Analysis of the relationship between ^{18}F-FDG PET/CT and ultrasound BI-RADS classification and their combined application in the diagnosis of breast diseases

Zhuanning Han[1] **MD,**
Xuping Shen[2] **MD,**
Rongrong Wang[3] **MD**

1. Department of Ultrasound, The Second Affiliated Hospital of Xi'an Medical University, Xi'an, China
2. Department of Ultrasound, Tongxiang First People's Hospital, Tongxiang, China
3. Department of Ultrasound, Xi'an Traditional Chinese Medicine Hospital, Xi'an, China

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Corresponding author:
Rongrong Wang MD,
Department of Ultrasound, Xi'an Traditional Chinese Medicine Hospital, Xi'an, China
357352663@qq.com

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Abstract

Objective: To analyze the relationship between fluorine-18-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography/computed tomography (PET/CT) and ultrasound breast imaging reporting and data system (BI-RADS) classification, and to evaluate the diagnostic value of their combined application in breast diseases. **Subjects and Methods:** A retrospective analysis was conducted on the ^{18}F-FDG PET/CT images and ultrasound BI-RADS classification data of 110 patients with suspected breast cancer treated at our hospital from July 2020 to May 2022. Pearson correlation analysis was used to assess the relationship between the maximum standardized uptake value (SUVmax) and BI-RADS classification. Using pathology or long-term follow-up results as the "gold standard," the diagnostic value of ^{18}F-FDG PET/CT, ultrasound BI-RADS classification, and their combined application in breast diseases was analyzed. **Results:** Based on the "gold standard" of pathology or long-term follow-up, of the 110 patients with suspected breast cancer, 49 were benign, and 61 were malignant. The SUVmax levels of malignant lesions were significantly higher than those of benign lesions ($P<0.05$). Pearson correlation analysis indicated a low correlation between SUVmax and ultrasound BI-RADS classification ($r=0.458$, $P<0.05$). Receiver operating characteristic (ROC) curve analysis showed that the area under the curve (AUC) of the combined application of SUVmax and ultrasound BI-RADS classification was higher than that of either method alone, both for breast tumors and for patients classified as BI-RADS category 3 to 4. **Conclusion:** The correlation between SUVmax and ultrasound BI-RADS classification is low ($r=0.458$), indicating that these two methods assess different biological aspects of breast tumors. However, the combined use of SUVmax and BI-RADS classification significantly enhances diagnostic accuracy, particularly for patients with BI-RADS 3 to 4 lesions. Although this combination improves diagnostic efficacy, ^{18}F-FDG PET/CT should not be used as a primary screening tool but rather as a complementary method in specific clinical scenarios where imaging findings are inconclusive or suspicion of malignancy is high.

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Introduction

Breast cancer is one of the most common malignant tumors in women worldwide, characterized by a high incidence, rapid disease progression, and significant variability in prognosis [1]. According to statistical data [2], breast cancer has surpassed lung cancer to become the most frequently diagnosed type of cancer globally, accounting for a major proportion of cancer-related deaths among women. The incidence of breast cancer in China is also increasing year by year, making early diagnosis and treatment crucial for improving patient survival and prognosis [3]. Effectively distinguishing between benign and malignant breast lesions and providing rapid and accurate clinical evidence for diagnosis and treatment is a significant challenge in the field of breast disease diagnosis.

In the imaging diagnosis of breast diseases, ultrasound examination is widely used for breast tumor screening and preliminary diagnosis due to its non-invasive nature, lack of radiation, and ease of operation [4]. The breast imaging reporting and data system (BI-RADS) classification provides clinicians with a standardized approach to breast imaging diagnosis [5]. Breast imaging reporting and data system classifies breast lesions into six categories, with categories 1 to 3 considered benign, category 4 suspicious for malignancy, category 5 highly suggestive of malignancy, and category 6 confirmed malignancy. Through this classification system, clinicians can make preliminary judgments on the nature of breast tumors and decide on further treatment plans. However, the BI-RADS classification system exhibits relatively low specificity in certain cases, such as BI-

RADS category 3 and 4, where the risk of misdiagnosis or missed diagnosis remains [6]. Therefore, optimizing existing diagnostic methods to improve accuracy has become a research focus.

