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FDG uptake in breast cancer and Quantitative Assessment of Breast Parenchymal Uptake on 18F-FDG PET/CT: Association with Histopathological, Hormonal status, and Clinical Features

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ABSTRACT

***Background*:** To evaluate the predictive value of the 18F-FDG PET/CT parameters on the histopathological features, receptor expression status, and molecular proliferation markers in breast cancer. Also, to assess the effect of the normal breast parenchymal uptake (BPU) on primary breast cancer. ***Materials and Methods*:** 287 patients were included, 198 patients with breast cancer (BC) and 89 patients with the healthy breast control group (CG). The metabolic parameters of breast carcinoma were compared with immunohistochemical subtypes, Ki-67 expression status, tumor size, axillary nodal involvement, and distant organ metastasis. We also analyzed the BPU using a 1.5 cm3 volume of interest (VOI) in the BC and CG groups. ***Results*:** There was a positive correlation between primary tumor SUVmax and tumor size (p=0.001), high Ki -67 expression (p<0.001), axillary nodal involvement (p<0,001), distant organ metastases (p=0.026), ER and PR negativity, and HER2 positivity (p=0.000, 0.001, and 0.021, respectively). Furthermore, the change in mean SUVmax in molecular subtypes was statistically significant (p<0.001). In addition, the SUVmax measured 0.5 cm from the tumor in the same quadrant is higher than the opposite quadrant and contralateral breast, suggesting that the distance to the tumor increases, the FDG uptake decreases (p<0.001 and 0.001, respectively). ***Conclusion*:** Strong relationships were detected between the ER and PR negativity, HER2-positivity, high Ki-67 expression, tumor size, axillary lymph node involvement, distant organ metastases, and SUVmax values. Therefore, we believe that metabolic parameters obtained with 18F-FDG PET/CT may provide relevant information about breast cancer tumor biology and suggest a potential role in identifying more aggressive behavior.

INTRODUCTION

Breast cancer is the most common cancer, representing nearly 1 in 4 cancer patients among women, and it is the leading cause of cancer deaths in developed countries [1].

There are many radiological imaging methods such as mammography, ultrasound, and MRI for breast cancer screening and diagnosis. In addition to tumor diagnosis, these studies have an undeniable function, providing information about normal breast tissue. Regarding normal breast tissue, the fibroglandular tissue (FGT) amount on the mammogram and background parenchymal enhancement (BPE) on MRI are the vital functional parameters [2]. Positron emission tomography (PET) is used globally with promising results in oncology and breast cancer [3]. The uptake of FDG is related to the density of viable tumor cells and mitotic activity rates. Therefore, the FDG uptake in breast cancer might be affected by tumor histopathology, the hormonal receptor expression status, and the Ki-67 proliferation index [4, 5]. Fluorine-18 fluorodeoxyglucose (18F-FDG) PET techniques can assess not only tumors but also background parenchymal uptake (BPU) [6, 7]. In this regard, we aimed to identify the predictive value of the PET/CT parameters on the histopathological features, receptor expression status, and molecular markers of proliferation, such as the Ki-67 index. Also, the effect of BPU on primary breast cancer was assessed in BC and CG patients.

MATERIALS AND METHODS

Patients

A total of 287 patients who underwent

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whole-body PET/CT imaging between April 2010 and November 2019 were included in our study. In addition to 198 breast cancer patients, a control group of 89 patients was added for BPU evaluation. The demographic features of the two groups are summarised in table 1. The local ethics committee approved our retrospective study (2020/2200). Verbal or written permission was obtained from all patients included in the study.

Table 1. Demographic information of BC and CG patients.

