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ORIGINAL ARTICLE

^{18}Fluorodeoxyglucose-positron emission tomography/computed tomography features of suspected solitary pulmonary lesions in breast cancer patients following previous curative treatment

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Keywords
^{18}Fluorodeoxyglucose-positron emission tomography/computed tomography; breast cancer metastasis; lung cancer; solitary pulmonary lesion.

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Abstract

Background: Differentiating pulmonary metastasis from primary lung cancer can be challenging in patients with breast malignancy. This study aimed to characterize the imaging features of ^{18}fluorodeoxyglucose-positron emission tomography/computed tomography (^{18}F-FDG-PET/CT) for distinguishing between these diseases.

Methods: We enrolled 52 patients who received curative treatment for breast cancer but later presented with suspected solitary pulmonary lesions (SPLs) and subsequently underwent ^{18}F-FDG-PET/CT to investigate.

Results: Subsolid lesions, ill-defined borders, lung lesions with negative maximum standardized uptake value, and lesions without ^{18}F-FDG-PET/CT-diagnosed hilar and/or mediastinal lymph nodes and pleural metastases were more likely to be associated with primary lung cancer.

Conclusions: CT border, FDG uptake, hilar and/or mediastinal lymph node metastasis, and pleural metastasis are potential markers for diagnosis.

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Introduction

According to *Cancer Statistics 2017*, breast cancer is the most commonly diagnosed and the second-leading cause of cancer death among women, contributing to an estimated 252 720 new cases and 40 610 deaths per year in the United States.[1] Approximately 20% of these patients present with distant metastasis at diagnosis that accounts for a poor prognosis and lower quality of life. Indeed, the lung is one of the most common sites targeted by metastatic cancer cells.[2]

Solitary pulmonary metastasis after curative treatment for breast cancer is rare in patients with breast malignancy. Although it is not difficult to detect lung lesions with advanced imaging technology, differentiating pulmonary metastasis from primary lung cancer and other benign conditions can be challenging after curative treatment for breast cancer.[2–5]

Approximately 12% of breast cancer patients show solitary pulmonary lesions (SPLs)[6] that mimic primary lung cancer, which is not concordant with the fact that pulmonary metastasis usually exhibits a multiple lesion pattern in various malignancies.[7] On the other hand, many studies have reported that a second primary tumor, such as lung cancer, is highly likely to be a concurrent condition in breast cancer patients.[2,4,8] An accurate diagnosis will also have a significant impact on future treatment plans,[5] as surgical resection is more appropriate for primary lung cancer patients, while pulmonary metastasis requires systemic therapy.[2,9] As a result, it is essential to make a precise diagnosis once SPLs are detected in women who have received prior curative treatment for breast cancer.

^{18}Fluorodeoxyglucose-positron emission tomography/computed tomography (^{18}F-FDG-PET/CT), a molecular imaging strategy, has been widely applied in oncology in recent decades.[10–14] Current international guidelines suggest that suspected pulmonary metastasis in breast cancer is an indication for an ^{18}F-FDG-PET/CT scan, which helps to achieve accurate diagnosis and restaging for subsequent treatment.[15–18] For patients with clinically suspected lung cancer or pulmonary lesions that cannot be confidently diagnosed, ^{18}F-FDG-PET/CT is also highly recommended.[19–21]

Recent studies have investigated the potential differences in clinical characteristics among breast cancer patients with SPLs[2–5,22–25] however, the ^{18}F-FDG-PET/CT features in this population have not been well researched. In this retrospective study, we characterize the imaging features of ^{18}F-FDG-PET/CT to differentiate highly suspected SPLs resulting from breast cancer metastasis with primary lung cancer among breast cancer patients who received prior curative treatment, as well as those with benign pathology.

Methods

Participants

Patients who underwent ^{18}F-FDG-PET/CT scanning at the Tianjin Medical University Cancer Institute and Hospital between June 2009 and October 2016 were retrospectively selected. The inclusion criteria were: (i) female patients who previously received curative treatment for breast cancer (surgery with or without adjuvant therapy and radiotherapy); (ii) patients who underwent ^{18}F-FDG-PET/CT scanning to investigate a newly found suspected SPL on CT after initial treatment, and the minimum axial diameter of the lung lesion was 8 mm;[26] and (iii) a pathological report of the SPLs was available (immunohistochemistry results were required; however in cases with benign lung lesions, a long-term follow-up result showing disease remission without treatment was also acceptable). The exclusion criteria were: (i) patients with a history of disease

recurrence or metastasis; and (ii) patients with other diagnosed malignancies.

