RESEARCH PAPER

The Additional Role of the Quantitative Measurements of 18F-FDG PEM Compared to PET/CT in the Evaluation of Post Interventional Breast Neoplasm

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ABSTRACT

Background: Breast cancer remains the most frequent malignancy between females globally. Accurate post-interventional assessment is essential for determining disease extent and guiding management. This research aimed to measure the additional role of quantitative measurements of 18F-FDG positron emission mammography (PEM) compared to 18F-FDG positron emission tomography/computed tomography (PET/CT) in assessing post-interventional breast neoplasms.
Methods: This prospective research was conducted on 36 female cases with pathologically proven breast cancer between December 2022 and April 2024. All cases had both 18F-FDG PET/CT and PEM on the same day. Semi-quantitative parameters, including SUVmax, PUVmax, and lesion-to-background (LTB) ratio, have been calculated and compared. Correlation analyses were performed, and changes in risk classification and management intent were assessed.
Results: PEM detected 42 lesions, while PET/CT detected 43. Three lesions (7.1%) were detected only by PEM—all approximately 1 cm—while four lesions (9.3%) were missed by PEM. The mean PUVmax was 6.3 ± 4.1, and the mean LTB was 6.2 ± 4.3. SUVmax illustrated a strong positive association with PUVmax (r value equal to 0.866, p value below 0.001). Risk stratification changed in 10 patients (27.7%) after incorporating PEM findings, with 6 lesions upgraded and 4 downgraded, directly affecting management decisions.
Conclusion: PEM offers superior spatial resolution and provides complementary metabolic information to PET/CT, particularly in small or multifocal lesions. Quantitative PEM indices enhance diagnostic accuracy and can significantly influence post-interventional breast cancer management.

Keywords: Positron Emission Mammography (PEM), 18F-FDG, PET/CT, Breast Neoplasm, Quantitative Imaging
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INTRODUCTION

Breast cancer is the most frequent neoplasm and primary reason for cancer-related death in females; its incidence continues to increase due to the widespread presence of its risk factors. Breast imaging is integral to breast cancer processes, encompassing secondary prevention via screening, clinical diagnosis, and subsequent follow-up (1).

PET/MR imaging is especially intriguing as a potential improvement over positron emission tomography/computed tomography oncologic whole-body imaging since MRI gives better lesion recognition in the brain, liver, breast, kidneys, in addition to bones, than CT. PET/MR can combine metabolic, anatomical, spectroscopic, diffusion, as well as perfusion data for breast cancer in a single examination. PET/MR has been proven to be more sensitive compared to PET/CT in whole-body imaging for breast cancer, especially for breast lesions as well as liver and bone metastases (2).

PET imaging, which is more sensitive for axillary nodes, seems to be complementary to MRI, which is more accurate for satellite lesions, in terms of local staging. PET/MR has been demonstrated to be more probable compared to PET/CT to accurately predict the tumor's maximal diameter (T stage), which may be important in surgical and oncological planning (3).

FDG (18F-Fluorodeoxyglucose) is a glucose analog that enters cells via glucose transporters and is phosphorylated by hexokinase. Throughout the initial enzymatic activities in the cells, FDG follows the same pathway as glucose; however, due to 18F-fluorodeoxyglucose lacking a hydroxyl group at the C-2 position, it is not further metabolized and is physically retained in cancer cells at a rate proportionate to glucose use (4).

Malignant cells have greater glycolytic activity and glucose metabolism than non-malignant cells due to raised glucose transporter (GLUT-1) expression in addition to greater concentrations of phosphofructokinase and hexokinase. This increased glycolytic activity facilitates the identification of cancer cells via 18F-FDG PET imaging. In breast cancer, 18F-FDG positron emission tomography/computed tomography is utilized to identify, stage, prognostic, evaluate treatment response, schedule radiotherapy, in addition detect recurrence (5).

