18F-Alfatide II for the evaluation of axillary lymph nodes in breast cancer patients: comparison with 18F-FDG

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Research Article

Keywords: 18F-Alfatide II, integrin αvβ3, positron emission tomography, breast cancer, axillary lymph node

Posted Date: February 15th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-166779/v1

Version of Record: A version of this preprint was published at European Journal of Nuclear Medicine and Molecular Imaging on February 9th, 2022. See the published version at https://doi.org/10.1007/s00259-021-05333-z.

Abstract

^{18}F-Alfatide II has been translated into clinical use and been proven to have good performance in identifying breast cancer. In this study, we investigated ^{18}F-Alfatide II for evaluation of axillary lymph nodes (ALN) in breast cancer patients and compared the performances with ^{18}F-FDG.

Methods: A total of 44 female patients with clinically suspected breast cancer were enrolled and underwent ^{18}F-Alfatide II and ^{18}F-FDG PET/CT within a week. Tracer uptakes in ALN were evaluated by visual analysis, semiquantitative analysis with maximum standardized uptake value (SUV_{max}), mean standardized uptake value (SUV_{mean}) and SUV_{max} ratio of target/non-target (T/NT).

Results: Among 44 patients, 37 patients were pathologically diagnosed with breast cancer with metastatic (17 cases) or non-metastatic (20 cases) ALN. The sensitivity, specificity, accuracy, positive predictive value (PPV) and negative predictive value (NPV) of visual analysis were 70.59%, 90.00%, 81.08%, 85.71% and 78.26% for ^{18}F-Alfatide II, 64.71%, 90.00%, 78.38%, 84.62% and 75.00% for ^{18}F-FDG, respectively. By combining ^{18}F-Alfatide II and ^{18}F-FDG, the sensitivity significantly increased to 82.35%, the specificity was 85.00%, the accuracy increased to 83.78%, the PPV was 82.35% and the NPV significantly increased to 85.00%. Three cases of luminal B subtype were false negative for both ^{18}F-Alfatide II and ^{18}F-FDG. The other 2 false negative cases of ^{18}F-Alfatide II were triple-negative subtype and 3 false negative cases of ^{18}F-FDG were luminal B subtype too. The AUCs of three semi-quantitative parameters (SUV_{max}, SUV_{mean}, T/NT) for ^{18}F-Alfatide II were between 0.8 and 0.9, whereas those for ^{18}F-FDG were more than 0.9. ^{18}F-Alfatide II T/NT had the highest Youden index (76.5%), specificity (100%), accuracy (89.19%) and PPV (100%) among these semi-quantitative parameters. ^{18}F-Alfatide II uptake as well as ^{18}F-FDG uptake in metastatic axillary lymph nodes (MALN) was significantly higher than that in benign axillary lymph nodes (BALN). Both ^{18}F-Alfatide II and ^{18}F-FDG did not show difference in primary tumor uptake irrespective of ALN status.

Conclusion: ^{18}F-Alfatide II can be used in breast cancer patients to detect metastatic ALN, however, like ^{18}F-FDG, with high specificity but relatively low sensitivity. The combination of ^{18}F-Alfatide II and ^{18}F-FDG can significantly improve sensitivity and NPV. ^{18}F-Alfatide II T/NT may serve as the most important semi-quantitative parameter to evaluate ALN.

Introduction

Axillary lymph nodes (ALN) are the most common spread site of breast cancer (1, 2). The status of ALN determines the staging, treatment strategy and prognosis for breast cancer patients (3). ALN involvement often means the more advanced stage, the greater extent of surgery, the need for systemic therapy and the lower survival rate. ALN metastasis is also the most important predictor of overall recurrence and survival (4). Therefore, the identification of ALN metastasis is crucial for patients with breast cancer. The gold standard for detecting ALN involvement is ALN dissection, which however can bring many adverse

complications such as arm edema, pain, neuropathy, and so on (5). Although minimally invasive methods including sentinel lymph node biopsy, core needle biopsy and fine needle aspiration cytology lead to fewer complications than ALN dissection, they have the risk of implantation metastasis (6). For these reasons, a non-invasive method of evaluating ALN is essential.

X-ray mammography, ultrasound, CT and magnetic resonance imaging (MRI) are traditional imaging methods, which can non-invasively evaluate ALN. However, the evaluation using these imaging methods is based on anatomical abnormalities and morphological changes, which often fail to reflect the status of ALN accurately (1). As a molecular imaging method, positron emission tomography (PET) has its superiority to traditional imaging methods in the clinic. It has been widely accepted for the diagnosis, staging, treatment evaluation and recurrence monitoring in cancer patients. As the most frequently used PET tracer, ^{18}F-FDG can provide glucose metabolism information in tissues. Many ^{18}F-FDG PET or PET/CT studies have also shown promising results for ALN evaluation. It has been reported that the specificity of ^{18}F-FDG for detecting metastatic ALN is up to 90–100%, but the sensitivity is relatively low to 50–80% (7–9). Accordingly, ^{18}F-FDG PET or PET/CT may underestimate the number of metastatic ALN. Therefore, more accurate ALN assessment entails some emerging PET tracers.

