

Diagnostic Potential of ^{68}Ga -NeoB PET/CT with Estrogen Receptor– and Progesterone Receptor–Positive Breast Cancer Undergoing Staging or Restaging for Metastatic Disease

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^{18}F -FDG PET/CT has low sensitivity for estrogen receptor and progesterone receptor (ER/PR)-positive breast cancer. By contrast, gastrin-releasing peptide receptor is overexpressed in ER/PR-positive breast cancer. This study assessed the diagnostic potential of ^{68}Ga -NeoB PET/CT in staging or restaging metastatic ER/PR-positive and human epidermal growth factor receptor 2 (HER2)-negative breast cancer.

Methods: Patients with ER/PR-positive and HER2-negative breast cancer with clinical suspicion for metastatic disease undergoing staging or restaging were prospectively enrolled. All patients underwent ^{68}Ga -NeoB PET/CT, in addition to standard ^{18}F -FDG PET/CT. ER/PR-positive and HER2-negative status was confirmed in prior biopsy samples (primary or metastatic). Conventional imaging (^{18}F -FDG PET/CT, bone scan, and diagnostic CT) was required within 3 wk of ^{68}Ga -NeoB PET/CT. ^{18}F -FDG PET/CT and ^{68}Ga -NeoB PET/CT were assessed visually and quantitatively. Visually, all scans were read masked by 2 readers, with a third reader if results were discordant.

Results: Twenty patients were enrolled, all with ER/PR-positive and HER2-negative histopathology. Of these, 75% (15/20) had lobular-subtype cancer, 40% (8/20) had suspected metastatic disease at diagnosis, and 60% (12/20) underwent restaging after systemic therapy. Overall, 75% (15/20) of the ^{68}Ga -NeoB PET/CT scans and 65% (13/20) of the ^{18}F -FDG PET/CT scans were positive on visual assessment. For 50% (10/20) of patients, both scans were positive, and for 10% (2/20) of patients, both scans were negative. In the staging group, 75% (6/8) of patients had positive ^{68}Ga -NeoB PET/CT and 50% (4/8) of patients had positive ^{18}F -FDG PET/CT. At restaging, 75% (9/12) of patients had positive ^{68}Ga -NeoB PET/CT and 75% (9/12) of patients had positive ^{18}F -FDG PET/CT. Sites of positive ^{68}Ga -NeoB PET/CT and negative ^{18}F -FDG PET/CT disease were identified in 50% (4/8) of staging patients and 42% (5/12) of restaging patients, whereas negative ^{68}Ga -NeoB PET/CT and positive ^{18}F -FDG PET/CT disease was found in none of the staging patients but 58% (7/12) of

the restaging cohort. Of these, 71% (5/7) of patients had a reduction in their ER status in the most recent biopsy samples. Quantitatively, the median SUV_{max} was higher for ^{68}Ga -NeoB PET/CT (20.5; interquartile range, 5.8–31.3) than for ^{18}F -FDG PET/CT (7.4; interquartile range, 4.9–9.8). **Conclusion:** ^{68}Ga -NeoB PET/CT has diagnostic potential in the staging of ER/PR-positive and HER2-negative breast cancer. Further evaluation is warranted.

Key Words: estrogen receptor; breast cancer; ^{68}Ga -NeoB PET/CT; GRPR

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Breast cancer is the second leading cause of cancer-related death in women, and estrogen receptor (ER)-positive breast cancer is the most common presentation (1,2). Although ^{18}F -FDG PET/CT shows high diagnostic accuracy in ER and progesterone receptor (ER/PR)-negative disease, its sensitivity is lower for women with ER/PR-positive disease (3–5). Better diagnostic tools are required for ER/PR-positive breast cancer. Gastrin-releasing peptide receptor (GRPR) correlates strongly with ER expression in breast cancer (6). NeoB (a bombesin analog) is a 14-amino-acid amphibian homolog of mammalian gastrin-releasing peptide, with a high affinity for GRPR (7), and its analogs have previously demonstrated promising safety and utility in the assessment of breast cancer (8). Preclinical studies suggest promising outcomes with various GRPR antagonists, highlighting their safety profile, but limited exploration has occurred in breast cancer settings (7,9,10). Recent findings suggest GRPR-targeted PET/CT may be more sensitive than ^{18}F -FDG PET/CT in detecting metastatic breast cancer, particularly the lobular subtype (8,11). The aim of this study is to compare the detection rate of ^{68}Ga -NeoB PET/CT with conventional imaging, including ^{18}F -FDG PET/CT, in women with ER/PR-positive, human epidermal growth factor receptor 2 (HER2)-negative breast cancer with suspected or confirmed metastatic disease.