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To confirm optimal scan quality, certain preparations are necessary involving instructions to cases which must be explained and communicated while scheduling the scan (6). This research aimed to detect additional role of the quantitative measurements of18 F FDG PEM in comparison with 18 F FDG positron emission tomography/computed tomography in the evaluation of post interventional breast neoplasm and to compare among PEM and PET/CT in recognition of post interventional breast neoplasm.

PATIENTS AND METHODS

Between December 2022 and April 2024, a private radiology center received 36 cases diagnosed with breast cancer for this prospective research. The research protocol has been approved by the investigation ethics committee of the Center of Clinical Oncology and Nuclear Medicine (NEMROCK) and Cairo University. All cases had pathologically proven breast cancer and were referred for evaluation after intervention.

Patients who underwent radical mastectomy have been excluded from the research. All cases provided written consent to expose the data that has been used for research purposes. All procedures used in research, including human subjects, have been subjected to the institutional research committee's ethical standards.

All cases had an 18F-FDG PET/CT examination and an 18F-FDG/PEM examination on the same day.

Regarding patient preparation for FDG PET/CT and PEM imaging includes: Avoiding exercise for 24 hours, oral hydration cases have been asked to drink plenty of water prior to the scan, typically starting four to six hours before the scan, to ensure adequate hydration and support the proper functioning of the kidneys.

The general recommendation was to consume about 500-1000 mL of water (depending on the case's age, size, and health status) in the hours leading up to the scan. Also, patients were advised not to over-hydrate right before the scan because overhydration could cause excessive urination or bloating, potentially making it uncomfortable for the patient, and to fast from food for 4 to 6 hours. Blood glucose level was checked (<200 mg/dl). Patients were kept warm and quiet for 30 to 60 minutes before injection. Patients received an intravenous bolus of radioactive tracer. cases received intravenous 18F-FDG injections of 4.62 megabecquerel/kilogram (0.125 millicurie/kilogram). Forty-five minutes following IV injection of the radiotracer, PET/CT images have been acquired utilizing a combined PET/CT scanner. Ninety minutes after the IV injection of the radiotracer, PEM images have been needed utilizing a PEM scanner.

Regarding FDG PET/CT and PEM imaging acquisition, the PET/CT Scanner utilized in this research was Ingenuity TF 64 (USA, OH, Cleveland, Philips Healthcare), an integrated positron emission tomography/computed tomography scanner combining a modular, LYSO-based PET component with a 64-channel CT component. The CT is depending on the Ingenuity CT (Philips Healthcare). The PET constituent has a ring diameter of ninety centimeters utilizing twenty-eight detector modules constructed as twenty-three (radial) by forty-four (axial) matrices of (4x4x22 mm^3) Lutetium-yttrium oxyorthosilicate (LYSO) crystal elements coupled to photomultiplier tubes and an eighteen-centimeter axial field of view. The system utilizes a 4.5 ns hardware coincidence window for its standard FOV, acquires information in 3D mode, and records events from all combinations of indicator rings in a list-mode format.

The PEM scanner used in this study is the NAVIscan PEM scanner; the scanner combines high-resolution PET technology with a dedicated breast imaging setup. It uses cerium-doped lutetium-yttrium oxyorthosilicate (LYSO) or similar scintillation crystals for the PET detectors, which are excellent for providing high light yield, timing resolution, and energy resolution. This results in high image quality with a shorter decay time and excellent spatial resolution. The PET detectors are arranged in a specific configuration to image breast tissue. The system typically uses two opposed detector panels placed around the breast, allowing for simultaneous detection of positron annihilation events from both sides of the breast. The system is capable of achieving sub-millimeter resolution (typically in the range of 2-3 mm), which is significantly better than whole-body PET systems. This great resolution allows for the recognition of small lesions, particularly in dense breast tissue. The field of view (FOV) of the Naviscan positron emission mammography scanner is optimized for imaging the breast and can cover the entire breast tissue. Unlike conventional PET, which has a much larger FOV for whole-body imaging, PEM focuses solely on breast tissue and achieves much higher resolution for this specific application.

