Special Relevance of FDG-PET as an Upfront Diagnostic Modality at Initial Diagnosis and in Suspected Recurrence in Patients of Breast Carcinoma Hailing From Lower Socioeconomic Status Owing to Relative Late Presentation: A Pilot Study in a Medical College Hospital Setting in India

Spoorthy S. Shetty · Mukund B. Tayade · Sandip Basu

Received: 20 September 2013 / Accepted: 27 January 2014 / Published online: 18 February 2014
© Indian Association of Surgical Oncology 2014

Abstract FDG-PET has found relatively limited use in routine management of breast carcinoma due to its limited utility in assessing the primary and axillary lymph node status. The aim of the study was to assess its role in a medical school and municipal hospital setting of Mumbai, where majority belongs to the lower socioeconomic status and presents relatively late and hence whole body FDG-PET could find important place for assessing whole body disease status that would justify being used upfront in this group of patients. Thus, the premise of this study was that FDG-PET will have special relevance in this particular setting for evaluation of patients of breast carcinoma with respect to initial staging, detection of locoregional recurrence and metastasis and assessing response to systemic treatment. A total of 52 patients proven to have breast carcinoma, who had undergone ^{18}F FDG-PET for disease staging at initial diagnosis and in recurrent disease staging with a few cases as a baseline study for early treatment monitoring purposes over a study period of 3 years, were included in this analysis. 33.3 % of patients with pretreatment baseline FDG-PET were upstaged with diagnosis of additional lesions in the adrenal gland, liver, internal mammary, cervical lymph nodes and the mediastinum. On a lesion specific

analysis, the percentage of increased lesion detection (including both lymph node with distant metastasis) by FDG-PET was 42.7 %. FDG-PET was found to be 100 % sensitive and specific for confirming recurrent breast cancer. Four out of 18 patients on chemotherapy underwent second FDG-PET after first cycle of chemotherapy, showed responsiveness to chemotherapy by decreased maximum standardized uptake value (SUVmax). FDG-PET showed 9 liver lesions in 6 patients, only 3 of them was reported in USG. In one patient USG abdomen was inconclusive between hemangioma and metastasis, FDG-PET ruled out liver metastasis in this patient. In the examined patient population belonging to lower socioeconomic status, where usual presentation is relatively late, upfront whole body survey with FDG-PET or PET/CT is of considerable value in view of higher probability of existence of metastatic disease, thus can be an important one-stop shop tool in assessing whole body disease status in a single examination. It also proved efficacious in diagnosing loco regional and distant recurrence, metabolic characterization of lump and early response to treatment in the examined few cases following one cycle of chemotherapy in locally advanced breast cancer.

Keywords Breast carcinoma · FDG-PET · PET-CT · Disease staging · Metastasis

S. S. Shetty · M. B. Tayade
Department of Surgery, Grant Medical College and Sir J J Hospital,
Mumbai, India

S. Basu (✉)
Radiation Medicine Centre, Bhabha Atomic Research Centre, Tata
Memorial Hospital Annexe, Jerbai Wadia Road, Parel, Mumbai 400
012, India
e-mail: drsanb@yahoo.com

Introduction

The utility of FDG-PET has been emphasized for its utility in disease staging at initial diagnosis especially for the non-axillary lymph nodes evaluation, distant metastases and in the setting of locally advanced breast carcinoma [1, 2]. Its

potential role in certain clinical questions in managing patients of carcinoma breast that is being critically examined are: (a) the ability to define extent of disease, (b) to monitor response of treatment and to (c) predict tumor behavior and biology [1–6]. These are the areas where the role of FDG-PET is continuing to evolve. Positron emission tomography (PET) is a noninvasive Nuclear Medicine study that has been in existence for almost 30 years, but has been accepted in oncologic imaging rapidly during past 10 years. The standard PET procedure mostly employs injection of a short lived positron emitting radiopharmaceutical, 2-deoxy-[f-18]fluoro-D-glucose (FDG), a glucose analogue with 18F having a half-life of 110 min. While radiologic studies such as mammography, sonography, CT, MRI provide anatomic information about size and location of masses, but cannot provide unique metabolic information available with PET. This feature has the potential of early detection/metabolic characterization of breast masses, differentiation of scar or benign tissue from active malignancy, detection of malignancy in normal sized lymph nodes and at distant sites and assessment of early tumor treatment response to administered chemotherapy.