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MATERIALS AND METHODS

Study Design

This prospective phase 2 imaging study was undertaken at a single Australian institution (St Vincent's Hospital Sydney). The study protocol was approved by the St Vincent's Hospital institutional review board (HREC/2022/SVH/ETH01188), and patients provided written informed consent. The study was registered with ClinicalTrials.gov (NCT05889728).

Patient Enrollment

Eligible participants had histopathologically confirmed ER/PR-positive, HER2-negative breast cancer and were undergoing either staging for suspected metastatic breast cancer at diagnosis or restaging with known metastatic breast cancer. Participants either had undergone or planned to undergo ^{18}F -FDG PET/CT, diagnostic CT, and bone scan for clinical purposes within 3 wk. Exclusion criteria include breastfeeding, pregnancy, or the presence of another active malignancy. Clinical data such as age, time since diagnosis, initial pathologic findings including stage, details of previous and ongoing treatments, locations of disease, and histology of subsequently biopsied metastatic lesions were collected as part of the study.

^{68}Ga -NeoB Production and Image Acquisition

^{68}Ga -NeoB was prepared using cold kits supplied by Advanced Accelerator Applications. A $^{68}\text{Ge}/^{68}\text{Ga}$ generator (IGG100-50 M-NT; Eckert-Ziegler) was eluted with 5.0 mL of 0.1 M hydrogen chloride. The eluent was sterile filtered via a Millex-GV 33-mm, 0.22- μm polyvinylidene fluoride membrane (Merck Millipore) and added to 50 μg of NeoB precursor. The reaction vial was supplemented with 0.5 mL of kit-provided buffer formulation and reacted at 95°C for 10 min to provide ^{68}Ga -NeoB with specific activity of $10.51 \pm 4.53 \text{ MBq}/\mu\text{g}$ ($n = 23$). Thin-layer chromatography analyses were performed using a 1- μL spot on $8 \times 2 \text{ cm}$ instant thin-layer chromatography silica gel plates developed with 50% v/v methanol in a 1.0 M ammonium acetate mobile phase and provided mean 98.99% radiochemical purity (Advanced Accelerator Applications specifications, free $^{68}\text{Ga} \leq 5\%$). High-performance liquid chromatography analyses, adapted from Pretze et al. (12), were performed.

Patients were injected with 200 MBq of intravenous ^{68}Ga -NeoB. PET imaging was performed at 1.5–2 h after injection. Image acquisition was performed on a Siemens Biograph Vision 600 64 PET/CT scanner at 2 min per field of view with an imaging direction from vertex to mid-thigh. This was preceded by a noncontrast low-dose CT scan using the following CT parameters: slice thickness of 2 mm with a 2-mm increment, soft-tissue reconstruction kernel at 120 kV and 50 mAs, pitch of 0.8, and a 440 matrix. Emission data were corrected for randoms, scatter, decay, and attenuation.

Imaging Analysis

^{68}Ga -NeoB PET/CT and ^{18}F -FDG PET/CT images were reported by 2 experienced nuclear medicine specialists who were masked to clinical data and prior imaging results. All images were reviewed and reported on Siemens Fusion Viewer (Syngo.via) software. Images were analyzed visually, and lesions were reported based on anatomic site, size, intensity of tracer uptake compared with surrounding tissue, and a 4-point scale of diagnostic certainty (definitely negative; equivocal, probably negative; equivocal, probably positive; and definitely positive). Each detected lesion was scored as definitely negative (0), probably negative (1), probably positive (3), or definitely positive (4). Scores 0 and 1 were considered negative, and scores 3 and 4 were considered positive. A definitely negative score was applied to lesions that were detected on low-dose CT and were consistent with breast cancer yet had no ^{68}Ga -NeoB or ^{18}F -FDG uptake. In cases of discordance between clinical readings, a third masked nuclear medicine

specialist provided a tiebreaker opinion. Images were reported and made available to treating clinicians. Subsequent treatment was documented but left to the treating clinician.

