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Correlation of primary tumor metabolic parameters with clinical, histopathological and molecular characteristics in breast cancer patients at pre-operative staging FDG-PET/CT study

Asmaa A. AbdElaal[1*], Ahmed M. Zaher[2], Marwa I. Abdelgawad[1], Mohamed A. Mekkawy[1] and Lamiaa M. Eloteify[1]

Abstract

Background: The aim of this prospective study was to evaluate the correlation of primary tumor metabolic activity parameters; maximum standardized uptake value (SUVmax) and tumor SUVmax/liver average SUV ratio (TLR) with clinical, histopathological and molecular characteristics of initial staging breast cancer (BC) patients using 18F-fluorodeoxyglucose (FDG) positron emission tomography / computerized tomography (PET/CT) scan.

Results: Forty female patients with newly diagnosed BC were enrolled in our study, age ranging from 31-78 years (mean 50.5 +/- SD11.7).
All the primary tumors were detected with mean SUVmax 10.8(+/-SD 7.9). The mean /median SUVmax values of primary tumor was higher in premenopausal , stage III and IV, Estrogen Receptors negative(ER-), Progesterone Receptors negative(PR-), Human epidermal growth factor receptor 2 positive (Her2neu+) patients, high nuclear grade (GIII), triple negative molecular subgroup (TN) and positive axillary lymph node (ALNs) metastasis,(P= 0.003, 0.017, 0.113, 0.089 0.01 ,0.002 , 0.007 and 0.016 respectively).
The mean/median TLR values was higher in premenopausal ,Her2neu+, GIII, TN molecular subtype patients, stage III and IV and in patients with positive ALNs , ER- and PR - patients (P= 0.002, 0.0476 , 0.005 , 0.018 , 0.039 and 0.022, 0.095 and 0.129 respectively).
SUVmax of the primary lesion and TLR were moderately negatively correlated with the age of the patients (P= 0.005 and 0.008 respectively), also they were moderately positively correlated with the size of the primary tumor (P= 0.019 and 0.036 respectively). TLR was predictive of nodal involvement AUC= 0.612 (95% CI: 0.431-792). The overall sensitivity and specificity of PET/CT for axillary staging was 100 % and 60 %, respectively (P= 0.006).

Conclusion: The SUVmax of the primary tumor and TLR values had similar significant associations with different prognostic factors in BC but only TLR can predict nodal involvement.

Keywords: Breast cancer, Initial staging, FDG PET/CT, SUVmax, TLR

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* Correspondence: asmaa2011@aun.edu.eg
[1]Department of Clinical Oncology and Nuclear Medicine, Faculty of Medicine, Assiut University, Assiut, Egypt
Full list of author information is available at the end of the article

Background

BC is the commonest cancer and the leading cause of cancer mortality among women worldwide [1].Classification can be done according to TNM stage, immunohistochemical features, grade, proliferation index and gene expression profiles, with histopathology remaining the cornerstone of characterization [2]. Immunohistochemistry (IHC) markers such as ER, PR and Her2neu, along with clinicopathological variables including; tumor size, grade and nodal involvement are commonly used for patient prognosis and management [3, 4]. Various imaging modalities are used in the diagnosis of BC including : ultrasound, mammography and magnetic resonance imaging [5]. Recently , functional imaging with F18-FDG PET/CT is increasingly used [6]. F18-FDG PET/CT is a non-invasive method, based on the principle of elevated glucose metabolism in malignant tumors; it detects distant metastasis as well as providing additional information about tumor histology [7, 8]. In patients with locally advanced BC, 18F-FDG PET/CT can be useful prior to surgery or neoadjuvant chemotherapy as it detects distant metastasis with a high rate (6% to 26%). 18F-FDG PET/CT can change the treatment plane in 1%–8% of patients with early-stage BC , in 7%–13% of those with locally advanced disease and in up to 52% of those with aggressive tumors [9].

Studies suggested that the quantitative PET parameter in the form of SUVmax is useful for predicting histologic, biologic characteristics of the tumor and patient's prognosis [8, 10]. Invasive tumors exhibit higher uptake values than lower-grade one [11].Many factors affect the SUVmax value, including the blood glucose level, body weight, duration after injection, size of the region of interest (ROI), and resolution of the scanner. Also it is susceptible to the impact of noise, partial volume effect, image resolution and determination of the volume of interest (VOI)- a single-voxel value representing the most intense FDG uptake in the tumor. These factors delimit the reliability of the absolute value to represent for the glucose metabolic rate of tumors [12, 13].So the SUVmax may not be an adequate measure for the metabolic rate of the tumor. It has been suggested that some of the problems may be eliminated by using TLR [14, 15]. The mediastinal vessels and normal liver tissue are the most commonly used parameters for individual background activity [16] .Using the SUV liver to represent individual normal uptake that is relatively constant regardless of which correction method, was more often used than using the mediastinal vessels [17]. Normalization of the SUVmax using normal liver uptake may minimize the effect of individual bias [18].

