BENHA MEDICAL JOURNAL bmj

Print ISSN 1110-208X.

Online ISSN 2357-0016

Original article

18F-FDG PET /CT for Monitoring of Treatment Response in Breast Cancer

Asmaa A. Ghalwash[a], Tamer A. Kamal[a], Rasha M. Dawoud[b], Ahmed S. Ali[a]

[a] Diagnostic Radiology Department, Faculty of Medicine Benha University, Egypt.

[b] Diagnostic Radiology Department, Faculty of Medicine Tanta University, Egypt.

Corresponding to: Asmaa A. Ghalwash. Diagnostic Radiology Department, Faculty of Medicine Benha University, Egypt.

Email: asmaaghalwashgh@gmail.com

Received: 12 December 2024

Accepted:22 December 2024

Abstract:

Background: Positron emission tomography (PET), with or without integrated computed tomography (CT), using 18F-Fluorodeoxyglucose (FDG) is based on the principle of increased glucose metabolism in malignant tumors and has been investigated frequently in breast cancer (BC). The aim of this work was to evaluate the potential role of 18F-FDG PET/CT in monitoring treatment of BC and assessment of recurrence after surgical or systemic treatment. **Methods:** This current study was carried out on 50 female patients aged from 24 to 73 years old, diagnosed with BC undergoing neoadjuvant chemotherapy, radio, hormonal or surgical treatment. All patients were subjected to 18F-FDG and PET /CT evaluation. **Results:** Detection of lesions by 18F-FDG PET /CT was positive in 37 (74%) patients. Local recurrence occurred in 7 (14%) patients. Distance metastasis occurred in brain in 1 (2%) patient, lymph node in 6 (12%) patients, liver in 6 (12%) patients, lung in 5 (10%) patients and bone in 7 (14%) patients. local recurrence and distance metastasis occurred in 5 (10%) patients. Distance metastasis occurred in brain in 1 (2%) patient, lymph node in 2 (4%) patients, liver in 5 (10%) patients, lung in 4 (8%) patients and bone in 6 (12%) patients. Progression occurred in 22 (44%) patients. Regression occurred in 13 (26%) patients. Stationary occurred in 3 (6%) patients. **Conclusions:** Whole body FDG-PET/CT must be considered a useful and golden tool in monitoring treatment of BC allowing an identification of the local recurrence of the BC and distance metastasis.

Keywords: 18F- Fluorodeoxyglucose; Positron Emission Tomography; Computed Tomography; Breast Cancer; Metastasis

Introduction

Breast cancer (BC) is the most common cancer and the second leading cause of cancer mortality in women. Accurate diagnosis and staging are essential for the selection of the most appropriate therapeutic strategy and major determinants of patient prognosis and survival [1].

The accurate staging of local, regional, and distant recurrences after initial diagnosis and treatment is critical for therapeutic planning. In general, systemic therapy is used at almost all disease stages; however, isolated local-regional disease or a single site of metastatic recurrence is also treated with surgery and radiation therapy. After treatment, follow-up examinations are required for the early detection and accurate staging of recurrences [2].

Fluorodeoxyglucose positron emission testing (FDG PET) has high accuracy for the diagnosis of recurrent or metastatic BC, because it provides functional information, and it often complements conventional imaging modalities, which are more dependent on morphologic changes to depict disease recurrence. FDG PET is particularly useful for discriminating between viable tumour and post-therapy changes such as necrosis or fibrotic scarring in patients with equivocal results of anatomic imaging. FDG PET also is useful in patients in whom the only indicator of cancer recurrence is an increase in the serum levels of tumour markers such as carcinoembryonic antigen or CA 15-3 antigen [3].

PET , with or without integrated Computed Tomography (CT), using 18F-FDG is based on the principle of increased glucose metabolism in malignant tumors and has been investigated frequently in BC [4].

Skeletal metastases are the most common site of distant disease in BC, accounting for 90% of all metastatic lesions as well as representing the most common site of initial metastatic involvement. The role of FDG PET and PET/CT for detection and evaluation of skeletal metastases remains unanswered. Although most lesions are mixed, with some combination of lytic and blastic components, some lesions are purely lytic or blastic, and these lesions can pose difficulties for imaging [2].

The aim of this work was to evaluate the potential role of 18F-FDG PET/CT in monitoring treatment of BC and assessment of recurrence after surgical or systemic treatment.