^{18}F-Alfatide II is an arginine-glycine-aspartate (RGD) based PET tracer targeting integrin $\alpha_v\beta_3$, which is highly expressed on activated endothelial cells of tumor neovasculature (10, 11). Some studies have shown the usefulness of ^{18}F-Alfatide II for tumor detection, therapy response prediction and prognosis evaluation (12–20). One of our previous clinical studies also demonstrated that ^{18}F-Alfatide II has good performance in identifying breast cancer. Particularly, ^{18}F-Alfatide II may be superior to ^{18}F-FDG in detecting breast cancer with strongly positive ER but negative HER-2 expression (21). Moreover, another clinical study also indicated that this tracer is valuable in the diagnosis of metastatic lymph nodes for non-small cell lung cancer patients (22). However, there is yet no report concerning ^{18}F-Alfatide II in detecting metastatic ALN of breast cancer.

In this work, ^{18}F-Alfatide II was further investigated in breast cancer patients for assessing ALN on the basis of our previous study (21). We obtained diagnostic parameters of ^{18}F-Alfatide II for identifying ALN metastasis using visual and semi-quantitative methods and assessed its diagnostic performance as compared to ^{18}F-FDG. We also compared diagnostic parameters of ^{18}F-Alfatide II and ^{18}F-FDG among different groups of ALN.

Materials And Methods

Patients

This study was approved by the ethics committee of Jinling Hospital (Approval No. 2015NZYW-007) and registered at ClinicalTrials.gov (NCT02582801). The including criteria include: (1) clinically suspected primary breast cancer according to conventional imaging, (2) no prior treatment for breast lesions, (3) 18

y < age < 70 y. The excluding criteria include: (1) pregnancy or lactation period, (2) some accompanied serious diseases (*e.g.*, impaired liver or renal function, active tuberculosis, another malignant tumor). Forty-four female patients (age range, 28–66 y, mean age, 50.73 ± 8.01 y) were included in this study and written informed consent was obtained from each patient.

PET/CT Acquisition

^{18}F-Alfatide II was synthesized according to the previously described method (23). PET/CT scans with ^{18}F-Alfatide II and ^{18}F-FDG were performed with an interval of at least one day and completed within one week. No specific patient preparation was requested before ^{18}F-Alfatide II injection, but fasting for at least 6 h was requested before ^{18}F-FDG injection. The injected activity was 306 ± 80 MBq (range 155–503 MBq) for ^{18}F-Alfatide II and approximately 3.7 MBq/kg body weight for ^{18}F-FDG. In addition, blood glucose level below 140 mg/dL needs to be confirmed before ^{18}F-FDG injection. After a rest for 60 min after injection, patients underwent the scans using an integrated PET/CT system (Biography 16, Siemens Healthcare). CT acquisition was initially performed with 120 kV, 140 mA, and a slice thickness of 5 mm. Subsequently, PET acquisition was performed with 3 min for each bed position. The CT data were used for PET attenuation correction and PET images were reconstructed using an iterative algorithm.

Image Analysis

PET, CT, and fused images were displayed on a Siemens/Syngo user interface. The images were interpreted by a consensus of two experienced nuclear medicine physicians, who were blinded to the histological diagnosis and other imaging results. It was defined as visually positive that the radioactive uptake of the ALN was higher than that of the surrounding normal tissue. The maximum standardized uptake value (SUV_{max}) and the mean standardized uptake value (SUV_{mean}) were semi-quantitatively measured by drawing regions of interest over the ALN. The SUV_{max} ratio of the ALN on the same side of the breast lesion to the node on the opposite side was calculated as T/NT (target/non-target).

Statistical Analysis

Statistical analysis was performed using SPSS software (version 17.0, SPSS, Inc., Chicago, IL, USA). All semi-quantitative data were expressed as the mean ± standard deviation. Differences both in independent samples and in paired samples were analyzed by *t*-test. The sensitivity, specificity, accuracy, PPV and NPV were calculated for each diagnostic parameter. Receiver operating characteristic (ROC) curve analysis was performed to evaluate the diagnostic performance. The area under the curve (AUC) and the cutoff value were further determined at the point with the highest Youden index. A *P* value less than 0.05 was considered statistically significant.

Results

Pathological Findings

All 44 patients received biopsy or surgery on breast lesion after two PET/CT scans. Among them, 39 patients were pathologically diagnosed with breast cancer and the other 5 were diagnosed with benign breast disease. In 39 patients with breast cancer, 2 patients did not undergo biopsy or surgery on ALN thus unclear about the metastasis status. The pathological results of ALN were obtained in the remaining 37 breast cancer patients, out of which 17 cases were confirmed with ALN metastasis and 20 cases were without. Characteristics of these 37 patients are presented in Table 1. Based on immunohistochemistry and fluorescence in situ hybridization (FISH), the invasive carcinomas in 33 patients (excluding 4 patients with ductal carcinoma in situ) were further divided into four molecular subtypes. ALN metastasis occurred in 2 cases of luminal A subtype (2/5), 8 cases of luminal B subtype (8/14), 3 cases of HER-2 overexpressing subtype (3/4) and 4 cases of triple-negative subtype (4/10).