The aim of this prospective study was to evaluate the association of primary tumor FDG uptake in form of SUVmax and TLR with clinical, histopathological and molecular characteristics of BC patients at the initial staging scanning.

Methods

Forty patients with pathologically proven BC were recruited in this prospective study. It was approved by local Institutional Committee of Medical Ethics and informed consent was obtained from all participants. Patients were referred for initial staging PET/CT scanning prior to their definite therapy.

Nodal staging was evaluated after axillary clearance or sentinel lymph node biopsies (SLNBs).

We excluded patients who underwent surgery, received chemotherapy or radiotherapy for their breast cancers prior to PET/CT examination, uncontrolled diabetics and pregnant females.

Positron emission tomography/computed tomography protocol.

Patients fasted for 6 h, and had blood glucose <180 mg/dl prior to the study. 0.1 mCi/kg F18-FDG was injected intravenously in a peripheral vein and scans were acquired at 45-60 min post-injection.

Imaging was performed using high –spatial-resolution, 3 full-ring PET/CT system (Biograph Horizon, Siemens Healthcare).Combining Bismuth Germanium Oxide (BGO) based PET crystal and 16 slice CT components. The patients were allowed to breathe normally. CT and PET scans were acquired from mid-thigh level to the top of the skull with the arms raised.

PET emission counts were collected over 2 min/table position, acquired in a three-dimensional mode. The imaging data were reconstructed using a point spread function and a time-of-flight algorithm (TrueX + time-of-flight, UltraHD-PET), with 2 iterations and 21 subsets. Subsequently, a Gaussian filter with 5 mm full-width half-maximum was applied to the reconstructed images. For attenuation and scatter correction, a CT without contrast agent was used. Here, slice thickness was 3 mm with a pitch of 0.9 and a tube voltage of 120 kV. The tube current was automatically modulated according to the patient's size and body shape; a 210 mAs maximum reference value was used to achieve good image quality.

Data Interpretation

PET/CT scans were interpreted by two experienced nuclear medicine physicians blinded to clinical and histopathological data. Gold standard for the evaluation of PET/CT findings was histopathology. The primary tumor was evaluated visually for its site in the breast and

quantitatively by measuring the lesion SUVmax and TLR as well as the lesion size. The SUV calculation was carried out using the manufacturer's workstation (MI Apps; Siemens). VOI was placed around the lesion, the SUVmax (maximum SUV value within the VOI of each lesion) was recorded automatically on the workstation.

The tumor to liver uptake ratio (TLR) was defined as the ratio of the tumor SUVmax to liver SUVavg. The liver SUVavg was calculated by drawing a circular 3cm diameter VOI over the relatively homogenous intense slice of normal liver parenchyma on the PET images.

When a multifocal disease was present, the VOI was placed over the largest visible tumor for calculation of the SUVmax value (Fig. 1).

To determine the metabolic N stage, any ALNs showing higher uptake than the mediastinal blood pool on PET/CT images was considered as positive; additionally, we reported quantitative data in form of size and SUVmax.

Any significant abnormal focal increased uptake with suspicious CT features in any part of the body, and not explained by clinically relevant alternative, was considered as positive for distant metastasis.

Statistical analysis:

Data were verified, coded by the researcher and analyzed using IBM-SPSS 21.0 (IBM-SPSS Inc., Chicago, IL, USA) [19]. Descriptive statistics: Means, standard deviations, medians and inter-quartile range (IQR) were calculated. Test of significances: Independent t-test analysis was carried out to compare the means of dichotomous data that follow normal distribution; otherwise Mann Whitney U and Kruskal–Wallis tests were used to compare the medians, . Spearman ranked correlation coefficient was used to test the associations between scale variables. Variables were entered in multivariable linear regression model to test the independent predictors of SUV of the primary lesion using OR, 95% CI, p-value. A significant P-value was considered when it is less than 0.05.

