocal or suspicious findings.
2. maybe a useful adjunct to standard imaging studies in detection of extra-axillary nodal metastasis or unsuspected distant metastasis
3. biopsy for conformation of stage IV disease whenever possible

Breast cancer staging (NCCN)



NCCN® Practice Guidelines in Oncology – V.2.2010

Invasive Breast Cancer

Guidelines Index
Breast Cancer TOC
Staging, Discussion, References

SURVEILLANCE/FOLLOW-UP

- Interval history and physical exam every 4-6 mo for 5 y, then every 12 mo
- Mammogram every 12 mo (and 6-12 mo post-radiation therapy if breast conserved [category 2B])
- Women on tamoxifen: annual gynecologic assessment every 12 mo if uterus present
- Women on an aromatase inhibitor or who experience ovarian failure secondary to treatment should have monitoring of bone health with a bone mineral density determination at baseline and periodically thereafter[bb]
- Assess and encourage adherence to adjuvant endocrine therapy.

RECURRENT WORKUP or INITIAL WORKUP FOR STAGE IV DISEASE

- History and physical exam
- CBC, platelets
- Liver function tests
- Chest imaging
- Bone scan
- X-rays of symptomatic bones and long and weight-bearing bones abnormal on bone scan
- Consider abdominal CT or MRI[cc]
- Biopsy documentation of first recurrence, if possible
- Consider determination of tumor ER/PR and HER2 status if unknown, originally negative or not over-expressed[b]
- Genetic counseling if patient is high risk for hereditary breast cancer[e]

Local disease only → See Treatment of Recurrence/ Stage IV Disease (BINV-16)

Systemic disease → See Treatment of Recurrence/ Stage IV Disease (BINV-16)

[b] See Principles of HER2 Testing (BINV-A).

[e] See NCCN Genetics/Familial High-Risk Assessment: Breast and Ovarian Guidelines.

[bb] The use of estrogen, progesterone, or selective estrogen receptor modulators to treat osteoporosis or osteopenia in women with breast cancer is discouraged. The use of a bisphosphonate is generally the preferred intervention to improve bone mineral density. Current clinical trials support the use of bisphosphonate for up to 2 years. Longer duration of bisphosphonate therapy may provide additional benefit, but this has not yet been tested in clinical trials. Women treated with a bisphosphonate should undergo a dental examination with preventive dentistry prior to the initiation of therapy, and should take supplemental calcium (1200-1500 mg/day) and vitamin D (400-800 IU/day).

[cc] The use of PET or PET/CT scanning should generally be discouraged for the evaluation of metastatic disease except in those clinical situations where other staging studies are equivocal or suspicious. Even in these situations, biopsy of equivocal or suspicious sites is more likely to provide useful information.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

Breast cancer staging (NCCN)

