Role of Positron Emission Tomography/Computed Tomography in Assessing Breast Cancer Recurrence

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Abstract

Breast cancer (BC) is the most prevalent malignancy and the most common leading cause of cancer-related deaths among females. This study evaluated the role of ¹⁸F-fluorodeoxyglucose positron emission tomography/ computed tomography (¹⁸F-FDG PET/CT) in detecting locoregional and distant metastatic recurrence during post-operative surveillance in BC cases. It was conducted on 60 BC females who underwent PET/CT imaging for suspected recurrence at the PET/CT unit of Radiology Department in Mansoura University Oncology Center. Preprocedural assessments included clinical evaluation, laboratory investigations, standardized FDG-PET/CT preparation protocols. Among the 60 patients, 113 suspected recurrent lesions were detected, and 97 were confirmed as recurrence by histopathologic evaluation &/or clinical and radiological follow-up. The commonest recurrence site was extraregional lymph nodes, followed by bone. The commonest indication for PET/CT scan was equivocal conventional imaging findings (43.3%), followed by elevated serum tumor markers (31.7%). The results showed that CECT had 89.7% sensitivity, 6.25% specificity, 77.9% accuracy, 85.3% PPV, and 9.1% NPV in detection of recurrence. The PET scan had 96.9% sensitivity, 68.8% specificity, 92.9% accuracy, 94.9% PPV, and 78.6% NPV in detection of recurrence. The PET/CT had 100% sensitivity, 75% specificity, 96.5% accuracy, 96% PPV, and 100% NPV in detection of recurrence. The 18F-FDG PET/CT thus demonstrated a superior diagnostic performance in detecting recurrence among BC cases compared with CECT and PET-alone, with significantly greater sensitivity, specificity, and accuracy. It outperformed CECT in identifying small lymph nodes, contralateral breast, liver, and bone recurrences, and corrected overestimations made by CECT.

Key words: Breast cancer, Positron Emission Tomography, Positron Emission Tomography/Computed Tomography, Recurrence, Tumor markers

Introduction

Breast cancer is the most prevalent malignancy in females and the commonest cause of cancer-related mortality globally ⁽¹⁾. It presents diverse histologic and molecular subtypes, leading to varied outcomes and significant therapeutic challenges. Several classifications on the basis of molecular and histological characteristics have been developed ^(2, 3). Histologic

classification depends on its pathological growth pattern. The most common is invasive ductal carcinomas, followed by invasive lobular carcinomas. The remainder are the less common types ⁽⁴⁾.

Estrogen Receptor, Progesterone Receptor, and Human Epidermal Growth Factor Receptor 2 (ER, PR, and HER2) assessment is routine in BC management. These are prognostic and predictive markers for hormonal and anti-HER2-targeted treatment. Breast cancer is categorized into 4 molecular subtypes based on immunohistochemistry: Luminal A, Luminal B, HER2-enriched subtype, and triple-negative (expresses none of these 3 markers) (5,6)

Effective BC treatment necessitates accurate diagnosis and determination of its extent ⁽⁷⁾. Recurrent BC can be suspected based on clinical and/or radiologic symptoms and/or an increase in tumour markers. Despite the poor prognosis of loco-regional recurrence and distant metastasis after the initial therapy, early recurrence determination can improve survival ^(8,9)

The ¹⁸F-FDG PET/CT combines morphological and functional imaging. FDG-PET provides information related to tumor's metabolic activity, while the CT provides the anatomical information for accurate interpretation of PET signal. It also provides a map for attenuation correction of PET images ^(10, 11). ¹⁸F-FDG PET/CT has become an important modality for cancer imaging. It has an emerging role in BC's diagnosis, staging, recurrence evaluation, planning of radiation therapy, restaging, and treatment response ^(7, 12).

This study evaluated the role of ¹⁸F-FDG PET/CT in evaluating suspected locoregional and distant metastatic recurrence during post-operative surveillance of BC cases. As well as comparing the CECT, PET, and PET/CT images with each other with reference to the final diagnosis.