Results

Patient Characteristics

Forty female patients; 19 (47.5%) premenopausal and 21 (52.5 %) postmenopausal with newly diagnosed BC were enrolled in this prospective study, age ranging
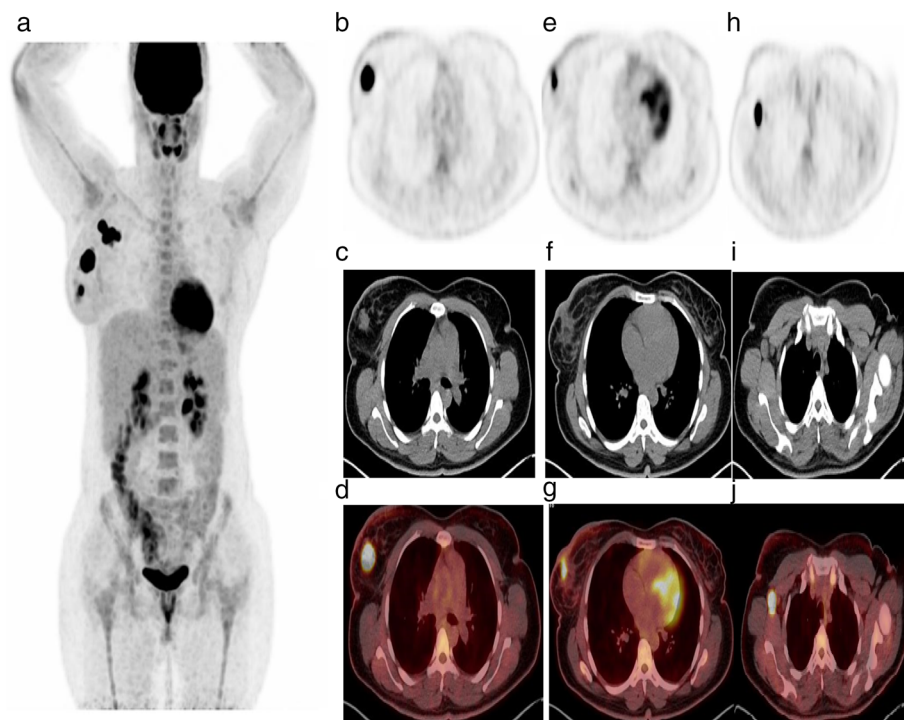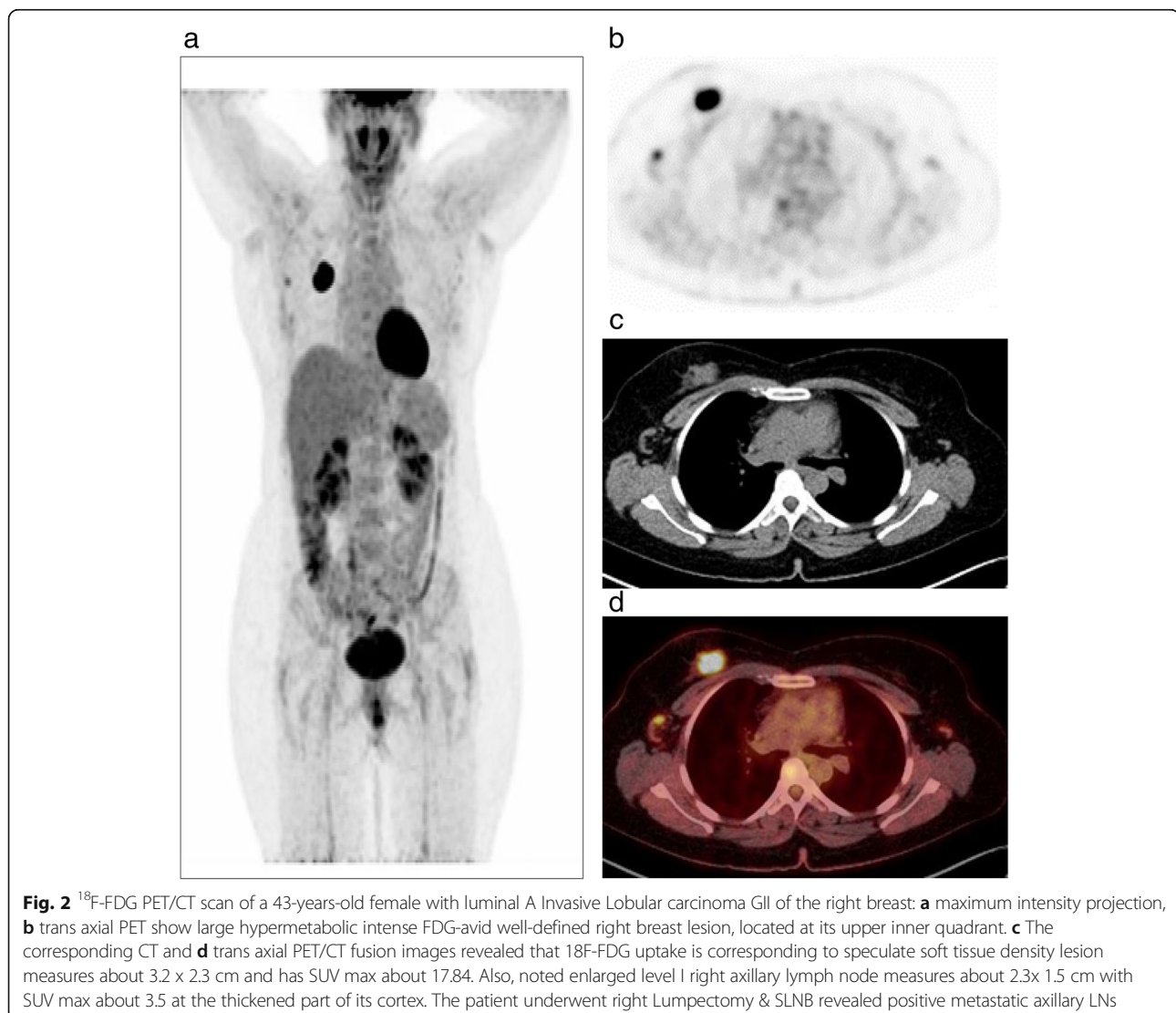