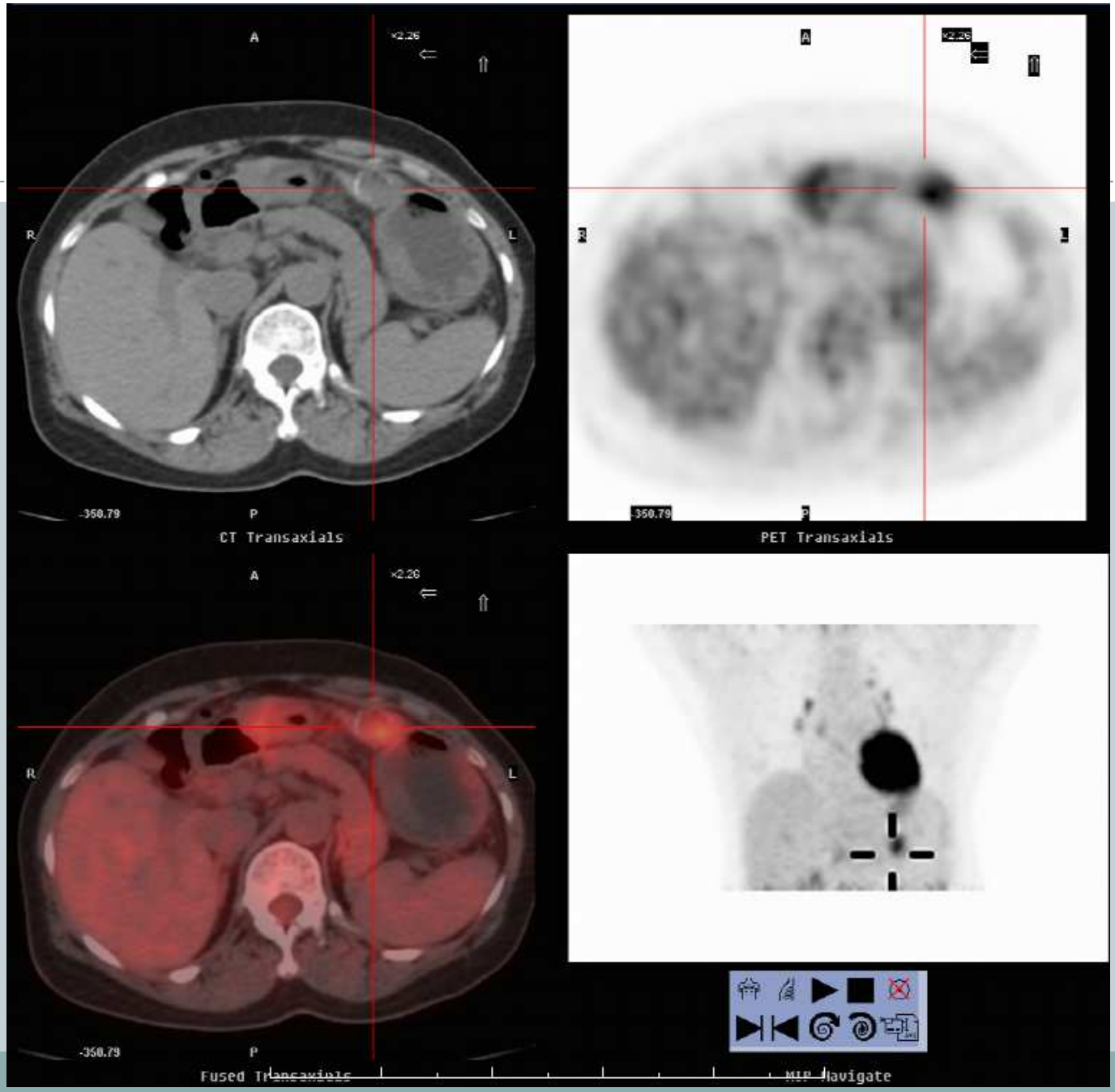
- PET or PET/CT for evaluation of recurrent breast cancer