Table 1
Characteristics of Breast Cancer Patients for Assessing ALN

Variable Breast Cancer (n)
Median Age (years, range) 53 (28–66)
Histology 37
Ductal Carcinoma in situ 4
Invasive Carcinoma 33
Molecular Subtype 33
Luminal A 5
Luminal B 14
HER-2 overexpressing 4
Triple-negative 10
Axillary Lymph Node 37
Metastasis 17
No Metastasis 20

Visual Assessment Findings

Among 17 cases with ALN metastasis, 12 cases were correctly recognized using ^{18}F-Alfatide II (Fig. 1) and 5 cases were false negative (Fig. 2). In comparison, 11 cases were correctly identified using ^{18}F-FDG (Fig. 1) and 6 cases were false negative (Fig. 2). By combining ^{18}F-Alfatide II and ^{18}F-FDG, the number of false negative cases was three. Among 20 cases without ALN metastasis, 18 cases were true negative, and 2 cases were false positive using ^{18}F-Alfatide II. Likewise, the number of true negative cases was 18 and that of false positive cases was 2 for ^{18}F-FDG. There was one false positive case for both ^{18}F-Alfatide II and ^{18}F-FDG. By combining the two tracers, the number of false positive cases was three. The

corresponding sensitivity, specificity, accuracy, positive predictive value (PPV) and negative predictive value (NPV) are shown in Table 2. Both ^{18}F-Alfatide II and ^{18}F-FDG had the same high specificity (90.00%) and relatively low sensitivity (70.59% *vs.* 64.71%). They both had similar accuracy (81.08% *vs.* 78.38%), PPV (85.71% *vs.* 84.62%) and NPV (78.26% *vs.* 75.00%). Moreover, the combined sensitivity and NPV significantly increased to 82.35% and 85.00%, while the combined accuracy increased to 83.78%.

Table 2
Visual Analysis of ^{18}F-Alfatide II and ^{18}F-FDG in Identifying ALN Metastasis

Variable	Sensitivity	Specificity	Accuracy	PPV	NPV
Alfatide II Visual	70.59%	90.00%	81.08%	85.71%	78.26%
FDG Visual	64.71%	90.00%	78.38%	84.62%	75.00%
Alfatide II + FDG Visual	82.35%	85.00%	83.78%	82.35%	85.00%
Alfatide II SUV_{max}	76.47%	90.00%	83.78%	86.67%	81.82%
Alfatide II SUV_{mean}	70.59%	95.00%	83.78%	92.31%	79.17%
Alfatide II T/NT	76.47%	100%	89.19%	100%	83.33%
FDG SUV_{max}	82.35%	90.00%	86.49%	87.50%	85.71%
FDG SUV_{mean}	82.35%	90.00%	86.49%	87.50%	85.71%
FDG T/NT	88.24%	85.00%	86.49%	83.33%	89.47%

There were three false negative cases for both ^{18}F-Alfatide II and ^{18}F-FDG. All the 3 cases belonged to luminal B subtype (Fig. 2). The other 2 false negative cases for ^{18}F-Alfatide II were triple-negative subtype (Fig. 3). The remaining 3 false negative cases for ^{18}F-FDG were all luminal B subtype (Fig. 4). One case of ductal carcinoma in situ was false positive for both ^{18}F-Alfatide II and ^{18}F-FDG (Fig. 5). The other false positive case for ^{18}F-Alfatide II was luminal B subtype and that for ^{18}F-FDG was HER-2 overexpressing subtype.

Semi-quantitative Assessment Findings

ROC curves of various semi-quantitative parameters are shown in Fig. 6. For both ^{18}F-Alfatide II and ^{18}F-FDG, the curves are located at the upper left of the chance line, indicating their strong potential for identifying ALN metastasis in breast cancer patients. However, the AUCs of ^{18}F-Alfatide II are slightly less than those of ^{18}F-FDG. The corresponding statistics of the ROC curves are presented in Table 3. The AUCs of ^{18}F-Alfatide II are between 0.8 and 0.9, while those of ^{18}F-FDG are all more than 0.9. The maximum Youden indices are close among these semi-quantitative parameters. ^{18}F-Alfatide II T/NT has the highest Youden index (76.50%), which indicates that the parameter has the highest diagnostic accuracy. Corresponding to the maximum Youden index, each semi-quantitative parameter has its cutoff

value. Based on these cutoff values, the sensitivity, specificity, accuracy, PPV and NPV values are calculated in Table 2. Although the sensitivity of each ^{18}F-Alfatide II parameter is less than that of ^{18}F-FDG, the specificity of the former is superior or equal to that of the latter. In particular, ^{18}F-Alfatide II T/NT has the highest specificity (100%), accuracy (89.19%) and PPV (100%) among all these parameters. The highest sensitivity (88.24%) is for ^{18}F-FDG T/NT, as well as the highest NPV (89.47%).

Table 3
ROC Quantitative Analysis of ^{18}F-Alfatide II and ^{18}F-FDG in Identifying ALN Metastasis

Parameter	AUC	*P*	Cutoff value	Youden index
Alfatide II SUV_{max}	0.812	0.001	1.095	66.50%
Alfatide II SUV_{mean}	0.804	0.002	0.81	65.60%
Alfatide II T/NT	0.851	0.000	2.5	76.50%
FDG SUV_{max}	0.924	0.000	1.265	72.40%
FDG SUV_{mean}	0.921	0.000	0.79	72.40%
FDG T/NT	0.922	0.000	2.745	73.20%

Comparisons Among Different Groups of ALN

The SUV_{max}, SUV_{mean} and T/NT for ^{18}F-Alfatide II between metastatic axillary lymph node (MALN) group and non-metastatic axillary lymph node (i.e. benign axillary lymph node, BALN) group are compared in Table 4, as well as those for ^{18}F-FDG. Using any of the three parameters, MALN had significantly higher ^{18}F-Alfatide II uptake than BALN ($P < 0.05$). The same result was obtained for ^{18}F-FDG. The SUV_{max}, SUV_{mean} and T/NT for the two tracers in the primary breast tumors with MALN and BALN are also compared in Table 5. No statistically significant differences between the two groups were found (all *P* values were greater than 0.05).