Fig. 1 ^{18}F-FDG PET/CT scan of a 32-years-old female with luminal B Invasive Duct carcinoma GIII of the right breast: **a** maximum intensity projection, **b,c** and **d** trans axial PET, The corresponding CT and trans axial PET/CT fusion images show intense FDG avid irregular speculated soft tissue mass at the upper outer quadrant of the right breast (the primary lesion) measures about 3.3 x 2.4 cm and has SUV max about 20. **e, f** and **g** show another FDG avid ill-defined retro areolar satellite lesion inferior to the primary lesion measures about 2.2 x 1 cm and has SUV max about 11.2, with mildly FDG avid diffuse thickening of the skin of right breast. **h, i** and **j** show intense FDG avid enlarged right axillary lymph nodes. Representative node measures about 2 x 1.9 cm and has SUV max about 23.8. TCNB of right axillary lymph nodes revealed positive metastatic axillary LNs

from 31-78 years (mean 50.5 +/- SD11.7). Twenty-One patients (52.5 %) had the primary lesion in the right breast while in the remaining 19 cases (47.5 %) the lesion was in the left one. In half of the patients the primary lesion was present in the upper outer quadrant (UOQ)(16 of them had positive ALNs uptake), 11 cases in the upper inner quadrant (UIQ) (6 of them had positive ALNs), 4 cases in the central region (all of them showed positive ALNs uptake), 3 cases in the lower outer quadrant(LOQ) (one of them had positive ALNs uptake) and 2cases in the lower inner quadrant(LIQ) with ALNs uptake in both (P=0.041).

Regarding the clinical staging, more than half of the patients were stage II (21 patients representing 52.5 %), stage III representing 27.5 %, stage I representing 15 %, while stage IV representing 5 % of our study population.

Most of the primary tumors; 36 (90%) were invasive ductal carcinoma (IDC) of no special subtype, 3 cases were invasive lobular carcinoma (ILC) (Fig. 2) and one case of mucinous type. As regard to the receptor status; ER+ were found in 31 (77.5%) and ER- were found in 9 (22.5 %) patients, 24 (60%) patients were PR+ while 16 (40%) patients were PR-, Her2neu receptors were positive in 14 patients (35 %) and negative in the remaining 26 (65 %) .Majority of our patients were luminal B (19), while luminal A, TN and HER2 neu overexpression represented in 10, 7 and 4 patients, respectively.

PET/CT detected all the primary tumors with mean SUVmax 10.8 (+/-SD 7.9). The mean SUVmax values of the primary tumor were significantly higher in premenopausal, stage III and IV, ER - , GIII, TN molecular subgroup and in patients with positive ALNs (P= 0.003,

Fig. 2 ^{18}F-FDG PET/CT scan of a 43-years-old female with luminal A Invasive Lobular carcinoma GII of the right breast: **a** maximum intensity projection, **b** trans axial PET show large hypermetabolic intense FDG-avid well-defined right breast lesion, located at its upper inner quadrant. **c** The corresponding CT and **d** trans axial PET/CT fusion images revealed that 18F-FDG uptake is corresponding to speculate soft tissue density lesion measures about 3.2x 2.3 cm and has SUV max about 17.84. Also, noted enlarged level I right axillary lymph node measures about 2.3x 1.5 cm with SUV max about 3.5 at the thickened part of its cortex. The patient underwent right Lumpectomy & SLNB revealed positive metastatic axillary LNs

Table 1 Determinants of the primary Lesion SUVmax among cases

	Lesion SUVmax		P-value
	Mean ± SD	Median (IQR)	
Pathology			
• IDC(n=36)	3.96±3.1	2.85(3.33)	**=0.258#**
• ILC(n=3)	2.41±2.98	0.8	
• Other (n=1)	1		
Menopausal State			
• Pre- (n=19)	14.55 ± 2.1	13 (6)	**0.003***
• Post- (n=21)	7.45 ± 1.0	7 (2)	
Disease Stage			
• I & II (n=27)	8.79 ± 1.1	7 (2)	**= 0.017***
• III & IV (n=13)	15.06 ± 2.9	14 (5)	
ER-Receptors			
Positive (n=31)	9.12 ± 5.7	7 (6)	**= 0.010****
Negative (n=9)	16.70 ± 9.6	12.5 (11)	
PR-Receptors			
Positive (n=24)	9.13 ± 6.2	7 (5)	**= 0.113****
Negative (n=16)	13.37 ± 9.7	9 (8.5)	
Her2-neu Receptors			
Positive (n=14)	12.35 ± 5.8	13 (9.5)	**=0.089****
Negative (n=26)	10.01 ± 8.9	7 (6.5)	
Tumor grad			
GI (n=5)	3.69±1.4	3.1(2.6)	
GII (n=18)	9.43±6.11	6.85(11.08)	**=0.002#**
GIII (n=15)	15.03±9.20	11.11(13.4)	
Molecular subtype			
Luminal A (n=10)	5.88±4.9	4.18(5.06)	**0.007#**
Luminal B (n=19)	10.93±5.55	8.4(9)	
Her2neu over expression (n=4)	8.03±5.24	7.98(9.13)	
Triple negative (n=7)	19.19±11.86	21.6(17.67)	
Axillary LN State			
Positive (n=27)	12.80 ± 8.6	10 (8.5)	**= 0.016****
Negative(n=13)	6.73 ± 4.1	6.5 (6)	

*Independent t-test
**Mann Whitney U
Kruskal Wallis test

0.017, 0.01, 0.002, 0.007 and 0.016 respectively). But it was insignificantly higher in PR- and Her2 neu + patients (P= 0.113 and 0.089) as shown in Table 1.