	BC patients	CG patients
Number of patients (%)	198 (69.0%)	89 (31.0%)
Age (range)	53.82±13.63 (25-86)	60.64±12.05 (24-87)
Patients over 50 years of age (%)	116 (58.6%)	72 (80.9%)
Patients under 50 years of age (%)	82 (41.4%)	17 (19.1%)

Histological analysis

The histopathological analysis of primary breast cancer was carried out on specimens obtained from fine-needle aspiration biopsy or tru-cut biopsy prior to 18F-FDG PET/CT, or breast surgery or excisional biopsy following initial 18F-FDG PET/CT. In the immunohistochemical (IHC) examination utilizing the streptavidin-biotin method, tumor blocks with minimal hemorrhage and necrosis best represent the tumor histological content of the tissues fixed with a 10% neutral buffered formalin were selected. The staining was utilized using BenchMark ULTRA (Ventana, Roche Diagnostics, Rotkreuz ZG, Switzerland) device. Ten percent or more nuclear immunostaining of hormone receptor expression was considered positive [8]. The antibody used for CerbB2 IHC analysis is Ventana HER-2/neu 4B5 (Roche Diagnostics, Rotkreuz ZG, Switzerland). The IHC features of CerbB2 (HER2-neu) were evaluated according to ASCO/CAP 2013 HER-2 Test guideline [9]. If the IHC score is 0 to 1+, the HER2 test result is reported as negative, and a score of 3+ is reported as positive. If the score is 2+, it is considered equivocal and later defined as negative or positive by Silver in situ hybridization (SISH) [10]. The system used for ISH is the Ventana Inform HER2 Dual ISH Automatic system, and the Kit is HER2 Dual ISH DNA probe (Ventana). In the slides prepared for CerbB2 and chromosome 17 by the ISH method, the signals in the nuclei of 40 cells were counted by 100x immersion in the evaluable invasive tumor areas. The HER2/CEP17 ratio, which is the ratio of HER2 signals per cell to CEP17 signals, is used following guideline recommendations and algorithms. Also, the mean number of tumor cell signals for Cerb B2 and chromosome 17 was measured. A dual-probe HER2/CEP17 ratio below 2 (<2) indicates Amplification negative, while a ratio above 2 (>2) was considered as Amplification positive.

Four molecular subtypes were included;

Luminal A: Hormone-receptor (+), HER2 (−) and Ki-67 less than 15%;

Luminal B: Hormone-receptor (+), HER2 (+), or HER2 (−), and Ki-67 higher than 15%

Triple-negative (TNBC): Hormone-receptor (−) and HER2 (−)

HER2 type: Hormone-receptor (−) and HER2 (+)

18F-FDG PET/CT imaging and analysis of imaging

18F-FDG PET/CT scans were performed using a Siemens mCT 20 ultra–HD LSO PET/CT system (Siemens molecular imaging, Hoffmann Estates, Illinois, USA). Patients with at least six hours of fasting and blood glucose levels lower than 150 mg/dl were admitted for the procedure. A standard 3.7–5.2 MBq/kg (0.1-0.15 mCi/kg) 18F-FDG intravenous injection was administered to the patients. Whole-body PET/CT imaging was obtained from the vertex area to the upper femur with the patients in the supine position 60min after intravenous injection. For the calculation of maximal standardized uptake values (SUVmax), mean SUV (SUVmean), and metabolic tumor volume (MTV) of the tumor, the volume of interest (VOI), which included the entire volume of index lesion, were drawn on PET/CT cross-sections in BC group. In addition, for BPU SUV calculations, a standard 1.5 cm^3 VOI was used in the areas of the breast parenchyma, which are described below;

For BPU in the BC group, SUV was measured at four locations;

1) 0.5 cm away from the tumor in the same quadrant

2) The contralateral quadrant of the ipsilateral breast

3) The same quadrant of the contralateral breast

4) 0.5 cm away from the areola (retroareolar region) in the contralateral breast

For BPU in the CG, SUV was measured at two locations;

1) Both of the healthy breasts, the two-quadrant that are appropriate

2) Both of the healthy breasts, 0.5 cm from the areola (retroareolar region), using a standard 1.5 cm^3 VOI as shown in figure 1.