Image Quantitation

Quantitative analysis was conducted to derive total tumor volume, SUV_{max} , and SUV_{mean} data for both ^{18}F -FDG PET/CT and ^{68}Ga -NeoB PET/CT (MIM Encore; MIM Software) using an SUV_{max} and a volume cutoff of 3 and 0.2 mL, respectively.

Patient Follow-up

Data on investigations, including histologic results of metastatic deposits and further confirmatory imaging, were documented.

Statistical Analysis

Quantitative PET findings were compared at the per-patient level, and all measurable lesions between the 2 PET tracers were compared. Only descriptive statistical analysis was performed because of the small sample size, and all findings were reported as number and percentage or as median and interquartile range (IQR).

RESULTS

Twenty patients were enrolled, all with ER/PR-positive and HER2-negative histopathology at diagnosis. Of these, 75% (15/20) had lobular-subtype cancer and 25% (5/20) had other subtypes on histopathologic analysis. Patient characteristics are listed in Table 1. Of the patients, 40% (8/20) had suspected metastatic disease at diagnosis and 60% (12/20) underwent restaging after systemic therapy. Patients underwent imaging with both ^{68}Ga -NeoB PET/CT and ^{18}F -FDG PET/CT on different days. The median time between ^{18}F -FDG PET/CT and ^{68}Ga -NeoB PET/CT was 3 d (IQR, 2–10.75). The median uptake time for ^{68}Ga -NeoB PET/CT was 99 min (IQR, 91–106). Discordant readings occurred for 25% (4/20) of the ^{68}Ga -NeoB PET/CT scans and 15% (3/20) of the ^{18}F -FDG PET/CT scans and needed a tiebreaker opinion from a third reader.

^{68}Ga -NeoB PET/CT and ^{18}F -FDG PET/CT

In total, 75% (15/20) of ^{68}Ga -NeoB PET/CT scans and 65% (13/20) of ^{18}F -FDG PET/CT scans were positive on visual assessment. Sites of ^{68}Ga -NeoB-positive disease were identified at the primary site or local recurrence in 27% (4/15), in lymph nodes in 33% (5/15), in bone in 27% (4/15), and in viscera in 53% (8/15) of the scans. In 50% (10/20) of patients, both ^{68}Ga -NeoB PET/CT and ^{18}F -FDG PET/CT were positive, and in 10% (2/20) of patients, both were negative. In addition, 25% (5/20) of patients had disease identified on ^{68}Ga -NeoB PET/CT alone and 15% (3/20) of patients had disease identified on ^{18}F -FDG PET/CT alone. On a region-based analysis, 15% (3/20) of patients had primary site or local recurrence, 30% (6/20) of patients had additional nodal sites, and 30% (6/20) of patients had visceral or skeletal sites detected only on ^{68}Ga -NeoB PET/CT (stomach, orbit, bone, peritoneum, esophagus, and rectum), whereas 10% (2/20) of patients had nodal sites and 15% (3/20) of patients had visceral or skeletal sites (bone) detected only on ^{18}F -FDG PET/CT. Patients with the lobular subtype had a high proportion of positive ^{68}Ga -NeoB PET/CT findings, 73% (11/15), versus 60% (9/15) with positive ^{18}F -FDG PET/CT findings.

Staging

In the staging group, 75% (6/8) of patients had positive ^{68}Ga -NeoB PET/CT and 50% (4/8) of patients had positive ^{18}F -FDG PET/CT. Both patients with negative ^{68}Ga -NeoB PET/CT scans also had negative ^{18}F -FDG PET/CT. All patients in the staging cohort had strongly positive ($\geq 80\%$ intensity) ER expression in

TABLE 1
Patient Characteristics

Characteristic	Data
Age (y)	59 (45–70)
Time from diagnosis (y)	3 (0–8)
Histologic subtype of primary cancer	
Lobular	
Classical	11
Pleomorphic	3
Mixed classical and pleomorphic	1
Ductal	1
Mixed lobular and ductal	2
Other	2
Ki-67 (%)	9 (5–21)
Grade	
2	14
3	4
2 and 3*	1
Not defined	1
ER expression from initial histopathology of primary cancer	90 (80–100)
Location of primary cancer	
Unilateral	16
Bilateral	4
Stage at diagnosis	
M0	18
M1	2
Lines of prior therapy	
0	8
1	6
2 or more	6
Current therapy	
Capecitabine, cyclophosphamide, vinorelbine, and/or sacituzumab govitecan	6
Letrozole and/or fulvestrant	6
Abemaciclib, ribociclib, and/or palbociclib	5
Zoledronic acid and/or denosumab	2

*In bilateral primary cancer.