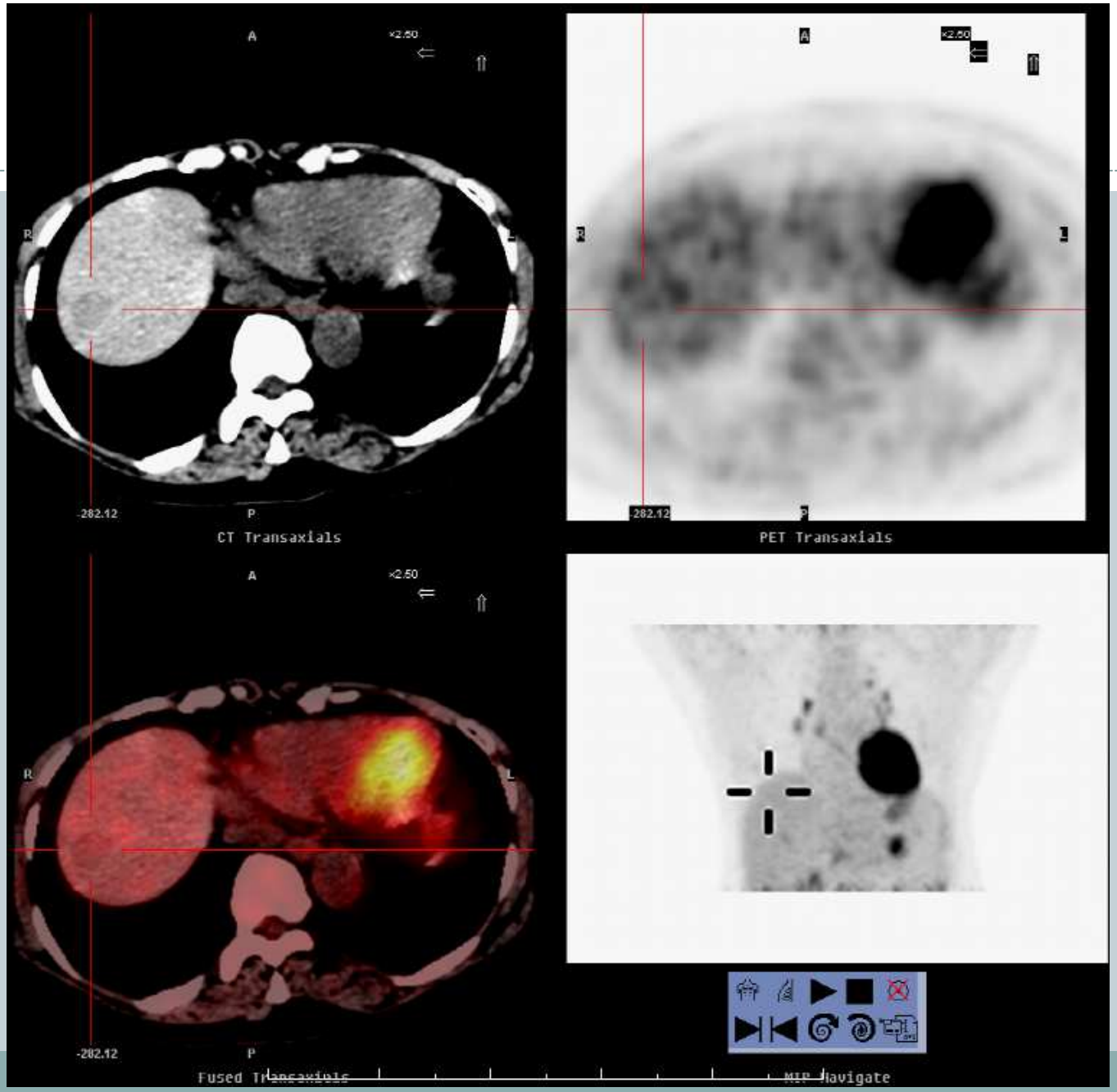
  1. standard imaging studies have equivocal or suspicious findings.
  2. biopsy for conformation whenever possible
  3. guide treatment planning through determination of disease extent (limited evidence)

- PET or PET/CT is not recommended in post-therapy follow-up of asymptomatic patients.

