# Comparison of PET-CT and MRI for evaluation of axillary lymph nodes in early breast cancer patients

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BACKGROUND: *Evaluation of axillary lymph node in women with breast cancer is very important as it can change the initial treatment decision. None of the noninvasive methods used for assessment of axilla is accurate as sentinel lymph node biopsy (SLNB) yet. This study compared the diagnostic performance of 18-fluorodeoxyglucose positron emission tomography/computed tomography (PET-CT) and Dynamic Contrast-Enhanced Magnetic Resonance Imaging (DCE-MRI) in preoperative axillary evaluation of women diagnosed with early breast cancer (EBC).*
METHODS: *The records of 1246 patients operated for EBC between 2016-2019 were analyzed retrospectively. Pathological evaluations of axillary lymph nodes and the data of these two imaging modalities were analyzed.*
RESULTS: *Forty patients operated for EBC had both DCE-MRI and PET-CT. Axillary metastasis were detected in 12 patients (27.5%). Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of DCE-MRI/ PET-CT for determining axillary lymph node metastases were 25/66.6%, 75/67.8%, 30/47%, 70/82.6%, and 60/67.5%, respectively.*
DISCUSSION: *Any method has yet reached the performance of sentinel lymph node biopsy in the axillary mapping of patients with EBC. If a clinically EBC patient is suspected of axillary involvement in DCE-MRI or PET-CT (since have low PPV and sensitivity), a biopsy should be performed.*

KEY WORDS: Breast Cancer, Magnetic Resonance Imaging, Positron Emission Tomography, Staging

## Introduction

Breast cancer is the most prevalent cancer type and the prominent cause of cancer-related mortality among women [1]. Axillary lymph node involvement is the primary determinant in predicting patient's survival, and is crucial in the decision of the type and timing of the treatment such as upfront surgery or neoadjuvant chemotherapy. Early breast cancer (EBC) is defined as T1 and T2 tumors are without axillary lymph node involvement according to TNM staging in American Joint Committee of Cancer 8th edition. Upfront surgery is the most preferred treatment type for EBC. Initial treatment strategy and prognosis of patients are based on the histochemical status and stage of tumor. Besides, determination of the local tumor status is mandatory to provide an accurate and individualized treatment plan for each patient.

Physical examination is usually insufficient to determine the axillary nodal status [2]. Ultrasonography (USG) of the axilla is the commonly preferred imaging technique to identify suspected nodal metastasis. However, the sensitivity and positive predictive value of USG alone remains inconclusive [3]. Depending on the burden of axillary metastasis, the role of conventional magnetic resonance imaging (MRI) to assess lymph node metastasis has been found to have moderate sensitivity and low-to-moderate specificity [4,5]. Thus, more accurate non-invasive techniques for preoperative diagnosis of axillary

nodal involvement are needed. In case the patient has a dense breast, Dynamic Contrast-Enhanced Magnetic Resonance Imaging (DCE-MRI) is preferred as preoperative imaging method before breast-conserving surgery [6]. The conventional local staging methods (clinical examination, breast ultrasound, conventional mammography, MRI) are not accurate enough to replace invasive procedures (i.e. needle biopsy, axillary lymph node dissection and sentinel lymph node biopsy) for nodal status evaluation [7].

When compared to the traditional imaging methods (i.e. Mammography, MRI, and USG), whole-body positron emission tomography (PET) and positron emission tomography/computed tomography (PET-CT) using [(18)F]2-fluoro-2-deoxyglucose (18F-FDG) as tracer has proven to provide more accurate results in the staging of both primary and locally advanced breast cancer. It is possible to detect lymph node metastases with high specificity ranges [8-10]. PET-CT, which is not recommended by current guidelines for axilla evaluation in EBC, is mainly preferred to detect distant metastases in metastatic breast cancer and to assess the response of neoadjuvant chemotherapy on the tumor [11,12].

The contribution of sentinel lymph node biopsy (SLNB) instead of axillary lymph node dissection (ALND), has significantly improved axillary disease management in breast cancer over the recent years. Being less invasive than ALND, SLNB has become gold standard especially in EBC [13]. Data collected from the American College of Surgeons Oncology Group (ACOSOG) Z0011 trial proposes that not all patients with involved lymph nodes imply completion axillary dissection[14]. The results of ACOSOG-Z0011 study reveals that patients with EBC can be managed without ALND even in the presence of metastatic lymph nodes (up to two in four sentinel lymph nodes [15]. The main purpose of the present study is the predictive performance comparison of PET-CT and DCE-MRI in detecting axillary nodal involvement in EBC diagnosed patients.

## Methods

### PATIENTS

The records of EBC diagnosed patients having undergone breast cancer surgery from October 2016 to September 2019 were examined retrospectively from hospital information system. Human epidermal growth factor receptor-2 (Her2) positive and triple negative breast cancer patients who received neoadjuvant chemotherapy despite having T1 or T2 tumors were excluded from the study. Patients' ages, physical examination findings, imaging techniques, type of surgery and histopathology results were recorded. The presence and number of suspicious lymph nodes in the ipsilateral axilla by the DCE-MRI and PET-CT images were recorded, if any.