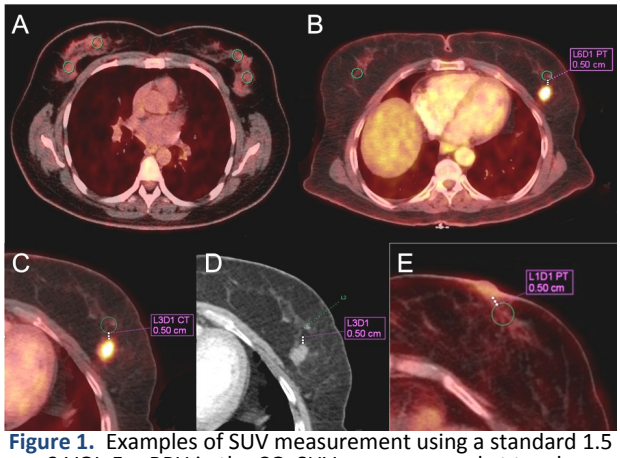

Figure 1. Examples of SUV measurement using a standard 1.5 cm3 VOI. For BPU in the CG, SUV was measured at two locations in both healthy breasts, the two-quadrant that are appropriate **(A)** and both of the healthy breasts, 0,5 cm from the areola in retroareloar region **(E)**. For BC, 0,5 cm from the tumor in the same quadrant **(B-D)**, The contralateral quadrant of the ipsilateral breast **(B)**.

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This formula was used to calculate the SUVmax value: the maximum activity in the VOI (MBq/ml)/ dose of 18F-FDG injected into the patient (MBq/kg body weight). MTV%40 is the total volume within a boundary determined by a specific threshold (SUV>40% of SUVmax). We reported the anatomical and metabolic characteristics of the primary breast tumor (MTV 40%, SUVmax, SUVmean) and metastatic features based on PET/CT results.

Statistical analysis

The statistical package for the social sciences (SPSS) software for Windows (v21.0; IBM, Armonk, New York, USA) was used for data analysis. Mean, median, SD, ranges, percentages, and frequency distributions were included in descriptive statistics. Kolmogorov-Smirnov test, histogram, detrended plots, skewness, and kurtosis were used for normality analysis. The comparison of normally distributed variables was made with Student's t-test. The categorical variables evaluation was done using the chi-square test. The relationships between SUVmax and histopathological findings were analyzed using Spearman's ρ correlation test. The κ statistic was calculated to evaluate the agreement. The statistically significant P value was accepted as less than 0.05.

RESULTS

In the BC group, we determined that 19.7% (n=39) of the primary lesions had low Ki-67 expression (<15%), and 80.3% (n=159) had high expression of Ki-67 (≥15%). According to the immunohistochemical subtype classification, 42 cases (21.2%) luminal A, 119 cases (60.1%) luminal B, 18 cases (9.1%) as TNBC, and 19 cases (9.6%) were HER2 types. Also, 162 cases (81.8%) were invasive ductal, 18 cases (9.1%) were invasive lobular, 9 cases (4.5%) were mucinous type, 4 cases (2.0%) were mixed type, and 5 cases (2.5%) were apocrine type.

Among the BC patients, all primary tumors (100%) demonstrated 18F-FDG uptake, and the mean SUVmax was 13.10±7.91 (median=11.24, range=1.67-45.48), and the mean SUVmean was 7.79±4.68 (median=6.90, range=0.99-26.69). No relationship was found between mean SUVmax values of the patients under 50 and those aged 50 and over (p=0.182). Our patient's mean tumor diameter was determined as 3.70±2.26 cm (range of distribution = 1.1-13.00 cm). The mean SUVmax was higher in the group with a primary tumor size greater than 2 cm than in the group with a primary tumor size less than 2 cm (p=0.001) (table 2).

In our study, 81.3% (n=161) of the tumors were ER-positive, 72.7% (n=144) were PR-positive, while 30.8% (n=61) were positive for Her-2 expression. ER and PR negativity and HER2 positivity demonstrated higher 18F-FDG uptake (p<0.001, 0.001, and 0.021, respectively). In addition, the mean SUVmax values were higher in cases with higher (≥15%) Ki-67 expression compared to the cases with low (<15%) Ki-67 expression (p<0.001) (table 2).