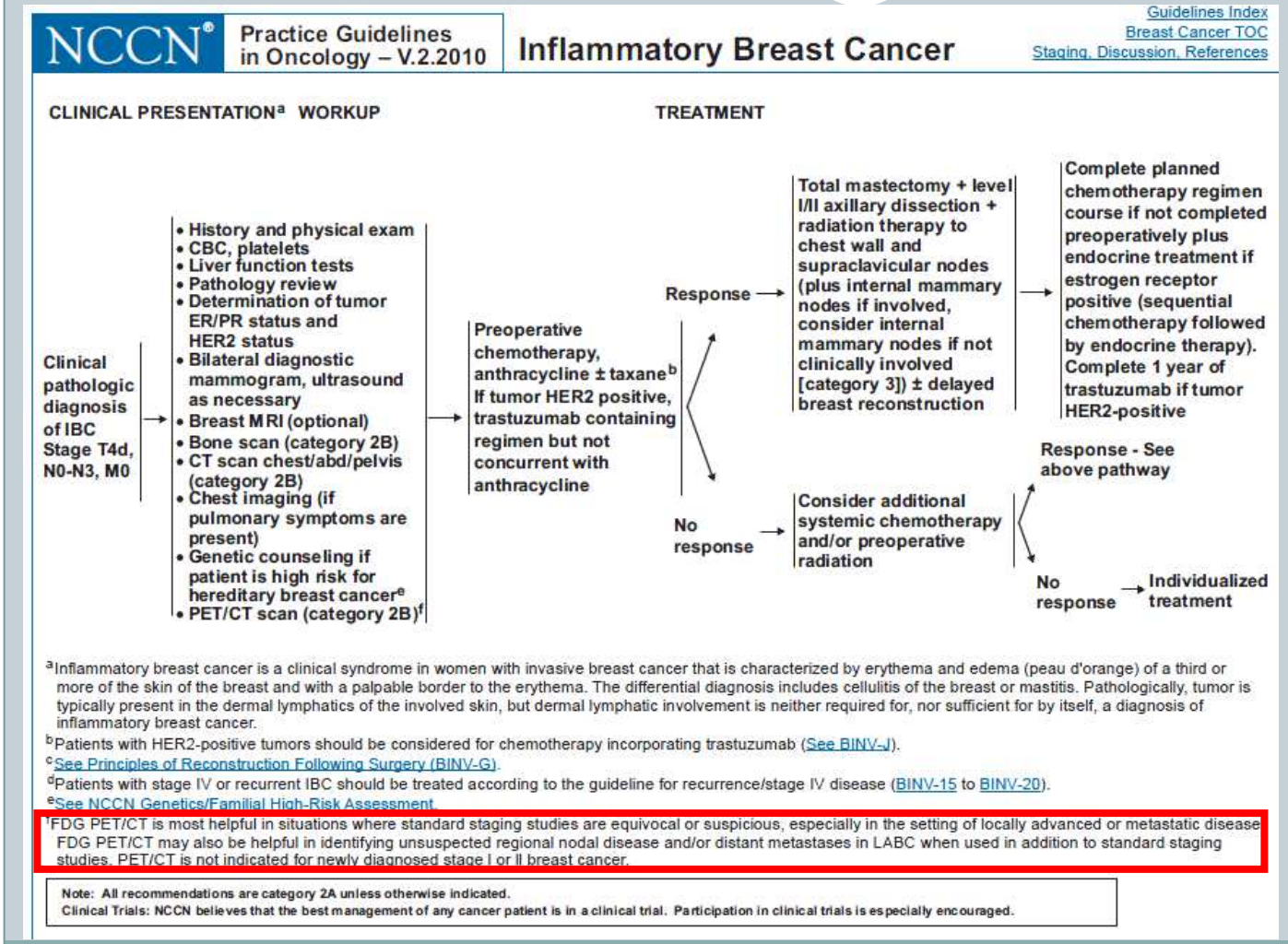
case

- 5602313
- *IDC of right breast s/p OP in 2004*
- *Suspected liver metastasis by CT on 2008-04-03*


A
R
L
P
-350.79
CT Transaxials
PET Transaxials
Fused Transaxials
MIP Navigate


A
×2.50
R
L
-282.12
P
CT Transaxials
A
×2.50
R
L
-282.12
P
PET Transaxials
A
×2.50
R
L
-282.12
P
Fused Transaxials
MIP Navigate

Breast cancer staging (NCCN)



Breast cancer staging (NCCN)

- PET or PET/CT is an optional additional study in inflammatory breast cancer

1. most useful when standard imaging studies have equivocal or suspicious findings.
2. maybe a useful adjunct to standard imaging studies in detection of extra-axillary nodal metastasis or unsuspected distant metastasis
3. biopsy for conformation of stage IV disease whenever possible

Breast cancer staging (健保)

編號	診療項目	基層院所	地區醫院	區域醫院	醫學中心	支付點數	備註
	正子造影 Positron emission tomography (PET)						修訂適應症
26072~~C~~B	一全身	V	V	V	V	36500	
26073~~C~~B	一局部	V	V	V	V	26500	
	註：實施本項目須符合 1. 腫瘤部分之適應症： (1)乳癌、淋巴癌之分期、治療及懷疑復發或再分期。 (2)大腸癌、直腸癌、食道癌、頭頸部癌(不包含腦瘤~~及甲狀腺癌~~)、原發性肺癌(~~非小細胞性~~)、黑色素癌、甲狀腺癌及子宮頸癌之~~診斷、~~分期及懷疑復發或再分期。 ~~(3)肺癌(SPN)。~~ ~~(4)甲狀腺癌復發後之再分期。~~ A.分期：評估腫瘤之期別。 B.治療：評估腫瘤對治療之反應，擬改變治療方式時。 C.懷疑復發或再分期：使用於患者已接受一階段之正統治療後，偵測疑似有復發或轉移及評估復發之程度(不得用於例行之追蹤檢查)。 D.~~以電腦斷層或核磁共振無法分期或診斷者~~以上各階段須符合：經電腦斷層、核磁共振、核子醫學掃瞄等檢查仍無法分期者，或認定電腦斷層、核磁共振等檢查不足以提供足夠資訊以供治療所需者，且須於病歷中說明施行正子造影之必要性理由。 E.配合腫瘤治療計畫者~~及療效評估~~方得以正子造影作為療效評估項目，未有後續積極處置之計畫者，不得施行。						