Positron emission tomography/computed tomography (PET/CT), which combines functional and anatomical imaging, has gradually been applied in the diagnosis of breast diseases in recent years [7]. Fluorine-18-fluorodeoxyglucose (^{18}F-FDG) PET/CT detects glucose metabolism in tumor cells, allowing for the evaluation of tumor metabolic activity. Malignant tumor cells typically exhibit a high metabolic rate, which is reflected as high uptake values on ^{18}F-FDG PET/CT images [8]. The maximum standardized uptake value (SUVmax), as a primary quantitative metric for assessing metabolic activity on PET/CT images, has been widely used in the diagnosis, staging, and therapeutic evaluation of breast cancer. A higher SUVmax usually indicates a higher degree of malignancy, providing critical clinical insights [9]. However, PET/CT has its limitations, with high examination costs making it unsuitable for breast cancer screening. Additionally, its sensitivity may decrease in detecting small lesions or tumors with low metabolic activity. Given these considerations, this study retrospectively analyzed the imaging data of 110 patients with suspected breast cancer to explore the relationship between ^{18}F-FDG PET/CT and ultrasound BI-RADS classification, and to assess the value of their combined application in the diagnosis of breast diseases, with the aim of providing more accurate clinical diagnostic evidence.

Subjects and Methods

Study subjects

This study used a retrospective analysis method, selecting patients who underwent breast examinations in the PET/CT center of our hospital from July 2020 to May 2022. The study subjects included patients who underwent PET/CT examinations due to breast nodules or breast space-occupying lesions, as well as cases where abnormal metabolic activity in breast tissue was incidentally found during other examinations. To ensure accuracy, the following patients were excluded: those without ultrasound BI-RADS classification results, those lacking clear pathological diagnoses, or those with a follow-up period of less than two years. Ultimately, 110 patients with suspected breast cancer were included in the study, none of whom had received any treatment related to breast disease (such as surgery, chemotherapy, or radiotherapy) prior to the examination. Additionally, all included patients were not pregnant or breastfeeding, avoiding interference with imaging results due to physiological changes. All patients were fully informed of the study's purpose and examination content before participating and signed a written informed consent form. The study protocol was approved by the Medical Ethics Committee of our hospital.

Examination methods

^{18}F-FDG PET/CT image acquisition

Fluorine-18-FDG PET/CT scans were performed using a Siemens Biograph 64 HD PET/CT instrument. To ensure accuracy, patients fasted for 6 hours before the scan, and blood glucose was controlled below 6.5mmol/L. After 15 minutes of rest in a supine position, ^{18}F-FDG was injected intravenously at a dose of 5.55MBq/kg. After the injection, the patient remained at rest for 60 minutes to allow the drug to fully distribute, followed by a whole-body PET/CT scan. The scan range extended from the base of the skull to the upper femur, ensuring coverage of all major areas of the body. The specific CT scan parameters were a voltage of 120kV, current adjusted between 40-100mA according to the patient's weight. The scan slice thickness was 3.75mm, and the bed movement speed was 3.7mm/bed position. Image reconstruction used a slice thickness of 0.625-5.000mm. Positron emission tomography scan parameters included 2 minutes per bed position with three-dimensional acquisition technology. OSEM image reconstruction was used, and the reconstructed images were displayed in coronal, sagittal, and transverse planes, merged with CT images to provide more intuitive anatomical and metabolic information.

Ultrasound examination

Ultrasound examinations were performed using a GE Logiq 9 ultrasound diagnostic instrument, with probe frequencies set between 10-12MHz. During the operation, the ultrasound physician recorded details based on the lesion's shape, edge clarity, internal echo distribution, long-axis orientation, and posterior echo characteristics. All important sonographic data were saved in the imaging workstation for subsequent analysis and comparison.