Patients and methods

Our study enrolled 60 previously-treated BC females, who underwent diagnostic PET/CT scan to assess suspiciously recurrent BC. It was performed at the PET/CT unit of the Radiology Department in Mansoura University Oncology Center, in the period between May 2023 and January 2025. We included female patients of any age group with a confirmed history of primary breast cancer who had undergone curative surgery, with or without adjuvant treatment after the initial diagnosis, presenting with suspicion of recurrence, either because of elevation of tumor markers, doubtful findings on other conventional imaging modalities (CIM), and/or suggestive clinical symptoms or physical examinations. We excluded pregnant women, women with previous reactions to contrast media and persons with allergies, patients with acute and chronic circulatory or respiratory failure, those having hepatic or renal failure, females with uncontrolled diabetes, extremely overweight females exceeding scanner dimensions, females who had recent chemotherapy within less than 14

days, surgical intervention within less than one month or radiation therapy within less than three months before scanning time, patients with a known other primary tumor (double/multiple primary malignancies) and females having metastases at the time of initial diagnosis.

Methods

Every patient was subjected to history taking including (personal history and history of present illness), medical history, current medications, past history about surgical operations, radiation or chemotherapy, and full complaint analysis and results of clinical examination. Laboratory, histopathological and radiological assessment included renal function tests including serum creatinine level, breast cancer serum tumor markers (CA15-3, CEA.), and histopathological examination results of the primary tumour by reviewing pathology reports.

Patients were asked to fast 4-6 h before scanning, oral hydration with water was encouraged. Patients were instructed to stop any strong activity or aggressive exercise 24 hours before scanning, to reduce skeletal muscles uptake. Patients were asked to wear comfortable clothes and remove any metals. A three-way valve system was utilized for injecting 18F-FDG (dose 0.1 mCi/kg), followed by a flush of 10 mL saline. Scan was performed 1h after injecting FDG, and patients waited and stayed in quiet and warm rooms after injection till scanning to avoid brown fat activation. Patients were instructed to void immediately prior to image acquisition, to reduce background urinary FDG activity and improve image clarity. Each patient was positioned supine on the table, both arms were placed in extension position above the heads.

Imaging technique

PET/CT was done on an integrated scanner (G.E discovery ST 16 PET/CT scanner) that superimposes the CT and PET components in 2 sequential gantries, without needing patients' motion between the CT and PET scanning, thus achieving accurate fusion and coregistration of data of CT and PET components. A CT scan was done first for anatomic localization and attenuation correction. Then a near whole-body PET scan (from skull to midthigh) was performed without patient movement (only in one case, the study was extended to the feet for knee assessment).

Scanning parameters were adjusted to minimize patient radiation exposure, yet to obtain the required information: tube current 60-140 mA, voltage 120 kVp, slice thickness 3-5 mm, rotation time 2-3 minutes/ bed position, with a whole-body scan typically requiring 5-6 bed positions, pitch 1, and matrix resolution 128x128 pixels. Images were reviewed before patients left the department to ensure examinations were satisfactory and any additional images were obtained depending on each case's needs.

After imaging, patients were asked to stay in the preparation room for the physician to confirm satisfactory examination. Patients were instructed to keep a distance from children (especially those less than 7 years) and pregnant women for at least a day. Drinking 1-1.5

liters of water after scanning was advisable, also patients were allowed to have light meals on the same day after scanning. All patients were told to change their clothes after 24 hours and the clothes should be washed separately by soap and running water.

Imaging interpretation

PET/CT images were reviewed at a workstation with fusion software (GE healthcare), which displayed CECT, PET and PET/CT fusion images. Both attenuation-corrected (AC-PET) and non- attenuation-corrected PET (NAC-PET) images were obtained. Axial, coronal, and sagittal images were evaluated. Patient's image data sets were blinded and separated into CECT, PET and PET/CT image data sets. Then comparison between them was carried out.

Histopathological examination and/or closely clinical and radiological follow-up (including bone scintigraphy, MRI, CT, and repeated PET/CT) for at least 6 months served as a reference standard to confirm recurrence. The diagnostic performance (sensitivity, specificity, PPV, NPV, and accuracy) of CECT, PET-alone and PET/CT was calculated for different recurrence sites.