Monitoring response to therapy

- Neoadjuvant systemic therapy in LABC

1. OS similar to adjuvant systemic therapy
2. improve surgical options

1. extent of residual disease is prognostic for DFS and OS
2. complete pathologic response has improved long-term outcome

Monitoring response to therapy

Neoadjuvent systemic therapy in LABC

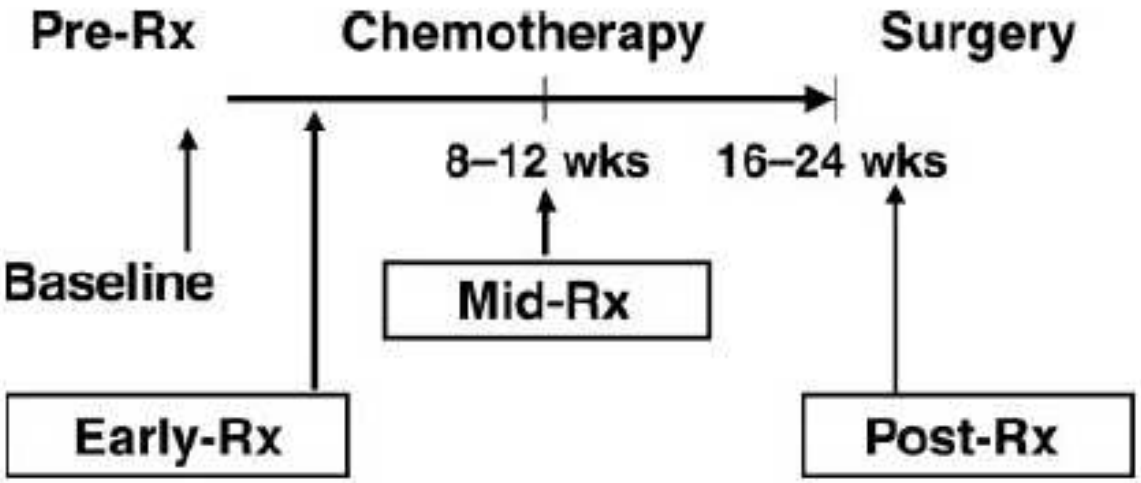


Figure 9. NST in women with LABC consists of preoperative systemic chemotherapy aimed at achieving long-term survival, assessing the response to systemic therapy, and improving surgical options. FDG PET has been evaluated at different time points along the course of neoadjuvant therapy *(Rx)*, and its results have been shown to be an accurate predictor of tumor response.

Monitoring response to therapy

Neoadjuvent systemic therapy in LABC

- Early response of NST in LABC

Table 7
Results of Studies of Early Response Evaluation with FDG PET

Authors and Year of Study	No. of Patients	Therapy*	Results†
Wahl et al 1993	11	AC	Response = 22% decrease in SUV, NR = no change
Schelling et al 2000	24	EC or ET	mCR = 54% decrease in SUV, no mCR = 19% decrease in SUV
Smith et al 2000	30	CVAP	mCR = 77% decrease in SUV, no mCR = 1% increase in SUV

*AC = doxorubicin and cyclophosphamide; CVAP = cyclophosphamide, vincristine, doxorubicin, and prednisolone; EC = epirubicin and cyclophosphamide; ET = epirubicin and paclitaxel.
†mCR = macroscopic complete response, NR = no response.

- Rousseau et al, >60% decrease in SUV

  1st cycle: 61% sensitive, 96% specific

  2nd cycle: 89% sensitive, 95% specific

  3rd cycle: less sensitive or specific

Monitoring early response to neoadjuvant chemotherapy in stage II and III breast cancer by 18F-FDG PET
J Clin Oncol 2006; 24(34):5366-5372