Patients and Methods:

This prospective study was carried out at the Radiodiagnosis Department, Benha University Hospitals, Qalyubiyya, Egypt, from 2021 to 2023. It included 50 female patients aged 24 to 73 years, diagnosed with breast cancer and undergoing neoadjuvant chemotherapy (NAC), radiotherapy, hormonal, or surgical treatment. The study was approved by the Ethical Committee of Benha University Hospitals, and informed written consent was obtained from all patients {Approval code: M.D.12.12.2022}

Exclusion criteria included pregnancy, blood glucose level (BG) greater than 140 mg/dl, and renal impairment. All patients underwent a comprehensive evaluation, including complete history taking, clinical examination, laboratory investigations [blood glucose level, blood urea nitrogen (BUN), and creatinine], and radiological investigations [PET and CT scans].

Technique of whole-body positron emission tomography-computed tomography imaging with 18F-fluorodeoxyglucose

It included CE-CT imaging from top of skull to midthigh; all scans were performed according to the European Association of Nuclear Medicine guideline [5]. The patient lies supine either with the arms above the head or by the side. The BC patients underwent 18F-FDG PET/CT, at baseline and after treatment. The patients fasted for a minimum of 4 h and had BG levels less than or equal to 200 mg/dL just before the intravenous injection of 18F-FDG dosage of (1 MCi/ 10kg)

followed by saline. After an uptake phase of 18F-FDG of approximately 60 to 90 min, after 18F-FDG administration and was instructed to remain quiet with minimal movement until the completion of the PET/CT scan. Intravenous and oral CT contrast agents were recommended in PET/CT studies. Intravenous agents were used for all body areas except the abdomen, for which oral contrast agents were used. IV contrast agents were administered 30 to 40 seconds before CT scanning. Oral contrast agents provide positive contrast by increase of CT attenuation (iodine, barium) or negative contrast by distension of the bowel (water-based contrast agents). A combined whole-body PET/CT scan (GE Medical Systems Discovery IQ) was performed. A single whole-body CT scan was performed with a sixteen-slice multidetector helical scanner for attenuation correction purposes. The CT study takes approximately 60-70 seconds to complete, and the PET study takes approximately 30-45 minutes, depending on the coverage required. The tumour was first identified on a pre-treatment FDG-PET scan, and subsequently an ROI was placed in the tumour bed on a post-treatment FDG-PET scan. The slice with the highest radioactivity concentration within the tumour was identified. SUVs were calculated using the maximum (SUV max) activity values within the ROIs, normalized to the injected activity and patient's body weight. FDG-PET results were obtained for two SUV thresholds: SUV 2.0 and SUV 1.5.

A positive PET result was defined as an SUV equal to or above the threshold level. A negative PET result was defined as an SUV below the threshold level. Histopathology served as a reference standard, as described above. To assess the metabolic response, the PET response criteria in solid tumours (PERCIST) was used [6]. To assess the anatomical response, the CT images of the PET scans were used.

Complications: Allergy from contrast media treated by corticosteroids. Renal impairment requires nephrologist consultation for treatment according to its degree were recorded.

Statistical analysis

Statistical analysis was done by SPSS v26 (IBM Inc., Chicago, IL, USA). The Shapiro-Wilks test and histograms were used to evaluate the normality of the distribution of data. Quantitative parametric data were presented as mean and standard deviation [7]. Quantitative non-parametric data were presented as median and interquartile range (IQR). Qualitative variables were presented as frequency and percentage (%).

Results:

The mean of age was 56.3 ±11.15. Detection of lesions by 18F-FDG PET /CT was positive in 37 (74%) patients. Local recurrence occurred in 7 (14%) patients. Distance metastasis occurred in brain in 1 (2%) patient, lymph node in 6 (12%) patients, liver in 6 (12%) patients, lung in 5 (10%) patients and bone in 7 (14%) patients. local recurrence and distance metastasis occurred in 5 (10%) patients. (**Table, 1)**

Distance metastasis occurred in brain in 1 (2%) patient, lymph node in 2 (4%) patients, and liver in 5 (10%) patients, lung in 4 (8%) patients and bone in 6 (12%) patients. (**Table, 2)**