Image Analysis

PET/CT images

All PET/CT scan results were interpreted by two experienced nuclear medicine specialists to ensure diagnostic reliability and consistency. First, visual interpretation was used to identify areas of high metabolic activity in the breast. Any area with ^{18}F-FDG uptake higher than the background breast tissue was considered an area of abnormal metabolic activity. After identifying areas of high metabolic activity, the physician measured the SUVmax of that region for semi-quantitative analysis. Maximum SUV reflects the maximum radiotracer uptake in a region of interest (ROI), and is calculated using the formula: SUV=radioactivity concentration in the ROI/injected dose/patient weight. To further analyze the diagnostic value of PET/CT and ultrasound BI-RADS classification in assessing breast lesions, only the primary lesions in the breast were analyzed during image interpretation, excluding factors such as lymph node metastasis and distant metastasis.

BI-RADS classification

Breast ultrasound examinations were performed by two experienced attending physicians or higher, and lesions were described according to BI-RADS standards [10]. The specific BI-RADS classification criteria and recommended treatment options are shown in Table 1.

Pathological examination

Table 1. Ultrasound BI-RADS classification criteria and recommended treatment options.

Classification	Diagnosis	Recommended Treatment
0	Incomplete imaging evaluation, requires further assessment	Suggest combination with other tests
1	Negative	Suggest follow-up
2	Consider benign	Suggest regular follow-up (1 year)
3	High likelihood of benign (2% malignancy)	Suggest regular follow-up (3-6 months)
4A	Low likelihood of malignancy	Suggest biopsy for confirmation
4B	Moderate likelihood of malignancy	Suggest biopsy for confirmation
4C	Atypical concern (non-typical malignant signs)	Suggest biopsy for confirmation
5	High suspicion of malignancy (95%)	Take appropriate action
6	Pathologically confirmed malignancy	Surgical resection

Diagnoses were made based on pathological and immunohistochemical results obtained from surgery or biopsy. For patients without pathological sampling, follow-up was conducted for more than two years, with the follow-up period ending in May 2024. Diagnoses were made based on the final follow-up results.

Statistical analysis

GraphPad Prism 8 software was used for graphing, and SPSS 22.0 software was used for data processing. Categorical data were expressed as [n(%)], and the chi-square test was used. Normally distributed continuous data were expressed as $\bar{x} \pm s$ and independent sample t-tests were used for intergroup comparisons. Pearson correlation analysis was used to examine the relationship between SUVmax and BI-RADS classification. The diagnostic value of ^{18}F-FDG PET/CT and ultrasound BI-RADS classification in breast disease was analyzed using pathology or long-term follow-up results as the "gold standard." P<0.05 was considered statistically significant.

Results

Pathological examination

Among the 110 patients who met the inclusion criteria, the minimum age was 23 years, the maximum age was 78 years, and the average age was (47.35±10.12) years. Of these, 49 cases were benign, and 61 cases were malignant. The 49 benign cases included 28 fibroadenomas, 4 inflammatory cases, 2 cases of fat necrosis, and 15 lesions identified as benign after more than two years of follow-up. The 61 malignant cases included 51 invasive ductal carcinomas, 5 intraductal carcinomas, 3 invasive lobular carcinomas, and 2 undifferentiated carcinomas.

Comparison of SUVmax levels

The average SUVmax of all lesions was (3.86±3.27), with the benign lesions having an average SUVmax of (1.85±1.12) and the malignant lesions having an average SUVmax of (5.49± 3.51). The SUVmax levels of malignant lesions were significantly higher than those of benign lesions (P<0.05), as shown in Figure 1.