### PET-CT PROCEDURE

The PET-CT method used in the acquisition of the patients' imagings from the study of Boellaard et al.[16] Any focal FDG uptake higher than the mediastinal blood pool activity was defined as a positive finding, in accordance with the anatomical lesion on corresponding CT.

### MRI PROCEDURE

The DCE-MRI method used in the acquisition of the patients' imagings from the study of Taskin et al.[17] Subtracted contrast-enhanced dynamic images were used as standard. MRI findings were assessed and issued in compliance with the breast imaging-reporting and data system (BI-RADS)[18] through two radiology specialists with 5 and 17 years of expertise in breast imaging. Any of following findings in MRI regarding axillary lymph nodes are considered suspicious: Round shape, diffuse cortical thickening, regionally thickened and oval, cortex medulla separation, and cortical irregularity.

### OPERATIONS AND HISTOPATHOLOGY

Surgical treatment was either breast-conserving surgery or mastectomy, combined with SLNB and/or ALND. Histologic tumor type, histological and nuclear grade of the tumor, pathological T stage, estrogen receptor (ER) expression, progesterone receptor (PR) expression, Her-2 status of tumor and lymph node status were evaluated. TNM staging was conducted in compliance with the American Joint Committee on Cancer (AJCC) 8th edition [19].

### REFERENCE STANDARD

The final pathological nodal status of each patient undergoing SNLB with or without ALND were determined based on the evaluation of the specimens. PET-CT and DCE-MRI findings were compared in terms of axillary lymph node involvement status and histopathological features.

The approval of Ethics Review Board numbered 2019/17 was obtained for this retrospective study and informed consent was waived because of retrospective nature of the study.

### STATISTICAL ANALYSIS

Categorical values were assessed with Mc-Nemar's test, Pearson's chi-square test, continuous variables were assessed with student's t-test, Mann-Whitney U test. P value of <0.05 was considered as statistically significant.

McNemar's test was conducted to find out any significant differences in axillary evaluation between PET-CT and DCE-MRI. The receiver operating characteristic (ROC) analysis was conducted to identify the optimum metastatic lymph node diameter cut-off values of PET-CT and DCE-MRI. All analysis was conducted with IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY.

## Results

Among 1246 patients undergone breast cancer surgery between 2016 and 2019, 865 were diagnosed with EBC, however, only 40 of these patients had both PET-CT and DCE-MRI preoperatively. All the patients included in the study were female with an average age of 46.1± 9.8 years(28-68years). Twenty-one (52.5%) lesions were T1 (<2 cm) and 19 (41.5%)were T2 (2–5cm). Twenty-four (60%) patients underwent breast-conserving surgery, while 16 (40%) had mastectomy. Of the 40 patients, 32 (75%) were ER positive and eight (%25) patients were ER negative. While PR was positive in 28 (70%) patients, it was negative in 12 (30%) patients. HER-2 was positive in five (12.5%) of 40 patients and rest were negative. Average time span between PET-CT and MRI was 4±2(1–9) days, and 14±3 (10–18) days between surgery and closest imaging methods.

Invasive ductal carcinoma (NOS, not other specified) was detected in 35 patients (87.5%). The remaining five patients had other kinds of invasive carcinomas; three of them (7.5%)was invasive lobular carcinoma and two (5%) invasive metaplastic carcinoma.

A tracer (radiotracer or isosulfan blue) was administered in all patients to identify sentinel lymph node, however, in one (2.5%) patient sentinel lymph node could not be identified and axillary lymph dissection was performed due to palpable and suspicious axillary lymph nodes. Metastasis was detected in nine of 20 lymph nodes in this patient; whose PET-CT and DCE-MRI revealed axillary lymph node suspicion. Axillary metastases were identified by SLNB in eight patients and these patients underwent ALND. Thus, in total ALND was performed in nine (22.5%) patients. However, final pathological examination revealed axillary nodal involvement in12 of 40 patients (30%).

One (2.5%) patient had no metastasis in sentinel lymph nodes according to frozen section result. However, in this patient also palpable non-sentinel lymph node was resected and frozen section revealed metastases. While axillary metastasis was suspected on PET-CT of this patient, there was no suspicious finding in MRI. This patient didn't undergo axillary dissection. ALND was not performed in one (2.5%) patient who has metastasis in sentinel lymph node according to frozen section, contrary to no suspicion of metastasis in axillary lymph nodes by MRI and PET-CT. In another (2.5%) patient,

TABLE I - *Histopathological and immunohistochemical characteristics, T-stage and grade of tumor, type of surgery to breast and axilla, nodal status of all primary breast tumors according to the reference standard and axillary lymph node status according to PET-CT and MRI reports.*