Monitoring response to therapy

Neoadjuvent systemic therapy in LABC

- Mid-therapy response of NST in LABC

Table 6
Results of Studies of Midtherapy Response Evaluation with FDG PET

Authors and Year of Study	No. of Patients	Therapy*	Results†
Wahl et al 1993	11	AC	Response = 48% decrease in SUV, NR = 19% decrease in SUV
Bassa et al 1996	15	FAC	51% decrease in SUV for all patients
Schelling et al 2000	24	EC or ET	mCR = 46% decrease in SUV, no mCR = 8% decrease in SUV
Smith et al 2000	30	CVAP	mCR = 86% decrease in SUV, no mCR = 40% decrease in SUV
Mankoff et al 2003	35	FAC or AC (weekly)	mCR = 65% decrease in MRFDG, PR = 49% decrease in MRFDG, NR = 40% decrease in MRFDG (DFS)

*AC = doxorubicin and cyclophosphamide; CVAP = cyclophosphamide, vincristine, doxorubicin, and prednisolone; EC = epirubicin and cyclophosphamide; ET = epirubicin and paclitaxel; FAC = fluorouracil, doxorubicin, and cyclophosphamide.
†mCR = macroscopic complete response, MRFDG = metabolic rate of FDG, NR = no response, PR = partial response.

Decline in FDG uptake by 50% or more is predictive of a good response to NST

Monitoring response to therapy

Neoadjuvent systemic therapy in LABC

- Post-therapy response of NST in LABC

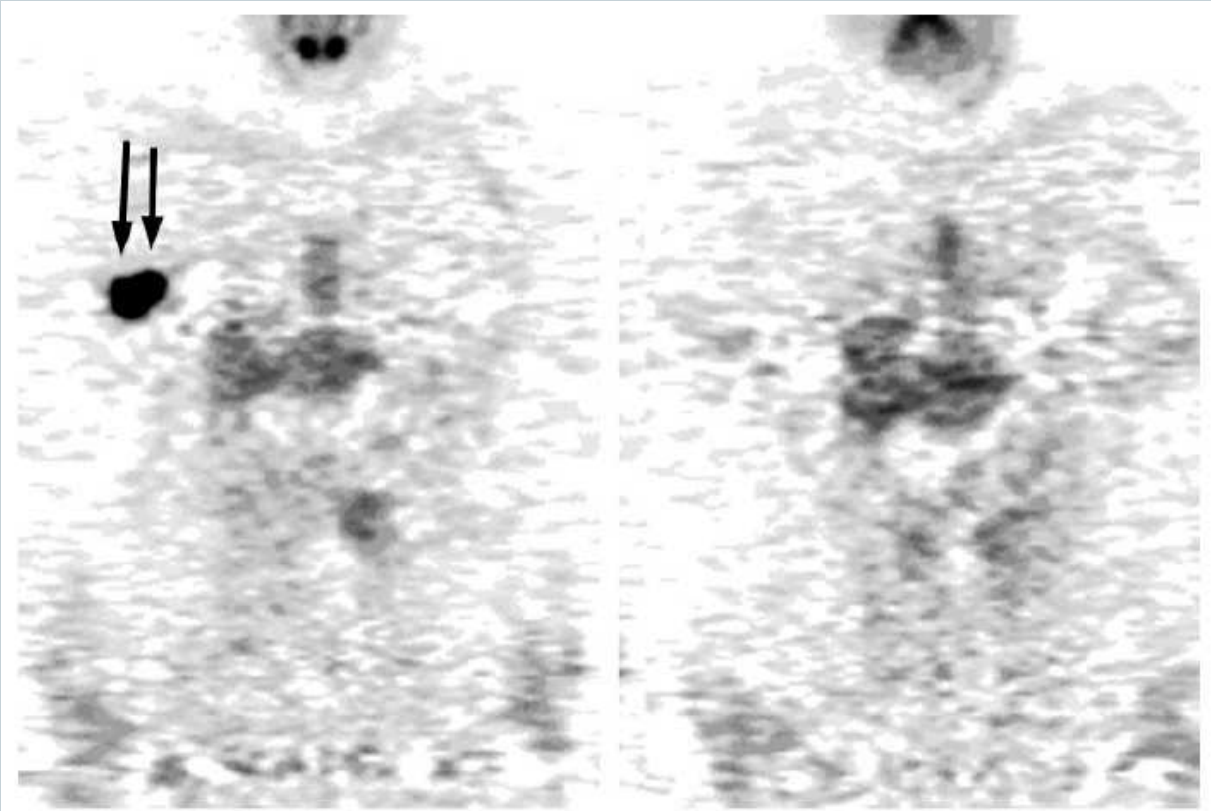
Table 8
Results of Studies of Posttherapy Response Evaluation with FDG PET