Qualitative data are number; continuous data are median followed by range in parentheses.

biopsy samples of primary sites of disease, except for 1 patient who had 40% ER expression (Table 2). This patient was 1 of 2 who had negative ^{68}Ga -NeoB PET/CT. Half (4/8) of the staging cohort had sites of disease that were positive on ^{68}Ga -NeoB PET/CT and negative on ^{18}F -FDG PET/CT (Figs. 1 and 2). No patient had sites of negative ^{68}Ga -NeoB PET/CT and positive ^{18}F -FDG PET/CT disease in the staging cohort. The number of lesions detected by ^{68}Ga -NeoB PET/CT was 28, versus 17 by ^{18}F -FDG PET/CT (Table 3).

Restaging

At restaging, 75% (9/12) of patients had positive ^{68}Ga -NeoB PET/CT scans and 75% (9/12) of patients had positive ^{18}F -FDG PET/CT scans at a per patient level. In addition, 42% (5/12) of

patients had positive sites on ^{68}Ga -NeoB PET/CT that were negative on ^{18}F -FDG PET/CT, and 58% (7/12) of the restaging cohort had positive sites on ^{18}F -FDG PET/CT that were negative on ^{68}Ga -NeoB PET/CT (Fig. 3). Of these, 71% (5/7) patients had a reduction in their ER status in the most recent biopsy samples from that of the initial histopathology before endocrine therapy (Table 2). In the restaging cohort, the number of lesions detected by ^{68}Ga -NeoB PET/CT was 110, versus 122 by ^{18}F -FDG PET/CT (Table 3).

Quantification

Quantitative analysis for ^{68}Ga -NeoB PET/CT showed a median total tumor volume of 55.1 mL (IQR, 5.8–83.5), median SUV_{max}

TABLE 2
Molecular Subtypes, ER/PR Status, Scan Findings at Biopsied Site, and Previous Lines of Therapy

Patient no.	Molecular subtype	ER/PR in most recent biopsy sample		Positive or negative ¹⁸ F-FDG PET/CT in biopsied lesion	Positive or negative ⁶⁸ Ga-NeOB PET/CT in biopsied lesion	Previous therapy lines	ER/PR in initial primary biopsy sample (%)
		%	Location or procedure				
Staging cohort							
2	Lobular	Not reported	Stomach	—	+	0	100/20
7	Other	90/80	Axillary lymph node	+	+	0	—
8	Lobular	100/100	Mastectomy	NA	NA	0	—
14	Lobular	40/70	Mastectomy	NA	NA	0	—
17	Lobular	90/30	Biopsy of primary site	—	+	0	—
18	Lobular	Left, 70/10; right, 100/100	Bilateral mastectomy	NA	NA	0	—
19	Lobular	80/90	Biopsy of primary site	+	+	0	—
20	Lobular	95/50	Biopsy of primary site	+	+	0	—
Restaging cohort							
1	Lobular	5/0	Stomach	—	+	5	80/0
3	Other	0/0	Axillary lymph node	—	—	2	90/80
4	Lobular	90/0	Axillary lymph node	—	+	2	65/40
5	Lobular	30/0	Bone marrow	+	—	3	90/0
6	Lobular	10/0	Bone	+	—	1	90/90
9	Left, ductal; right, mixed lobular and ductal	0/0	Bone	+	—	1	Left, 80/80; right, 90/75
10	Mixed lobular and ductal	60/0	Bone	+	+	1	95/95
11	Lobular	10/0	Retropertitoneal lymph node	+	—	1	100/100
12	Ductal	0/0	Axillary lymph node	+	—	1	100/0
13	Lobular	90/0	Peritoneum	+	+	4	30/60
15	Lobular	Left, 95/85; right, 100/100	breast	—	+	1	Not reported
16	Lobular	95/15	Chest wall	—	+	4	90/80

— = Most recent biopsy is initial primary biopsy sample, as stated in columns 3 and 4; NA = not applicable.

