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Original article

# Role of FDG PET/CT in Diagnosis & Staging of Breast Cancer

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## Abstract

**Background**: Cancer breast is a leading cause of death and the most common cancer in women. Early and accurate diagnosis remains a challenge. If breast cancer is found early, prompt treatment could save life. PET is a useful test for staging or re-staging breast cancer because its higher accuracy for finding local or distant disease. PET is sensitive in detection of clusters of tumor cells that have taken hold in other tissues or organs in the body. **Aim of the study:** The aim of the present study is to evaluate role of FDG PET/CT in diagnosis &staging of breast cancer. **Patients and methods:** This prospective study was conducted on female patients known to have malignant breast lesion /lesions who were referred to radio-diagnosis & oncology departments. The present study demonstrated in correlation with other studies that PET/CT is sensitive in detection the primary breast masses but till now not the modality of choice in breast cancer diagnosis as PET/CT has important limitation such as high cost , significant radiation exposure and inability to detect small sized primary tumors. **Results:** The overall sensitivity of PET/CT in diagnosis &staging of breast was about 97%. **Conclusion:** The present study demonstrated in correlation with other studies that PET/CT is sensitive in detection the primary breast masses but till now not the modality of choice in breast cancer diagnosis as PET/CT has important limitation such as high cost , significant radiation exposure and inability to detect small sized primary tumors.

**Keywords:** breast cancer ; FDG PET/CT, PET/CT

## Introduction

Cancer breast is a leading cause of death and the most common cancer in women. Early and accurate diagnosis remains a challenge. The current standard relies on physical examination, mammography and/or ultrasound, and fine needle aspiration. If breast cancer is found early, prompt treatment could save life. (1)

PET helps in assessment of axillary and mammary lymph node involvement, which may reduce the need of axillary lymph node dissection in patients who show no lymph

node involvement, thus reducing its complications as well. [2]

PET is a useful test for staging or re-staging breast cancer because its higher accuracy for finding local or distant disease, when compared to other imaging modalities. PET is sensitive in detection of clusters of tumor cells that have taken hold in other tissues or organs in the body. [2]

PET/CT is superior to other radiological modalities in assessment of the response of treatment and for follow up. [3, 4]

Positron emission tomography with 18fluorodeoxyglucose (FDG-PET) has been used for diagnosis, staging, monitoring response to therapy, and restaging patients with breast cancer. [5]

FDG is a glucose analog transported via glucose transporters into the cells, phosphorylated by hexokinase. FDG mimics glucose during the first enzymatic reactions in the cells. [6, 7]

Changes in metabolic activity generally occur earlier than changes in tumor size so that functional/morphological imaging techniques such as PET/CT can be used earlier than morphologic imaging methods to evaluate treatment response. [8]

## Patients and methods

This prospective study was conducted on (20) female patients over a period of 6 months. Those patients were referred to Radio diagnosis & nuclear medicine departments in Tanta university hospital.

Every patient was subjected to the following:

***Inclusion criteria:**

1. Histological proven breast cancer.
2. Blood urea nitrogen and serum creatinine within normal range.
3. Availability of follow up imaging study.

***Exclusion criteria:**

1. Women of childbearing age, inquiry about pregnancy was done for fear of risk of radioactive material upon the fetus and in cases of suspicion a pregnancy test was done.
2. Women with renal impairment.

***Pretreatment evaluation and diagnostic work up:**

Each patient underwent the following before inclusion in our study:

***Clinical evaluation:**

1. Complete history and physical examination.
2. Local examination: including breast and axillae.

***Diagnostic Work Up:**

1. **Laboratory studies including:**

- Complete blood picture.
- Blood urea nitrogen and creatinine.

2. **Radiological studies and imaging including:**

- *FDG PET/CT* (for all patients).
- *Mammography*(18 patients had mammographic examination, two young patients below 25 years did not undergo mammography)
- *Ultrasound* (for all patients)
- *FNA* ( for all patients)
- *Bone scintigraphy* ( for only 10 patients of suspected bone metastases)
- *Chest x-ray* ( for all patients)

***Imaging:**

Exams were done and data were obtained using Siemens Bio-graph true point PET/CT scanner. PET images had been reconstructed using standard vendor-provided reconstruction algorithms. CT images had been acquired in helical mode from the skull to the mid-thigh during suspended mid expiration at a 120 kV, 300 mA.

***Patient Preparation:**

**Before examination**

All patients were asked to fast for six hours prior to scan. All metallic items were removed from the patients and they were given gown to wear. Patients were asked to empty their bladders before the procedure.