An important role for FDG-PET is thought to be especially useful in detecting distant metastases/recurrent disease. Thus we believed that in a given medical college set-up, where majority of the patients belong to the lower socioeconomic status and present late with relatively advanced disease, the role of FDG-PET will have special relevance compared to a tertiary care setting. Thus the premise of the study was to examine the precise role of upfront FDG-PET in this group of population with relatively advanced disease. Another important aim was to examine its role in monitoring systemic therapy early in the course which could be potentially superior to the anatomically based measure of response.

Material and Methods

This prospective study was undertaken with enrolment of patients presenting with carcinoma breast admitted in the surgical wards of a medical school in India over a study period of 3 years (2010 to 2012). Selected patients had undergone ^{18}F -FDG PET study in a neighboring Nuclear Medicine centre. Patients were

Table 1 Age distribution of patients recruited in the study

SL no	Age range	Number of patients
1	20–30	02
2	31–40	13
3	41–50	22
4	51–60	07
5	61–70	06
6	71–80	02

Table 2 The profile of the histopathological characteristics (grade and type) of the primary tumor included in the study population

SL no	Histopathological type and grade	No of patients
1	IDC GRADE III	45(86 %)
2	IDC GRADE II	06(12 %)
3	PAPILLARY CYSTIC VARIANT	01(2 %)

categorized into various subgroups for the purpose of systematic analysis: (a) pre-surgery, for treatment monitoring purposes and those who were examined for detecting recurrence. The aspects for which FDG-PET findings were assessed included (a) determining Initial diagnosis of breast cancer, (b) Initial disease staging (of loco regional lymph nodes and distant metastases), (c) detection of loco regional recurrence and distant metastasis and (d) evaluating early response to administered systemic treatment.

Inclusion Criteria

1. All patients of age group 20–80 year. having diagnosed carcinoma breast on fine needle aspiration cytology (FNAC)/biopsy.
2. Operated carcinoma breast with histopathological report, tumor grade, ER/PR status and axillary lymph node status.
3. Recurrent carcinoma breast patients diagnosed on biopsy.
4. Carcinoma breast patients planned for radiotherapy or chemotherapy with FDG-PET before and after treatment.

Exclusion Criteria

1. Patients with uncontrolled diabetes mellitus.
2. Pregnant and lactating female.
3. Patients with Renal failure.

Methods

Patients fasted for at least 6 h prior to the FDG-PET study. A random blood sugar level was done prior to scan and patients

Table 3 Receptor status

Receptor status of the primary lesion	Number of patients (%)
ER+PR+HER-	19(51.3 %)
ER-PR-HER-	13(35.1 %)
ER-PR-HER+	4(10.8 %)
ER+PR+HER+	1(2 %)

Fig. 1 A patient of recurrent breast carcinoma with ER—PR- and HER 2 + disease demonstrating extensive metastasis to multiple vertebrae, femur, shoulder, sternum, chest wall and lung on FDG PET scan

with blood sugar level below 150 mg were injected with ^{18}F labeled FDG of 12 mCi. History, clinical examination and informed valid written consent was taken for all patients included in this prospective research study. The FDG-PET scan was performed 60 min post injection of FDG. Maximum standardized uptake value (SUVmax) was calculated and delayed scan was undertaken in relevant cases

Results

A total of 52 patients of carcinoma breast were prospectively studied using the aforementioned protocol. Out of 52 cases, 24 underwent primary FDG –PET (undertaken at initial diagnosis and before surgery), 18 were post-treatment cases (post-surgery or during chemotherapy) and 10 cases were examined for recurrent breast cancer with suggestive history of metastasis.

Fig. 2 Male breast carcinoma demonstrating metastasis to axilla, multiple vertebrae, chest and bilateral pleura

Fig. 3 Fungating growth of the Right breast in male breast cancer

Among the 52 patients, the mean age of presentation was 48.4 years. The most common age group was from 41 to 50 years. The detailed age distribution of the patients has been described in Table 1. The histopathological grade and type of the primary tumor in this study population has been depicted in Table 2. The most common histopathological subtype was infiltrating ductal carcinoma grade III. With regard to the hormonal receptor status, 19 patients (51.3 %) was ER positive, PR positive and HER 2 negative (ER+/PR+Her2-); four patients (10.8 %) had with ER negative, PR negative and HER 2 positive (ER-/PR- Her2+). 13 patients (35.1 %) were triple negative cancers. One patient (2 %) was ER positive, PR positive and HER2 positive. The details have been tabulated in Table 3.