All cases had imaging in the arms-up position, covering the area from the skull to the upper thighs. Following the completion of CT imaging, the PET scan has been conducted in the caudal–cranial direction. The period of the scan varied based on the case's body size and usually contained twelve bed positions. The dose of the CT contrast (if not contraindicated) was 1.5 ml/kg body weight. Following completion of acquisition, the images have been reconstructed with a standard iterative algorithm. All images have been analyzed by a minimum of 2 experienced nuclear medicine physicians in reporting PET and with special training in 18F-FDG PET/CT reporting in addition to an experienced radiologist.

For PEM imaging, the case’s breast is positioned and compressed in the PEM device, similar to conventional mammography, but designed to accommodate the PET detector. Bilateral cranio-caudal and medio-lateral oblique 3D volume acquisitions analogous to tomographic mammography were obtained using gentle compression. Tomographic PEM images were produced at a thickness range from 3 to 8 mm. The PEM system acquires images from multiple angles around the breast, producing high-resolution images that combine anatomical details with metabolic activity.

Regarding FDG PET/CT and PEM imaging interpretation,

For the visual and qualitative interpretation of FDG PET/CT scans, a positive result of visual analysis has been identified when focal FDG activity exhibited greater intensity compared to surrounding tissues and couldn't be associated with benign or physiological uptake, as observed in the corresponding area of other anatomical modalities. **For the quantitative analysis of primary tumor FDG uptake,** the maximum standardized uptake value (SUVmax) has been assessed using a circular region of interest (ROI) surrounding the primary breast cancer site.

Lymph node metastasis has been recognized as a lymph node with suspicious localized elevated uptake greater than the surrounding background, independent of the short-axis diameter, or as a lymph node without any uptake but having a short axis above eight millimeters in the pelvis and above ten millimeters outside the pelvis. Bone metastases were defined as obvious focal tracer avidity with underlying bone abnormality in CT images depending on response evaluation criteria in solid tumors (RECIST criteria) after exclusion of benign osseous lesions. Other deposits, such as hepatic, lung, brain lesions, were identified as soft tissue deposits.

The SUV is a semi-quantitative evaluation of the radiotracer uptake from a static PET image. SUV = (μCi/gram in tissue) / (total mCi injected) x body weight. Where tissue tracer activity is in microcuries per gram, injected radiotracer dose is in millicuries, and case weight is in kilograms. **Maximal standardized uptake values (SUVmax)** have been measured for every lesion. Manually determined zones of interest have been drawn on attenuation-corrected emission images during the axial planes in lesions recognized as areas of focally raised uptake.

For PEM, the visual and qualitative interpretation of FDG PEM scan images was identified visually, and the abnormalities in breast tissue were characterized by their appearance and metabolic activity. The high spatial resolution of PEM allows for detailed visualization of small lesions and subtle differences in tissue metabolism. Tumors often appear as irregularly shaped areas with higher metabolic activity compared to surrounding tissues.

For the quantitative analysis of PEM, ROIs were drawn on areas of increased activity to calculate PUVmax as well as another area of normal parenchymal tissue to calculate the background activity, and then calculate lesion to background ratio by dividing the PUVmax of the lesion over the PUV of the background. PEM Uptake Value (PUVmax) has been calculated as a quantitative assessment of the highest FDG uptake within a tumor or lesion. It reflects the maximum level of glucose metabolism in the area of interest. PUVmax is typically measured in units of SUV (Standardized Uptake Value). The PUV is measured as the ratio of the FDG concentration in the lesion to the injected dose of FDG, normalized by the case's body weight or other factors. High PUVmax values often correlate with aggressive tumors and can provide insights into the metabolic activity and potential malignancy of the lesion.

Formula: PUV = (Activity concentration in the region of interest / (Injected dose / Body weight).

We also calculated the Lesion-to-Tissue Background (LTB) Ratio. The Lesion-to-Tissue Background (LTB) ratio is a metric utilized to measure the contrast among the FDG uptake in a lesion and the surrounding normal tissue.

The LTB ratio is measured by separating the FDG uptake value in the lesion (often expressed as SUV) by the FDG uptake in the surrounding normal tissue.