In linear regression model, the statistically significant independent predictor factors of the primary lesion SUVmax are; age, advanced stage, postmenopausal, ER- and ALNs positive cases, as shown in Table 2 & Fig. 3.

The mean TLR values were significantly higher in premenopausal, Her2neu +, GIII and TN molecular subtype patients (P= 0.002, 0.0476, 0.005 and 0.018 respectively).The median of TLR values were significantly higher in stage III and IV as well as in patients with positive ALNs (P= 0.039 and 0.022 respectively), also it was higher in ER and PR negative patients but with no statistically significant differences (P= 0.095 and 0.129 respectively) Table 3.

SUVmax of the primary lesion and TLR were significantly moderately negatively correlated with the age of the patients (r = 0.405 and 0.414

respectively with P= 0.005 and 0.008 respectively). Also they were significantly moderately positively correlated with the size of the primary lesion (r = 0.328 and

Table 2 Independent Predictors of SUVmax of the primary Lesion: Linear Regression Model

Variable	β (95% CI)	T-Statistics	P-value
• **Constant**	23.50 (12.79 – 34.23)	4.437	< 0.001
• **Age/years**	-0.25 (-0.46 : –0.04)	-2.455	**= 0.019**
• **Disease Stage (III & IV)**	6.27 (1.16 – 11.37)	2.485	**= 0.017**
• **Post-menopausal**	-7.10 (-11.71 : -2.49)	-3.12	**= 0.003**
• **ER-Receptors (Negative)**	7.58 (1.93 – 13.23)	2.717	**= 0.010**
• **PR-Receptors (Negative)**	4.24 (-0.84 – 9.31)	1.691	= 0.099
• **Her2 neu -Receptors (Negative)**	-2.35 (-7.70 - 3.00)	-0.889	= 0.379
• **Tumor Size/cm**	2.24 (-0.14 – 4.63)	1.903	= 0.065
• **Axillary LN (Positive)**	-6.07 (-0.93 – -11.20)	2.393	**= 0.022**

CI, Confidence Interval

0.337 respectively with P = 0.019 and 0.036 respectively) as shown in Table 4.

Nodal staging

In the Twenty-Three patients who underwent nodal staging (axillary dissection in 7/23 patients and SLNBs in 16/23 patients Fig. 4), 13/23 and 10/23 patients were positive and negative for metastases respectively.

PET/CT was positive in 27 patients with ALNs; out of them 13 proved true positive, 4 were false positive by histopathology and in the remaining 10 cases no pathology report was available. PET/CT negative axillary cases were 13 out of them 6 were true negative by histopathology and in the remaining 7 cases no pathology

report were available. The overall sensitivity and specificity of PET/CT for axillary staging was 100 % and 60 %, respectively (P = 0.006).

M staging

PET/CT identified distant metastases in five cases; one skeletal, one hepatic and three cases with mediastinal nodal metastasis.

ROC analysis

The ROC analysis was performed to examine which parameter (SUVmax or TLR) better reflects the nodal involvement as both parameters were significantly associated with it. Only TLR was poorly predictive of

Fig. 3 Linear regression model: Correlation between SUV of the primary lesion, age and tumor Size

Table 3 Determinants of TLR among cases

	TLR		
	Mean ±SD	**Median (IQR)**	**P-value**
Pathology:			=0.158#
IDC(n=36)	3.96±3.10	2.85(3.4)	
ILC	2.41±2.98	0.80(5.3)	
Others	1		
Menopausal State			
Pre- (n=19)	5.27±3.55	4.7 (5.1)	= 0.002*
Post- (n=21)	2.41± 1.72	1.88 (2)	
Disease stage			
I & II (n=27)	3.21±2.28	2.32(3.37)	= 0.039**
III & IV (n=13)	4.93±4.15	2.9(6.36)	
ER-Receptors			
Positive (n=31)	3.12 ±2.32	2.5 (2.97)	= 0.095**
Negative (n=9)	5.99±4.62	4.7 (7.6)	
PR-Receptors			
Positive (n=24)	3.12±2.32	2.56 (3.39)	= 0.129**
Negative (n=16)	4.74±3.81	3.25 (6.25)	
Her2 neu -Receptors			
Positive (n=14)	4.26±2.46	4 (4.23)	= 0.0476*
Negative (n=26)	3.51±3.37	2.17 (2.68)	
Axillary LN Stat			
Positive (n=27)	4.58±3.39	3.52 (5.54)	= 0.022**
Negative(n=13)	2.10±1.26	1.86 (1.96)	
Tumor grade **• GI (n=5)** **• GII (n=18)** **• GIII (n=15)**			
GI (n=5)	1.35±0.6	1.16 (1.13)	= 0.005#
GII (n=18)	3.21±2.26	2.38 (3.35)	
GIII (n=15)	5.42±3.38	3.31± (6)	
Molecular subtype **• Luminal A (n=10)** **• Luminal B (n=19)** **• Her2neuover expression (n=4)** **• Basal Like (n=7)** **(triple negative)**			
Luminal A **(n=10)**	1.96±1.6	1.45 (1.77)	= 0.018#
Luminal B **(n=19)** **• Luminal A (n=10)** **• Luminal B (n=19)** **• Her2neuover expression (n=4)** **• Basal Like (n=7)** **(triple negative)**	3.85±2.27	3 (3.66)	
Her2neu-overexpression expression (n=4)	2.57±1.74	2.26 (3.25)	
Triple negative (n=7)	6.9±4.82	8.12(8.29)	