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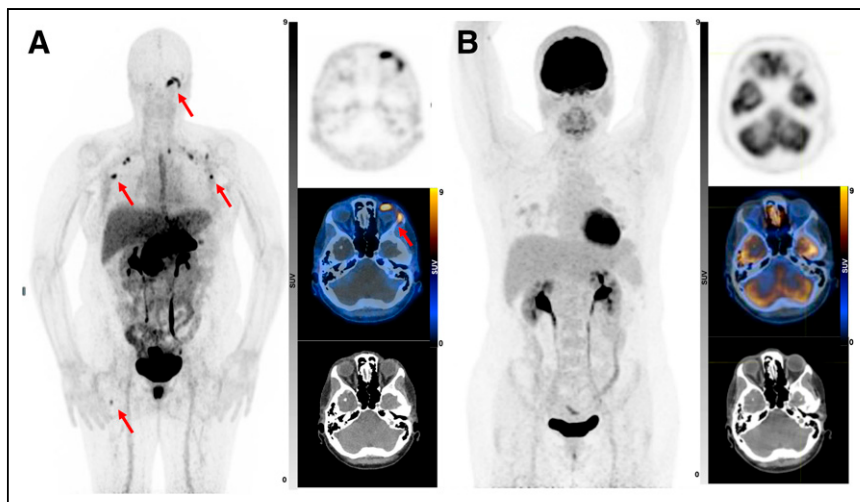


FIGURE 1. 50-y-old woman with newly diagnosed lobular carcinoma, 100% ER, 100% PR, and HER2-negative histopathology. (A) After bilateral mastectomy and axillary dissections, ^{68}Ga -NeoB PET/CT demonstrated multiple bilateral axillary and infraclavicular lymph nodes, left orbital metastases, and right femoral metastases on whole-body maximum-intensity projection (left) and axial (right) images (arrows). (B) Preoperative staging with ^{18}F -FDG PET/CT showed primary right breast lesion and right axillary lymph nodes on whole-body maximum-intensity projection (left) and axial (right) images.

of 20.5 (IQR, 5.8–31.3), and median SUV_{mean} of 5.6 (IQR, 2.4–7.2). ^{18}F -FDG PET/CT had a median total tumor volume of 17.8 mL (IQR, 10.9–31.2), median SUV_{max} of 7.4 (IQR, 4.9–9.8), and median SUV_{mean} of 3.4 (IQR, 3.0–3.6).

In the staging cohort, the median SUV_{max} was 16.8 (IQR, 5.1–38.9) for ^{68}Ga -NeoB PET/CT and 4.3 (IQR, 3.6–5.4) for ^{18}F -FDG PET/CT. In the restaging cohort, the median SUV_{max} was 20.5 (IQR, 7.3–24.6) for ^{68}Ga -NeoB PET/CT and 9.6 (IQR, 7.4–10.2) for ^{18}F -FDG PET/CT.

DISCUSSION

Accurate staging of ER-positive breast cancer, particularly the lobular subtype, with ^{18}F -FDG PET/CT and conventional imaging

has significant limitations, with ^{18}F -FDG PET/CT often demonstrating only low metabolic activity and frequently demonstrating negative findings (3,13,14). This study demonstrates that ^{68}Ga -NeoB PET/CT has potential in the staging of ER/PR-positive, HER2-negative breast cancer, particularly the lobular subtype, with a higher detection rate than that of ^{18}F -FDG PET/CT, but there are more heterogeneous findings in restaging after systemic therapy. The detection rate of ^{68}Ga -NeoB PET/CT for sites of metastatic disease appears to be superior to that of ^{18}F -FDG PET/CT in this study in patients undergoing initial staging, with an increased number of lesions compared with ^{18}F -FDG PET/CT, particularly in the detection of additional nodal disease, and potentially a higher volume of disease that may affect the initial staging and subsequent management of these patients. ^{18}F -FDG PET/CT is the standard of care for the staging of metastatic breast cancer (15). With low ^{18}F -FDG PET/CT avidity in hormone-positive disease, alternative molecular imaging for the staging of breast cancer is a current unmet need (16). 16α -[^{18}F]-fluoro-17 β -estradiol is a molecular imaging agent with potential in the staging of ER-positive breast cancer. It directly binds to the ER in the nucleus of ER-expressing cells (17). However, recent research directly comparing 16α -[^{18}F]-fluoro-17 β -estradiol PET to ^{18}F -FDG PET/CT in a metastatic cohort has not shown its superiority over ^{18}F -FDG PET/CT (18,19). In a study by Ulaner et al. (20), assessing the 16α -[^{18}F]-fluoro-17 β -estradiol PET detection rate compared with ^{18}F -FDG PET/CT in 62 patients undergoing staging for ER-positive breast cancer with correlation to histopathologic findings, 16α -[^{18}F]-fluoro-17 β -estradiol PET detected 11 of 14 true-positive lesions, versus 12 detected by ^{18}F -FDG PET/CT. The current study analyzed detection rate rather than sensitivity but had a significantly higher detection rate than that of ^{18}F -FDG PET/CT in the staging of ER-positive patients at high risk of metastatic disease, suggesting ^{68}Ga -NeoB PET/CT may improve on available molecular imaging options for the staging of ER-positive breast cancer patients.