Relationship between SUVmax and ultrasound BI-RADS classification

During the collection of ultrasound BI-RADS classification data, it was found that the number of patients in specific subcategories of BI-RADS 4 was small, so these patients were combined into the BI-RADS 4 category for analysis. Among all lesions, 14 cases were classified as category 1 (12.73%), 5 cases as category 2 (4.55%), 18 cases as category 3 (16.36%), 31 cases as category 4 (28.18%), and 42 cases as category 5 (38.18%). In benign lesions, 14 cases were category 1 (28.57%), 4 cases were category 2 (8.16%), 16 cases were category 3 (32.66%), 14 cases were category 4 (28.57%), and 1 case was category 5 (2.04%). In malignant lesions, there were no cases in category 1 (0.00%), 1 case in category 2 (1.64%), 2 cases in category 3 (3.28%), 17 cases in category 4 (27.87%), and 41 cases in category 5 (67.21%). In Pearson correlation analysis, SUVmax sho-a low correlation with ultrasound BI-RADS classification (r= 0.458, P<0.05), as shown in Figure 2.

Analysis of diagnostic efficacy of SUVmax, ultrasound BI-RADS classification, and their combined application

Receiver operating characteristic curve analysis showed that for both breast tumors and patients classified as BI-RADS 3-4, the combined application of SUVmax and ultrasound BI-RADS classification had a higher AUC than single diagnosis methods, as shown in Table 2, Figure 3, and Table 3, Figure 4.

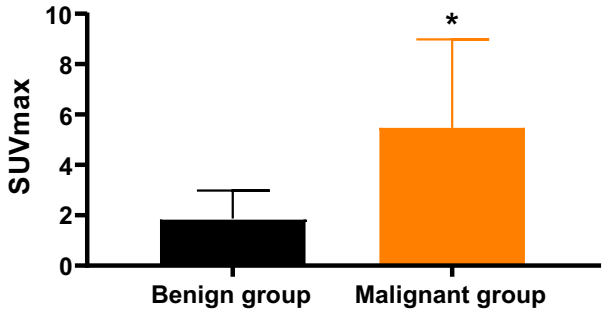

Figure 1. Comparison of SUVmax levels $\bar{x} \pm s$. Note: *P<0.05, indicates a statistically significant difference between groups.

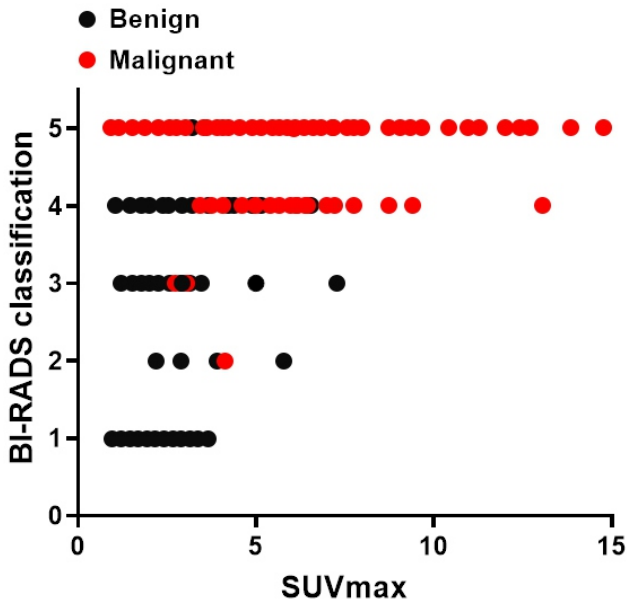

Figure 2. Relationship between SUVmax and ultrasound BI-RADS classification.