Statistical Analysis

Data were analysed by SPSS (IBM/SPSS Inc., Chicago, IL, version 25). Quantitative data were first tested for normality by Kolmogorov-Smirnov and Shapiro-Wilk's tests; if the significance level is >0.05, then normality is assumed. For normally distributed continuous data, results were presented in means $(\bar{X}) \pm SDs$. For non-normally distributed data, data were represented as medians (Med) and ranges. Qualitative (categorical) data were summarized as number (n) and percent (%). Independent Samples t-test was utilized to evaluate the statistical significance of difference between normally distributed data between two groups. The statistical significance of a result was set at p-value <0.05.

Ethical Considerations

Throughout its implementation, the study complied with the Helsinki Declaration. Approval was obtained from Mansoura University Institutional ethics committee (Code Number: MS.22.08.2096). Written consents were obtained from all patients after explaining the purpose and methodology of the study. All data was collected by the researcher himself.

Results

Table (1) shows age distribution in the cases of the study. The mean age was 50.32 ± 12.13 years (range = 19 and 76 years). There were 2 cases (3.3%) with bilateral breast cancer, while the remaining 58 cases (96.7%) were with unilateral breast cancer.

Regarding their histologic subtypes, invasive ductal carcinoma was the most common histologic subtype (81.7%) followed by invasive lobular carcinoma (13.3%); the most common grade was grade II detected in 42 cases (70%), followed by grade III detected in 14 cases (23.3%). Regarding the molecular subtypes, Luminal subtypes were detected in 46 cases

(76.7%), HER2-enriched in 8 cases (13.3%), and TNBC in 6 cases (10%). Luminal A was shown in 17 cases (28.3%), Luminal B-HER2- in 20 cases (33.3%), and Luminal B-HER2+ in 9 cases (15%). Variable lines of treatment had been received by the patients. All patients in our study underwent surgical management for primary breast cancer, other lines of treatment included hormone therapy in 46 cases (76.7%), chemotherapy in 10 cases (16.7%), radiotherapy in 19 cases (31.7%), and anti-HER2 therapy in 16 cases (26.7%).

Different types of surgical management were performed for the included cases; they included breast-conserving surgery (BCS) in 17 breasts (27.4%), modified radical mastectomy (MRM) in 42 breasts (67.7%), and nipple-sparing mastectomy (NSM) with muscle flap reconstruction/silicone implant in 3 breasts (4.8%). The mean time after surgical management was 3.88 ± 3.5 years (range =9 months and 14 years)

Patients were referred for PET/CT for different indications; the most common indication was equivocal or suspicious conventional imaging findings in 43.3%, followed by elevated serum tumor marker in 31.7%, and suspicious clinical symptoms or physical examinations in 25%.

Table 1. Age, characterization of primary breast cancer, primary tumor treatment and surgery type, time after surgery and PET/CT indication in the 60 studied cases

| Age | Years | Years | | |
|----------------------------|-------------------|-------|--|--|
| Mean±SD | 50.32 ± 12.13 | | | |
| Median (Range) | 50 (19–76) | | | |
| Primary breast cancer | Number (60) | % | | |
| Laterality | • | | | |
| Bilateral | 2 | 3.3 | | |
| Unilateral | 58 | 96.7 | | |
| Left | 32 | 53.3 | | |
| Right | 26 | 43.3 | | |
| Histologic subtypes | | | | |
| Invasive ductal carcinoma | 49 | 81.7 | | |
| Invasive lobular carcinoma | 8 | 13.3 | | |
| Others | 3 | 5.0 | | |
| Grade | | | | |
| I | 1 | 1.7 | | |
| II | 42 | 70.0 | | |
| III | 14 | 23.3 | | |
| Unknown | 3 | 5.0 | | |
| Molecular subtypes | | | | |
| Luminal | 46 | 76.7 | | |
| Luminal A | 17 | 28.3 | | |
| Luminal B-HER2- | 20 | 33.3 | | |
| Luminal B-HER2+ | 9 | 15.0 | | |