Table 4

Comparisons of ^{18}F-Alfatide II and ^{18}F-FDG Uptake between MALN and BALN

Parameter	MALN	BALN	*t*	*P*
Alfatide II SUV_{max}	2.608 ± 2.034	0.675 ± 0.379	4.175	0.000
Alfatide II SUV_{mean}	1.594 ± 1.191	0.487 ± 0.230	4.075	0.000
Alfatide II T/NT	5.922 ± 4.452	1.335 ± 0.550	4.579	0.000
FDG SUV_{max}	4.173 ± 3.762	0.833 ± 0.796	3.879	0.000
FDG SUV_{mean}	2.658 ± 2.304	0.580 ± 0.490	3.941	0.000
FDG T/NT	12.348 ± 12.370	2.079 ± 1.580	3.687	0.001

Table 5

Comparisons of ^{18}F-Alfatide II and ^{18}F-FDG uptake between Primary Tumors with MALN and Primary Tumors with BALN.

Parameter	Primary Tumors with MALN	Primary Tumors with BALN	*t*	*P*
Alfatide II SUV_{max}	4.205 ± 2.186	3.563 ± 1.552	1.043	0.304
Alfatide II SUV_{mean}	2.521 ± 1.251	2.186 ± 0.954	0.925	0.361
Alfatide II T/NT	6.330 ± 4.015	4.719 ± 2.177	1.549	0.130
FDG SUV_{max}	6.927 ± 3.585	7.510 ± 5.002	0.401	0.691
FDG SUV_{mean}	4.230 ± 2.198	4.686 ± 3.215	0.494	0.625
FDG T/NT	7.672 ± 5.099	11.385 ± 15.809	0.926	0.361

Discussion

^{18}F-Alfatide II is a PET probe to target integrin $\alpha_v\beta_3$. Our previous study demonstrated the clinical usefulness of ^{18}F-Alfatide II in breast cancer, suggesting that it is comparable to ^{18}F-FDG for identification of breast cancer and can exert a complementary role to ^{18}F-FDG for some subtypes (21). When using ^{18}F-Alfatide II to detect lymph node metastases, Zhou's study (22) showed encouraging results with the sensitivity of 100%, the specificity of 94.90% and the accuracy of 95.40% for non-small cell lung cancer patients.

In this study, visual assessment findings showed that the false negative rate of ^{18}F-Alfatide II (5/17) was similar to that of ^{18}F-FDG (6/17) for detecting metastatic ALN, whereas the false positive rate of ^{18}F-Alfatide II (2/20) was about the same as that of ^{18}F-FDG (2/20). The relatively low sensitivity (64.71%)

and high specificity (90.00%) of ^{18}F-FDG in our study were consistent with the numbers reported in previous studies (24–31). Compared with ^{18}F-FDG, ^{18}F-Alfatide II had the same high specificity (90.00%) and relatively higher sensitivity (70.59%). Moreover, the accuracy, PPV and NPV of ^{18}F-Alfatide II were somewhat higher than those of ^{18}F-FDG. Although ^{18}F-Alfatide II was non-inferior to ^{18}F-FDG in detecting metastatic ALN, its sensitivity (70.59%) was much lower than that reported by Zhou *et al.* in lung cancer patients, which was almost 100% (22). For both ^{18}F-Alfatide II and ^{18}F-FDG, the relatively high number of false negative cases is the main cause for the compromised sensitivity. However, combining ^{18}F-Alfatide II and ^{18}F-FDG together can significantly improve sensitivity and NPV, suggestive of their mutually complementary role.

For ^{18}F-FDG, all 6 false negative cases were of luminal B subtype. Although there are still controversies on the correlation between hormonal receptor status, HER-2 overexpression and ^{18}F-FDG uptake (32, 33), ALN without ^{18}F-FDG foci should remain alerted for breast cancer patients of luminal B subtype. For ^{18}F-Alfatide II, three of the five false negative cases were also luminal B subtype, which may be attributed to the small sized ALN in the three patients. The other two false negative cases of ^{18}F-Alfatide II were triple-negative subtype. Our previous study also demonstrated that primary tumors of triple-negative subtype had the lowest ^{18}F-Alfatide II uptake compared with the other three subtypes (21). Thus ^{18}F-Alfatide II appears to bring about false negative results for assessing ALN of triple-negative subtype just like what we observed in assessing primary tumors. Based on our findings, ^{18}F-Alfatide II can play a complementary role to ^{18}F-FDG in assessing ALN of luminal B subtype, while ^{18}F-FDG can make up for the deficiency of ^{18}F-Alfatide II in evaluating ALN of triple-negative subtype.