ER/PR/HER2 NEU Status and Recurrent Disease Setting

Out of the patients who were examined for recurrence following completion of treatment, two patients had ER- PR- and HER 2+. The other 8 patients with recurrence did not have receptor status available at the time of presentation. Both of these patients showed extensive metastasis to femur, vertebra, shoulder, sternum, chest wall and lung on PET scan (an example is shown in Fig. 1).

Table 4 Lesions on FDG-PET undertaken at initial diagnosis

Sl no	Lesion site	No of patients
1	Axillary lymph nodes	15
2	Internal mammary lymph nodes	7
3	Mediastinum	2
4	Liver	1
5	Skin satellite nodules	1
6	Adrenal	1
7	Cervical lymph nodes	1
8	Tuberculosis chest	1

Fig. 4 Graphical representation of lesions on primary FDG PET undertaken at the time of initial diagnosis

Gender Distribution

Out of the 52 patients in the study group, there were two male breast carcinoma patients. Both the patients had locally advanced breast cancer, one presenting with fungating growth. This was consistent with the notion of male breast cancer behaving aggressively. According to the hormonal receptor status, both of them were ER +PR+HER2-ve. On FDG-PET, both patients demonstrated extensive distant metastasis. One patient presented with 3 cm lump had metastasis to axilla, sternum, cervical lymph nodes and vertebrae (Fig. 2). The other patient (Fig. 3) presented with 8 cm fungating growth with metastasis to right pleura, axilla, and anterior chest wall with cutaneous satellite nodules on FDG-PET scan. Both the patients presented in stage 4 and were undertaken for palliative treatment

Evaluation of FDG PET at Initial Diagnosis In Patients With Pre Treatment FDG-PET

In the study population of 52 patients, FDG-PET at initial diagnosis was done in 24 patients. The disease sites depicted by

FDG-PET in this group of patients are depicted in Table 4 and Fig. 4. Among the 24 patients with pretreatment FDG-PET, 8 patients (33.3 %) were upstaged with diagnosis of extra lesions in adrenal, internal mammary, cervical lymph nodes, liver and mediastinum in all 8 patients there was change in plan of management from surgery to chemotherapy due to detection of metastatic lesions (Table 5). All 8 patients with internal mammary node metastasis were interestingly outer quadrant tumor. CT thorax was not done in any of these 8 patients since it was not cost effective, would deliver high radiation dose (the effective dose from a high resolution diagnostic scan can be quite high up to 25–30 mSv for a whole body CT scan) and unnecessarily would delay definitive management in the given setting. In one interesting case (Fig. 5) FDG-PET showed increased uptake in peri bronchial, pre tracheal and hilar lymph nodes suggestive of metastasis which turned out to be false positive. On thorough history and analysis of SUV of FDG PET images patient was found to be a case of tuberculosis on treatment. One of 24 patients had a doubtful enhancing lesion in liver on CT and USG abdomen which was suggestive of metastasis or hemangioma. But on PET there was no enhancing lesion ruling out metastasis. Mean tumor size in the present study population was 4 cm and mean age was 48.4 years. With histopathology

Table 5 Change in treatment after FDG-PET scan

Patient list	Lesion before FDG PET	Additional lesions on FDG PET	Change in plan of management
Patient 1	Breast, axilla	Mediastinal and internal mammary lymph node	Surgery to chemotherapy
Patient 2	Breast lesion alone	Mediastinal and internal mammary lymph node	Surgery to chemotherapy
Patient 3	Breast lesion alone	Liver and internal mammary lymph node	Surgery to chemotherapy
Patient 4	Breast lesion alone	Adrenal and internal mammary lymph node	Surgery to chemotherapy
Patient 5	Breast lesion alone	Internal mammary lymph node and axilla	Surgery to chemotherapy
Patient 6	Breast lesion alone	Axilla and cervical lymph node	Surgery to chemotherapy
Patient 7	Breast lesion alone	Internal mammary lymph node and axilla	Surgery to chemotherapy
Patient 8	Breast lesion alone	Internal mammary lymph node and axilla	Surgery to chemotherapy

Fig. 5 FDG-PET showing uptake in right breast, hilar and mediastinal lymph nodes. The hilar lymph nodes found to be positive due to tuberculosis

as reference standard sensitivity and specificity of PET scan is 100 % and 100 % respectively for the diagnosis and characterization of the primary.

