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Which type of breast cancers is undetectable on ring-type dedicated breast PET?

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ABSTRACT

Objectives: To assess the factors causing tumor undetectability on ring-type dedicated breast positron emission tomography (DbPET).
Methods: A total of 265 patients (288 tumors) underwent DbPET and contrast-enhanced magnetic resonance imaging (MRI) in a prone position. The distance between the shallowest part of the breast tumor and the front end of the pectoralis major muscle on MRI was considered as the tumor-to-chest wall distance.
Results: Twenty-four tumors (8.3%) were not visualized via DbPET. The tumor-to-chest wall distance for undetectable tumors was shorter than that of the detectable tumors (23.0 mm vs 38.5 mm, $P < 0.001$). Multivariate analysis indicated that proximity to the chest wall and low-grade tumors were independent predicting factors for undetectable cancers. Among the 24 undetectable cancers, 15 tumors were proximal to the chest wall, suggesting that they were outside or at the edge of field of view (FOV), and 7 were low-grade tumors, suggesting insignificant ^{18}F-fluorodeoxyglucose (FDG) uptake.
Conclusions: The factors of undetectable breast cancers on DbPET are classified into two types; outside or at the edge of FOV and insignificant FDG uptake.

1. Introduction

Breast cancer is the most common cancer occurring in adult women and accounts for approximately 30% of the total cancer incidence [1]. Mammography screening has been shown to reduce the breast cancer mortality in randomized controlled trials [2]. However, small tumors, particularly in dense breasts characteristic of young women, are hard to detect on mammography. Positron emission tomography (PET) is a molecular approach for cancer imaging, and dedicated breast PET (DbPET) was developed for high-resolution molecular breast imaging. DbPET may overcome the limitation of mammography for young women and small breast cancers. Molecular breast imaging in addition to mammography for screening tumors in dense breast was reported to reduce the cost per cancer diagnosis compared with mammography alone [3].

DbPET is classified into opposite- and ring-type scanners [4]. The opposite-type DbPET, such as positron emission mammography (PEM), has higher sensitivity for breast imaging than whole-body PET (WBPET) [5], whereas the sensitivity of ring-type DbPET is comparable to WBPET [6,7]. However, ring-type DbPET may be particularly ideal for small lesions (< 5 mm) because it has improved resolution and thus better lesion detection capability compared with WBPET [7]. Previous studies of DbPET highlighted only the detectability of breast cancer, and the cause of undetectability has not been investigated.

We hypothesized that DbPET has limited detection capability in lesions with lesser ^{18}F-fluorodeoxyglucose (FDG) accumulation as with WBPET and also has an imaging range not applicable to WBPET. Therefore, we investigated the tumor location including the tumor-to-chest wall distance and the histological malignant features, to determine how to address such limitations of DbPET. This is the first report considering the objective factors for the undetectability of breast cancer on DbPET.

Abbreviations: AUC, area under the curve; CI, confidence interval; DbPET, dedicated breast positron emission tomography; FDG, ^{18}F-fluorodeoxyglucose; FOV, field of view; HER2, human epidermal growth factor receptor 2; MRI, magnetic resonance imaging; PEM, positron emission mammography; PET, positron emission tomography; SUVmax, maximum standardized uptake value; WBPET, whole-body positron emission tomography

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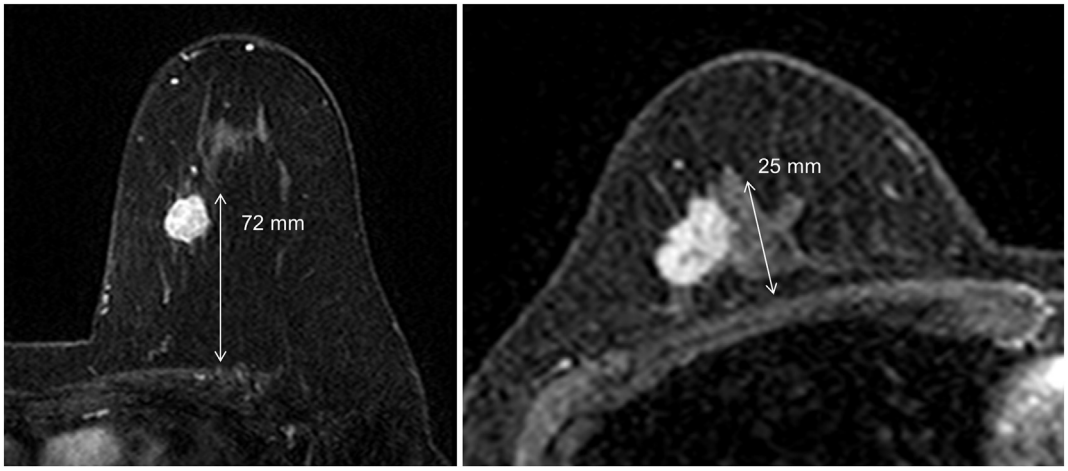

Fig. 1. Method of measuring the tumor-to-chest wall distance. The distance between the shallowest part of the breast tumor and the front of the large pectoralis muscle on contrast-enhanced magnetic resonance imaging was measured.