|  | n (%) |
|---|---|
| *Tumor Stage* | |
| T1 | 21 (52.5%) |
| T2 | 19 (47.5%) |
| *Tumor Grade* | |
| Grade I | 5 (12.5%) |
| Grade II | 15 (37.5%) |
| Grade III | 20 (50%) |
| *Estrogen receptor expression* | |
| Positive | 32 (80%) |
| Negative | 8 (20%) |
| *Progesterone receptor expression* | |
| Positive | 28 (70%) |
| Negative | 12 (30%) |
| *Her-2 overexpression* | |
| Positive | 5 (12.5%) |
| Negative | 35 (87.5%) |
| *Histopathological Type* | |
| Invasive Ductal Carcinoma | 35 (87.5%) |
| Invasive Lobular Carcinoma | 3 (7.5%) |
| Metaplastic Carcinoma | 2 (5%) |
| *Axillary Status by PET-CT* | |
| Positive | 17 (42.5%) |
| Negative | 23 (57.5%) |
| *Axillary Status by DCE-MRI* | |
| Positive | 10 (25%) |
| Negative | 30 (75%) |
| *Axillary Involvement (SLNB/ALND)* | |
| Positive | 12 (30%) |
| Negative | 28 (70%) |
| *Surgery Type in Breast* | |
| Breast Conserving Surgery | 24 (60%) |
| Mastectomy | 16 (40%) |
| *Axillary Surgery Type* | |
| SLNB | 31 (77.5%) |
| SLNB+ALND | 8 (20%) |
| ALND | 1 (2.5%) |

PET-CT; positron emission tomography-computed tomography, DCE-MRI; dynamic-contrast-enhanced magnetic resonance imaging, SLNB; sentinel lymph node biopsy, ALND; axillary lymph node dissection, Her-2; human epidermal growth factor receptor-2

frozen result of sentinel lymph node was negative despite suspicion of axillary metastasis in PET-CT and no suspicion in MRI. However, micrometastasis was detected in the final pathology and ALND was not performed. In total, axillary lymph node dissection was not performed on the above mentioned three patients even though metastasis was found out in frozen section or final pathology report, according to the ACOSOG-Z011 study.

DCE-MRI revealed metastatic lymph nodes in 10 (25%) of 40 patients, however only three (30%) of them were true positive. Though, DCE-MRI of nine (75%) patients with metastasis by SLNB/ALND did not reveal any metastatic lymph nodes (Figs. 1, 2).
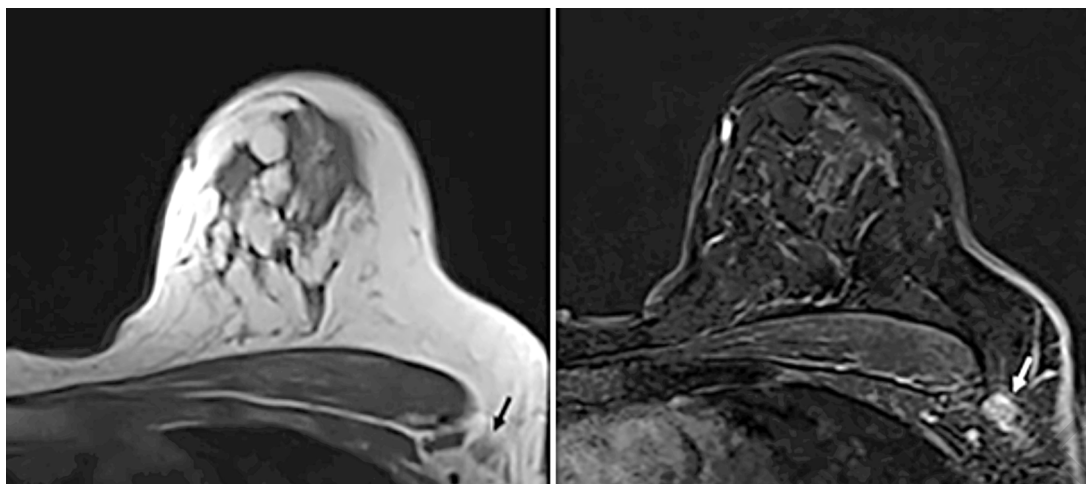
Fig. 1: Magnetic resonance imaging (MRI) of breast. A 38-year-old woman with a 22 mm mass of grade III invasive ductal carcinoma in the left breast, estrogen receptor (+), progesterone receptor (-), Human Epidermal Growth Factor Receptor-2 (-). (1a) T1-weighted axial without fat suppression and (1b) T1-weighted post-contrast fat-suppression images of a suspicious lymph node (marked with arrow) in round shape, with no visible fatty hilus. Metastasis was not detected in 7 sentinel lymph nodes.
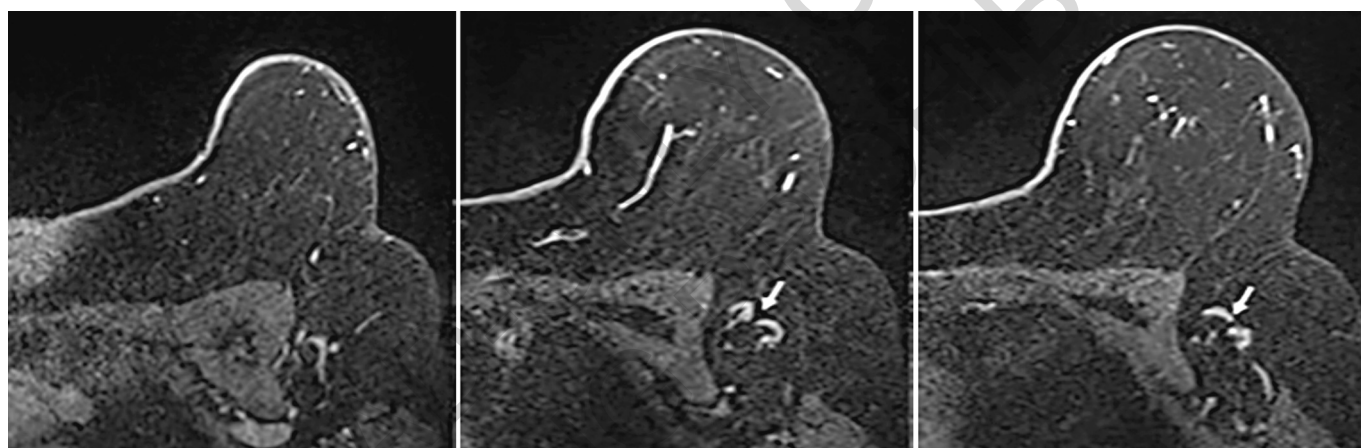