Comparison of FDG-PET and Conventional Radiological Imaging (CRI) in Lymph Node Detection

Table 6 and Fig. 6 depicts comparison of lymph node lesions detected on FDG PET compared to conventional radiological imaging (that included USG abdomen, sonomammography, x ray, CT scan, MRI, bone scan). From the tabulation clearly FDG-PET has a better diagnostic ability in detecting lymph node metastasis, especially in the non-axillary lymph nodes, a major advantage of FDG-PET evaluation compared to

conventional staging. PET detected an addition of 55 lesions (lymph nodes) in 52 patients. (40.1 %)

Case examples are depicted in Figs. 7, 8, 9 and 10

Role of FDG-PET in Detecting Distant Metastasis

A lesion based analysis of number of total lesions detected on FDG-PET vs. CRI is depicted in Table 7 and Fig. 11. Distant metastasis detected by FDG PET compared to CRI as tabulated above shows a 47.3 % increase in diagnosis with FDG-PET on a lesion specific analysis. FNAC was done for all accessible lesions. Not all lesions could be verified histopathologically for ethical and practical reasons. A more aggressive correlative radiology and follow up data were used as applicable in a particular case (Tables 8, 9, 10).

Case examples are depicted in Figs. 11, 12, 13, 14 and 15

Locoregional Recurrence

In this study out of 52 patients 10 patients were a case of previously operated breast cancer post treatment with symptoms suggestive of recurrence. Out of them, 8 patients presented with operative site induration and nodules. One presented with bone pain (backache) and other with arm edema. FNAC of local induration and skin nodules was done in all 8 patients. In 5 patients it was confirmatory of recurrence but in rest 3 patients FNAC was non confirmatory but PET was helpful by confirmation of recurrence with additional distant metastasis. Thus, FDG-PET showed local as well as distant metastasis and hence would definitely confirm recurrence as well as define extent of disease.

PET was done in all 10 patients and was 100 % sensitive and specific for confirming recurrent breast cancer.

Case examples are depicted in Figs. 16 and 17

Table 6 Lymph node lesions detected on FDG-PET: Classification according to station and sites

Site of lesion	No of lesions on FDG-PET	No of lesions on CRI ^a	Added lesions on FDG-PET
Mediastinal lymph nodes	13	00	13
Axillary lymph nodes	77	70	07
Internal mammary lymph nodes	23	00	23
Cervical lymph nodes	09	05	04
Inguinal lymph nodes	01	00	01
Abdominal lymph nodes	06	05	01
Supraclavicular lymph nodes	08	02	06
Total	137	82	55

^a conventional radiological imaging (USG abdomen, sonomammography, x ray, CT scan, MRI, bone scan)

Fig. 6 Lymph node lesions demonstrated on FDG PET: comparison with conventional radiological imaging (CRI)

Evaluating Response to Treatment

Four patients underwent second FDG-PET after first cycle of chemotherapy. All four showed reduced uptake (SUV) in follow up scan and decrease in two lymph node lesions in two patients. Since all four showed responsiveness to chemotherapy by decreased standard uptake value with a sensitivity of FDG-PET is 100 %.

Adjuvant Polychemotherapy (iv bolus or infusion) used in our study was:

CAF: D1 only at 3 weekly intervals $\times$ 6 cycles
 Cyclophosphamide 600 mg/m²
 Adriamycin 60 mg/m²
 5-fluorouracil 600 mg/m²

Since the number is too small to conclude regarding the role FDG-PET in judging responsiveness to treatment and chemotherapy, further follow up studies are necessary which is ongoing at present for report in larger number of patients.

Fig. 7 FDG PET Scan (MIP Image) showing lesions in internal mammary lymph nodes, left subclavian lymph node and mediastinum

Histopathological Correlation of FDG-PET Lesions and Comparison of FDG-PET with Other Imaging Modalities (CT scan, MRI, bone scan)

A correlation was undertaken wherever feasible for the FDG-PET detected additional metastatic lesions. FNAC/biopsy was done for lesions that were accessible (Table 11). 19 lesions (nodal lesions in the axillary, cervical and inguinal nodes as detailed in the Table 11) were confirmatory of metastases. In some patients invasive biopsy could not be done due to obvious ethical and practical reasons. In addition, FDG-PET proved to be a problem solving tool in some cases where CT, MRI, Bone scan was done but were inconclusive (Tables 8, 9 and 10). The pattern and uptake of FDG in certain images in the given clinical background itself were conclusive of malignancy. These images were analyzed by experienced

Fig. 8 FDG-PET (MIP Image) in a right sided breast Carcinoma detecting left axillary and inguinal lymph node proven on histopathology

Fig. 9 FDG-PET (MIP Image) showing right axillary, mediastinal and gastric lymph nodes hypermetabolism in a patient with right sided breast cancer

nuclear medicine physician with more than 10 years of experience.