Formula: LTB Ratio = PUV of the lesion / PUV of the background tissue.

RESULTS

Table (6) Demographic data of 36 patients

Age		**Mean ± SD**			**Range**			
		47.3 ± 11.3			**28.0-72.0**			
	Site of the primary			**Type of intervention**		**Pathological data**		
	Right breast	**Left breast**	**Bilateral**	**Biopsy**	**Lumpectomy**	**IDC**	**ILC**	**other**
Patients No	20	15	1	31	5	23	10	3
Percentage	55.5 %	41.6%	2.7%	86.1%	13.9%	63.9%	27.7%	8.3%
Total	36 (100%)							

Table (7) PET/CT results of the 43 breast lesions

	Mean ± SD	**Range**
Size (cm)	3.5 ± 1.9	1.0 - 8.3
SUVmax	9 ± 6	1.6 - 27.5

Considering the results of FDG-PET/CT to assess the rest of the body of the patients, axillary nodal deposits were detected in 28 patients (77.8%), 4 patients (11.1%) had bone deposits, and 5 patients (13.9%) had soft tissue deposits (table 8).

Table (8): positron emission tomography/computed tomography results for the rest of the body.

Site of deposits	**Number of patients**	**Percentage**
Axillary nodal deposits	28	77.8
Bone deposits	4	11.1
Soft tissue deposits	5	13.9

Regarding FDG PEM imaging results, the 4 free patients in PET/CT imaging were also negative in PEM imaging. The total lesions detected by PEM imaging were 42 lesions. PUVmax and the lesion-to-background ratio (LTB) of the lesion were calculated for all 42 lesions. The PUVmax ranged from 1.4 to 19.6 with a mean of 6.3 ± 4.1. The LTB varied from 1.4 to 17.4, with a mean of 6.2 ± 4.3.

Table (9) PEM results of the 42 breast lesions

	Mean ± SD	**Range**
PUV	6.3 ± 4.1	1.4- 19.6
LTB	6.2 ± 4.3	1.4- 17.4

Table (10): PET/CT risk classification of 43 lesions.

Risk classification by PET	**Number of lesions**	**Percentage**
High risk	26	60.5%
Intermediate risk	17	39.5%
Low risk	0	0.0%
Total	43	100

Lesion-based analysis of PEM

According to the risk classification of the L/BG ratio in PEM results within the detected 42 lesions, 30 lesions (72%) were classified as high risk, 9 lesions (21%) were classified as intermediate risk, and 3 lesions (7.0%) were classified as low risk (table 6) (fig 5).

Table (11): PEM risk classification of 42 lesions

Risk classification by PET	**Number of lesions**	**Percentage**
High risk	30	72
Intermediate risk	9	21
Low risk	3	7.0
Total	42	100

Change in risk stratification according to quantitative data of PET and PEM: (table 12) (fig 24).

PET and PEM were matched in risk classification in 29 lesions (56.9%). PEM had changed risk stratifications of 10 patients (21.7%); PEM imaging downgraded 4 lesions (7.8%), 3 patients from intermediate risk to low risk, and one patient from high risk to intermediate risk. PEM imaging upgraded 6 lesions (11.8%) from intermediate risk to high risk.

Table (12): change in risk classification

	Number	**Percentage**
PEM Detected New	**3**	**5.9**
Downstage by PEM	**4**	**7.8**
No Change by PEM	**29**	**56.9**
Not Detected by PEM	**4**	**7.8**
Upstaging by PEM	**6**	**11.8**

High Risk Agreement: There is a strong correlation between PEM and PET when both modalities identify a patient as high risk.

Intermediate Risk Discrepancy: There are some discrepancies, as seen in intermediate risk categories, where the assessments do not always align.

Low Risk by PEM: No patients classified as low risk by PEM were classified as high risk by PET, which might indicate that PEM tends to be less likely to miss higher-risk lesions. Table (13)

Table (13): risk classification agreement between both modalities.