Fig. 2: Magnetic resonance imaging (MRI) of breast. Axillary lymph nodes were normal in the preoperative staging MRI examination of a 61-year-old patient diagnosed with estrogen receptor (+), progesterone receptor (+), Human Epidermal Growth Factor Receptor-2 (-), grade I invasive ductal carcinoma detected by routine screening in the left breast. Sentinel lymph node biopsy was positive and axillary dissection was performed. Metastasis was detected in two of 16 lymph nodes. T1 weighted images with axial post-contrast fat suppression showed oval-shaped lymph nodes with fat hilus and evaluated normally (arrows in 2b and 2c).

Seventeen (42.5%) patients had metastases to the axillary lymph nodes, as revealed by PET-CT, eight (47.1%) of them was false positive. No metastases were detected in the PET-CT of four patients with axillary lymph node metastasis (Figs. 3, 4). Patients' age, histologic type, pathological T stage, nuclear grade, pathological lymph node status, ER expression, PR expression, Her2 status of tumor, axillary lymph node status according to PET-CT and DCE-MRI are demonstrated in Table I. With reference to histopathological evaluation of axilla as the golden standard, true positive (TP), true negative (TN), false positive (FP), false negative (FN), sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of PET-CT and DCE-MRI are demonstrated in Table II.

TABLE II - *Assessment of axillary lymph node status with PET-CT and DCE-MRI*

| Parameters | PET-CT | DCE-MRI |
|---|---|---|
| True Positive (n) | 8 | 3 |
| True Negative (n) | 22 | 23 |
| False Positive (n) | 8 | 7 |
| False Negative (n) | 4 | 9 |
| Sensitivity (%) | 66.6 | 25 |
| Specificity (%) | 67.8 | 75 |
| PPV (%) | 47 | 30 |
| NPV (%) | 82.6 | 70 |
| Accuracy (%) | 67.5 | 60 |

PET; positron emission tomography, CT; computed tomography, DCE; dynamic-contrast-enhanced, MRI; magnetic resonance imaging, PPV; positive predictive value, NPV; negative predictive value.

TABLE III - *Comparison of PET-CT and DCE-MRI rates in evaluation of axillary involvement by McNemar's test.*

| | | Axillary involvement detected by DCE-MRI | | |
| | | Negative (n) | Positive (n) | p-value |
| --- | --- | --- | --- | --- |
| Axillary Involvement detected by PET-CT | Negative (n) | 18 | 5 | 0.143 |
| | Positive (n) | 12 | 5 | |

PET; positron emission tomography, CT; computed tomography, DCE; dynamic-contrast-enhanced, MRI; magnetic resonance imaging
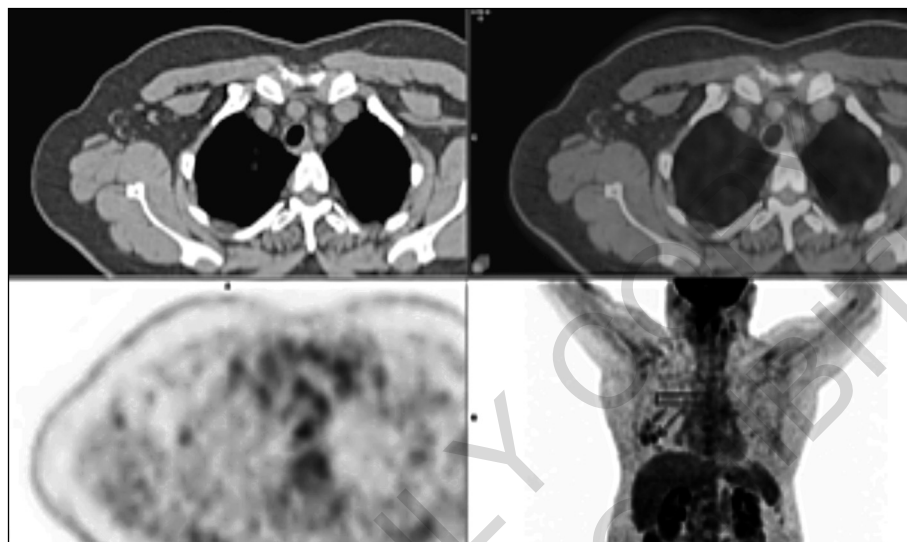