This study was approved by the ethics committee of Tianjin Medical University Cancer Institute and Hospital, and was conducted in accordance with the Declaration of Helsinki. Informed consent was waived because of the retrospective nature of this work.

Positron emission tomography/computed tomography (PET/CT) scanning and image interpretation

^{18}F-FDG-PET/CT scanning was conducted using a Discovery ST PET/CT scanner (GE Healthcare, Milwaukee, WI, USA). Patients were required to fast for six hours before the scan. Serum glucose was closely monitored before the intravenous injection of ^{18}F-FDG. The administered activity of the radiotracer was 4.1–4.8 MBq (0.11–0.13 mCi) per kilogram of body weight. Scanning was conducted from the mid thigh to the vertex approximately one hour after ^{18}F-FDG injection. CT scanning was performed with the following parameters: current, 120–170 mA; voltage, 120 kV; slice thickness, 5 or 3.75 mm; and reconstruction interval, 5 or 3.75 mm. Attenuation-corrected PET images were gathered at two minutes per frame and were reconstructed with iterative algorithms. A non-contrast CT scan targeted at the lung nodule with a slice thickness of 1.25 mm was also obtained.

Three senior radiologists in nuclear medicine reviewed the images on an Advantage Workstation (Version 4.4, GE Healthcare). Suspicious cases were resolved by discussion. Hilar and mediastinal adenopathy was diagnosed as malignant according to the following criteria: short-axis diameter larger than 1 cm, increased uptake of FDG (higher than mediastinal blood pool uptake), and visually lower attenuation (< 70 Hu). A volume of interest (VOI) was automatically marked using an isocontour method with a fixed maximum standardized uptake value (SUV_{max}) threshold of 2.5.

The following metabolic parameters were measured: the SUV_{max}, metabolic tumor volume (MTV), and total lesion glycolysis (TLG) of the lung lesion; and the SUV_{max}, MTV, and TLG of whole body lesions. SUVs were automatically generated via software using the following equation: SUV = radioactivity concentration/(injected activity/body weight). The MTVs were the volume of VOIs. TLGs were calculated by multiplying the average SUV by the MTV of VOIs.

Statistical analysis

Categorical variables were recorded as numbers and percentages. Continuous variables were recorded as median (range) or mean ± standard deviation, depending on the distribution of data. Variable comparisons were performed using the independent Student's *t*, Mann–Whitney *U*, or chi-squared test, as appropriate. Logistic regression was used for multivariate analyses. $P < 0.05$ was considered statistically significant. All statistical data were analyzed using SPSS version 17.0.

Results

Patient characteristics

A total of 52 patients met the inclusion criteria and were included in this study. None of the patients had cancer in situ or had undergone breast conserving surgery or neoadjuvant treatment. The clinicopathological characteristics of the study population are shown in Table 1.

Imaging and pathology

On ^{18}F-FDG-PET/CT, the lung lesion was ^{18}F-FDG avid in 41 (78.8%) patients, with a SUV_{max} of > 2.5. The mean SUV_{max} in all patients was 7.8 ± 6.1 (including both positive and negative SPLs). In 14 (26.9%) patients, additional potentially malignant lesions were discovered on ^{18}F-FDG-PET/CT. The detected metastases were as follows: hilar and/or mediastinal lymph node (LN, 14/14, 100.0%); pleural (4/14, 28.6%); bone (4/14, 28.6%); cervical and/or supraclavicular (3/14, 21.4%); brain (2/14, 14.3%); liver (2/14, 14.3%); and axillary (1/14, 7.1%). Thirty of the 52 patients also underwent hilar and/or mediastinal LN dissection. The sensitivity, specificity, and accuracy of detecting hilar and/or mediastinal LN metastasis in these patients were 55.5%, 100%, and 86.7%, respectively.