Fig. 10 FDG -ET/CT (PET and fusion PET-CT images) showing cervical, axillary and internal mammary lymph nodes in a patient of right sided breast carcinoma with avid FDG uptake in the primary

Table 7 Comparison of distant metastasis on FDG PET versus CRI

Site of lesion	No of FDG-PET lesions	No of lesion on CRI conventional radiologic imaging	Added PET lesions
Chest wall	12	07	05
Liver	9	3	6
Lung and pleura	17	07	10
Bone marrow	1	0	1
Adrenal	3	0	3
Brain	1	0	1
Peritonem	4	1	3
skeleton	29	22	7
Total lesions	76	40	36

Discussion

The present study addressed the efficacy of FDG-PET/PET-CT in a busy medical college setting, where the presentation is usually late, hence the utility of this modality assumes a greater significance (compared to a tertiary care setting) in

Fig. 11 Distant metastasis on FDG-PET: Comparison with CRI **Table 8** FDG PET compared with other imaging modalities (MRI Chest)

Patient list	Lesions on CT scan	Lesions on PET scan	Comments (additional lesions)
Patient 1	Lung and pleura mediastinal lymph node	Lung, pleura, mediastinal nodes	—
Patient 2	Lung, b/l pleura	Lung, pleura, internal mammary nodes	Nodes detected on FDG PET
Patient 3	Adrenal, liver	Adrenal, liver, peritoneum	Peritoneal deposit detected
Patient 4	Liver single lesion	Liver two lesions, perigastric lymph nodes	Extra lesion in liver and lymph nodes
Patient 5	Adrenal, liver	Adrenal and liver	—
Patient 6	Normal study	Abdominal lymph nodes and liver	FDG PET detected metastasis in liver and abdominal nodes

assessing whole body disease status. Mean tumor size was 4 cm and mean age was 48.4 years consistent with other studies. With histopathology as reference standard sensitivity and specificity of PET scan is 100 % and 100 % respectively, which is comparable with other reported studies in this domain. In 24 patients with pretreatment PET, 8 patients (33.3 %) were upstaged with diagnosis of extra lesion

in adrenal, internal mammary, cervical lymph nodes and mediastinum. Tuberculosis was the cause of false positive in one patient in peri bronchial, pre tracheal and hilar lymph nodes.

Multiple studies have demonstrated the usefulness of FDG-PET in the detection of metastasis [5–12], though the detection of unsuspected distant metastases, in initial staging and

Table 9 FDG PET scan compared with (Bone Scan)

Patient list	Lesions on bone scan	Lesions on FDG PET	Comments
Patient 1	Chest wall, humerus, pelvis	Chest wall, humerus, pelvis, axilla, breast	—
Patient 2	Vertebrae, chest wall	Vertebrae, chest wall axilla	—
Patient 3	Vertebrae, femur, humerus, sternum, chest wall	Vertebrae, femur, humerus, sternum, chest wall	—
Patient 4	Femur, pelvis	Femur, pelvis	—
Patient 5	Vertebrae, chestwall	Vertebrae, chest wall, femur marrow	Additional femur marrow involvement (findings confirmatory from pattern)
Patient 6	vertebrae	vertebrae	—
Patient 7	Vertebrae, ribs	Vertebrae, ribs	—
Patient 8	vertebrae	vertebrae	—

Table 10 FDG PET compared with (MRI Chest)

Patient list	Lesion on MRI chest	Lesion on FDG PET	Comment
Patient 1	Local recurrence over chest wall	Local recurrence with axillary uptake	–
Patient 2	Recurrence in axilla	Axillary lesions	–
Patient 3	Recurrence in axilla	Recurrence in axilla	–
Patient 4	Residual tumor? Post operative inflammation	PET Proved malignancy confirmed on Biopsy	PET superior in differentiating fibrosis and malignancy-

modification in treatment plan varied widely between different studies. In the aforementioned 8 studies, detection of unsuspected distant metastases varied from 7.5 to 38 %, detection of unknown extraaxillary node metastases varied from 5 to 56 %. The change in initial staging was seen in two of these studies (which was 17–18 %) and the modification in treatment plan 6.5 % to 13 % as was observed 4 of these studies. We believe the selection of patient population group could be one of the major factors for the heterogeneous results obtained in the various studies. It is presumable that the impact of FDG-PET/PET-CT will be more in patients presenting late or with locally advanced disease where the probability of distant metastases is substantially high.