Table 2. Relationship between primary tumor SUVmax and histopathological, clinical features.

	Variables	n (%)	SUVmax (Mean±SD)	P-value
Age	< 50 > 50	82 (41.4%) 116 (58.6%)	13.56±7.34 12.77±8.31	0.182
Tumor Size (cm)	< 2 ≥ 2	27 (13.6%) 171 (86.4%)	8.86±6.04 13.77±7.98	0.001*
ER	Negative Positive	37 (18.7%) 161 (81.3%)	17.08±7.28 12.21±7.79	0.000*
PR	Negative Positive	54 (27.3%) 144 (72.7%)	15.90±7.97 12.07±7.66	0.001*
HER2	Negative Positive	137 (69.2%) 61 (30.8%)	12.43±8.05 14.58±7.45	0.021*
Ki-67 %	< 15 ≥ 15	39 (19.7%) 159 (80.3%)	6.62±3.02 14.70±7.93	0.000*
Axillary involvement	Absent Present	32 (16.2%) 166 (83.8%)	8.50±3.73 13.99±8.20	0.000*
Distant Organ Metastasis	Absent Present	116 (58.6%) 82 (41.4%)	12.09±7.40 14.51±8.43	0.026*

*= p<0.05 statistically significant.

The axillary lymph node metastasis was detected in 83.8% (n=166) of our patients in 18F-FDG PET/CT. According to this, the primary tumor mean SUVmax (13.99±8.20) in patients with axillary involvement was higher than the group without axillary involvement (8.50±3.73) (p<0,001) (table 2).

Bone and bone marrow metastases 74.4% (n=61) are the most common sites in patients with distant organ metastases, followed by multiple sites metastases with a rate of 17.1% (n=14) and liver-lung metastases with a rate of 3.7% (n=3). Besides, the mean primary tumor SUVmax in distant metastasis cases was higher than those without metastasis (p=0.026) (table 2).

According to molecular subtypes; the mean SUVmax in the luminal A group was 6.84±3.32, 13.96±7.83 in the luminal B group, 18.02±9.14 in the TNBC cases, and 17.12±6.62 in the HER2 cases. The mean SUVmax in the molecular subtypes was statistically different (p<0,001) (table 3).

Table 3. SUVmax correlation across breast cancer subtypes.

	N	%	SUVmax (Mean±SD)	P-value
Luminal A	42	21.2	6.84±3.32	**0.000***
Luminal B	119	60.1	13.96±7.83	
TNBC	18	9.1	18.02±9.14	
HER2 Type	19	9.6	17.12±6.62	

*= p<0.05 statistically significant.

The mean primary tumor SUVmax was higher than the mean BPU SUVmax as expected; 0.5 cm away from the tumor in the same quadrant (p<0.001), in the same quadrant of the contralateral breast (p<0.001), and in the contralateral quadrant of the ipsilateral breast (p<0.001). More importantly, the mean SUV values at 0.5 cm away from the tumor were higher than the contralateral quadrant and the contralateral breast BPU SUV values, indicating that

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FDG uptake decreases as the distance to the tumor increases (p<0.001 and <0.001, respectively) (figure 2, 3) (table 4).

Table 4. Mean SUVmax and SUVmean correlation amongst regions.

Regions	(Mean ±SD)	SUVmax (Mean±SD)	SUV Mean (Mean±SD)	P-value[a]	P-value[b]
SUVmax 0.5cm from primer (1.5cm^3)	2.03± 0.70	13.11±7.94	-	0.000*	
SUVmax Opposite Quadrant (1.5cm^3)	1.59± 0.57	13.11±7.94	-	0.000*	0.000*
SUVmax Opposite Breast (1.5cm^3)	1.58± 0.60	13.11±7.94	-	0.000*	
SUVmean 0.5cm from primer (1.5cm^3)	1.31± 0.50	-	7.80±4.70	0.000*	
SUVmean Opposite Quadrant (1.5cm^3)	1.109± 0.456	-	7.80±4.70	0.000*	0.000*
SUVmean Opposite Breast (1.5cm^3)	1.103± 0.450	-	7.80±4.70	0.000*	

a= Comparisons between the primary lesion and adjacent regions.
b= Group comparison of SUVmax and SUVmean between adjacent