In case of diabetic patients (3 cases); serum glucose was routinely measured prior to 18F-FDG injection, and fasting levels were 70–170 ng/dl. In one case an injection of one unit of act-rapid/200cc saline was done with monitoring of the blood glucose level to ensure that it is less than 150 mg/dl, when it was within the accepted range; FDG was injected one hour later.

**At examination:**

An I.V. cannula was inserted in the patient's arm for administration of 18F-FDG. The patients were instructed to avoid any kind of strenuous activity prior to the examination and following injection of the radioisotope to avoid physiologic muscle uptake of FDG.

***Dosage Administration:**

One liter of negative oral contrast agent (5% mannitol) approximately one hour before the exam. A dose of 3-7 MBq/Kg of 18F-FDG IV injection 45–90 minutes before examination was administered**.** This period is referred to as the uptake phase and is the necessary amount of time for the FDG to be adequately bio-distributed and transported into the patient's cells. Patients were asked to rest in a quiet room, devoid of distractions, and they were also asked to keep their movements, including talking, at an absolute minimum. This minimizes physiologic uptake of FDG into skeletal muscle, which can confound interpretation of the scan. Patients should be comfortable and relaxed

*** Patient position:**

The patients were positioned on the PET\CT machine table in supine position with arms above the head.

***CT Technique:**

Helical CT was performed following injection of 125 mL of a low-osmolarity iodinated contrast medium at a rate of 4 m /sec using a power injector. For a typical whole body PET -CT study (skull, neck, chest, abdomen, and pelvis), scanning began at the level of the skull and extended caudally to the level of the upper thighs. The total length of CT coverage was an integral number of bed positions scanned during acquisition of PET data. The study was performed with the patient breathing quietly. Scanning parameters are collimation width of 5.0 mm, pitch of 1.5, and gantry rotation time of 0.8 second and field of view of 50cm. The helical data are retrospectively reconstructed at one mm intervals.

***PET Technique:**

PET was performed following the CT study without moving the patient. Approximately six to seven bed positions are planned for the three dimensional acquisition modes for scanning the entire patient with 3-5 minute acquisition at each bed position.

***PET/CT Fusion**

Trans-axial PET and CT images were first reconstructed. These are then reformatted into coronal and Sagittal images to facilitate image interpretation. For each of these sets of PET and CT images, corresponding fusion images, combining the two types of data, also were generated. The whole acquisition time for an integrated PET/ CT scan was approximately 25-30 minutes. PET image data sets were reconstructed using CT data for attenuation correction and co-registered images were displayed using special software.

***Examination time:**

A whole body PET study follows an enhanced whole body CT study. 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 study was done after the approval of the Research and Ethical committee , Informed consent was obtained before performing the study**.

**Results**

Statistical analysis: Data analysis was done using SPSS program version 20. Data presented as number and percentage.

Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy was calculated

**Distribution of the cases according to different lines of treatment:**

Sixteen patients underwent surgical, chemo therapy, radiotherapy or hormonal treatment (80% of the studied patients) .Two patients underwent only chemotherapy, radiotherapy or hormonal treatment without surgical interference (10% of the studied patients) .Two patients not received any treatment (10% of the studied patients). (Table 1)

**Patients with breast mass:**

Six patients of the present study showed breast mass ,two young patients below 25 years old admitted for first diagnosis, two patients presented with advanced breast cancer, only one patient came with recurrence to right breast after left MRM, one patient presented with hypoechoic small sized soft tissue lesion in the right breast measured 1x1 cm by ultrasound with microcalcification by mammographic examination. (Table 2)

**B)-axillary and extra axillary LNs**

Eight cases showed axillary and extra axillary LNs as the following distribution (four as mediastinal LN, 3 as axillary LN and one as cervical , supraclavicular &iliac LNs).

One of the axillary LNs showed equivocal FDG uptake 4 SUV , after follow up with CT disappeared. (Table3)

**C) - bone lesions:**

Seven cases showed bone metastasis as follow (one osteolytic , 2 osteoblastic and four as mixed type )

Bone scan detected the osteoblastic and mixed bony lesions as hot areas however the osteolytic lesions were equivocal.

PET/CT detected all bony lesions with abnormal increase FDG uptake (max SUV ranged between 9-38)

**D)-visceral distant metastasis:**

Seven cases showed visceral distant metastasis as follow (4 cases with liver focal lesions , 2 cases with pulmonary nodules & one case with brain metastasis )

CT is equal to PET/CT in detection of these lesions, FDG uptake ranged between 12-26 SUV.

**E): Tumor response to the different parameters of treatment:**

The study included 8 patients with previously documented metastatic disease who underwent PET/CT scanning to monitor treatment response.