Among the 52 patients, the confirmed pathological results of the lung lesions were as follows: pulmonary metastasis (22/52, 42.3%); primary lung cancer (22/52, 42.3%); and benign pulmonary disease (8/52, 15.4%). Of the 22 patients with pulmonary metastasis, 1 (4.5%) was FDG-negative. Of the 22 patients with primary lung cancer, 6 (27.3%) were FDG-negative with the following pathologies: adenocarcinoma (18/22, 81.8%), adenosquamous carcinoma (2/22, 9.1%), squamous carcinoma (1/22, 4.5%), and small cell lung cancer (1/22, 4.5%). Typical presentations of FDG-positive cases are shown in Figure 1. Among the eight patients with benign disease, four were FDG-negative (50%). In these eight patients, two were identified with fibroma and focal fibrosis combined with lymphocyte infiltration, respectively; two had tuberculosis; and two had sclerosing hemangioma. The remaining two patients did not undergo pathological examination but long-term follow-up data showed that their lung lesions disappeared without antitumor treatment (Fig 2).

Table 1 Clinicopathological characteristics of the enrolled patients

Variable	N	%
Administered activity of tracer, MBq (mCi),	296.0 (188.7–421.8)	
Median (range)	8.0 (5.1–11.4)	
Age, median (range) (years)	56 (28–74)	
Maximum axial diameter of lung lesions, median (range) (cm)	2.2 (1.0–5.6)	
Minimum axial diameter of lung lesions, median (range) (cm)	1.7 (0.6–4.9)	
Smoking history		
Yes	3	5.8
No	49	94.2
DFI, median (range), months	65.6 (4.7–313.6)	
T stage of breast cancer†		
T_1	23	44.2
T_2	28	53.8
T_3	0	0.0
T_4	1	1.9
N stage of breast cancer†		
N_0	33	63.5
N_1	15	28.8
N_2	4	7.7
TNM stage of breast cancer†		
I	17	32.7
II	30	57.7
III	5	9.6
IV	0	0.0
Treatment for breast cancer		
Adjuvant chemotherapy		
Yes	49	94.2
No	3	5.8
Adjuvant radiotherapy		
Yes	18	34.6
No	34	65.4
Confirmation of lung lesions		
Pathology	50	96.2
Surgery	40	76.9
With LN dissection‡	30	57.7
Without LN dissection‡	10	19.2
Puncture	7	13.5
Bronchoscopy	3	5.8
Clinical follow-up	2	3.8

†Pathological stage of breast cancer according to the American Joint Committee on Cancer staging system. None of the patients had carcinoma in situ of breast cancer. ‡Some patients also underwent hilar and/or mediastinal lymph node (LN) dissection because intraoperative frozen pathology cannot differentiate pulmonary metastasis from primary lung cancer. DFI, disease-free interval; TNM, tumor node metastasis.

Differences between primary lung cancer and pulmonary metastasis

No significant differences in clinicopathological characteristics were found between patients presenting with primary lung cancer and pulmonary metastasis (Table 2).

CT characteristics were also evaluated to investigate their impact on the accuracy of diagnoses (Table 3). Of the 22 patients with pulmonary metastasis, only 1 patient (4.5%) had a subsolid lesion, which was a significantly lower incidence compared to patients with primary lung cancer (27.3%; $P = 0.04$). In addition, patients with primary lung cancer were more likely to present with ill-defined lesions compared to those with pulmonary metastasis (78.6% vs. 50%; $P = 0.001$). Other CT characteristics were not significantly different between the two patient groups.

As shown in Table 4, SUV_{max}, MTV, and TLG of both lung lesions and whole-body malignant lesions (diagnosis of ^{18}F-FDG-PET/CT) were included in the analysis. We found that when using a traditional cutoff point of 2.5, the positivity or negativity of SUV_{max} is a significant diagnostic factor. Most patients with negative SUV_{max} results had primary lung cancer (6/7, 85.7%) ($P = 0.04$). In addition, the SUV_{max} of whole-body lesions seemed a little higher in patients with pulmonary metastasis (11.1 ± 6.0) compared to those with primary lung cancer (7.8 ± 5.7), although the difference was not statistically significant ($P = 0.07$).