| HER2-enriched | 8 | 13.3 |
|---|----------------|------|
| Triple-negative breast cancer | 6 | 10.0 |
| Primary tumor treatment | | |
| Surgery | 60 | 100 |
| Hormone therapy | 46 | 76.7 |
| Chemotherapy | 10 | 16.7 |
| Radiotherapy | 19 | 31.7 |
| Anti-HER2 therapy | 16 | 26.7 |
| Surgery type | Number (62)* | % |
| Breast-conserving surgery | 17 | 27.4 |
| Modified radical mastectomy | 42 | 67.7 |
| Nipple-sparing mastectomy with reconstruction | 3 | 4.8 |
| Time after surgery | Years | |
| Mean±SD | 3.88 ± 3.5 | |
| Median (Range) | 2.5 (0.75–14) | |
| PET/CT indication | | |
| Elevated serum tumor marker | 19 | 31.7 |
| Equivocal or suspicious conventional imaging | 26 | 43.3 |
| findings | | |
| Suspicious clinical symptoms or physical | 15 | 25.0 |
| examinations | | |

Continuous data represented in means±SDs and medians (ranges)

Categorical data represented in Numbers (%)

Among 60 patients suspected to have recurrence, absence of tumor recurrence was seen in 10 cases based on clinical/imaging follow-up for at least 6 months. All these cases were correctly diagnosed with CECT, PET-alone, and PET/CT. In the remaining 50 cases, there were 113 suspected recurrent lesions detected; each lesion was detected with at least one modality. Of these 113 lesions, 97 lesions were confirmed as recurrence by pathological examinations or clinical/radiological follow-up. The distribution of recurrence localizations in the 50 patients is displayed in Table 2.

Table 2. Distribution of recurrence localizations in 50 patients.

| Site | Number Suspected | Number Confirmed |
|---------------------------------|-------------------------|-------------------------|
| Local recurrence | 10 | 9 |
| Regional LNs recurrence | 8 | 7 |
| Contralateral breast recurrence | 4 | 4 |
| Distant metastatic recurrence: | | |
| Extra-regional LNs | 27 | 25 |
| Bone | 23 | 22 |

^{*}N=62 breasts as two cases were bilateral breast cancer.

| Lung | 13 | 8 | |
|---------------|-----|----|---|
| Liver | 18 | 15 | |
| Brain | 2 | 2 | |
| Spleen | 2 | 0 | |
| Adrenal gland | 1 | 0 | |
| Peritoneum | 3 | 3 | |
| Ovaries | 1 | 1 | |
| Pleura | 1 | 1 | • |
| Total | 113 | 97 | |

LNs: lymph nodes.

One patient might have more than one site of recurrence.

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Contrast-enhanced CT images were reviewed for detection of recurrent lesions, and it was correct in 88 out of 113 suspected lesions (Table 3). PET images were reviewed for detection of recurrent lesions, and it was correct in 105 out of 113 suspected lesions (Table 4). PET/CT fused images were reviewed for detection of recurrent lesions, and it was correct in 109 out of 113 suspected lesions (Table 5).

Table 3. Detection of recurrence by CECT in 113 suspected lesions in 50 patients.

| Site | N | TP | TN | FP | FN |
|----------------------|-----|----|----|----|----|
| Local | 10 | 9 | 0 | 1 | 0 |
| Regional LNs | 8 | 5 | 1 | 0 | 2 |
| Contralateral breast | 4 | 3 | 0 | 0 | 1 |
| Extra-regional LNs | 27 | 25 | 0 | 2 | 0 |
| Bone | 23 | 19 | 0 | 1 | 3 |
| Brain | 2 | 2 | 0 | 0 | 0 |
| Lung | 13 | 8 | 0 | 5 | 0 |
| Liver | 18 | 11 | 0 | 3 | 4 |
| Spleen | 2 | 0 | 0 | 2 | 0 |
| Adrenal gland | 1 | 0 | 0 | 1 | 0 |
| Peritoneum | 3 | 3 | 0 | 0 | 0 |
| Ovarian | 1 | 1 | 0 | 0 | 0 |
| Pleura | 1 | 1 | 0 | 0 | 0 |
| Total | 113 | 87 | 1 | 15 | 10 |

N: Number of suspected lesions by either modality; One patient might have more than one site of recurrence.