These 8 cases divided as follow:

*Two cases showed additional sites of metastases (25% of these 8patients) whereas CT detected only one case (12.5% of these 8 patients)

*One case showed stationary course (12.5% of these 8patients) whereas CT detected 5 cases (62.5% of these 8 patients)

*Three cases showed progressive course (37.5% of these 8 patients) whereas CT detected only one case (12.5% of these 8 patients).

*One case showed improvement in CT(12.5% of these 8patients) and two cases in PET-CT (25% of these 8 patients) (table5) &( figure 1).

**Table (1):** Different lines of treatment

| | No. | % |
|---|---|---|
| **Surgery &therapy** | 16 | 80% |
| **Only therapy** | 2 | 10% |
| **No surgery or therapy** | 2 | 10% |

**Table (2):** Breast masses detection:

| **Case no** | **CT** | **PET/CT** | **Max.SUV** |
|---|---|---|---|
| Four cases | -Abnormal soft tissue density are noticed either in the right or left breast<br>-Size of masses ranged between 2.5-5 cm | Abnormal increase FDG uptake of these masses | Ranged between 9-15 |
| 5th Case | Patient had left MRM showed abnormal soft tissue density in the right breast measured 2x1.5 cm | Abnormal increase FDG uptake of the mass | 10 |
| 6th Case | No detection of any abnormal soft tissue density | No abnormal FDG uptake | ------ |

**Table 3:** axillary and extra axillary LNs detection

| **LNs** | **CT** | **PET/CT** | **Max SUV** |
|---|---|---|---|
| Axillary LNs | Enlarged with average size 2cm | Abnormal increase FDG uptake | Ranged between 4-18 |
| Mediastinal LNs | Enlarged with average size 3cm | Abnormal increase FDG uptake | Ranged between 9-22 |
| Cervical ,supraclavicular& iliac LNs | Enlarged with average size 1.5cm | Abnormal increase FDG uptake | 10 |

**Table4:** Results of CT and PET-CT in the 4 cases of discordant staging:

| NO. | CT | PET/CT | Results |
|---|---|---|---|
| **1** | Only primary tumour + ipsilateral axillary LN | Primary tumour + axillary & mediastinal LNs | Upstaging from II to III |
| **2,3** | Only primary tumour | Primary tumour + Bone lesions | Upstaging from I to IV |
| **4** | Only primary tumour + ipsilateral axillary LN | Primary tumour + Axillary LN &Bone lesions | Upstaging from II to IV |

**Table 5:** Comparison between CT & PET-CT regarding the response to treatment.

| | CT No. (%) | PET/CT No. (%) |
|---|---|---|
| **Additional sites of metastasis** | 1(12.5%) | 2(25%) |
| **Stationary course** | 5(62.5%) | 1(12.5%) |
| **Progression** | 1(12.5%) | 3(37.5%) |
| **Improvement** | 1(12.5%) | 2(25%) |

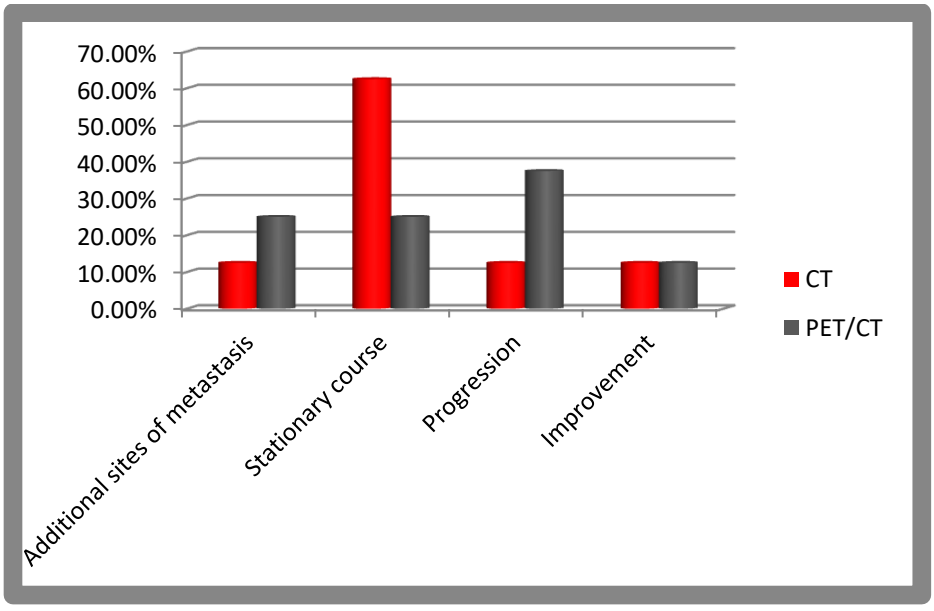


**Figure1:** Comparison between CT & PET-CT regarding the response to treatment

## Discussion

Out of the 20 cases of the present study, eight cases showed axillary and extra axillary LNs as the following distribution (four as mediastinal LN, 3 as axillary LN and one as cervical, supraclavicular &iliac LNs). One of the axillary LNs showed equivocal FDG uptake 4 SUV, after follow up with CT disappeared.