Fig. 3: 18-fluorodeoxyglucose positron emission tomography/computed tomography (PET-CT) image. Axillary lymph nodes were normal in the preoperative staging PET-CT examination of a 38-year-old patient diagnosed with estrogen receptor (+), progesterone receptor (+), Human Epidermal Growth Factor Receptor-2 (-), Grade II Invasive lobular carcinoma detected by routine screening in the left breast. When sentinel lymph node biopsy was positive, axillary dissection was performed and metastasis was detected in two of 21 lymph nodes.
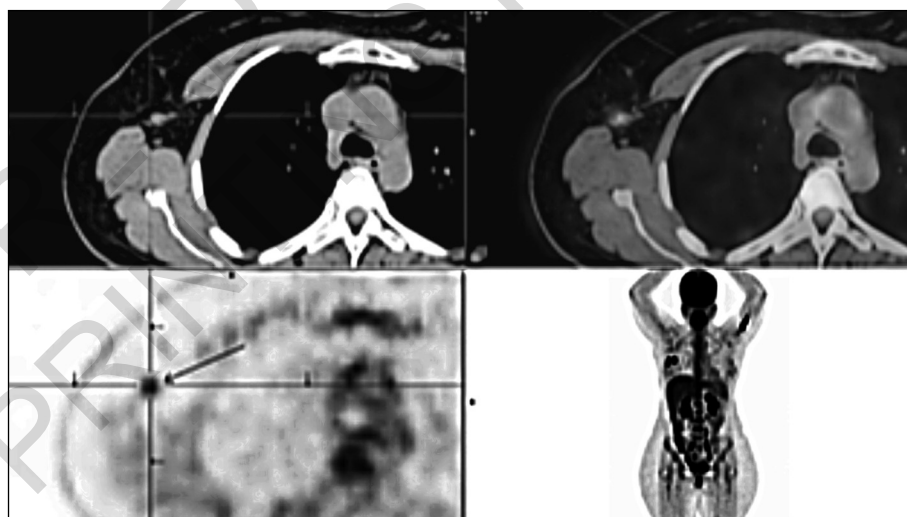


Fig. 4: 18-fluorodeoxyglucose positron emission tomography/computed tomography (PET-CT) image. A 40-year-old woman with a mass of 26 mm, estrogen receptor (+), progesterone receptor (-), Human Epidermal Growth Factor Receptor-2 (-), grade III invasive ductal carcinoma in the right breast and a suspicious lymph node in the right axilla by preoperative staging PET-CT images (arrows). Metastasis was not detected in four lymph nodes in sentinel lymph node biopsy.

In 23 of 40 patients with EBC, features of axillary lymph node involvement in PET-CT and DCE-MRI were consistent, while 17 patients were incompatible. The McNemar's test compared the status of axillary involvement between PET-CT and DCE-MRI showed no difference (p=0.143) (Table III). Additionally, correlation
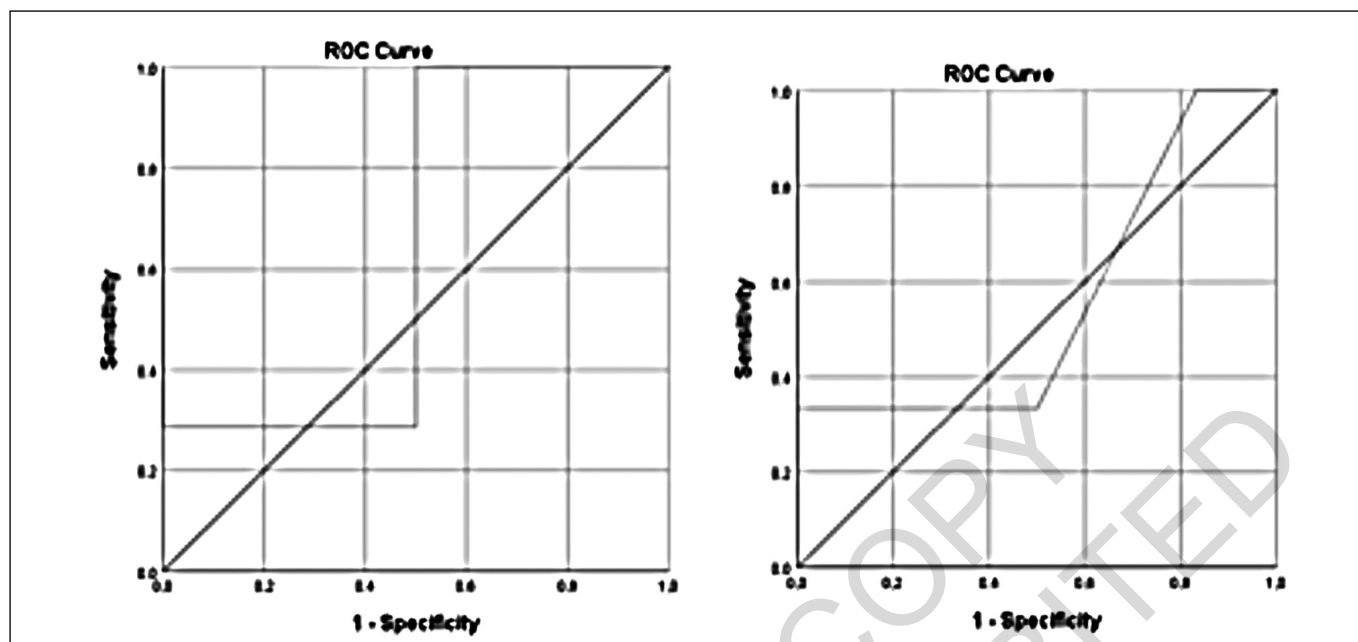
Fig. 5: Receiver operating characteristic (ROC) analysis diagram for 18-fluorodeoxyglucose positron emission tomography/computed tomography (PET-CT) and dynamic contrast enhanced-magnetic resonance imaging (MRI). The ROC analysis curves for PET-CT (left) and MRI (right) according to diameter of metastatic foci in axillary lymph nodes are given.