As previously mentioned, in the present study, FDG-PET/CT proved to be superior to conventional radiological imaging where PET detected extra 55 lymph node lesions. The overall detection of added lesion in comparison to CRI in this group of patients was 40.2 %. One of the shortcomings in this study is that not all patients underwent CT scan, MRI and Bone scan. Only affording patient who had suspected metastasis underwent CT (6 patients), MRI (4 patients) and Bone scan (8 patients). But all patients had USG abdomen, sonomammography and x ray chest. Instead of multiple

investigations like CT thorax, CT abdomen pelvis, Bone scan, MRI, Ultrasonography of abdomen, FDG PET is one stop shop where anatomic extent and biological activity of tumor was very well defined and was confirmatory from the pattern of abnormality in a given clinical context.

Among 8 patients with supraclavicular lymph node metastasis on FDG-PET, all patients were found to have wide spread dissemination: (a) to lung ($n=3$), liver ($n=1$ patient), Skeleton ($n=3$ patients), mediastinum ($n=2$) adrenal($n=1$) . From the above observation in patients with supraclavicular lymph node metastasis additional site of systemic dissemination should be sought for in FDG-PET studies.

In the present study out of 52 patients 10 patients were a case of previously operated breast cancer post treatment with symptoms suggestive of recurrence. Out of them, 8 patients presented with operative site induration and nodules. One presented with bone pain (backache) and other with arm edema. PET was done in all 10 patients and was 100 % sensitive and specific for confirming recurrent breast cancer. Out of 10 patients 3 of them had extensive skeletal metastasis which was confirmed by both bone scan and PET scan, 2

Fig. 12 FDG-PET showing right breast lump with satellite nodules with axillary, hilar, retroperitoneal lymph nodes with lung involvement **Fig. 13** FDG-PET showing extensive metastasis to bilateral axillary lymph nodes, mediastinum, chest wall and abdominal lymph nodes

Fig. 14 FDG-PET/CT in a multifocal breast cancer showing liver and pelvic bone metastasis in addition to metastatic axillary lymph nodes

patients with extensive metastasis to skeleton, liver, mediastinum died during palliative treatment and two patients had lung, chest wall involvement and two patients had liver metastasis. One of the patients had only axillary uptake representing viable disease and she was treated with local surgical excision and second line chemotherapy. On follow up after 1 year the FDG-PET showed no residual tumor. In six studies that addressed FDG-PET/PET-CT in the evaluation of recurrent disease setting the sensitivity overall was in excess of 80 % whereas the specificity varied from 70 to 100 % [13–18]. We believe, here too, the heterogeneity in patient selection could have an important role in defining the

specificity, wherein those with late presentation will have higher specificity as demonstrated in our study.

Goerres et al. [13] compared FDG-PET with MRI in 32 patients with a suspected chest wall, contralateral breast, or locoregional recurrence. FDG-PET appeared to have a superior sensitivity of 100 % compared with 79 % for MRI, but had a lower specificity of 72 % compared with 94 % for MRI. FDG-PET detected additional distant metastases in five patients. Another prospective study was done to evaluate FDG-PET role in detecting suspected relapse in 25 women. Abnormal FDG-PET uptake was noted in 43 areas. FDG-PET had a high sensitivity of 95 %, but a low specificity of

Fig. 15 FDG-PET/CT showing extensive liver and splenic metastasis, vertebral and skull metastasis in addition to demonstrating avid FDG uptake in the primary in the left breast and left axilla

only 20 %. A total of 22 sites were correctly identified as areas of relapse, and 21 additional sites of metastasis were discovered. [19]

The total number of distant metastasis lesions detected on FDG PET was 76 in 52 patients, out of which the percentage of increased lesion detection by FDG-PET was 47.3 %. With regard to early assessment of treatment response, in present study 4 out of 18 patients underwent second PET after first cycle of chemotherapy. All four showed reduced uptake (SUV) in progressive scan and decrease in two lymph node lesion in two patients. Since all four showed responsiveness to chemotherapy by decreased standard uptake value sensitivity of PET is 100 %. Since the number is too small to conclude regarding role PET in judging responsiveness to treatment and chemotherapy, further follow up studies are necessary. This finding is commensurate with the reported results in this domain. Mortimer et al. [20] gave tamoxifen to 40 ER PR positive patients with locally advanced recurrent metastatic breast cancer. After 7 to 10 days of treatment patients were assessed for temporary flare response on quantitative PET measure (7–10 % rise in FDG). The presence or absence of flare was highly predictive of response assessed by standard criteria. On follow up sensitivity was 95 % and specificity was