We found the distribution of metastasis could help to differentiate primary lung cancer and pulmonary metastasis. The hilar and/or mediastinal LN was a significant factor. However, unexpectedly, there were far more pulmonary metastasis patients with hilar and/or mediastinal LNs (diagnosis via ^{18}F-FDG-PET/CT) than patients with primary lung cancer ($P = 0.01$). Pleural metastasis was also a risk factor of pulmonary metastasis ($P = 0.04$). Indeed, we found that all four patients with pleural metastasis discovered via ^{18}F-FDG-PET/CT were from the pulmonary metastasis group.

Multivariate analysis revealed that a CT border characteristic was the only significant predictor for pulmonary metastasis after breast cancer curative treatment, unlike other factors, such as lesion type, FDG uptake of the lung lesion, and metastasis pattern (Table 5).

Discussion

In this work, we focused on a small group of female breast cancer patients who received curative treatment and then developed SPLs. Our data revealed that among these patients, the chance of developing new primary lung cancer and pulmonary metastasis were similar. In these two groups of patients, subsolid lesions, ill-defined border lesions, lesions with negative FDG uptake, and SPLs without ^{18}F-FDG-PET/CT diagnosed hilar and/or mediastinal LNs or pleural metastasis were more likely to be associated with primary lung cancer than with pulmonary metastasis. Of these diagnostic factors, lesion border status was found to be an independent predictor.