*Independent t-test
**Mann Whitney U test
#Kruskal Wallis test

Table 4 Correlation between metabolic PET parameters, Age and Tumor size

Parameter	SUVmax		TLR	
	rho*	p-value	rho*	p-value
Age/years	-0.405	0.005	-0.414	0.008
Tumor Size/cm	0.328	0.019	0.337	0.036

*Spearman's Rank Correlation Coefficient

nodal involvement with AUC of 0.612 (95% CI: 0.431-792) Fig. 5.

Discussion

BC is a heterogeneous malignancy owing to several factors affecting its behavior and prognosis [20] . Due to this heterogeneity, the optimal treatment and expected therapy response may vary substantially for each patient [21].PET/CT is a combined imaging of anatomy and function as well. It does not only show the morphological features of the lesion but it may also report its metabolic information, offering new opportunities for breast cancer's diagnosis, staging, re-staging, and treatment response assessment [22].
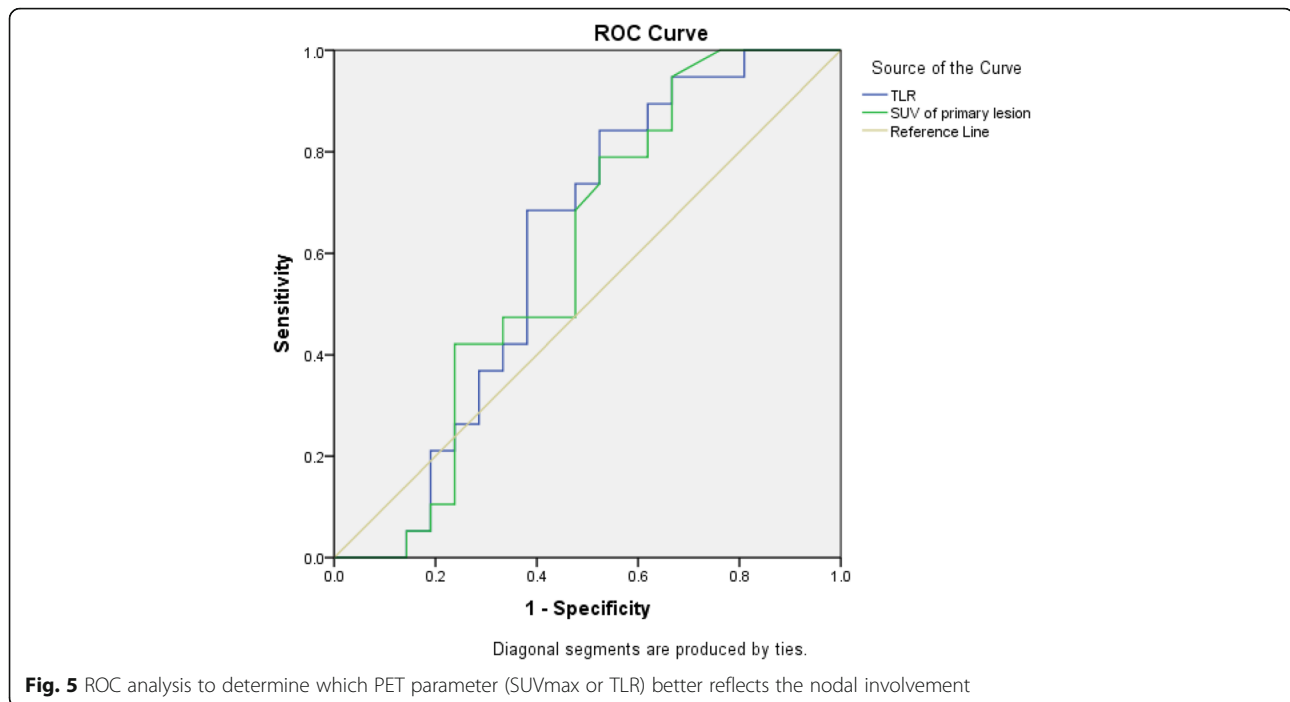
SUVmax is a semi quantitative value, and it indicates the degree of 18F-FDG uptake. The density of 18F-FDG uptake in the tumor is related to increased proliferative activity in tumor cells [23].