89 %. Wahl et al. [21] included 11 patients who were given a non-standard regimen for locally advanced disease included cyclophosphamide, doxorubicine, methotrexate, fluorouracil and tamoxifen. After first cycle of treatment all patients responding by clinical criteria had significant decrease in PET quantitative measurements. Smith et al. [22] in 2000 selected patients with newly diagnosed noninflammatory breast cancer with large primary or locally advanced disease. 30 patients were enrolled in a trial comparing 2 neoadjuvant chemotherapy regimens: cyclophosphamide, vincristine, doxorubicine and prednisolone or primary paclitaxel. The key responses were histology at the time of surgery pathologic complete response (PCR) or pathologic partial response (PPR) at the end of first cycle of chemotherapy. PET results were assessed quantitatively a drop of 10 % or more in the PET measure had following diagnostic performance for predicting either PCR or PPR: sensitivity 82 % and specificity of 66 %. The proper assessment of therapeutic response would require a prospective study where both pre and post treatment PET scans are to be evaluated where in the treatment protocol is a standardized one. The preliminary results in different studies are a definite pointer toward effectiveness of PET as a better tool for therapy evaluation than other imaging modalities.

Fig. 16 Recurrent breast cancer with FDG-PET (MIP view) showing left chest wall, skin, axilla, left arm and pelvic metastasis

Table 11 Accessible lesions where fnac/biopsy done for histopathological correlation

Site of lesions	No of patients
Axillary lymph nodes	15
Cervical lymph nodes	13
Inguinal lymph nodes	1

Thus, FDG PET and PET/CT have been shown to be particularly useful in the restaging of breast cancer in recurrent staging, in evaluation of response to therapy, and as a problem-solving method when results of conventional imaging are equivocal. In these situations, FDG PET often demonstrates locoregional or unsuspected distant disease that affects management. PET has demonstrated a particular capability for early evaluation of chemotherapy response in both patients with locally advanced breast carcinoma and those with metastatic disease.

Conclusion

In the examined patient population with relatively late presentation (a characteristic in the various medical colleges and the

Fig. 17 Recurrent right breast cancer with extensive metastasis to chest wall, internal mammary lymph nodes and bilateral axillary lymph nodes

government hospital setting), whole-body FDG-PET can provide a more precise understanding of the extent of disease in patients with breast cancer at initial staging and at recurrent disease setting and is thus a valuable complementary to the conventional staging modalities of physical examination and cross-sectional imaging. FDG-PET helps differentiating local axillary recurrence in the scenario of postoperative scarring and is more sensitive than CT in the evaluation of non-axillary locoregional and mediastinal lymph nodes. Because the uptake of FDG is not entirely specific to tumor, FDG PET findings need to be confirmed with biopsy when possible or at least with corroborative conventional imaging. The high sensitivity of FDG PET for detection of distant metastases, including non axillary regional lymph nodes, in a single examination makes it extremely useful for directing appropriate therapy.

The results of this study indicate that [18F]-FDG PET, using a simple imaging protocol, may be of considerable value in the early prediction of metastasis, loco regional recurrence, characterization of lump and response to treatment in both primary and locally metastatic breast cancer. Further studies, involving larger patient numbers, are currently underway in an attempt to validate its role in early treatment response monitoring. Given the increasing number of PET scanners (total 95 in number at present) and cyclotrons in India, ¹⁸F-FDG-PET may prove to be a very effective diagnostic whole-body imaging modality for metastatic survey in this particular setting in future.

Conflict of Interest None.