According to semi-quantitative assessment findings in this study, three parameters (SUV_{max}, SUV_{mean}, T/NT) of ^{18}F-Alfatide II showed AUCs of more than 0.8, indicating their strong potential for detecting metastatic ALN. As presented in Table 3, the optimal cutoff value is 1.095 for ^{18}F-Alfatide II SUV_{max}, 0.81 for ^{18}F-Alfatide II SUV_{mean} and 2.5 for ^{18}F-Alfatide II T/NT. Although the AUCs (< 0.9) of ^{18}F-Alfatide II are all less than those (> 0.9) of ^{18}F-FDG, ^{18}F-Alfatide II T/NT has the highest Youden index (76.50%), specificity (100%), accuracy (89.19%) and PPV (100%) among all these parameters. These data suggested that ^{18}F-Alfatide II T/NT may have the potential to serve as the most important semi-quantitative parameter to be used for evaluation of ALN.

In the previous study, ^{18}F-Alfatide uptakes in malignant lymph nodes were significantly higher than those in benign lymph nodes for non-small cell lung cancer patients (22). Our results also showed that MALN had higher ^{18}F-Alfatide II uptake than BALN, as well as ^{18}F-FDG uptake. These data suggested that both ^{18}F-Alfatide II and ^{18}F-FDG are suitable to distinguish between MALN and BALN. However, no difference was found in ^{18}F-Alfatide II and ^{18}F-FDG uptakes among the primary breast tumors with MALN and with BALN. Several previous studies demonstrated that the higher ^{18}F-FDG uptake of the primary breast lesion could mean a higher incidence of ALN metastasis (8, 34–36). Other studies however revealed no

significant difference between MALN and BALN in terms of primary breast mass in ^{18}F-FDG PET/CT (37, 38), which was also found in the present study for both ^{18}F-Alfatide II and ^{18}F-FDG. Song *et al.* thought molecular subtypes should be considered as a possible factor to affect ^{18}F-FDG uptake by primary breast cancer lesion for predicting ALN metastasis (8). Kim *et al.* demonstrated that ^{18}F-FDG uptake of primary breast cancer lesion has a significant predictive value for ALN metastasis in patients with ER-positive/HER-2-negative and HER-2-positive subtypes (39). More luminal B subtype and triple-negative subtype were included in our study, which could cause no significant difference in primary breast tumors with MALN versus BALN for ^{18}F-FDG and ^{18}F-Alfatide II.

There are some limitations in the present study. Particularly, the number of cases is not large enough. Due to the small number of luminal A and HER-2 overexpressing subtype, the evaluation of ALN using ^{18}F-Alfatide II in each subtype was not conducted in this study. In the future, further investigations are required to concentrate on exploring the preference of ^{18}F-Alfatide II in assessing ALN for some certain subtypes of breast cancer.

Conclusion

^{18}F-Alfatide II can be used to detect metastatic ALN like ^{18}F-FDG with high specificity but relatively low sensitivity. Combining ^{18}F-Alfatide II and ^{18}F-FDG can significantly improve sensitivity and NPV. ^{18}F-Alfatide II is insufficient for assessing ALN of triple-negative subtype but complementary to ^{18}F-FDG for ALN of luminal B subtype. Having the highest specificity, accuracy and PPV, ^{18}F-Alfatide II T/NT may be the most important semi-quantitative parameter for the evaluation of ALN. PET/CT can distinguish between MALN and BALN based on ^{18}F-Alfatide II uptake of the ALN, but can't do based on ^{18}F-Alfatide II uptake of the primary breast tumor.

Declarations

Compliance with Ethical Standards:

Conflict of Interest:

All authors declare no conflict of interest.

Ethical approval:

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent:

Informed consent was obtained from all individual participants included in the study.

Funding: This study was funded by X (grant number X).

This work was supported by the National Key Basic Research Program of China (973 program, 2014CB744504), the National Natural Science Foundation of China (81971675), the Natural Science Foundation of Jiangsu Province (BK20160610), Jiangsu Province Social Development Program (BE2017772), Jiangsu Planned Projects for Postdoctoral Research Funds (1601090C), and the National University of Singapore Start-up Fund (R-180-000-017-133, R-180-000-017-733, R-180-000-017-731).