This agrees with several studies report success with FDG PET in staging the presence or absence of axillary nodal metastases in patients with breast cancer. Accuracy for characterization of the axilla as a whole as positive or negative for axillary nodal metastatic disease ranges from 82% to 95%. **(9 & 10)**

In the series of sensitivity of FDG PET to nodal metastases was 17 of 18 (94%) in patients with primary lesions >2 cm, and only 2 of 6 (33%) in those with smaller primaries. **(11 & 12)**

Studied 167 consecutive breast cancer patients, and axillary involvement was detected in 68 of 72 patients, resulting in a sensitivity of 94.4% and a specificity of 86.3%; overall accuracy of lymph node staging with PET was 89.8%. **(13)**

Although the sensitivity of PET may be low for small nodal metastases, PET is able to noninvasively depict metastases to the internal mammary lymph nodes. **(14)**

The skeleton is the most common site of distant metastasis in breast cancer; nearly 70% of patients who have advanced disease have bone metastasis. Bone scintigraphy is considered the most sensitive method for detecting and determining the extent of skeletal metastases; however, purely osteolytic lesions or metastases confined to the marrow cavity may be difficult to detect on bone scintigraphy, because of a lack of sufficient osteoblastic response. **(15)**

Out of 20 cases in the present study, Seven cases showed bone metastasis as follow (one osteolytic, 2 osteoblastic and four as mixed type) Bone scan detected the osteoblastic and mixed bony lesions as hot areas however the osteolytic lesions were equivocal. PET/CT detected all bony lesions with abnormal increase FDG uptake (max SUV ranged between 9-38)

This agrees with **(16)** showed that FDG PET depicted a mean of 14.1 lesions in the skeleton versus 7.8 by 99mTc-MDP bone scan. Furthermore, they showed a poorer prognosis for patients with osteolytic lesions with higher FDG uptake levels**.**

Several studies comparing the sensitivity of bone scintigraphy to FDG-PET in the detection of skeletal metastases in patients who have advanced disease have shown conflicting results. Some studies have shown FDG-PET to be equal or superior to planar bone scintigraphy in the detection of skeletal metastases whereas others have shown FDG-PET to be less sensitive on a lesion-based analysis. **(16) (17) (18)**

[18] In the study of 23 breast cancer patients who had known skeletal metastases and underwent both bone scintigraphy and FDG-PET, FDG-PET detected more lesions than bone scintigraphy, except in a subgroup of patients who had osteoblastic metastases. Moreover, the level of FDG uptake in osteolytic lesions was significantly greater compared with osteoblastic lesions, and the prognosis of patients who had osteolytic-predominant disease was significantly worse

This agrees with [15] that PET has been shown to be superior to bone scintigraphy in detecting bone metastases .

The presence of distant metastases is an important prognostic factor in patients with breast cancer and has a significant influence on determining therapy. Because breast cancer can metastasize to many organs (bone, liver, lung, brain, etc.).

Seven cases showed visceral distant metastasis as follow (4 cases with liver focal lesions, 2 cases with pulmonary nodules & one case with brain metastasis). CT is equal to PET/CT in detection of these lesions& FDG uptake ranged between 12-26 SUV.

This disagrees with a recent study by [19] in 80 patients with operable breast cancer who were considered high risk for metastatic disease (patients with T3 lesions and/or clinically positive N1/N2), demonstrated that the rate of false-positive results was greater with conventional imaging (CT or bone scintigraphy) than FDG PET (17% vs. 5%). The findings on the conventional imaging generated additional tests and biopsies that eventually had negative results. In addition, eight patients (10%) had metastatic disease detected by both conventional imaging and PET; however, four (5%) other patients had additional metastatic disease seen only on PET that altered management.

**Conclusion**

PET-CT was far more sensitive than CT in follow up of breast cancer where stationary size of the lesion or residual smaller masses are detected after treatment yet they are metabolically non-active. This helps in guiding further treatment and establishing risk adapted chemotherapy.

The use of standard uptake value (SUV) proved to be more efficient in follow up studies after chemotherapy being more related to the functional activity of the residual tumor cells rather than to the size of the tumor itself.

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