Progression occurred in 22 (44%) patients. Regression occurred in 13 (26%) patients. Stationary occurred in 3 (6%) patients. (**Table, 3)**

Case 1: A 53-year-old female with MRM for right BC, followed by chemotherapy. PET CT is requested for status evaluation/assessment of therapy response. PET/CT findings: clear right breast operative bed with no residual/recurrent masses or FDG-avid foci. FDG avid left axillary nodal lesion noted, measuring 2.5 cm SUV max 4.5. FDG avid few right internal mammary sub-cm nodal lesions noted, SUV max 2.5 dense left breast parenchyma noted with sub-areolar density

SUV max 1associated with stranding of fat planes. FDG avid marrow based, and osteolytic lesions noted involving multilevel spine marked at DV11 and LV1. Metastatic disease with recurrence. De-novo FDG avid enlarged left axillary as well as few right internal mammary sub-cm nodal lesions. Denovo FDG avid marrow based and osteolytic deposits as described. Dense left breast parenchyma noted with low grade sub-areolar density associated with stranding of fat planes for U/S and MRI. (**Figure, 1- A and B)**

Case 2: A 48-year-old female with left BC under hormonal treatment. PET/CT is requested for status evaluation. PET/CT findings: FDG-avid left breast upper inner quadrant lobulated soft tissue mass lesion 2.4 X1.9 cm. No enlarged or FDG-avid axillary or other mammary-related LNs. FDG-avid bi-lobar hepatic focal lesions are seen, largest 39 mm. Enlarged porta-hepatis LN seen (1.7x1.5 cm). Whole-body PET/CT study for a known patient with left breast Ca. under hormonal therapy showing: Left breast soft tissue lesion. Bi-lobar hepatic focal lesions. Enlarged porta-hepatis LN. (**Figure, 2- A and B)**

Case 3: A 40-year-old female with history of surgically managed left BC followed by chemotherapy. PET/CT is requested for status evaluation. PET/CT findings: Clear left mastectomy bed with no masses or dense tracer fixing foci. No enlarged or dense tracer fixing mammary-related lymph nodes. FDG-avid multiple hepatic bi-lobar hypodense focal lesions are seen; the largest at segment III (2.5 cm), eliciting SUV max 18.7. FDG-avid mixed sclerotic/lytic osseous lesions are seen at sternum, few bilateral ribs, multi-levels of the spine, scapulae, eliciting SUV max up to 15.5, at the sternum. Whole-body PET/CT study showing: Glucose-avid multiple hepatic and osseous lesions as described; in keeping with active tumor biology (metastatic deposits). Free rest-surveyed body from any pathological glucose-avid lesions; including the left mastectomy bed and mammary-related lymph nodes. (**Figure, 3- A and B)**

Table 1: Age, detection of lesions by 18F-FDG PET /CT, local recurrence and distance metastasis and both of them of the studied patients

		N=50
Age (years)		56.3±11.15
Detection of lesions by18F-FDG PET /CT		37(74.0%)
Local recurrence		7(14.0%)
	Brain	1(2.0%)
	Lymph node	6(12.0%)
Distance metastasis	**Liver**	6(12.0%)
	Lung	5(10.0%)
	Bone	7(14.0%)
Local recurrence and distance metastasis		5(10.0%)

Data are presented as mean ± SD or frequency (%). FDG: fluorodeoxyglucose, PET /CT: positron emission tomography-computed tomography.

Table 2: Detection of distance metastasis in follow up of the studied patients

		N=50
	Brain	1(2.0%)
	Lymph node	2(4.0%)
Distance metastasis	**Liver**	5(10.0%)
	Lung	4(8.0%)
	Bone	6(12.0%)

Data are presented as frequency (%).

Table 3: Outcomes of the studied patients

	N=50
Progression	22(44.0%)
Regression	13(26.0%)
Stationary	3(6.0%)

Data are presented as frequency (%).