Lobular-subtype breast cancer is often difficult to detect on conventional imaging, and as a consequence, it is often diagnosed later and hence has a poorer prognosis related to the more advanced stage (21). Most patients demonstrate high levels of ER expression, and it often spreads to visceral sites, including invasion of hollow organs and peritoneal seeding (22,23). Given that lobular carcinomas often have lower metabolic activity on ^{18}F -FDG PET/CT, the use of GRPR-targeted imaging agents appears to provide a more accurate representation of disease burden, at least at presentation, when the tumor is more homogeneous in ER expression. In this study, 73% of patients with

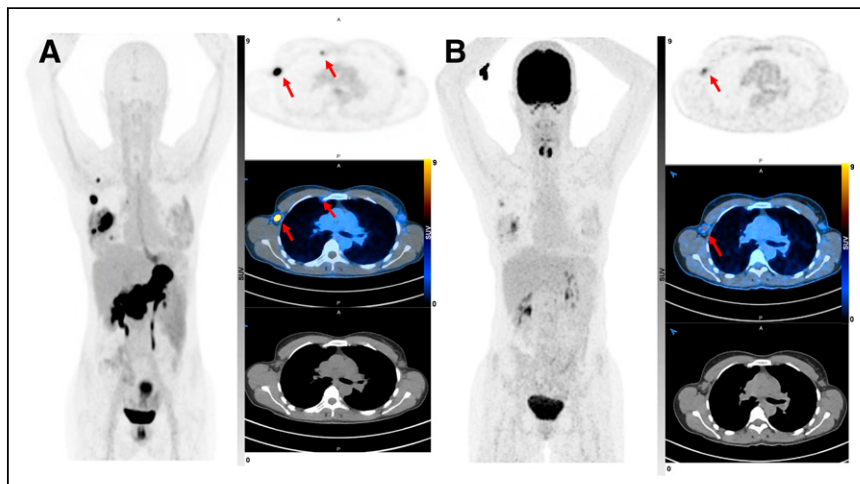


FIGURE 2. 44-y-old woman with newly diagnosed lobular carcinoma, 80% ER, 90% PR, and HER2-negative histopathology. (A) On staging, imaging ^{68}Ga -NeoB PET/CT detected multifocal primary right breast lymph nodes, right axillary or subpectoral lymph nodes, and right internal mammary lymph node in whole-body maximum-intensity projection (left) and axial (right) views (arrows). (B) ^{18}F -FDG PET/CT shows primary lesion, 1 axillary lymph node, and no internal mammary lymph node on whole-body maximum-intensity projection (left) and axial (right) images (arrows).

TABLE 3

Site and Number of Visually Identified Lesions on ^{68}Ga -NeoB PET/CT and ^{18}F -FDG PET/CT in Staging and Restaging Cohorts

Site	Visually identified lesions (n)	
	^{68}Ga -NeoB PET/CT	^{18}F -FDG PET/CT
Staging cohort		
Primary breast	4	3
Lymph nodes	23	14
Bone	0	0
Viscera	1	0
Total	28	17
Restaging cohort		
Primary breast	2	1
Lymph nodes	38	42
Bone	24	68
Viscera	46	11
Total	110	122

lobular-subtype breast cancer were positive on ^{68}Ga -NeoB PET/CT, with a median SUV_{max} of 20.5. This aligns with the results of a previous study by Wong et al. (8) that demonstrated more avid [^{64}Cu]Cu-SAR-BBN uptake than with ^{18}F -FDG in the lobular subtype of metastatic disease. These results are promising for the future use of GRPR-targeted PET for more accurate staging of lobular-subtype breast cancer, and it warrants further evaluation both for staging and in treatment response.