		Risk by PET N	
		High	**Intermediate**
Risk by PEM	**High**	23	6
	Intermediate	1	6

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	Low	0	3

Regarding 36 patients, four were already free in both PET and PEM imaging.

Three patients discovered the four lesions that PEM had missed. In 26 patients (72.2%), PEM did not change the management of their lesions (including the patients who were free in PET and PEM). PEM modified disease management intent in 10 patients (27.7%). The 3 lesions detected in PEM and missed by PET were found in 3 patients; all show a change in the disease management plan. In case of a newly discovered lesion in the same breast, the management plan may change from lumpectomy to mastectomy (in case of multifocal/multicentric breast neoplasm).

In case of a newly discovered lesion in the contralateral breast (this may need follow-up by sonomammography if low risk; close follow-up and even core biopsy are needed in cases of intermediate risk). All lesions detected only by PEM were around 1 cm. The 6 upgraded lesions were found in 5 patients; all showed change in disease staging. The 4 downgraded lesions were found in 3 patients; all showed a change in management intent. One lesion detected by PEM and one upgraded lesion were found in the same patient.

Table (14): Change in disease management plan by adding PEM results.

Change in disease change/management	Number of patients	Percentage
Unchanged by PEM	26	72.2
Changed by PEM	10	27.7
Total	36	100

SUVmax were positively correlated with PUVmax with correlation Coefficient (r): 0.866. SUVmax were positively correlated with LTB with correlation Coefficient (r): 0.805. PUVmax were positively correlated with LTB with correlation Coefficient (r): 0.854

Table (15): shows Correlation between semi-quantitative measurements of PET and PEM.

Semi-quantitative measurements		r	p value
PET lesions SUV max	**PEM lesions PUVmax**	0.866	**<0.001**
PET lesions SUVmax	**PEM lesions LTB**	0.805	**<0.001**
PEM lesions PUVmax	**PEM lesions LTB**	0.854	**<0.001**

DISCUSSION

In the current research we aimed to estimate the role of the quantitative measurements of PEM compared to PET/CT in the estimation of post-interventional breast neoplasm.

We enrolled 36 female cases with breast cancer, the mean age was 47.3 ± 11.3, in harmony with Pourriahi et al., (7) study that has a mean age of the cases of forty-eight years.

In the present research, regarding the lesion site (55.5%) of the cases had right breast cancer, (41.6%) had left breast cancer, and (2.7%) had bilateral disease involvement. This agreed with Bravo-López et al., (8) that found a similar rate in cases on the right and left breasts.

In our study, 3 lesions were detected by PEM and not detected in PET. Because of the high spatial resolution of PEM, all of them were around 1 cm. Two of them were found in the same breast as the primary lesion as small nodular lesions; one was adjacent to the primary lesion in the same quadrant, the other lesion was found in a different quadrant away from the primary lesion. The third lesion was found in the contralateral breast.

This was in harmony with Fuzuki Yano, et al. (9), who concluded that 18F-fluorodeoxyglucose PET had limited ability in identifying small breast tumors measuring less than ten millimeters. Combined positron emission tomography/computed tomography and positron emission mammography illustrated greater accuracy and sensitivity in comparison with PET/CT alone. Also, Kalinyak et al., (10) The study indicated that the sensitivity of positron emission mammography exceeded that of positron emission tomography/computed tomography, especially for cancers measuring one centimeter or smaller, with PEM identifying twenty-six/twenty-eight (ninety-three percent) compared to PET/CT's twenty-one/twenty-eight (seventy-five percent; p-value equal to 0.059). The enhanced outcomes with PEM probably indicate better spatial resolution, a closer proximity of crystals to the breast, & reduced respiratory motion in comparison to PET/CT.

We found 4 lesions detected by PET were missed in PEM; the reasons varied from very small breasts to adjacency of the lesion to the chest wall or axillary tail that cannot be totally assessed or adequately assessed by PEM. One of the patients showed a small breast with a lesion very close to the chest wall.

Regarding FDG PET/CT imaging of breast results in our study, 4 patients had no residual breast neoplastic lesions by PET. The other 32 patients showed 43 lesions. The SUVmax of the detected lesions varied from 1.6 to 27.5, with a mean value of 9.0 ± 6.0.