Primary breast tumors with high 18F-FDG uptake have been associated with poor prognosis compared with those with lower uptake [24]. Several studies investigated the correlations between 18F-FDG uptake described by SUVmax, distinct histopathological and
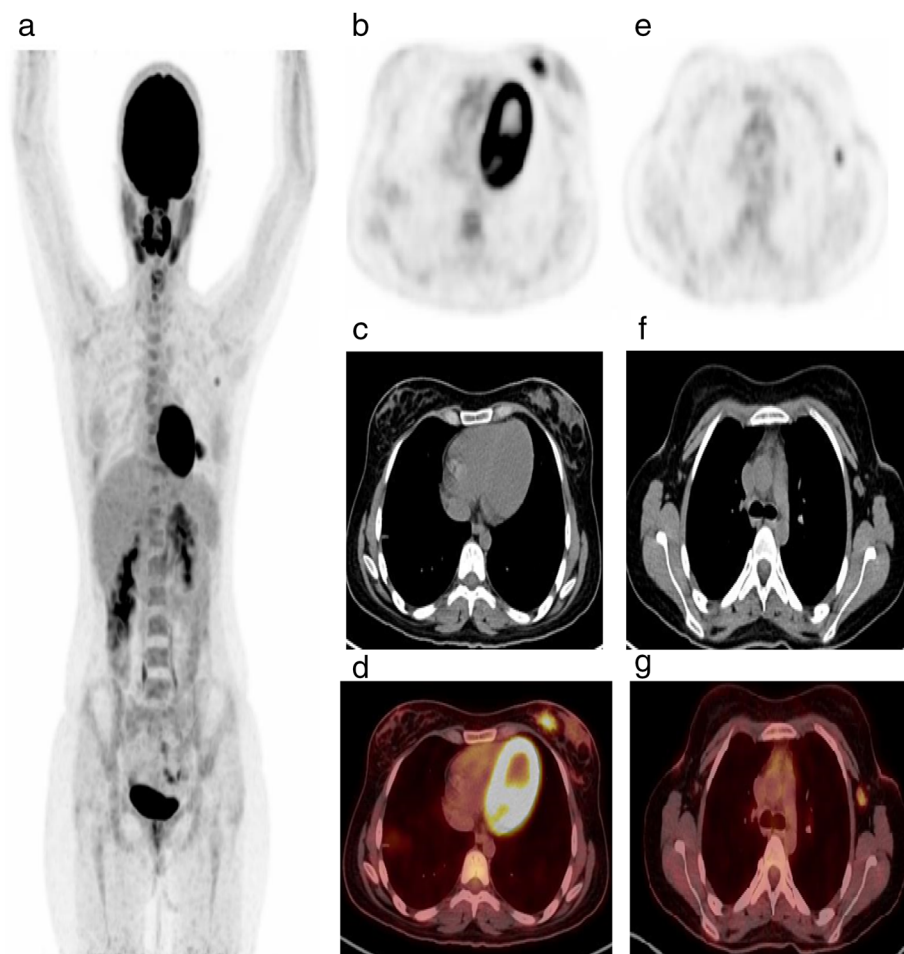
Fig. 4 18F-FDG PET/CT scan of a 20-years-old female with luminal B Invasive Duct carcinoma GII of the Left breast: **a** maximum intensity projection, **b**, **c** and **d** trans axial PET, The corresponding CT and trans axial PET/CT fusion images show intense FDG avid irregular speculated soft tissue mass at the lower inner quadrant of the Left breast measures about 1.5 x 1.3 cm and has SUV max about 6.18. **e**, **f** and **g** show small sized FDG avid left axillary level I lymph nodes measuring 0.9 ×0.9 cm, showing focal cortical thickening reaching 5mm with SUV max about 3.2. SLNB of Left axillary lymph nodes reveal positive metastatic axillary LNs

Fig. 5 ROC analysis to determine which PET parameter (SUVmax or TLR) better reflects the nodal involvement

immunhistochemical factors in BC [18, 24–36]. In our study ,PET CT detected all the primary tumors with mean SUVmax of 10.8(+/-SD 7.9), in concordance with results of Antunovic et.al [28, 37].Several studies reported a significant lower F-18 FDG uptake in ILC compared with IDC; the authors stated that the lower intensity of tumor cells in lobular carcinomas, lower expression of GLUT1, lower proliferation rates, and diffuse infiltrative tumor growth patterns of the surrounding tissue could explain their results [25, 29, 38]. In agreement with these studies ,we found that the median SUV max was lower in ILC compared with IDC ,but with no statistically significancant difference. This is may be explained by smaller numbers of patients included.

The mean SUVmax of the primary tumor was significantly higher in premenopause and advanced stages (stage III and IV); these results are similar to those concluded by Önner et al. and Groheux et al. [18, 29]. The median SUVmax values of the primary tumor in our study was significantly higher in ER - tumors and in PR - ones and these results are similar to those concluded by Ravinaetal [27]..