between two tests was also similar (r=0.088, p=0.591). According to the ROC analysis, PET-CT has 71% sensitivity and 50% specificity (AUC: 0.643; 95% CI: 0.107-1) in 4.5 mm and larger lesions for detecting metastatic foci in axillary area. On the other hand, according to the ROC analysis; DCE-MRI has 67% sensitivity and 33% specificity (AUC: 0.556; 95% CI: 0.113-0.999) in 4.5 mm and larger lesions in detection of metastatic foci in the axillary region (Fig. 5).

## Discussion

We retrospectively evaluated the performance of DCE-MRI and PET-CT to diagnose axillary lymph node status in EBC patients in current study. Although there are previous studies comparing MRI and PET-CT to identify axillary region, it is difficult to conclude the which imaging technique to prefer for the evaluation of axillary metastases from these studies as most of them were applied in clinics where only one technique (DCE-MRI or PET-CT) was preferred.

Consequently, only two studies in literature directly compared diagnostic performance of DCE-MRI and PET-CT in axilla. Ergul et al. [20] studied DCE-MRI and PET-CT performance of detecting axillary metastases in twenty-four patients and found sensitivity, specificity, PPV, NPV and accuracy values as 47%, 78%, 78%, 47%, 58% and 67%, 89%, 91%, 62%,75%, respectively. Similarly, in the present study, the diagnostic ability indicators of PET-CT were better than DCE-MRI, except for specificity.

In another prospective study by Gruneisen et al.[21], the ability of DCE-MRI and PET-CT was compared to find out axillary lymph node metastasis in forty-nine patients and found out sensitivity, specificity, PPV, NPV and accuracy as 67%, 87%, 75%, 82%, 80% and 78%, 94%, 88%, 88%, 88%, respectively.

Since that study included breast cancer diagnosed patients at all stages and the diameter of the metastatic lymph nodes were larger, we propose that these parameters indicating diagnostic predictability are high. However, in present study, only EBC patients were included and therefore we found the diagnostic performance to be lower in both radiological techniques.

Detection of axillary metastases is very important for decision-making of an appropriate surgical treatment and has importance in planning of patients' treatment. Therefore, imaging modalities that provide safer determination of patients for whom ALND is necessary will be of well utility.

Robertson et al. [22] reported 60% sensitivity and 97% specificity for detecting axillary metastases in PET-CT, in a systematic review. In another study including 236 EBC patients, Veronesi et al. [23] compared the diagnostic validity of PET-CT and SLNB to assign lymph node involvement. They showed that ALND should be applied to patients with signs of axillary lymph node involvement in PET-CT, despite low sensitivity (37%). In current study, we PET-CT was fount out to have a higher sensitivity (65%) in axillary lymph node status evaluation than their study.

In another retrospective study by Hwang et al. [24] the utility of axillary US, DCE-MRI and PET-CT was com-

pared in the axillary assessment of T1 stage breast cancer patients and DCE-MRI was shown to have the ultimate sensitivity. On the other hand, PET-CT had the highest specificity, PPV and accuracy. Three tests were compared for more than 300 T1 breast cancer diagnosed patients in terms of ALND. In that study, NPV and PPV values were calculated to evaluate axillary lymph node metastasis when these three tests were positive or negative simultaneously. NPV was found to be 84% when three tests were negative. In addition, PPV was found to be 94% when three tests were positive. Despite these high predictive values, they didn't suggest conducting PET-CT and DCE-MRI together to evaluate the axillary lymph node in EBC, since these tests are expensive.

Considering current study, DCE-MRI has lower sensitivity, PPV and NPV than PET-CT and its specificity was found to be higher. In addition, when both tests were positive, PPV was 60%, whereas both tests were negative, NPV as 74% in current patient group. When two tests were used together, PPV (PET-CT; %47, DCE-MRI;30% and both positive;60%) and NPV (PET-CT % 82.6, DCE-MRI; 70% and both negative 74%) seems to rise.

However, we don't recommend using both tests together because of the high costs.

In a meta-analysis involving 21 studies, it was shown that the sensitivity of MRI and PET-CT was 82% (95% CI: 0.78-0.85) and 64% (95% CI: 0.59-0.69), respectively, and MRI had a higher sensitivity in the screening of axillary lymph node involvement. Besides, none of the techniques was found out to have a significant difference in terms of specificity (MRI 93%, PET-CT 93%). The most important factor causing this insignificance was increasing FN and FP of DCE-MRI in addition to FN of PET-CT by decreasing diameter of the metastatic focus [25]. As a result of the ROC analysis applied in the present study, it was determined that DCE-MRI and PET-CT had balanced sensitivity and specificity in axillary metastatic foci about 4.5mm. Since the possible metastatic foci are expected to be small in clinically early stage tumors, the sensitivity and specificity of both imaging methods were found to be low in current study.