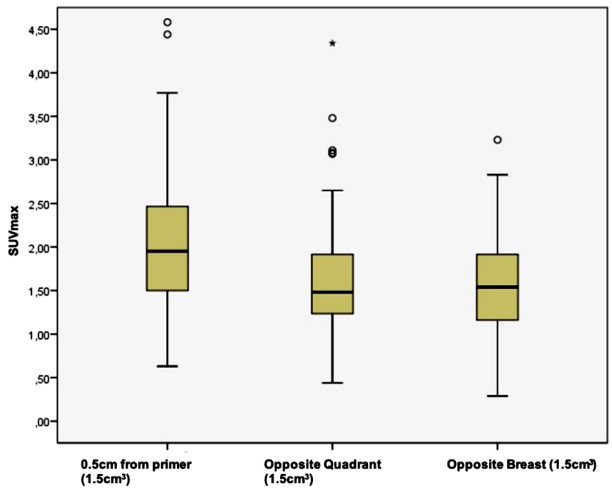

Figure 2. Box-and-Whisker Plots. The boxes show the interquartile range (25-75th percentile), and the Median (50th percentile) SUVmax values in tumor-adjacent regions are shown as horizontal black lines. The whiskers outside the boxes show other than upper and lower quartiles. The outliers are shown as circles (mild outliers) and stars (extreme outliers). BPU SUVmax at 0,5 cm away from the tumor is statistically significantly higher than other regions.

A correlation was found between the primary tumor SUVmax, and the BPU SUVmax measured at 0,5 cm away from the tumor and in the contralateral quadrant (r=0.281, p<0.001, and r=0.180, p=0.012, respectively) (figure 4). Similarly, there was a statistically significant correlation between the SUVmean values. (r=0.241, p=0.001, and r=0.168, p=0.019, respectively) (figure 5) (table 5).

The mean MTV 40% of primary tumor lesions was 18.19±49.44 (median=5.87, range=0.40-499.53). There was a statistically significant relationship between high mean MTV and increased tumor diameter, high Ki-67 rates, axillary LN involvement, and distant organ metastasis (table 6).

According to mean BPU SUVmax and SUVmean in the control group, no statistically significant relationship was found between the group under the age of 50 and the group over the age of 50 (p>0.05 and p>0.05, respectively) (table 7). Our study of 287 subjects showed no significant difference in 18F-FDG uptake between right and left healthy breast FGT.

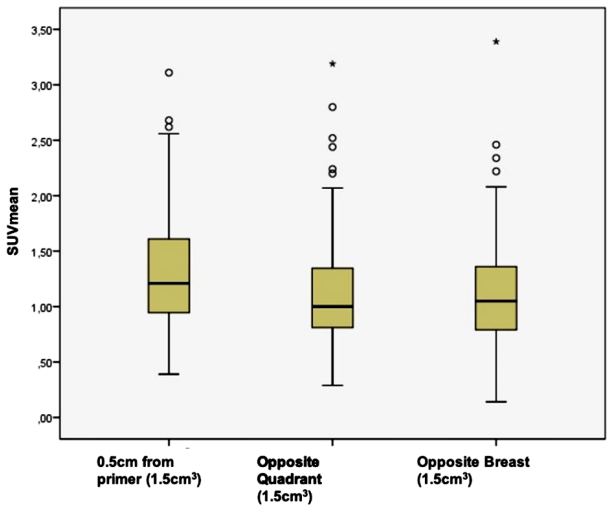

Figure 3. Box-and-Whisker Plots. The boxes show the interquartile range (25-75th percentile), and the Median (50th percentile) SUVmax values in tumor-adjacent regions are shown as horizontal black lines. The whiskers outside the boxes show other than upper and lower quartiles. The outliers are shown as circles (mild outliers) and stars (extreme outliers). BPU SUVmean at 0,5 cm away from the tumor is statistically significantly higher than other regions.