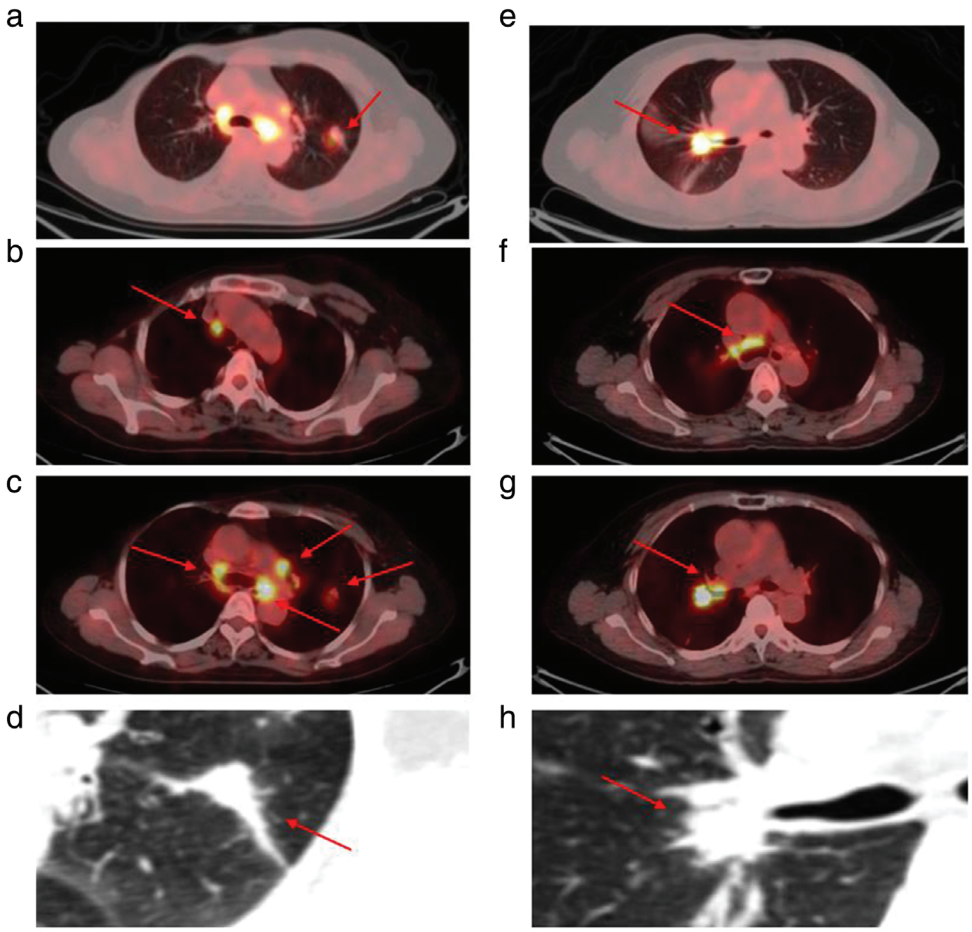

Figure 1 ^{18}Fluorodeoxyglucose-positron emission tomography/computed tomography (^{18}F-FDG-PET/CT) images of primary lung cancer and pulmonary metastasis. (**a–d**) A 54-year-old woman underwent surgery for stage II breast cancer followed by adjuvant chemotherapy. ^{18}F-FDG-PET/CT revealed a suspected solitary pulmonary lesion (SPL) (with a maximum standardized uptake value [SUV_{max}] of 4.83) 181 months after surgery. Hilar and mediastinal lymph nodes (LNs) were also positive. The patient underwent lung biopsy and mediastinoscopy surgery, which confirmed primary lung adenocarcinoma combined with multiple hilar and mediastinal LN metastases. (**e–h**) A 60-year-old woman underwent surgery for stage II breast cancer followed by adjuvant chemotherapy. PET/CT revealed a suspected SPL (SUV_{max} of 8.74) 259 months after surgery. Hilar and mediastinal LNs were also positive. Later surgery confirmed pulmonary metastasis combined with multiple hilar and mediastinal LN metastases from breast cancer. All lesions are marked with arrows.

SPLs after curative treatment for breast cancer, which mimic primary lung cancer and pulmonary metastasis and require significantly different management, are a rare condition that is seldom accurately diagnosed.[2,3,9,27–30] In particular, careful observation by an experienced pathologist and immunohistochemistry staining might not be sufficient to differentiate primary lung cancer (especially adenocarcinoma) from pulmonary metastasis of breast cancer. A few previous studies have reported how to make a diagnosis using regular radiological methods. The results varied because of small sample sizes and different study methods.[2–5,22–25] To the best of our knowledge, our research is the first to describe the imaging features of ^{18}F-FDG-PET/CT for differentiating highly suspected SPLs resulting from breast cancer metastasis and primary lung cancer among breast cancer patients who have received prior curative treatment.

Because primary lung cancer and pulmonary metastasis after breast cancer curative treatment are both uncommon in real clinical settings, there is no international guideline available in regard to differential diagnosis. ^{18}F-FDG-PET/CT is a powerful radiological method for detecting primary lung cancer and breast cancer metastasis.[15–21] Therefore, based on current research data and general guidelines for both lung cancer and breast cancer diagnosis, an ^{18}F-FDG-PET/CT scan is an appropriate management option.