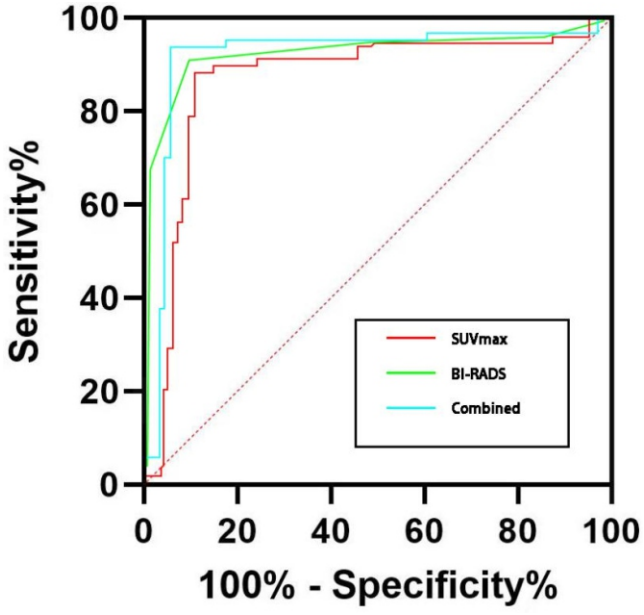

Figure 3. ROC curve for diagnostic efficacy in breast tumors.

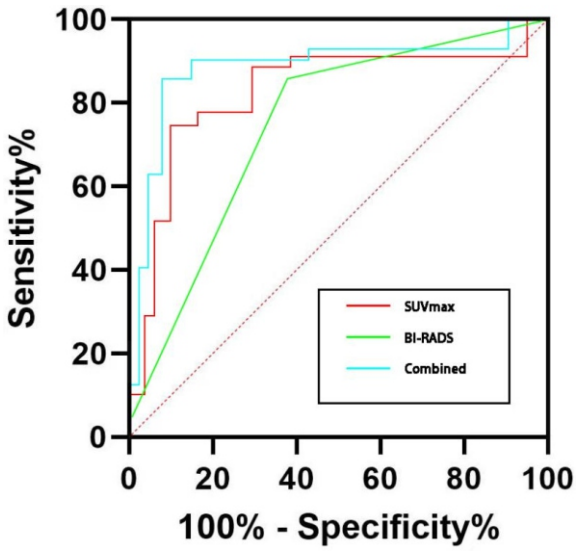

Figure 4. ROC curve for diagnostic efficacy in patients with BI-RADS classification 3-4.

Table 2. *Analysis of diagnostic efficacy in breast tumors.*

Index	Cut-off value	AUC	95% CI	P	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
SUVmax	2.113	0.882	0.795~0.941	＜0.05	89.09	73.64	80.91	84.55
Ultrasound BI-RADS	-	0.917	0.832~0.959	＜0.05	94.55	69.55	79.09	91.36
Combined application	-	0.948	0.867~0.976	＜0.05	97.67	89.82	90.13	95.48

Table 2. *Analysis of diagnostic efficacy in patients with BI-RADS classification 3-4.*

Index	Cut-off value	AUC	95% CI	P	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
SUVmax	2.179	0.861	0.784~0.913	＜0.05	88.78	71.43	67.35	90.82
Ultrasound BI-RADS	-	0.707	0.653~0.776	＜0.05	87.76	44.90	51.05	86.73
Combined application	-	0.906	0.845~0.947	＜0.05	93.51	82.96	72.69	94.17

Discussion

At present, the primary screening methods for breast tumors rely heavily on mammography and breast ultrasound examinations [11]. With continuous advancements in ultrasound technology, the accuracy and sensitivity of breast ultrasound in detecting breast masses have significantly improved [12]. However, despite its advantages of being non-invasive, convenient, and providing real-time imaging, ultrasound results are often limited by the lack of standardized diagnostic criteria, leading to significant subjectivity in diagnoses and variability based on physician experience [13]. The introduction

of the BI-RADS classification has effectively standardized ultrasound reporting, improving diagnostic consistency and reducing subjectivity [14]. While BI-RADS improves diagnostic accuracy, particularly in distinguishing between benign and malignant lesions, its specificity decreases in BI-RADS categories 3 and 4, leading to higher rates of false positives [15]. This is corroborated by this study, which found that while the sensitivity of the BI-RADS classification in diagnosing all patients was 94.55%, its specificity was only 44.90% in patients classified as BI-RADS 3 and 4. This limitation results in higher rates of unnecessary biopsies or surgeries [16].