TP: true positive; TN: true negative; FP: false positive, FN: false negative.

Table 4. Detection of recurrence by PET-alone in 113 suspected lesions in 50 patients.

| Site | N | TP | TN | FP | FN |
|----------------------|-----|----|----|----|----|
| Local | 10 | 9 | 1 | 0 | 0 |
| Regional LNs | 8 | 7 | 0 | 1 | 0 |
| Contralateral breast | 4 | 4 | 0 | 0 | 0 |
| Extra-regional LNs | 27 | 25 | 0 | 2 | 0 |
| Bone | 23 | 20 | 0 | 1 | 2 |
| Brain | 2 | 2 | 0 | 0 | 0 |
| Lung | 13 | 7 | 4 | 1 | 1 |
| Liver | 18 | 15 | 3 | 0 | 0 |
| Spleen | 2 | 0 | 2 | 0 | 0 |
| Adrenal gland | 1 | 0 | 1 | 0 | 0 |
| Peritoneum | 3 | 3 | 0 | 0 | 0 |
| Ovarian | 1 | 1 | 0 | 0 | 0 |
| Pleura | 1 | 1 | 0 | 0 | 0 |
| Total | 113 | 94 | 11 | 5 | 3 |

N: Number of suspected lesions by either modality; One patient might have more than one site of recurrence.

Table 5. Detection of recurrence by PET/CT in 113 suspected lesions in 50 patients.

| Site | N | TP | TN | FP | FN |
|----------------------|-----|----|----|----|----|
| Local | 10 | 9 | 1 | 0 | 0 |
| Regional LNs | 8 | 7 | 1 | 0 | 0 |
| Contralateral breast | 4 | 4 | 0 | 0 | 0 |
| Extra-regional LNs | 27 | 25 | 0 | 2 | 0 |
| Bone | 23 | 22 | 0 | 1 | 0 |
| Brain | 2 | 2 | 0 | 0 | 0 |
| Lung | 13 | 8 | 4 | 1 | 0 |
| Liver | 18 | 15 | 3 | 0 | 0 |
| Spleen | 2 | 0 | 2 | 0 | 0 |
| Adrenal gland | 1 | 0 | 1 | 0 | 0 |
| Peritoneum | 3 | 3 | 0 | 0 | 0 |
| Ovarian | 1 | 1 | 0 | 0 | 0 |
| Pleura | 1 | 1 | 0 | 0 | 0 |
| Total | 113 | 97 | 12 | 4 | 0 |

N: Number of suspected lesions by either modality; One patient might have more than one site of recurrence.

TP: true positive; TN: true negative; FP: false positive, FN: false negative.

TP: true positive; TN: true negative; FP: false positive, FN: false negative.

The CECT had 89.7% sensitivity, 6.25% specificity, 77.9% accuracy, 85.3% PPV, and 9.1% NPV in detection of recurrence. The PET scan had 96.9% sensitivity, 68.8% specificity, 92.9% accuracy, 94.9% PPV, and 78.6% NPV in detection of recurrence. The PET/CT had 100% sensitivity, 75% specificity, 96.5% accuracy, 96% PPV, and 100% NPV in detection of recurrence (Table 6).

Table (7) shows that recurrence was detected in 50 cases (83.3%). Isolated locoregional recurrence (LRR) was reported in 8 cases (13.3%), distant metastatic recurrence (DMR) in 33 cases (55%), DMR & contralateral breast recurrence (CLBR) in 3 cases (5%), DMR & LRR in 5 cases (8.3%), and DMR, LRR & CLBR in 1 case (1.7%).

Table 6. Diagnostic performance of CECT, PET-alone and PET/CT in 113 suspected lesions in 50 patients

| | Sensitivity | Specificity | Accuracy | PPV | NPV |
|---------------|-------------|-------------|----------|------|------|
| CECT (%) | 89.7 | 6.25 | 77.9 | 85.3 | 9.1 |
| PET-alone (%) | 96.9 | 68.8 | 92.9 | 94.9 | 78.6 |
| PET/CT (%) | 100 | 75 | 96.5 | 96 | 100 |

PPV: positive predictive value; NPV: negative predictive value.