Authors and Year of Study	No. of Patients	Therapy*	Results
Bassa et al 1996	11	FAC	In the primary tumor, sensitivity = 75%; in the axilla, sensitivity = 42% and specificity = 100%
Burcombe et al 2002	9	FEC	In the primary tumor, sensitivity = 0% (0 of 9 patients); in the axilla, sensitivity = 0% (0 of 3 patients)
Kim et al 2002	50	AT or XT	In the primary tumor, sensitivity = 86% and specificity = 83%

*AT = doxorubicin and docetaxel; FAC = fluorouracil, doxorubicin, and cyclophosphamide; FEC = fluorouracil, etoposide, and cisplatin; XT = capecitabine and docetaxel.

1. conformation of gross residual tumor
2. not allow exclusion of microscopic residual tumor

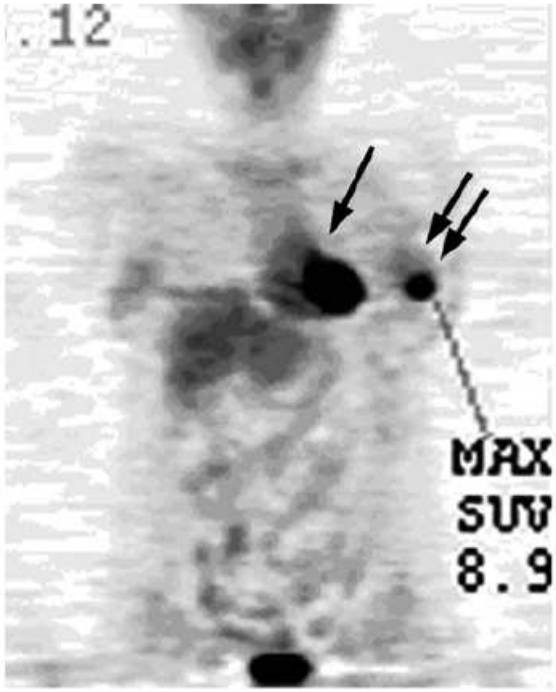
Monitoring response to therapy

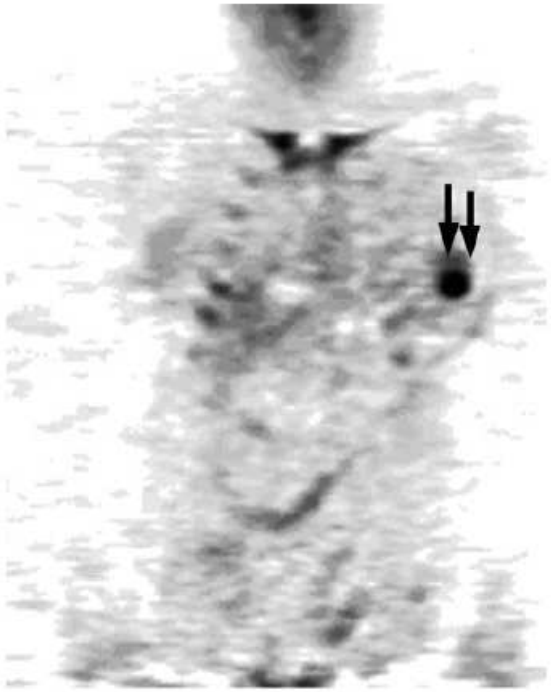


a. b.

Figure 10. Assessment of tumor response to NST. Coronal FDG PET images of a patient with right LABC (arrows in a), obtained before (a) and 2 months after (b) chemotherapy, show an excellent response. The tumor response was subsequently confirmed at posttherapy

Monitoring response to therapy





a. b.

Figure 11. Poor response to preoperative chemotherapy in a patient with left LABC. **(a)** Coronal FDG PET image obtained before therapy shows uptake in the breast primary tumor (double arrows) and myocardial uptake (single arrow), which is a normal variant. **(b)** Image obtained after 2 months of chemotherapy shows little qualitative change in the appearance of the breast tumor (arrows); there was only a small quantitative decline in uptake. The diffuse uptake in the marrow spaces is due to the effect of granulocyte colony-stimulating factor. The poor response to treatment was confirmed with multiple subsequent imaging studies and surgical histopathologic analysis.