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Figures

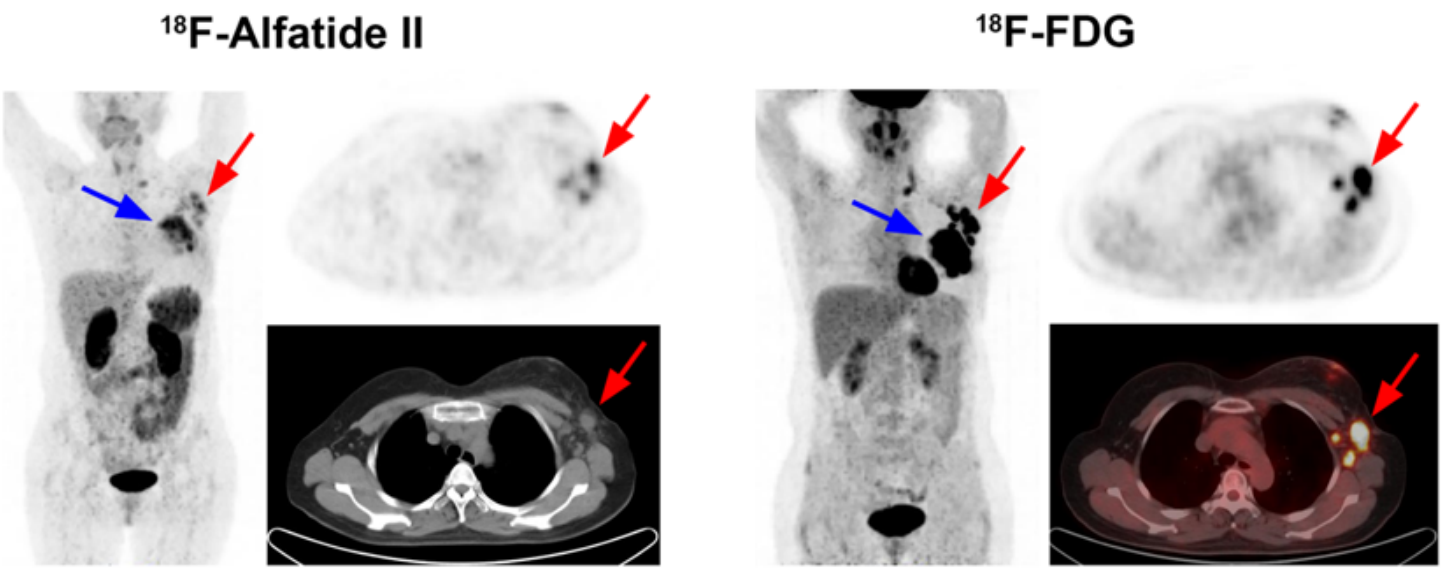

Figure 1

A 49-y-old patient with HER-2-overexpressing breast cancer (blue arrows) and ALN metastases (red arrows) showing high uptakes of both 18F-Alfatide II and 18F-FDG.

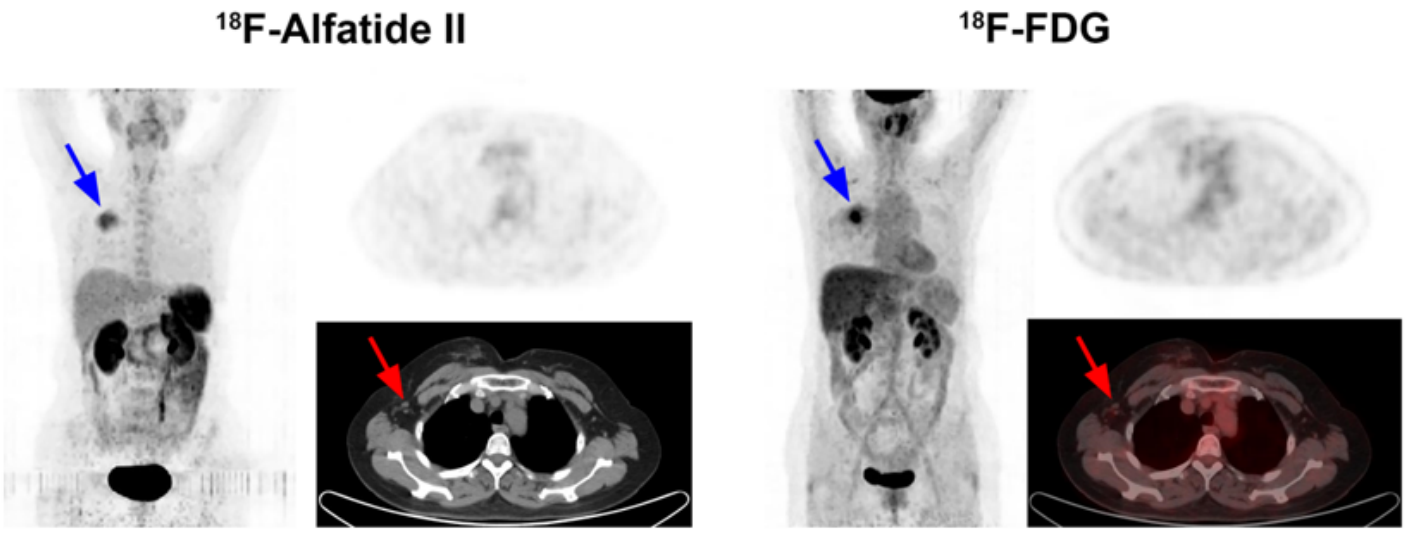

Figure 2

A 47-y-old patient with luminal B breast cancer (blue arrows) showing intense uptake of both 18F-Alfatide II and 18F-FDG, but no uptake of neither tracer in metastatic ALN (red arrows).