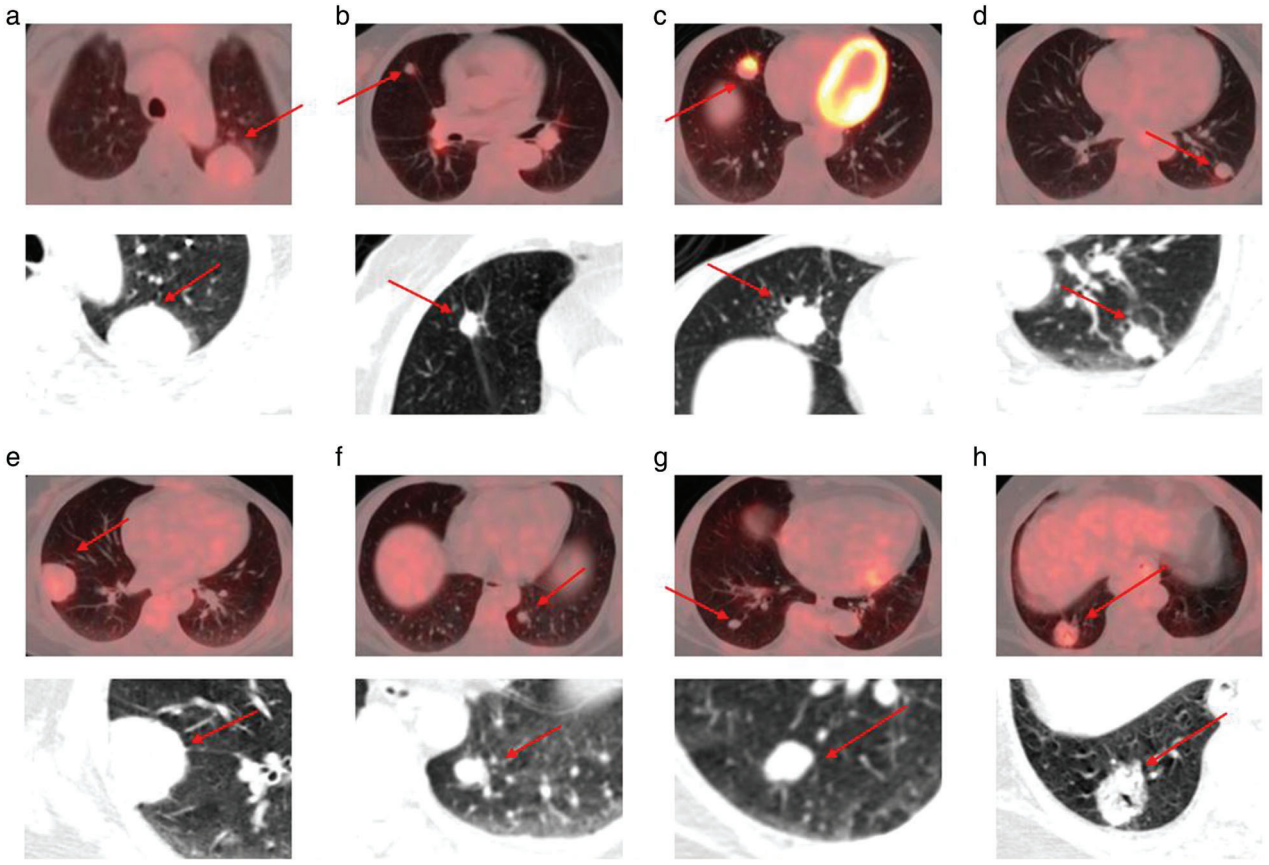

Figure 2 ^{18}Fluorodeoxyglucose-positron emission tomography/computed tomography (^{18}F-FDG-PET/CT) and non-contrast CT imaging results of all patients with benign diseases. (**a**) A 40-year-old woman presented with a lung lesion with a maximum standardized uptake value (SUV_{max}) of 2.3 and a maximum axial diameter of 3.8 cm. Pathology confirmed fibroma. (**b**) A 74-year-old woman presented with a lung lesion with an SUV_{max} of 4.3 and a maximum axial diameter of 1.3 cm. Pathology confirmed focal fibrosis combined with lymphocyte infiltration. (**c**) A 51-year-old woman presented with a lung lesion with an SUV_{max} of 8.3, and a maximum axial diameter of 2.3 cm. Pathology confirmed tuberculosis. (**d**) A 48-year-old woman presented with a lung lesion with an SUV_{max} of 1.7 and a maximum axial diameter of 1.7 cm. Pathology confirmed tuberculosis. (**e**) A 47-year-old woman presented with a lung lesion with an SUV_{max} of 3.1 and a maximum axial diameter of 4.5 cm. Pathology confirmed sclerosing hemangioma. (**f**) A 28-year-old woman presented with a lung lesion with an SUV_{max} of 0.9 and a maximum axial diameter of 1.2 cm. Pathology confirmed sclerosing hemangioma. (**g**) A 64-year-old woman presented with a lung lesion with an SUV_{max} of 0.7 and a maximum axial diameter of 1.3 cm. The patient did not receive antitumor treatment and the lesion disappeared during follow-up. (**h**) A 64-year-old woman presented with a lung lesion with an SUV_{max} of 3.9, and a maximum axial diameter of 3.3 cm. The patient did not receive antitumor treatment and the lesion disappeared during follow-up. All lesions are marked with arrows.

According to our data, approximately 15% of all patients were false positive cases. Similar results have been reported in other studies.[5,23] Thus, we should note that the proportion of benign patients is not low, even in these patients. In patients with definite malignant pulmonary lesions, the proportions of primary lung cancer and pulmonary metastasis were similar in this study. This finding could assist physicians in their clinical work and is in accordance with the results of previous research. We anticipated that older patients with advanced breast cancer and a shorter disease-free interval (DFI) were more likely to have pulmonary metastasis. Interestingly, none of these parameters was a significant predictor. A few studies have indicated that age could be a significant factor for differential diagnosis, as the incidence peak of breast cancer presents at a younger age than lung cancer.[3] In this work, a similar trend was observed, however the difference was not significant. It is well known that most breast cancer recurrence occurs during the first five years since initial treatment.[16] Hence, it is logical that patients with longer DFI are less likely to have metastasis. However, an adverse finding was revealed in our study (as shown in Table 2): the mean DFI of the metastasis group was approximately seven years, and therefore these tumors were "indolent metastases." We suggest that as a seven-year period is already beyond the common