This study had following limitations. First, it was retrospective, which could result in selection bias. Second limitation was the small sample space.

In EBC, the volume of patients included in the study was low since PET-CT was only performed to a limited number of patients with special conditions such as anxiety or internal quadrant tumors.

PET-CT and DCE-MRI have low sensitivity and PPV to detect axillary lymph node involvement in comparison to SLNB in patients with EBC. Thus, routine use of PET-CT or DCE-MRI for pre-operative evaluation of axillary status is not recommended for early breast cancer patients.

## Riassunto

La valutazione dello stato del linfonodo ascellare nelle donne con carcinoma mammario è molto importante in quanto può modificare la decisione iniziale sul trattamento da adottare. Nessuno dei metodi non invasivi utilizzati per la valutazione dell'ascella è ancora accurato come la biopsia del linfonodo sentinella (SLNB). Questo studio ha confrontato le prestazioni diagnostiche della tomografia a emissione di positroni con 18-fluorodeossiglucosio/tomografia computerizzata (PET-CT) e della risonanza magnetica a contrasto dinamico (DCE-MRI) nella valutazione ascellare preoperatoria di donne con diagnosi di carcinoma mammario precoce (EBC).

Sono state analizzate retrospettivamente le cartelle cliniche di 1246 pazienti operate per EBC tra il 2016 e il 2019, analizzando i referti anatomo-patologici dei linfonodi ascellari e confrontati i dati di queste due modalità di imaging.

RISULTATI: Quaranta pazienti operate per EBC avevano sia DCE-MRI che PET-CT. Metastasi ascellari sono state rilevate in 12 pazienti (27,5%). La sensibilità, la specificità, il valore predittivo positivo (PPV), il valore predittivo negativo (NPV) e l'accuratezza di DCE-MRI/PET-CT per la determinazione delle metastasi linfonodali ascellari erano rispettivamente 25/66,6%, 75/67,8%, 30/47%, 70/82,6% e 60/67,5%.

Nessun metodo ha ancora raggiunto le prestazioni della biopsia del linfonodo sentinella nella mappatura ascellare dei pazienti con EBC. Se una paziente EBC è clinicamente sospettata di coinvolgimento ascellare in DCE-MRI o PET-CT (poiché ha PPV e sensibilità sono bassi), deve essere eseguita una biopsia.

## References

1. Grabenstetter A, Lazaro C, Turashvili G: *Editorial: Hereditary breast and ovarian cancer: current concepts of prevention and treatment.* Front Oncol 1 2020; 0:618369. doi:10.3389/fonc.2020.618369

2. Tate J, Lewis V, Archer T, Guyer P, Royle G, Taylor I: *Ultrasound detection of axillary lymph node metastases in breast cancer.* Eur J Surg Oncol, 1989; 15(2):139-41.

3. Bedi DG, Krishnamurthy R, Krishnamurthy S, Edeiken BS, LePetross H, Fornage BD, Bassett Jr RL, Hunt KK: *Cortical morphologic features of axillary lymph nodes as a predictor of metastasis in breast cancer: In vitro sonographic study.* AJR Am J Roentgenol, 2008; 191(3):646-52.

4. Cooper KL, Meng Y, Harnan S, Ward SE, Fitzgerald P, Papaioannou D, Wyld L, Ingram C, Wilkinson ID, Lorenz E: *Positron emission tomography (PET) and magnetic resonance imaging (MRI) for the assessment of axillary lymph node metastases in early breast cancer: Systematic review and economic evaluation.* Health Technol Assess, 2011; 15(4):III.

5. Kvistad KA, Rydland J, Smethurst HB, Lundgren S, Fjosne HE, Haraldseth O: *Axillary lymph node metastases in breast cancer:*

*preoperative detection with dynamic contrast-enhanced MRI.* Eur Radiol, 2000; 10 (9):1464-471. doi:10.1007/s003300000370

6. Sardanelli F, Boetes C, Borisch B, Decker T, Federico M, Gilbert FJ, Helbich T, Heywang-Köbrunner SH, Kaiser WA, Kerin MJ: *Magnetic resonance imaging of the breast: Recommendations from the EUSOMA working group.* Eur J Cancer, 2010; 46 (8):1296-316.

7. Valente SA, Levine GM, Silverstein MJ, Rayhanabad JA, Weng-Grumley JG, Ji L, Holmes DR, Sposto R, Sener SF: *Accuracy of predicting axillary lymph node positivity by physical examination, mammography, ultrasonography, and magnetic resonance imaging.* Ann Surg Oncol, 2014; 19 (6):1825-830.

8. Heusner T, Freudenberg L, Kuehl H, Hauth E, Veit-Haibach P, Forsting M, Bockisch A, Antoch G: *Whole-body PET/CT-mammography for staging breast cancer: Initial results.* Br J Radiol, 2008; 81(969):743-48.

9. Heusner TA, Kuemmel S, Umutlu L, Koeninger A, Freudenberg LS, Hauth EA, Kimmig KR, Forsting M, Bockisch A, Antoch G: *Breast cancer staging in a single session: whole-body PET/CT mammography.* J Nucl Med, 2008; 49 (8):1215-222.