However, regarding Shin et al., (11) study, the median SUVmax in the malignant group was 4.2 (range, 1.3-16.0; IQR, 2.5-6.7), which was significantly greater compared to that in the benign group (median, 2.3; range, 1.0-5.7; IQR, 1.7-2.9; p-value below 0.001).

By positron emission tomography/computed tomography imaging in this research, 28 cases (77.8%) showed axillary nodal deposits, 4 patients (11.1%) with bone deposits, and 5 patients (13.9%) with soft tissue deposits. Similarly, out of the 20 cases of the Osman et al., (12) study aimed to assess the role of FDG PET/CT in the identification and staging of breast cancer, 8 cases illustrated axillary and extra-axillary LNs.

In the present study regarding FDG PEM imaging, the 4 free patients in PET/CT imaging were still free in PEM imaging. The total number of lesions detected by PEM imaging was 42. The PUVmax ranged from 1.4 to 19.6; the mean PUVmax was 6.3 ± 4.1. The LTB ranged from 1.4 to 17.4; the mean LTB was 6.2 ± 4.3.

The imaging sensitivity of positron emission mammography is greater compared to that of WBPET in Japanese females younger than fifty years of age. PEM illustrated significant sensitivity for cancers smaller than one centimeter, which has been a weak point for WBPET; these results supported our results that all lesions discovered by PEM only and not identified by PET CT were around one centimeter.

In the comparison of PET/CT and FDG PEM imaging in our study, 4 individuals exhibited concordant PET and PEM results with no breast lesions, 39 lesions have been identified by both PET/CT and PEM, 3 lesions were discovered solely by PEM, and 4 lesions identified by PET were not recognized by PEM.

We assumed that this change in risk stratification by adding PEM results may change the management plan/intent of the patients. For the lesions that were downgraded from intermediate to low risk, the standard approach is usually routine monitoring with no need of immediate intervention, according to Ibrahim, N. K., et al. (13), so they can be managed conservatively with periodic imaging (e.g., mammography, ultrasound). The lesions were downgraded from high risk to intermediate risk, often requiring close surveillance and, in some cases, excision to exclude more serious pathology. The decision to excise or observe depends on lesion characteristics and patient risk factors, according to LaTrenta et al. (14).

On the other hand, the lesions were upgraded from intermediate to high risk and found in five patients. Regarding the American College of Radiology (ACR) and Society of Breast Imaging (SBI) guidelines on breast cancer management, the treatment approach typically involves surgical excision, possibly followed by chemotherapy, radiation, or hormonal therapy, depending on the tumor's characteristics.

In addition, in Yamamoto et al., (15) research, which aimed to compare the sensitivity of positron emission mammography and PET methods, they concluded that the sensitivity of the positron emission mammography diagnostic method was greater compared to that of PET, and thereforePEM screening seems to have potential for breast cancer screening.

Keshavarz et al., (16) mentioned that the positron emission mammography technique is preferred to the PET method for efficacy. The comparison of PEM and PET diagnostic procedures indicated variances in sensitivity, specificity, PPV, NPV, as well as accuracy of 0.25, -0.013, 0.15, 0.072, and 0.081, correspondingly. As illustrated, all indices, with the exception of the specificity index, were positive, demonstrating that the usage of positron emission mammography for breast cancer cases is better compared to that of PET.

In our research, we aimed to assess the role of PEM quantitative indices compared to PET quantitative indices in detecting breast lesions post- intervention.

CONCLUSION:

PEM and PET may yield supplementary information. When PEM results are consistent with PET findings, this reinforces the reliability of both modalities in lesion detection and management. Discrepancies between PEM and PET, such as cases where PEM led to upstaging (13.0%) or detected new lesions not seen by PET, highlight the importance of using multiple diagnostic tools to obtain a comprehensive view of the disease. Quantitative PEM methods could be valuable for decision-making regarding management strategies based on the risk of change.

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