Table 2 Clinicopathological differences between patients with primary lung cancer and pulmonary metastasis

Variable	Primary lung cancer	Pulmonary metastasis	*P*
Age, median (range) (years)	60 (39–73)	55 (38–68)	0.17
BMI, median (range) (kg/m^2)	25.2 (18.4–33.7)	25.0 (17.9–30.1)	0.69
Smoking history			1.00
Yes	1	1	
No	21	21	
TNM stage of breast cancer			0.66
I	8	6	
II	11	14	
III	3	2	
Treatment of breast cancer			
Adjuvant chemotherapy			1.00
Yes	21	20	
No	1	2	
Adjuvant radiotherapy			0.54
Yes	8	10	
No	14	12	
DFI, months	105.4 ± 81.5	81.4 ± 65.7	0.29
DFI			
Cutoff point of 5 and 10			0.41
> 10 years	7	4	
5–10 years	8	7	
< 5 years	7	11	
Cutoff point of 15			0.22
< 15 years	17	20	
> 15 years	5	2	
Laterality of breast cancer			0.13
Left	7	12	
Right	15	10	
Laterality of pulmonary lesion			0.76
Left	9	10	
Right	13	12	
Laterality between breast cancer and pulmonary lesion			0.54
Ipsilateral	10	8	
Contralateral	12	14	

BMI, body mass index; DFI, disease-free interval; TNM, tumor node metastasis.

Table 3 Computed tomography characteristics of lung lesions in patients with primary lung cancer and lung metastasis

Variable	Primary lung cancer	Pulmonary metastasis	*P*
Size of pulmonary lesion, cm			
Maximum axial diameter	2.3 ± 0.8	2.3 ± 1.2	0.94
Minimum axial diameter	1.8 ± 0.7	1.8 ± 1.0	0.75
Lesion type			0.04
Solid	16	21	
Subsolid	6	1	
Border			0.01
Well-defined	3	11	
Ill-defined	19	11	
Lobulation			1.00
Yes	18	18	
No	4	4	
Spiculation			0.50
Yes	17	15	
No	5	7	
Pleural indentation			0.55
Yes	11	9	
No	11	13	
Cavity			0.66
Yes	4	2	
No	18	20	
Location of pulmonary lesion			0.34
Peripheral	18	21	
Central	4	1	

surveillance period for breast cancer metastasis, prior data could be biased because of a lack of follow-up.

Common CT characteristics were included in our analysis. We found that both lesion type and border were significant predictors of primary lung cancer. It is well known that a radiological subsolid pulmonary lesion is one of the typical characteristics of primary lung adenocarcinoma,[31] even though it could also be pulmonary metastasis (in rare cases), such as pulmonary metastasis with lepidic growth.[3,31] When examining ^{18}F-FDG-PET/CT characteristics, the SUV_{max} cutoff point of 2.5 was a significant predictor in multivariate analysis. Most FDG-negative lesions were primary lung cancer and all of these patients had adenocarcinoma with subsolid radiological presentation. The value of metabolic parameters, such as SUV_{max}, MTV, and TLG, has a limited diagnostic effect.

Axillary LNs, the lung, bone, and the liver are the most common sites of metastasis in breast cancer patients,[32] while metastasis to hilar and mediastinal LNs, bone, the adrenal gland, liver, and brain are common in primary lung cancer.[33] Our data revealed that hilar and/or mediastinal LN metastasis was a significant predictor of pulmonary metastasis, which is contradictory to the traditional perspective. ^{18}F-FDG-PET/CT is reported to have a sensitivity of 50–79% and a specificity of 72–94% for the diagnosis of lung cancer mediastinal LN metastasis.[34–38] However, no prior data is available regarding the use of the same imaging strategy for a diagnosis of breast cancer mediastinal LN metastasis. Our results indicated that ^{18}F-FDG-PET/CT has a high level of specificity and accuracy for detecting hilar/mediastinal metastasis. Although such metastasis could not be definitively confirmed by ^{18}F-FDG-PET/CT, it is the most applicable and precise method available compared to a pathological examination. Therefore, metastasis from breast cancer should first be considered once suspected hilar and/or mediastinal LNs are found on ^{18}F-FDG-PET/CT among the target population. ^{18}F-FDG-PET/CT-detected pleural metastasis was also a significant diagnostic factor. Indeed, all four patients who presented