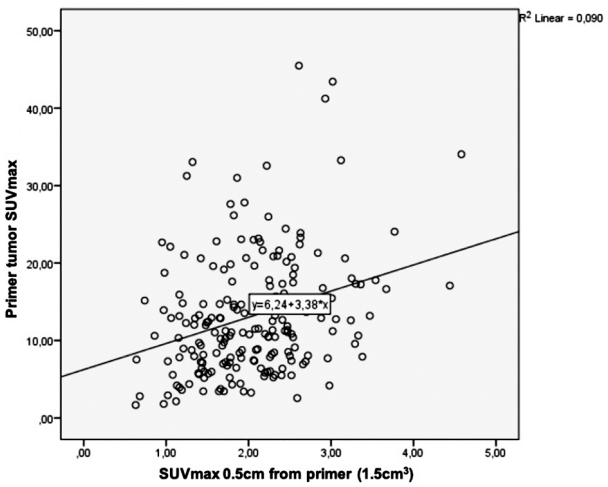

Figure 4. Correlation between primary tumor SUVmax and BPU SUVmax at 0.5 cm from the tumor.

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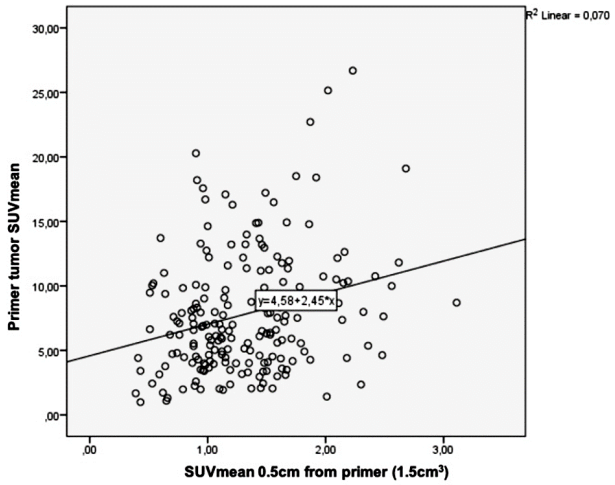

Figure 5. Correlation between primary tumor SUVmean and BPU SUVmean at 0.5 cm from the tumor.

Table 5. Correlation analyzes of primary tumor SUVmax and SUVmean in patients.

	SUVmax		SUVmean	
	R	*p*	*R*	*p*
SUVmax 0.5cm from primer (1.5cm³)	0.281	0.000*	-	-
SUVmax Opposite Quadrant (1.5cm³)	0.180	0.012*	-	-
SUVmax Opposite Breast (1.5cm³)	0.096	0.181	-	-
SUVmean 0.5cm from primer (1.5cm³)	-	-	0.241	0.001*
SUVmean Opposite Quadrant (1.5cm³)	-	-	0.168	0.019*
SUVmean Opposite Breast (1.5cm³)	-	-	0.091	0.207

*= p<0.05 statistically significant.

Table 6. Relationship between SUVmean, MTV%40 and histopathological, clinical features.

	SUV mean (Mean±SD)	P-value	MTV 40% (Mean±SD)	P-value
Age				
< 50	8.13±4.48	0.173	20.59±44.38	0.260
> 50	7.56±4.83		16.48±52.88	
Tumor Size				
< 2 cm	5.52±4.02	0.001*	1.76±1.28	0.000*
≥ 2 cm	8.16±4.69		20.80±52.77	
ER				
Negative	10.36±4.65	0.000*	36.65±95.30	0.052
Positive	7.22±4.51		14.06±30.23	
PR				
Negative	9.52±4.96	0.001*	31.74±85.72	0.302
Positive	7.16±4.43		13.20±24.19	
HER2				
Negative	7.37±4.72	0.014*	14.76±28.53	0.524
Positive	8.74±4.50		25.82±77.89	
Ki67				
< 15%	3.97±1.82	0.000*	6.04±9.84	0.001*
≥ 15%	8.74±4.70		21.19±54.61	
Axillary involvement				
Absent	5.19±2.47	0.000*	4.29±3.63	0.000*
Present	8.30±4.85		20.88±53.61	
Distant Organ Metastasis				
Absent	7.33±4.58	0.058	8.71±18.18	0.000*
Present	8.44±4.78		31.49±71.71	

*= p<0.05 statistically significant.