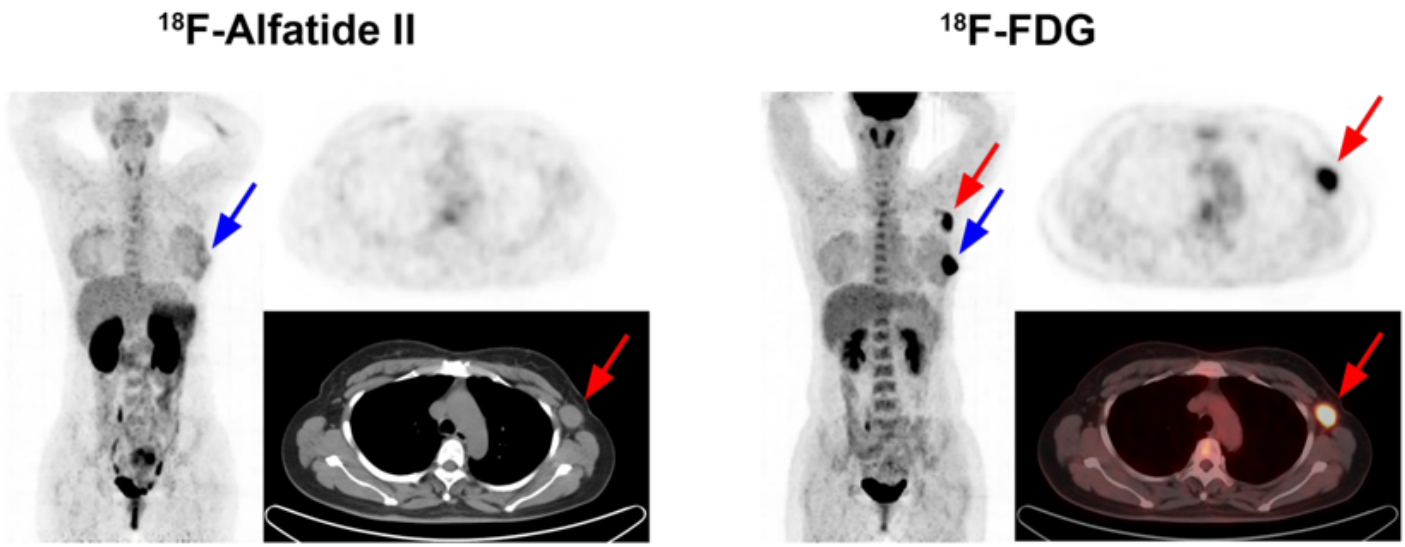

Figure 3

A 46-y-old patient with triple-negative breast cancer (blue arrows) and ALN metastasis (red arrows) showing no increased 18F-Alfatide II uptake but high 18F-FDG uptake.

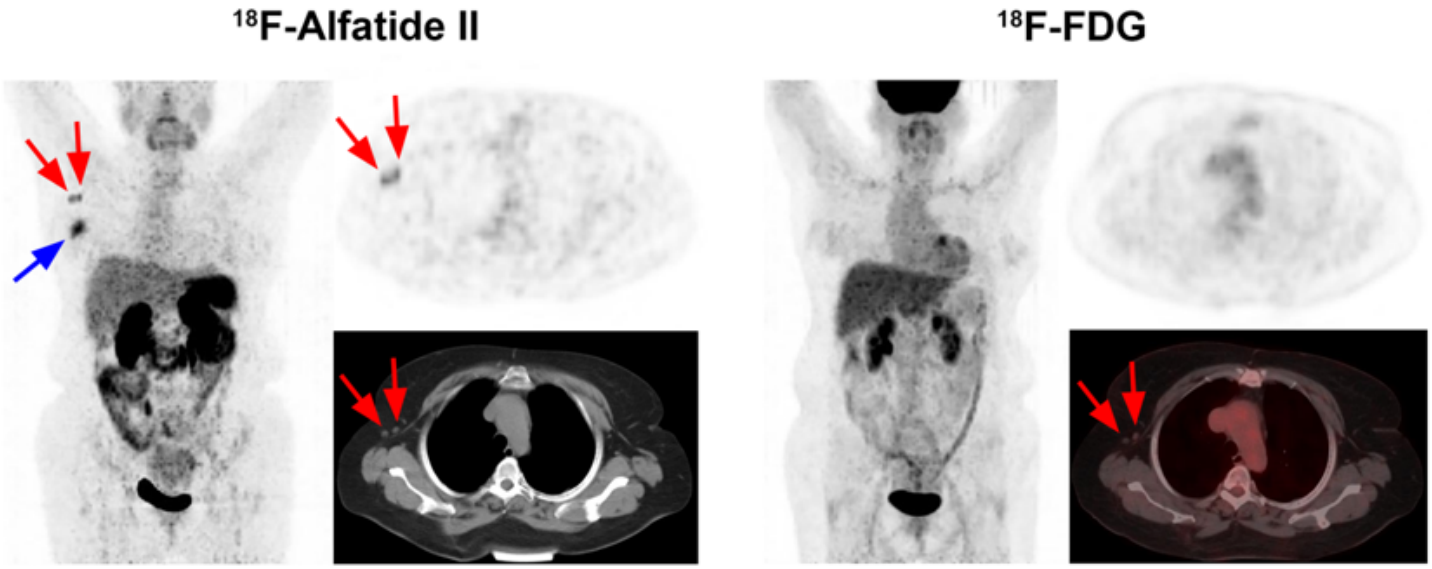

Figure 4

A 60-y-old patient with luminal B breast cancer (blue arrow) and ALN metastasis (red arrows) showing intense 18F-Alfatide II uptake but no 18F-FDG uptake in neither the primary tumor nor metastatic ALN.