Table 7. Final diagnosis and type of recurrence in the 60 studied cases

| Final diagnosis | Number (60) | % |
|------------------|-------------|------|
| No recurrence | 10 | 16.7 |
| Isolated LRR | 8 | 13.3 |
| DMR | 33 | 55 |
| DMR + CLBR | 3 | 5 |
| DMR + LRR | 5 | 8.3 |
| DMR + LRR + CLBR | 1 | 1.7 |

Categorical data expressed as Number (%)

LRR: Loco-regional recurrence
DMR: Distant metastatic recurrence
CLBR: Contralateral breast recurrence

Discussion

In our study, PET/CT was the most accurate for recurrence detection among BC cases (accuracy = 96.5%, compared to CECT = 77.9% and PET-alone = 92.9%). PET/CT sensitivity and specificity in detecting recurrence were 100% and 75%, respectively. CECT sensitivity and specificity were 89.7% and 6.25%, respectively. While PET-alone sensitivity and specificity were 96.9% and 68.8%, respectively. This is consistent with **Chang et al.** (13) study in which PET/CT was performed in BC cases with high serum levels of CA 15-3 and/or clinical/radiologic suspicion of recurrent lesions. The control group included asymptomatic

patients who had FDG-PET/CT in the post-therapy surveillance of BC. The sensitivity and specificity of FDG-PET/CT were 87.5% and 87.1% in cases with suspected recurrent lesions compared to 77.8% and 91.7% in control group.

Also, **Dong** *et al.* ⁽¹⁴⁾ compared the efficacy of ¹⁸F-FDG PET/CT versus conventional techniques in detecting the recurrence and metastasis of BC. The sensitivity and specificity of PET/CT were 95.0% and 71.43% versus 78.95% and 57.14% for conventional methods. Likewise, **Vercher-Conejero** *et al.* ⁽¹⁵⁾ demonstrated that ¹⁸F-FDG PET/CT had a sensitivity of 86-100% and specificity of 90-98% for detecting recurrence in BC, closely aligning with our study results. They also emphasized PET/CT's superiority in identifying distant metastases and its ability to provide whole-body imaging. This demonstrates PET/CT's reliability and diagnostic accuracy in comprehensive post-operative BC surveillance.

Consistently, **Shawky** *et al.* ⁽¹⁶⁾ assessed the diagnostic value of PET/CT compared to CECT in detecting recurrence and metastasis of BC. Their results demonstrated PET/CT's superiority, with 100% sensitivity, 95.4% specificity, 88.9% PPV, and 100% NPV in detecting recurrence, while the CECT alone had 81.2% sensitivity, 90% specificity, 76.4% PPV and 93% NPV. As well as PET/CT showed greater sensitivity and specificity in detecting distant metastases.

Retrospectively, **Murakami et al. (2012)** performed PET/CT for 47 cases with suspected recurrent BC. Twenty-five (53%) patients had recurrence. The sensitivity, specificity, PPV, NPV, and accuracy of PET/CT were 96%, 91%, 92%, 95%, and 94%, respectively. Compared to PET-alone, PET/CT demonstrated superior sensitivity and accuracy (96% versus 80% and 94% versus 81%, respectively).

The finding in our study that PET/CT achieved 100% sensitivity and NPV indicates its exceptional capability to accurately rule out recurrence, ensuring no false negatives. This high sensitivity suggests that PET/CT can reliably identify metabolically-active lesions, including small or challenging-to-detect recurrences, due to the superior spatial and functional integration of PET and CT imaging. The 75% specificity of PET/CT reflects its ability to differentiate true recurrences from benign conditions, although some false positives may arise from inflammatory or benign lesions that mimic malignancy on FDG uptake. The overall accuracy of 96.5% and high PPV of 96% underscore PET/CT's clinical value in confirming recurrent disease, guiding treatment decisions by providing precise localization and characterization of recurrence.

In the present study, the most frequently observed site of distant metastases was extraregional LNs, followed by bone. This finding differs slightly from the results reported by **Piva** *et al.* ⁽¹⁷⁾ who identified the skeleton as the commonest site of distant metastasis among BC patients. Similarly, **Shawky** *et al.* ⁽¹⁶⁾ reported bone metastases in 12 out of 30 cases (40%). However, in our study, bone represents the second most prevalent site of metastasis,

highlighting potential variations in metastatic patterns across different populations and study designs.