Table 7. Correlation analyzes of primary tumor SUVmax and SUVmean in control patients.

PET/CT Results	< 50 years (Mean±SD)	> 50 years (Mean±SD)	Total (Mean±SD)	p-value
Right Breast SUVmax (1.5cm3)	1.85±0.64	1.62±0.47	1.66±0.51	0.190
Right Breast SUVmean (1.5cm3)	1.34±0.50	1.11±0.34	1.16±0.38	0.096
Right Breast SUVmax 0.5cm from Retroareolar	1.86±0.45	1.80±0.53	1.81±0.51	0.667
Right Breast SUVmean 0.5cm from Retroareolar	1.14±0.39	1.02±0.34	1.04±0.35	0.214
Left Breast SUVmax (1.5cm3)	1.75±0.56	1.57±0.46	1.60±0.49	0.168
Left Breast SUVmean (1.5cm3)	1.21±0.45	1.06±0.32	1.09±0.35	0.165
Left Breast SUVmax 0.5cm from Retroareolar	1.88±0.42	1.75±0.55	1.73±0.52	0.362
Left Breast SUVmean 0.5cm from Retroareolar	1.18±0.33	1.02±0.32	1.05±0.33	0.076

DISCUSSION

PET/CT has low sensitivity in detecting small breast tumors. It has been reported that low FDG uptake is observed due to the partial volume effect in T1 tumors [11]. Some authors reported a positive correlation between 18F-FDG uptake and tumor size [12, 13, 17, 18], while others reported no correlation [7, 14]. This diversity in these studies might be associated with the IHC findings, histological subtypes, and variations (necrotic/fibrotic tissue and tumor cell density) across the tumors. We found, like other authors, that FDG uptake was strongly related to tumor size.

Breast cancer represents a heterogeneous disease characterized by different histopathological features, diverse treatment responses, and survival [15]. ER and PR are important prognostic factors for breast cancer, and ER-positive patients have excellent long-term survival [16]. Although many studies have shown that 18F-FDG uptake is higher in the ER-negative condition [14, 17, 18, 19, 22], there are also studies stating no clear relationship between SUVmax and ER status [7, 20, 21, 23]. Although Basu *et al.* [20] reported that tumors in 29 TNBC patients showed intense FDG uptake regardless of tumor size, the small sample size in the study was insufficient for statistical analysis. In the study of Dehdashti *et al.* [23], there was no significant relationship between ER status and tumor FDG uptake. Ekmekcioglu *et al.* [13] found high SUVmax in the ER-negative group; in contrast, De Cicco et al. and Mavi *et al.* found no significant difference between the PR-positive and PR -negative groups [18, 24]. Gil Rendo *et al.* [17] found a positive relationship between the SUV and ER status,

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but the study did not assess PR status. Negative hormone receptor status was statistically correlated with high SUV levels in the study of Ueda *et al.* and Heudel *et al.* [19, 22]. Our study found the high 18F-FDG uptake to have a significant correlation with ER and PR-negative status.

There are conflicting results regarding the relationship between HER2 overexpression and 18F-FDG uptake. There was no relationship between CerbB2 oncogene expression and 18F-FDG uptake [7, 13, 14, 24, 25, 26], although other studies have reported a significant relationship [10, 18, 19, 27, 28]. Garcia et al. [27] found statistically high SUV values in the HER2-positive and TNBC group compared to luminal HER2-negative tumors. Sanli et al. [28] demonstrated that tumors with C-erbB-2 overexpression were associated with higher SUVmax. Similarly, our study showed a positive correlation between HER2 overexpression and tumor SUVmax.