References

- Groheux D, Moretti J, Baillet G et al (2008) Effect of ¹⁸F-FDG PET/CT imaging in patients with clinical stage II and III breast cancer. *Int J Radiat Oncol Biol Phys* 71:695–704
- Cermik TF, Mavi A, Basu S, Alavi A (2008) Impact of FDG PET on the preoperative staging of newly diagnosed breast cancer. *Eur J Nucl Med Mol Imaging* 35(3):475–483
- Mavi A, Cermik TF, Urhan M, Puskulcu H, Basu S, Yu JQ, Zhuang H, Czerniecki B, Alavi A (2007) The effects of estrogen, progesterone, and C-erbB-2 receptor states on ¹⁸F-FDG uptake of primary breast cancer lesions. *J Nucl Med* 48(8):1266–1272
- Basu S, Chen W, Tchou J, Mavi A, Cermik T, Czerniecki B, Schnall M, Alavi A (2008) Comparison of triple-negative and estrogen receptor-positive/progesterone receptor-positive/HER2-negative breast carcinoma using quantitative fluorine-18 fluorodeoxyglucose/positron emission tomography imaging parameters: a potentially useful method for disease characterization. *Cancer* 112(5):995–1000
- Basu S, Mavi A, Cermik T, Houseni M, Alavi A (2008) Implications of standardized uptake value measurements of the primary lesions in proven cases of breast carcinoma with different degree of disease burden at diagnosis: does 2-deoxy-2-[F-18]fluoro-D-glucose-positron emission tomography predict tumor biology. *Mol Imaging Biol* 10(1):62–66
- Heusner TA, Kuemmel S, Umutlu L et al (2008) Breast cancer staging in a single session: whole-body PET/CT mammography. *J Nucl Med* 49:1215–1222
- Fuster D, Duch J, Paredes P et al (2008) Preoperative staging of large primary breast cancer with [18F]fluorodeoxyglucose positron emission tomography/computed tomography compared with conventional imaging procedures. *J Clin Oncol* 26:4746–4751
- Yang WT, Le-Petross HT, Macapinlac H et al (2008) Inflammatory breast cancer: PET/CT, MRI, mammography, and sonography findings. *Breast Cancer Res Treat* 109:417–426
- Carkaci S, Macapinlac HA, Cristofanilli M et al (2009) Retrospective study of ¹⁸F-FDG PET/CT in the diagnosis of inflammatory breast cancer: preliminary data. *J Nucl Med* 50:231–238
- Alberini J, Lerebours F, Wartski M et al (2009) ¹⁸F-fluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET/CT) imaging in the staging and prognosis of inflammatory breast cancer. *Cancer* 115:5038–5047
- Aukema TS, Straver ME, Peeters MTFDV et al (2010) Detection of extra-axillary lymph node involvement with FDG PET/CT in patients with stage II-III breast cancer. *Eur J Cancer* 46:3205–3210
- Segaert I, Mottaghy F, Ceyssens S et al (2010) Additional value of PET-CT in staging of clinical stage IIB and III breast cancer. *Breast J* 16:617–624
- Goerres GW, Michel SC, Fehr MK et al (2003) Follow-up of women with breast cancer: comparison between MRI and FDG PET. *Eur Radiol* 13:1635–1644
- Bender H, Kirst J, Palmedo H et al (1997) Value of ¹⁸F-fluorodeoxyglucose positron emission tomography in the staging of recurrent breast carcinoma. *Anticancer Res* 17(3B):1687–1692
- Kamel EM, Wyss MT, Fehr MK et al (2003) [18F]-Fluorodeoxyglucose positron emission tomography in patients with suspected recurrence of breast cancer. *J Cancer Res Clin Oncol* 129:147–153
- Lin WY, Tsai SC, Cheng KY et al (2002) Fluorine-18 FDG-PET in detecting local recurrence and distant metastases in breast cancer—Taiwanese experiences. *Cancer Invest* 20:725–729
- Kim TS, Moon WK, Lee DS et al (2001) Fluorodeoxyglucose positron emission tomography for detection of recurrent or metastatic breast cancer. *World J Surg* 25:829–834
- Hathaway PB, Mankoff DA, Maravilla KR et al (1999) Value of combined FDG PET and MRI in the evaluation of suspected recurrent loco regional breast cancer: preliminary experience. *Radiology* 210(3):807–814
- Landheer ML, Steffens MG, Klinkenbijn JH et al (2005) Value of fluorodeoxyglucose positron emission tomography in women with breast cancer. *Br J Surg* 92:1363–1367
- Mortimer JE, Dehdashti F, Siegel BA et al (2001) Metabolic flare: indicator of hormone responsiveness in advanced breast cancer. *J Clin Oncol* 19:2797–2803
- Wahl RL, Zasadny K, Helvie M et al (1993) Metabolic monitoring of breast cancer chemohormonal therapy using positron emission tomography: initial evaluation. *J Clin Oncol* 11(11):2101–2111
- Smith IC, Welch AE, Hutcheon AW et al (2000) Positron emission tomography using [(18)F]-fluorodeoxy-D-glucose to predict the pathologic response of breast cancer to primary chemotherapy. *J Clin Oncol* 18:1676–1688