A higher proportion of patients had ^{68}Ga -NeoB-positive and ^{18}F -FDG-negative disease in the staging setting before systemic endocrine therapy than in the restaging setting after systemic therapy. In this study, 58% of patients undergoing restaging had sites of ^{18}F -FDG-positive and ^{68}Ga -NeoB-negative disease. Most of these patients (71%) had a reduction in their ER expression in

biopsy samples of the metastatic sites. This may be partly due to increased heterogeneity in the ER expression of treated metastatic disease. This suggests that a proportion of metastatic deposits have transformation to a low ER expression clone and that ^{68}Ga -NeoB PET/CT imaging will have more heterogeneous results, depending on the proportion of clones that have transformed to low ER status. This may have implications for the use of ^{68}Ga -NeoB as a theranostic agent in later lines of therapy, with the assumption that heterogeneous expression is important in the development of an effective treatment strategy.

Although the results are promising, this study is limited by its small sample size and the single-center design. Hence, data are presented descriptively, and no statistical test was applied. The high proportion of lobular carcinomas in this study may reflect a selection bias from the referring clinicians, because this subtype often poses diagnostic dilemmas, as mentioned in the discussion. Future research should focus on larger, multicenter trials to validate these findings. The other limitation of the study is the lack of histopathologic correlation for all lesions detected on PET imaging to confirm diagnostic accuracy, because it was not feasible to biopsy all detected sites.

CONCLUSION

^{68}Ga -NeoB PET/CT holds promise as a diagnostic tool in ER/PR-positive, HER2-negative breast cancer, particularly in the lobular subtype and in the staging setting. Further evaluation in larger prospective trials is warranted.

DISCLOSURE

The study was partially funded by Novartis. The authors were not paid by the company. No other potential conflict of interest relevant to this article was reported.

KEY POINTS

QUESTION: Is ^{68}Ga -NeoB PET/CT a better diagnostic tool than ^{18}F -FDG PET/CT in hormone-positive breast cancer?

PERTINENT FINDINGS: ^{68}Ga -NeoB PET/CT offers a better detection rate than ^{18}F -FDG PET/CT in the staging of hormone-positive breast cancer in this small-cohort, prospective phase 2 imaging study.

IMPLICATIONS FOR PATIENT CARE: Staging of newly diagnosed hormone-positive breast cancer patients may be more accurate, with a potential effect on patient management.

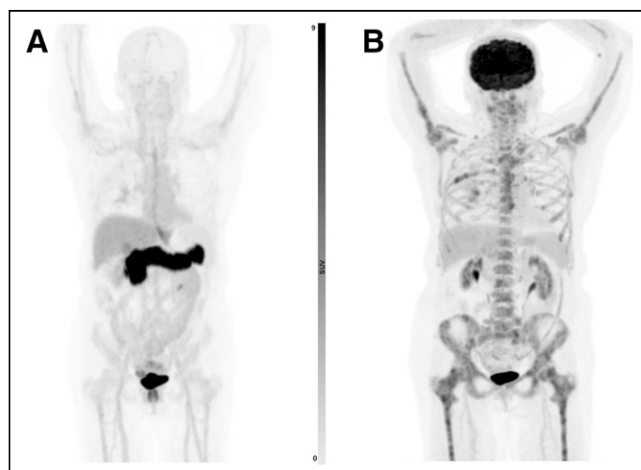


FIGURE 3. 71-y-old woman with recurrent lobular breast cancer in bone marrow. Initial histopathologic examination showed 90% ER, 0% PR, and negative HER2. Recent bone marrow biopsy samples show lobular breast carcinoma, 30% ER, 0% PR, and negative HER2. (A) ^{68}Ga -NeoB PET/CT is negative. (B) ^{18}F -FDG PET/CT shows extensive bone marrow involvement.

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