Compared to ultrasound, ^{18}F-FDG PET/CT has certain advantages in detecting early-stage breast cancer and differentiating between benign and malignant lesions, as it assesses the metabolic activity of tumors [17]. Malignant tumors tend to exhibit higher ^{18}F-FDG uptake, reflected by elevated SUVmax values, which correlate with tumor metabolic intensity, size, and location [18]. Positron emission tomography/CT is particularly useful in evaluating lymph node and distant metastases, providing comprehensive information for clinical decision-making. Multiple meta-analyses have demonstrated the sensitivity of PET/CT for breast cancer diagnosis to be between 85% and 95%, with specificity ranging from 80% to 95% [19, 20]. These findings are consistent with this study, which showed that the combined application of SUVmax and BI-RADS classification significantly improved diagnostic accuracy over either method used alone.

However, ^{18}F-FDG PET/CT has limitations in certain histological subtypes of breast cancer, such as lobular carcinoma, and in smaller tumors, particularly those less than 1 cm in size. Fluorine-18-FDG uptake is not exclusive to malignant tumors; benign tumors, such as fibroadenomas, and inflammatory lesions can also exhibit high ^{18}F-FDG uptake, which reduces the specificity of PET/CT in these cases. Therefore, this study does not advocate the use of PET/CT as a primary screening tool. Instead, the focus is on its diagnostic advantages when combined with ultrasound BI-RADS classification. The results suggest that this combined diagnostic approach significantly improves accuracy in challenging cases, particularly in patients categorized as BI-RADS 3 and 4, where ultrasound alone often struggles to differentiate between benign and malignant lesions.

The correlation between SUVmax and BI-RADS classification was found to be relatively low (r=0.458) in this study. This reflects the differing mechanisms by which these two modalities assess breast lesions. Maximum SUV evaluates metabolic activity, whereas BI-RADS classification is based on morphological characteristics seen on ultrasound [22, 23]. Since metabolism and morphology do not always align, combining both approaches offers a more comprehensive view of tumor biology, thus improving diagnostic performance. For example, PET/CT metabolic assessment can enhance diagnostic confidence in BI-RADS 3 and 4 cases, where ultrasound findings may be ambiguous, thereby reducing unnecessary biopsies or surgeries.

Limitations

There are several limitations to this study. First, the sample size was relatively small, particularly in the subset of patients classified as BI-RADS 3 and 4, which may limit the generalizability of the findings. Second, the retrospective design may introduce selection bias and information bias. Additionally, the study focused on SUVmax and BI-RADS classification at the time of diagnosis, without assessing patients' treatment responses or long-term prognosis. Therefore, it was not possible to evaluate the role of SUVmax and BI-RADS in predicting treatment outcomes. Finally, the accessibility and cost of PET/CT remain barriers to widespread clinical use, as many patients may not have access to this technology. This study was conducted in a single center, and the results may not be applicable to other healthcare settings with different populations or diagnostic capabilities. Future research should focus on larger, multi-center studies and incorporate long-term follow-up to better understand the clinical value of combining ^{18}F-FDG PET/CT with ultrasound BI-RADS classification.

In conclusion, this study demonstrates that the combined application of ^{18}F-FDG PET/CT and ultrasound BI-RADS classification significantly enhances the diagnostic accuracy for breast diseases, particularly in patients categorized as BI-RADS 3 and 4. The findings suggest that the combined use of these two methods allows for a more comprehensive assessment of breast tumors, reducing misdiagnosis rates and improving clinical decision-making. However, it is not recommended that PET/CT be routinely applied to all BI-RADS 3-4 patients. Instead, PET/CT should be considered a supplementary tool in specific clinical contexts, particularly when ultrasound findings are inconclusive or there is a strong suspicion of malignancy. Future studies should further explore the clinical value of this combined diagnostic approach to align it with current breast cancer screening and diagnostic guidelines.

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