Patients with a high Ki-67% constitute a highly proliferative subgroup of patients with ER-positive breast cancer [29]. According to the literature, the relationship between PET and the Ki-67 proliferation index is controversial. While some authors defined significant correlations between SUVmax and the Ki-67 proliferation index [7, 14, 15, 18, 30], others did not. Groheux *et al.* [31] found no association between SUVmax and Ki-67 in 55 TNBC patients. In the study of Koo *et al.* [32] with 103 TNBC patients, a positive correlation was found between Ki-67 and SUVmax. In a meta-analysis with 25 studies, Surov *et al.* [33] reported that SUVmax correlated moderately with the expression of Ki-67. The present study found a significant relationship between the Ki-67 proliferation index and 18F-FDG uptake.

Several groups have reported an association between axillary nodal status and FDG uptake [12, 13, 17, 19, 28, 30, 34], while others could not confirm this finding [7, 14, 21, 25, 26, 32]. In this study, primary tumor SUVmax was higher in patients with axillary nodal metastases. Cermik *et al.* [34], Koolen *et al.* [35], and some authors [27, 30] mentioned that a higher TNM stage was associated with higher SUVmax. However, the others suggested that this does not apply to all tumors [26]. In our study, a higher TNM stage was associated with high SUVmax. Based on these data, high primary tumor SUVmax may indicate a higher risk for metastatic disease and is a prognostic factor in IDC patients.

Previous studies have described relationships between tumor metabolism in molecular subtypes of BC [20, 24]. Koolen *et al.* [35] reported higher primary tumor SUVmax in TNBC than in Luminal A-B and HER 2 types (13.3 vs. 6.3, 8.9, and 6.3 respectively) (P<0.001). Garcia-Vicente *et al.* [27] reported that HER2-positive and TNBC tumors displayed higher primary tumor SUVmax than luminal HER2-negative tumors. In our study, the HER2 group showed the same level of FDG uptake as TNBC and was significantly higher than the luminal subtypes. Although HER2 status in ER-negative tumors did not affect SUVmax in contrast to the studies mentioned above, it should be confirmed in studies with more extensive series.

Since most of the data published have concentrated on the SUVmax difference between the TNBC type, HER 2 type, and luminal types, limited information is available in differentiating luminal B from luminal A. Yoon *et al.* [26] found no significant differences in SUVmax of molecular subtypes. On the other hand, Miyake *et al.* [36] reported that luminal A SUVmax (4.4±2.2) was lower than non–luminal A SUVmax values (8.1±4.4; p<0.0001) and concluded that FDG PET/CT contributed to distinguishing between luminal A and non–luminal A tumors. Similarly, in our study, a significantly lower SUVmax level was found in the Luminal A subtype compared to other subtypes. Although the overall effect of PR-negativity has been highlighted, the impact of PR in Luminal subtypes has not been evaluated.

Hruska et al. displayed the first evidence for BPU as a risk factor for breast cancer [37]. The results of our study show that BPU is inversely proportional to the distance from the index cancer. As the distance to the tumor increases, BPU SUV decreases. In addition, BPU SUV values were consistent in all normal breast tissues, and this finding is essential in cases who underwent PET/CT for indications other than breast cancer. In evaluating the breast parenchyma, PET findings should be carefully examined in addition to CT findings, and FDG uptakes higher than BPU should not be overlooked in terms of possible pathologies.

Limitations of the study

This is a retrospective study conducted in a single institution with a small sample size. The patient's menstrual cycle timing was not adequately controlled, suggesting that the menstrual cycle status may have affected the BPU measurements.

CONCLUSION

Strong relationships were detected between the HER2 positivity, hormone-receptor negativity, higher Ki-67%, tumor size, axillary lymph node involvement, distant organ metastases, and SUVmax values. Therefore, 18F-FDG PET/CT metabolic parameters could give essential data about breast cancer tumor biology, suggest a potential role in determining more aggressive behaviors, and guide treatment options.

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equally in the study. The manuscript has been read and approved by all the authors, the requirements for authorship as stated earlier in this document have been met and, each author believes that the manuscript represents honest work.

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