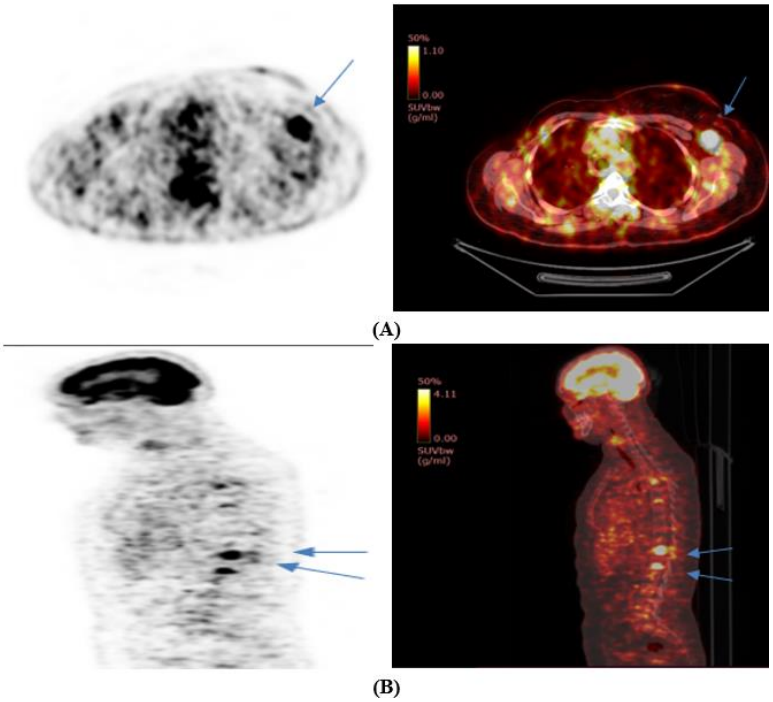

Figure 1:(A) Axial few positron emission tomography-computed tomography chest showing left axillary nodal lesion with avid uptake (line arrow) and (B) Sagittal view dorso-lumbar spine positron emission tomography-computed tomography scan showing multi-level bony metastasis with avid uptake (line arrow)

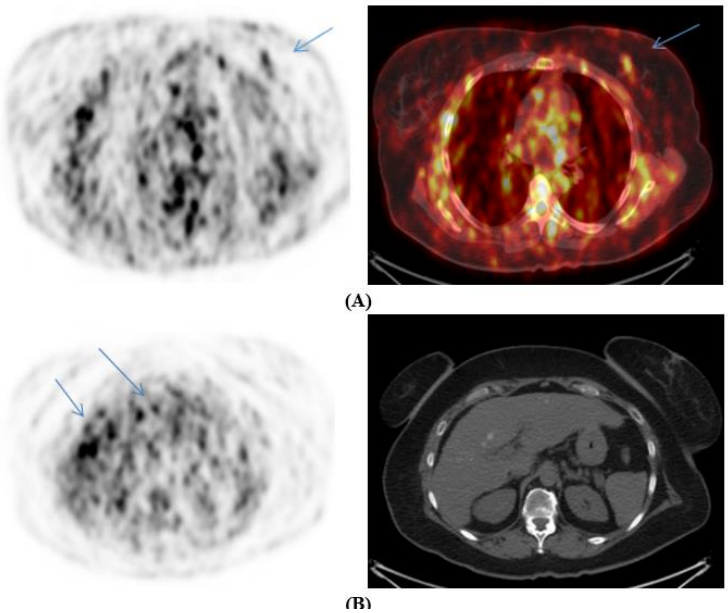

Figure 2: Axial positron emission tomography-computed tomography chest shows fluorodeoxyglucose -avid (A) left breast upper inner quadrant lobulated soft tissue mass lesion (line arrow) and (B) bi-lobar hepatic focal lesions