10. Rosen EL, Eubank WB, Mankoff DA: *FDG PET, PET/CT, and breast cancer imaging.* Radiographics, 2007; 27 Suppl 1 (suppl_1):S215-229. doi:10.1148/rg.27si075517

11. Gradishar WJ, Anderson BO, Balassanian R, B;lair SL, Burstein HJ, Cyr A, Elias AD, Farrar WB, Forero A, Giordano SH: *Breast cancer, NCCN clinical practice guidelines in oncology.* J Natl Compr Canc Netw, 2018; 16 (3):310-20.

12. Kumar A, Kumar R, Seenu V, Gupta SD, Chawla M, Malhotra A, Mehta SN: *The role of 18 F-FDG PET/CT in evaluation of early response to neoadjuvant chemotherapy in patients with locally advanced breast cancer.* Eur Radiol, 2009; 19 (6):1347-357.

13. Seok JW, Kim Y, An YS, Kim BS: *The clinical value of tumor FDG uptake for predicting axillary lymph node metastasis in breast cancer with clinically negative axillary lymph nodes.* Ann Nucl Med, 2013; 27 (6):546-553. doi:10.1007/s12149-013-0720-x

14. Giuliano AE, McCall L, Beitsch P, Whitworth PW, Blumencranz P, Leitch AM, Saha S, Hunt KK, Morrow M, Ballman K: *Locoregional recurrence after sentinel lymph node dissection with or without axillary dissection in patients with sentinel lymph node metastases: The American College of Surgeons Oncology Group Z0011 randomized trial.* Ann Surg, 2010; 252 (3):426

15. Jung J, Kim BH, Kim J, Oh S, Kim SJ, Lim CS, Choi IS, Hwang KT: *Validating the ACOSOG Z0011 Trial Result: A Population-Based Study Using the SEER Database.* Cancers (Basel) 2020; 12 (4). doi:10.3390/cancers12040950

16. Boellaard R, Delgado-Bolton R, Oyen WJ, Giammarile F, Tatsch K, Eschner W, Verzijlbergen FJ, Barrington SF, Pike LC, Weber WA: *FDG PET/CT: EANM procedure guidelines for tumour imaging: version 2.0.* Eur J Nucl Med Mol Imaging, 2015; 42 (2):328-54.

17. Taskin F, Kalayci CB, Tuncbilek N, Soydemir E, Kurt N, Kaya H, Aribal E: *The value of MRI contrast enhancement in biopsy decision of suspicious mammographic microcalcifications: A prospective multicenter study.* Eur Radiol, 2021; 31 (3):1718-726. doi:10.1007/s00330-020-07265-y

18. Magny SJ, Shikhman R, Keppke AL: *Breast imaging reporting and data system.* In: StatPearls. Treasure Island (FL), 2021.

19. Shao N, Xie C, Shi Y, Ye R, Long J, Shi H, Shan Z, Thompson AM, Lin Y: *Comparison of the 7th and 8th edition of American Joint Committee on Cancer (AJCC) staging systems for breast cancer patients: a Surveillance, Epidemiology and End Results (SEER) Analysis.* Cancer Manag Res, 2019; 11:1433-1442. doi:10.2147/CMAR.S185212

20. Ergul N, Kadioglu H, Yildiz S, Yucel SB, Gucin Z, Erdogan EB, Aydin M, Muslumanoglu M: *Assessment of multifocality and axillary nodal involvement in early-stage breast cancer patients using 18F-FDG PET/CT compared to contrast-enhanced and diffusion-weighted magnetic resonance imaging and sentinel node biopsy.* Acta Radiol, 2015; 56 (8):917-23.

21. Grueneisen J, Nagarajah J, Buchbender C, Hoffmann O, Schaarschmidt BM, Poeppel T, Forsting M, Quick HH, Umutlu L, Kinner S: *Positron emission tomography/magnetic resonance imaging for local tumor staging in patients with primary breast cancer: a comparison with positron emission to mography/computed tomography and magnetic resonance imaging.* Invest Radiol, 2015; 50 (8):505-13.

22. Robertson IJ, Hand F, Kell MR: *FDG-PET/CT in the staging of local/regional metastases in breast cancer.* Breast, 2011; 20 (6):491-94.

23. Veronesi U, De Cicco C, Galimberti V, Fernandez J, Rotmensz N, Viale G, Spano G, Luini A, Intra M, Veronesi P: *A comparative study on the value of FDG-PET and sentinel node biopsy to identify occult axillary metastases.* ESMO Open, 2007; 18(3):473-78.

24. Hwang SO, Lee SW, Kim HJ, Kim WW, Park HY, Jung JH: *The Comparative Study of Ultrasonography, Contrast-Enhanced MRI, and (18)F-FDG PET/CT for Detecting Axillary Lymph Node Metastasis in T1 Breast Cancer.* J Breast Cancer, 2013; 16 (3):315-21. doi:10.4048/jbc.2013.16.3.315

25. Liang X, Yu J, Wen B, Xie J, Cai Q, Yang Q: *MRI and FDG-PET/CT based assessment of axillary lymph node metastasis in early breast cancer: A meta-analysis.* Clin Radiol, 2017; 72(4):295-301.