Monitoring response to therapy

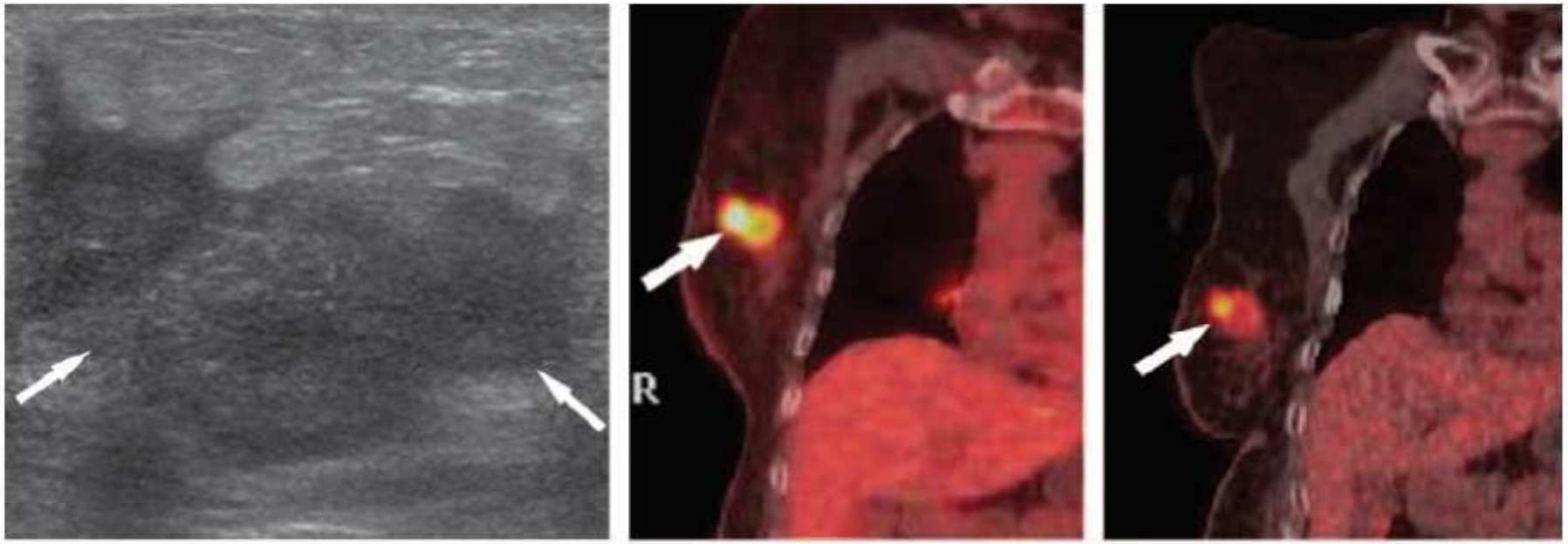


Figure 9. Initial and follow-up imaging of recurrent invasive ductal carcinoma in a 60-year-old woman with a palpable right breast mass after a left total mastectomy. **(a)** Initial US image shows an irregular hypoechoic mass (arrows) in the right breast. The mass was diagnosed on the basis of US-guided biopsy as invasive ductal carcinoma. Because of the patient's generally poor clinical condition, chemotherapy was administered. **(b)** Pretreatment coronal PET/CT image shows increased FDG uptake (maximum SUV, 8.7) indicative of hypermetabolism in the lesion (arrow). **(c)** Posttreatment coronal PET/CT image shows decreased FDG uptake (maximum SUV, 5.6) indicative of a chemotherapy-induced reduction in metabolic activity in the tumor (arrow).

Monitoring response to therapy

systemic therapy in metastatic or recurrent breast cancer

- Gennari et al:

  after 1st cycle of chemotherapy, >50% decrease in SUV

  good response to treatment in metastatic disease

Role of 18F-FDG PET in the early assessment of response to chemotherapy in metastatic breast patients
Clin Breast Cancer 2000; 1(2):156-161

- Dose Schwarz et al:

  after 1st cycle of chemotherapy

Early prediction of response to chemotherapy in metastatic breast cancer using sequential F18-FDG PET
J Nucl Med 2005; 46(7):1144-1150

- Stafford et al:

  bone metastasis

Use of serial FDG PET to measure the response of bone-dominant breast cancer to therapy
Acad Radiol 2002; 9(8):913-921