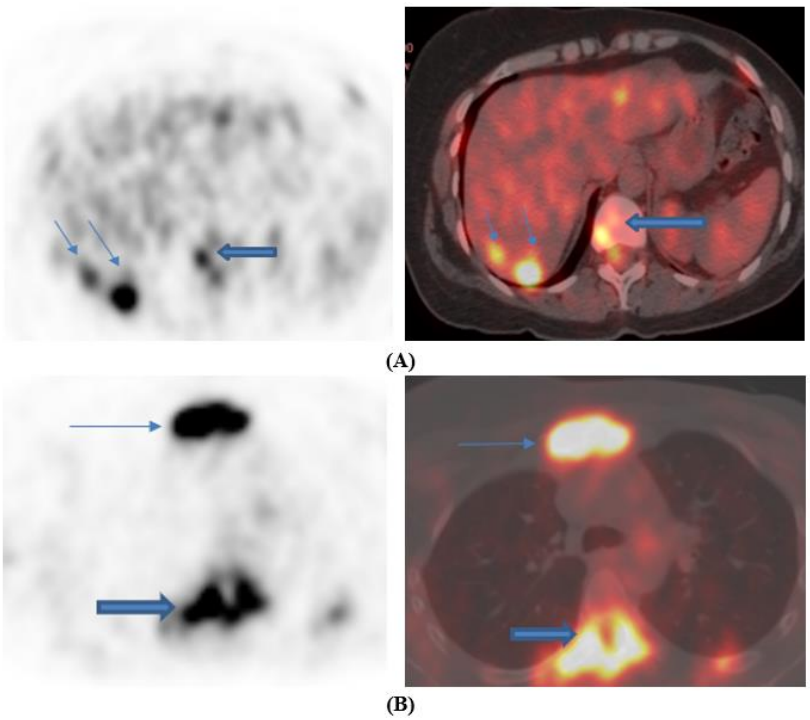

Figure 3: Axial positron emission tomography-computed tomography (A) abdomen showing fluorodeoxyglucose -avid multiple hepatic bi-lobar focal lesions (line arrow) and fluorodeoxyglucose -avid sclerotic osseous lesion at related vertebral body (thick arrow) and (B) chest showing fluorodeoxyglucose -avid sclerotic osseous lesion at sternum (line arrow) and at related vertebral body (thick arrow)

Discussion

BC has the fifth highest mortality rate with death rates for female breast and cervical cancers being considerably higher in developing versus developed countries (15.0 vs. 12.8 per 100,000 and 12.4 vs. 5.2 per 100,000, respectively). In females, it accounts for one in four cases and for one in six deaths [8].

In the current study, detection of lesions by 18F-FDG PET /CT was positive in 37 (74%) patients. Supporting our results, it was reported that 18F-FDG PET/CT has higher sensitivity and accuracy compared to CT alone (reaching 100% for PET/CT and 96% for CT) in detecting malignant breast lesions, regional and distant nodal deposits as well as distant deposits [9]. In the same line, it was demonstrated that positive findings for 18F-FDG-PET/CT were found in 28/37 patients (75.7%) [10]. Also, 18F-FDG-PET/CT for the follow-up and restaging of soft tissue sarcomas in adults showed an overall diagnostic accuracy of 91.8%, sensitivity of 90% and a specificity of 100%. The positive predictive value and negative predictive value were 100 and 70%, respectively. This agreed with prior research which reported 97% sensitivity of PET/CT in detecting the breast tumours [7].

This study revealed that local recurrence occurred in 7 (14%) patients while local recurrence and distance metastasis occurred in 5 (10%) patients. The most important current clinical applications of 18F-FDG PET/CT in BC patients are for the detection and evaluation of recurrent or metastatic disease and for monitoring response to therapy [11]. As [12] showed that 18F-FDG PET/CT has a high overall sensitivity, specificity and accuracy for the detection of locoregional recurrence (89%, 84% and 87%, respectively) and distant metastases (100%, 97% and 98%, respectively). This agreed with another study which reported that local recurrence

occurred in 16% of patients [13]. Also, it was claimed that there was 7% had local recurrence after treatment [14].

In the current study, distance metastasis occurred in brain in 1 (2%) patient, lymph node in 6 (12%) patients, liver in 6 (12%) patients, lung in 5 (10%) patients and bone in 7 (14%) patients.

In the same line, it was reported that bone-only disease was present in 26.4% (majority) of the patients [15]. However, it was illustrated that site of metastasis was in lymph nodes accounting for 32% of cases liver in 24%, bone in 20% and lung in 16%[13]. The different sample size could explain this difference from our results. This came in line with other study that reported that distance metastasis in follow up occurred in lymph node in 8% patients, liver in 20% patients, lung in 12% patients and bone in 16% [13]. It was proved that bone is the most common site of distant metastasis in BC; nearly 70% of patients who have advanced disease have bone metastasis [16].

In the current study, progression occurred in 22 (44%) patients. Regression occurred in 13 (26%) patients. Stationary occurred in 3 (6%) patients. Supporting our results, is the study which demonstrated that progression was detected first by 18F-FDG PET/CT in 43/87 patients (49.4%)[15]. This was in harmony with [13] showed that progression occurred in 40% of patients, Regression occurred in 20% of patients and stationary occurred in 4% of patients.