Kajáry et al. reported that the median SUVmax values of 1ry tumor was significantly higher in Her2-neu + patients but in our study the difference was not statistically significant ; this is may be attributed to the lower number of cases with Her2neu + (14 versus 58 patients) [33]. TN breast cancer has a more aggressive biology than other subtypes; also it is associated with a poorer outcome than luminal subtypes [39]. Inspite of the few number of TN cases in the

present study the results confirmed significantly higher 18F-FDG uptake in this group than in other molecular subtypes , which comes in line with the results of several studie s[33, 36, 40].The histological grade of the tumor is a major prognostic factor in BC. Several studies proved that the SUVmax of primary tumor was significantly higher in cases with high nuclear grade tumors similar to ours [32, 33].ALNs metastasis is considered the most important prognostic factor in the BC . Patients with positive ALNs had significantly higher median SUVmax values similar to several studies [35, 41]. Larger tumors contain more tumor cells than the smaller ones , thus requiring a greater glucose supply to maintain the metabolism and proliferation of tumor cells, which would result in an increase in SUVmax. Several studies have demonstrated the association of the maximum tumor size and the tumor SUVmax [42, 43].The SUV max of the primary tumor was positively correlated with the size of the lesion ; this is similar to the results concluded by Abubakar et al. [26]. Additionally, it was negatively correlated with the age of the patients as concluded by Kimet al [44]. ; this is in contrast to several studies that found that there was no statistically significant association between the SUVmax and age [34, 36].

In contrast to our results, Ravinaetal. stated that there was no statistically significant correlation between patient age, tumor size and SUVmax [27].

TLR may provide a better understanding of the metabolic activity of the tumor and a better diagnostic

performance than SUVmax [45, 46]. Several recent studies have used TLR as an alternative approach to predicts ALNs metastasis , evaluate the prognosis and treatment response as in assessment prognosis of nodal metastasis in locally advanced BC, predicts poor prognosis in stage IIA colorectal cancer and predict occult lymph node metastasis of non–small cell lung cance r[18, 24, 42, 46].

In our study, we also examined the association of TLR with the aforementioned prognostic factors examined with the SUV max of the primary lesion.

Önner et al. found that the TLR value seems to be more informative than the tumor SUVmax in predicting ALNs involvement and that the median of TLR values was significantly higher in stage III and IV, patients with positive ALNs ,higher tumor grade , ER-, PR-, Her2neu negative and in TN molecular subtype ,which were similar to ours [18]. These markers may provide significant information about tumor biology and behavior [18] .We found significantly higher TLR values in premenopausal patients. Also, these values were significantly negatively correlated with the age of the patients and significantly positively correlated with the size of the primary tumor. TLR were found to be more predictive of ALNs involvement than SUVmax similar to those concluded by Önner et al. [18].The main Limitations of our study is the small sample size .

Conclusion

Semi quantitative PET parameters in the form of SUVmax of the primary tumor and TLR values had significant association with different prognostic factors in BC but only TLR was a poor predictor of nodal metastasis. So these parameters could provide possible relevant information about tumor behavior and biology.

Abbreviations
FDG-PETCT: Fluorodeoxyglucose positron emission tomography computerized tomography; SUV max: Maximum Standardized Uptake value; TLR: Tumor SUVmax/Liver average SUV Ratio; BC: Breast Cancer; ER+: Estrogen Receptors positive; ER-: Estrogen Receptors negative; PR+: Progesterone Receptors positive; PR-: Progesterone Receptors negative; Her2neu+: Human epidermal growth factor receptor 2 positive; TN: Triple negative; ALNs: Axillary lymph node; AUC: Area under the curve; IHC: Immunohistochemistry; ROI: Region of interest; VOI: Volumetric region of interest; SLNBs: Sentinel lymph node biopsies; BGO: Bismuth Germanium Oxide; IQR: Inter-quartile range; UOQ: Upper outer quadrant; UIQ: Upper inner quadrant; LOQ: Lower outer quadrant; LIQ: Lower inner quadrant; IDC: Invasive ductal carcinoma; ILC: Invasive lobular carcinoma; GLUT1: Glucose transporter 1

Acknowledgements
Not applicable

Authors' contributions
Study concepts: MAM, AMZ, MIA. Study design: AAA Data acquisition: AAA. Data analysis and interpretation: AAA. Statistical analysis: AAA. Manuscript preparation: AAA, LME. Manuscript editing: AAA, LME. Manuscript review: AAA, LME, MIA. All authors read and approved the final manuscript.

Declarations

Ethics approval and consent to participate
This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of faculty of medicine, Assiut University, Egypt, with IRB number**17200543.** written informed consent had taken from all patients .

Consent for publication
All patients included in this research gave written informed consent to publish the data contained within this study.

Competing interests
The authors declare that they have no competing interests.

Author details
[1]Department of Clinical Oncology and Nuclear Medicine, Faculty of Medicine, Assiut University, Assiut, Egypt. [2]Nuclear medicine department, National Cancer Institute, Cairo University, Cairo, Egypt.

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