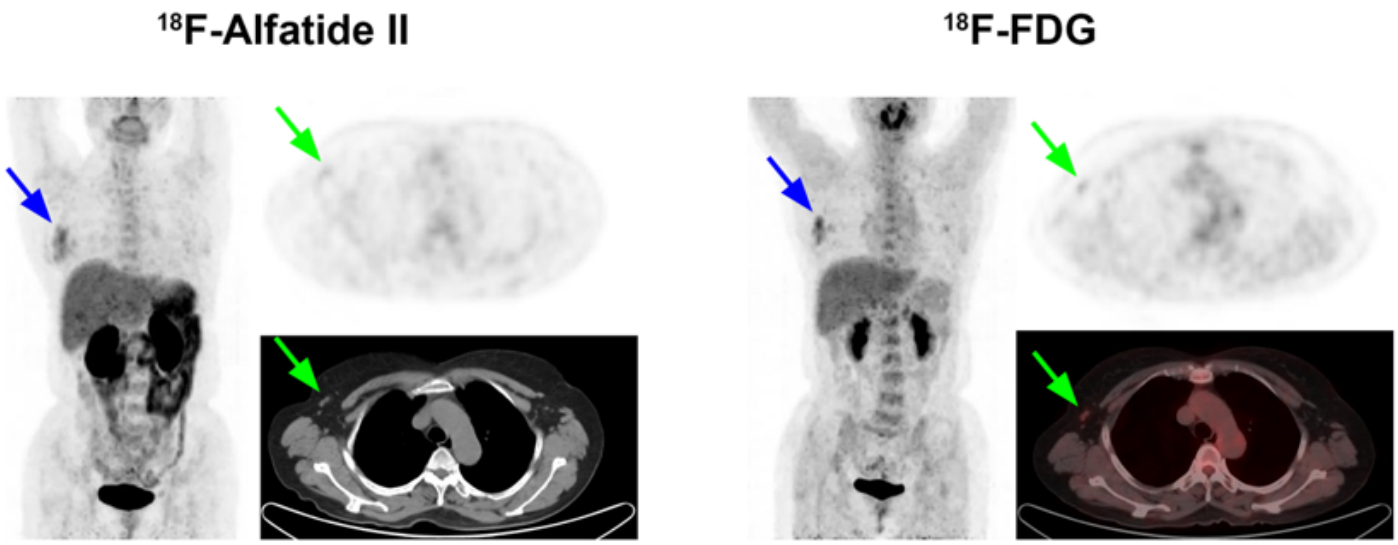

Figure 5

A 57-y-old patient with ductal carcinoma in situ (blue arrows) showed intense uptakes of both 18F-Alfatide II and 18F-FDG, and non-metastatic ALN (green arrows) had slightly increased uptakes of both 18F-Alfatide II and 18F-FDG.

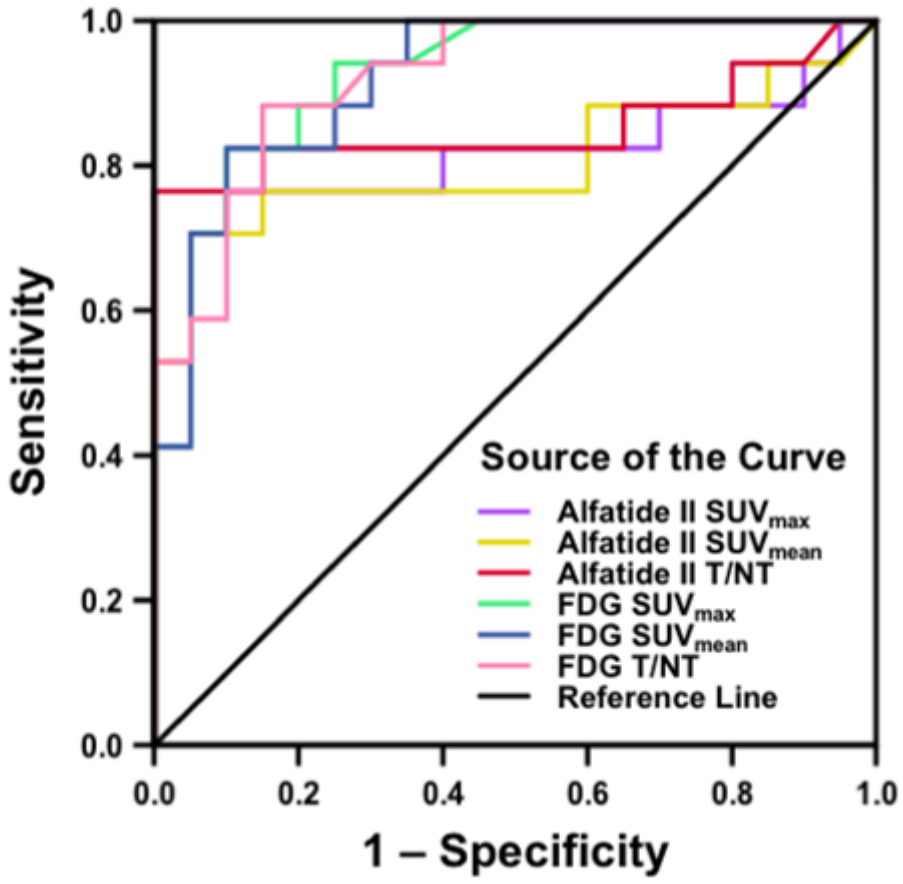

Figure 6

ROC curves of 18F-Alfatide II and 18F-FDG parameters in identifying ALN metastasis.