Conclusions:

Whole body FDG-PET/CT must be considered a useful and golden tool in monitoring treatment of BC allowing an identification of the local recurrence of the BC and distance metastasis. These results suggest that 74% of patients were positive in detecting lesions by 18F-FDG PET/CT. Also, regarding outcomes progression occurred in 44% of patients, regression in 26% of patients and stationery occurred in 6% of patient. So 18F-FDG PET/CT is recommended for monitoring treatment of BC.

References:

1. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer statistics, 2022.CA Cancer J Clin 2022;72:70-20.
2. Rania AM, Noha FE-Q, Salama M, Asmaa M. 18F-FDG PET/CT for monitoring of treatment response in breast cancer.Med J Cairo Univ 2021;89:473-9.
3. Murakami R, Kumita S-i, Yoshida T, Ishihara K, Kiriyama T, Hakozaki K, et al. FDG-PET/CT in the diagnosis of recurrent breast cancer.Acta radiol.2012;53:12-6.
4. Koolen B, Vogel W, Vrancken Peeters M, Loo C, Rutgers ET, Valdes Olmos R. Molecular imaging in breast cancer: from whole-body PET/CT to dedicated breast PET.J Oncol.2012;50:438-647.
5. Boellaard R, Delgado-Bolton R, Oyen WJ, Giammarile F, Tatsch K, Eschner W, et al. FDG PET/CT: EANM procedure guidelines for tumour imaging: version 2.0.Eur J Nucl Med Mol Imaging.2015;42:328-54.
6. Wahl RL, Jacene H, Kasamon Y, Lodge MA. From RECIST to PERCIST: Evolving considerations for PET response criteria in solid tumors.J Nucl Med.2009;50 122-50.
7. Bernsdorf M, Berthelsen A, Wielenga V, Kroman N, Teilum D, Binderup T, et al. Preoperative PET/CT in early-stage breast cancer.Ann Oncol.2012;23:2277-82.
8. Hadebe B, Harry L, Ebrahim T, Pillay V, Vorster M. The role of PET/CT in breast cancer. Diagn.2023;13:50-30.
9. Kamal AM, Kamal OA, Sakr HM, Ali SA. Role of 18F-FDG PET/CT in evaluation of recently diagnosed breast cancer patients.Egypt J Radiol Nucl Med.2022;53:178-40.
10. Kassem TW, Abdelaziz O, Emad-Eldin S. Diagnostic value of 18F-FDG-PET/CT for the follow-up and restaging of soft tissue sarcomas in adults.Diagn Interv Imaging.2017;98:693-8.
11. Almuhaideb A, Papathanasiou N, Bomanji J. 18F-FDG PET/CT imaging in oncology.Ann Saudi Med.2011;31:3-13.
12. Kamel EM, Wyss MT, Fehr MK, von Schulthess GK, Goerres GW. [18F]-Fluorodeoxyglucose positron emission tomography in patients with suspected recurrence of breast cancer.J Cancer Res Clin Oncol.2003;129:147-53.
13. Rania AM, Noha FE-Q, Salama M, Asmaa M. 18F-FDG PET/CT for monitoring of treatment response in breast cancer.Med J Cairo Univ.2021;89:473-9.

14. Nguyen DV, Kim SW, Oh YT, Noh OK, Jung Y, Chun M, et al. Local recurrence in young women with breast cancer: breast conserving therapy vs. mastectomy alone.Cancers 2021;13:70-30.
15. Vogsen M, Harbo F, Jakobsen NM, Nissen HJ, Dahlsgaard-Wallenius SE, Gerke O, et al. Response monitoring in metastatic breast cancer: a prospective study comparing 18F-FDG PET/CT with conventional CT.J Nucl Med.2023;64:355-61.
16. Nakai T, Okuyama C, Kubota T, Yamada K, Ushijima Y, Taniike K, et al. Pitfalls of FDG-PET for the diagnosis of osteoblastic bone metastases in patients with breast cancer.Eur J Nucl Med Mol Imaging.2005;32:1253-8.

To cite this article: Asmaa A. Ghalwash, Tamer A. Kamal, Rasha M. Dawoud, Ahmed S. Ali. 18F-FDG PET /CT for Monitoring of Treatment Response in Breast Cancer. BMFJ 2025;42(6):90-97.