2. Patients and methods

2.1. Patients

Among patients histologically diagnosed with breast cancer between January 2016 and May 2017 at the Hiroshima University Hospital, 303 patients (329 tumors) who received ring-type DbPET were included in this study. Of them, 271 patients (294 tumors) who underwent contrast-enhanced magnetic resonance imaging (MRI) were included, and 6 patients (6 tumors) whose tumors were not detected via MRI were excluded because the tumor-to-chest wall distance could not be measured. Finally, 265 patients (288 tumors) were assessed. The Institutional Review Board of the Hiroshima University Hospital approved this study. All procedures performed involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. For this type of study, formal consent is not required.

2.2. DbPET examination

All DbPET examinations were performed with whole-body PET. Patients fasted for at least 4 h before the FDG injection (3–3.7 MBq/kg). Whole-body PET scanning was performed 1 h after the FDG administration, and DbPET was performed immediately thereafter while patients are in prone position using an Elmammo scanner (Shimadzu, Kyoto, Japan; LGSO/1.44 × 1.44 × 18 mm). The field of view (FOV) was 185 × 156.5 mm; the scan time was 7 min per bed position; and the acquired data were reconstructed as 236 × 236 matrix images (pixel size, 0.78 × 0.78 mm) using 3-dimensional dynamic row-action maximum likelihood algorithm.

PET image evaluation and quantification of the maximum standardized uptake value (SUVmax) were performed using Xeleris workstation version 1.1452 (GE Healthcare, Little Chalfont, UK). Regions of interest were delineated within the primary tumor on attenuation-corrected FDG-PET images and within the ipsilateral normal breast tissue for the background uptake, and the SUVmax was measured. All PET images were read by two professionals: a radiologist and a breast cancer specialist.

2.3. Pathological diagnosis

The breast tumor samples were collected via core-needle biopsy or surgery. The histopathological characteristics, such as histology, nuclear grade, hormonal receptor and human epidermal growth factor receptor 2 (HER2) status, and Ki-67 labeling index were evaluated.

2.4. Measuring the tumor-to-chest wall distance

The tumor-to-chest wall distance, defined as the length between the shallowest part of the breast tumor and the front of the large pectoralis muscle, was measured on the axial image of contrast-enhanced MRI by a breast cancer specialist (Fig. 1).

2.5. Statistics

The summarized data are presented as numbers and percentages or means ± standard deviation unless otherwise stated. Frequencies were compared using Fisher's exact test for categorical variables. Meanwhile, the continuous variables were compared using *t*-test. Receiver operating characteristic curves of the parameters were drawn to determine the cutoff value. Logistic regression analysis was used to predict the obscured tumors. $P < 0.05$ was considered statistically significant. All statistical analyses were performed with EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria) [8].

3. Results

The characteristics of the 265 patients (288 tumors) are summarized in Table 1. Twenty-four tumors (8.3%) were undetectable on DbPET. DbPET detected 90.9% of carcinoma in situ and 93.8% of microinvasive carcinoma, whereas 25.0% of invasive lobular carcinoma tumors were not visualized. A total of 14 (13.7%) of the 102 tumors in the upper-inner and lower-inner quadrants of the breast were undetectable. The tumor-to-chest wall distance of the undetectable tumors was shorter than that of the detectable tumors (23.0 ± 18.1 mm vs 38.5 ± 21.1 mm; $P < 0.001$; Fig. 2a), and the cutoff for predicting undetectable tumors was 16 mm (area under the curve [AUC]: 0.744; 95% confidence interval [CI]: 0.617–0.870; Fig. 2b). We considered 3 parameters as the tumor-to-chest wall distance, namely, the deepest part, the center, and the shallowest part of the breast tumor, and the shallowest part was found to be the most suitable (Supplementary Fig. S1). The relationship between location and biological features and detectability of breast cancers on DbPET is shown in Table 2. Inner location (i.e., upper- and lower-inner quadrants of the breast), small-sized tumor (≤10 mm), proximity to the chest wall (≤15 mm), and low-grade tumor were associated with undetectability on DbPET. The breast cancers proximal to the chest wall were fewer at outer location than inner location, and the AUCs of the tumor-to-chest wall distance for undetectability were 0.821 (95% CI: 0.667–0.974) at inner location and