Table 4 PET/CT characteristics of lung lesions in patients with primary lung cancer and pulmonary metastasis

Variable	Primary lung cancer	Pulmonary metastasis	*P*
SUV_{max} of pulmonary lesion	7.1 ± 5.7	10.2 ± 6.3	0.10
FDG uptake of pulmonary lesion			0.04
Positive	16	21	
Negative	6	1	
SUV_{max} of whole lesions	7.8 ± 5.7	11.1 ± 6.0	0.07
MTV of pulmonary lesion (cm^3)	8.0 ± 11.7	12.5 ± 18.7	0.34
MTV of whole lesions (cm^3)	14.8 ± 27.0	151.9 ± 573.3	0.27
TLG of pulmonary lesion, median (range)	17.2 (0.0–351.9)	27.2 (0.0–532.7)	0.29
TLG of whole lesions	70.0 ± 128.7	700.5 ± 2529.3	0.25
Metastasis detected on PET/CT			
Hilar and/or mediastinal LN metastasis			0.01
Yes	3	11	
No	19	11	
Skeletal metastasis			0.60
Yes	1	3	
No	21	19	
Axillary metastasis			1.00
Yes	0	1	
No	22	21	
Brain metastasis			1.00
Yes	1	1	
No	21	21	
Pleural metastasis			0.04
Yes	0	4	
No	22	18	
Cervical and/or supraclavicular metastasis			1.00
Yes	2	1	
No	20	21	
Liver metastasis			0.47
Yes	0	2	
No	22	20	

FDG, ^{18}fluorodeoxyglucose; LN, lymph node; MTV, metabolic tumor volume; PET/CT, positron emission tomography/computed tomography; SUV_{max}, maximum standardized uptake value; TLG, total lesion glycolysis.

with pleural metastasis were finally diagnosed with pulmonary metastasis. This result was also contradictory to usual clinical practice, as pleural metastasis is more common in lung cancer patients.[39]

There are some limitations to this study. Firstly, because of the retrospective design, missing data was inevitable, as patients with multiple distant metastases usually refused biopsy and thus were subsequently lost to follow-up. Secondly, patients who underwent breast conservation surgery and neoadjuvant therapy were not observed in this work, indicating that the enrolled population did not generally represent the target population and thus there was selection bias. Finally, the status of important pathological parameters – such as ER, PR, HER2, and Ki-67 – were not available for this research because of the long enrollment period and significant difficulties in retrieving accurate data.

In conclusion, ^{18}F-FDG-PET/CT features are useful to predict pulmonary metastasis in breast cancer patients who have received prior curative treatment. Among them, CT border status, FDG uptake of the lung lesion, hilar and/or mediastinal LN metastasis, and pleural metastasis are potential imaging markers for accurate diagnoses.

Table 5 Multivariate analysis in patients with pulmonary metastasis after curative treatment for breast cancer

Variable	OR (95% CI)	*P*
Lesion type	0.83 (0.03, 23.30)	0.91
Solid		
Subsolid		
Border	8.76 (1.37, 56.21)	0.02
Well-defined		
Ill-defined		
FDG uptake of pulmonary lesion	0.14 (< 0.01, 4.31)	0.26
Positive		
Negative		
Metastasis detected on PET/CT		
Hilar and/or mediastinal LN metastasis	4.50 (0.79, 25.71)	0.09
Yes		
No		
Pleural metastasis	< 0.01 (0.00, –)	1.00
Yes		
No		

CI, confidence interval; FDG, ^{18}fluorodeoxyglucose; LN, lymph node; OR, odds ratio; PET/CT, positron emission tomography/computed tomography.

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Disclosure

No authors report any conflict of interest.

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