In this study, 10 patients presented with suspected local recurrence in the breast; 9 of them were confirmed by PET/CT as local recurrences while the PET/CT ruled out recurrence in one case as it was shown to be a post-operative scarring.

In our study, there were 8 suspected regional LNs recurrences; one of them was axillary focal nodular uptake of brown adipose tissue (BAT) seen at PET-alone images, and it was easily excluded by reviewing the fused PET/CT images. Two small regional LN metastases were missed by CECT (as they did not fulfill size criteria by CT standards, i.e., <10 mm in short axis diameter), yet, they were FDG-avid in PET and PET/CT images. The remaining LNs were assigned by CECT, PET, and PET/CT as regional LNs recurrences. This reflects the effectiveness of PET/CT in detecting recurrence even in normal-sized lymph nodes. These small micro-metastases significantly decrease the sensitivity and accuracy of morphologic imaging.

Two cases in our study with suspected extra-regional LNs (cervical in location), were mistakenly diagnosed by CECT and PET/CT as nodal recurrence and were shown to be inflammatory. 18F-FDG uptake in a lesion is dependent upon the lesional metabolic activity, with the extent proportional to the number of tumour cells and their proliferative activities. But, increased uptake by an inflammatory lesion might not represent high metabolic activity but rather the activity of leukocytes, as macrophages and neutrophils utilize glucose for chemotaxis and phagocytosis (18).

In our study, PET/CT could detect a recurrent lesion in the **contralateral breast** without corresponding morphological finding in CECT. This agrees with **Shawky** *et al.* ⁽¹⁶⁾ who used PET/CT and could detect lesions in the contralateral breast in 2/30 cases (6.7%) that were not detected by CECT study. Cancer-related metabolic changes often precede structural alterations and are readily detected using PET.

In terms of bone metastases in our study, 23 patients had suspected osseous metastatic recurrence, 22 were correctly classified as osseous metastases by PET/CT, and 1 case was mistakenly classified as metastatic by CECT and PET/CT but proven to be a giant cell tumor upon pathological evaluation. This is consistent with **Shawky et al.** (16) findings and **Wafaie et al.** (19) who claimed that when there are no obvious structural alterations on CT scans, PET can identify early bone marrow-based metastases. Even though two of the sclerotic bony metastases were not FDG-avid, the fused PET/CT images clearly showed them. This is consistent with the findings of **Mohamed et al.** (20) who said that when osteogenic bone metastasis occurs, PET may yield false-negative lesions.

Despite the known limited sensitivity of PET for brain metastasis due to physiological FDG uptake in normal brain tissue, the two cases in our study exhibited increased metabolic

activity more than the surrounding brain parenchyma, and were correctly assigned by CECT, PET and PET/CT as recurrences. **Zidan** *et al.* ⁽²¹⁾ assessed the effectiveness of FDG-PET/CT in detecting brain metastases among 420 patients with extra-cranial malignancies, and their findings demonstrated a moderately good sensitivity of 78.1% and a specificity of 92.6%, indicating a reasonable degree of diagnostic accuracy; however, the study also emphasized the potential for false-negative results, particularly in lesions with low metabolic activity or those isometabolic to normal brain parenchyma.

Finally, recurrent pleural, peritoneal, and ovarian lesions were correctly assigned by CECT, PET, and PET/CT. Suspected splenic and adrenal lesions were correctly ruled out by PET and PET/CT (were positive by CECT).

Conclusion

Our findings indicate that ¹⁸F-FDG PET/CT demonstrates superior diagnostic performance in detecting recurrent breast cancer compared to CECT and PET-alone, with significantly higher sensitivity, specificity, and accuracy. It outperformed CECT in identifying small lymph nodes, contralateral breast, liver, and bone recurrences, and corrected overestimations made by CECT. With no missed lesions and few false positives, ¹⁸F-FDG PET/CT is considered a reliable imaging modality for evaluating loco-regional and distant metastatic recurrence in BC patients.

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