Original Article

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What is the Diagnostic Performance of 18F-FDG-PET/MRI in the Detection of Bone Metastasis in Patients with Breast Cancer?

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ABSTRACT

Objective: To evaluate the diagnostic performance of 18F-fluorodeoxyglucose (FDG)-positron emission tomography (PET)/magnetic resonance imaging (MRI) in the detection of bone metastasis in patients with breast cancer.

Materials and methods: From August 2018 to January 2019, a total of 23 patients with pathologically confirmed invasive breast cancer underwent whole-body hybrid 18F-FDG -PET/MRI for initial staging and follow-up of their malignancies. The number of the bone metastasis was recorded for each patient. The total 18F-FDG-PET/MRI protocol was compared with PET only and the contrast enhanced fused (CE) component for the detection of bone metastasis.

Results: Eight (26%) of 23 patients had bone metastasis. Bone metastases were dominantly localized in the spine (63%) and pelvis (25%). In terms of the total number of detected bone metastasis, there was a statistically significant difference between 18F-FDG-PET/MRI (mean 3.57; median 0; range, 0-2) and PET only component (mean 2.87; median 0; range, 0-1) (p=0.026), but no statistically significant difference was detected between 18F-FDG-PET/MRI and whole-body CE MRI (mean 3.43; median 0; range 0-2) (p=0.083).

Conclusion: Whole-body hybrid 18F-FDG-PET/MRI is superior to PET component only, but no statistically significant difference between hybrid 18F-FDG-PET/MRI and whole-body CE MRI is found for the detection of bone metastasis in patients with breast cancer.

Keywords: 18F-fluorodeoxyglucose (FDG) positron emission tomography (PET)/magnetic resonance imaging (MRI), breast cancer, bone metastasis

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Introduction

Breast cancer is the most frequent cancer in women and initial staging and follow-up is very important for treatment and survival. The presence of distant metastases at the initial examination changes the treatment strategy and options. The most frequent locations for breast cancer metastasis include the liver, lungs, and bone (1). 18F-fluorodeoxyglucose (FDG)-positron emission tomography (PET) and whole-body magnetic resonance imaging (MRI) are generally used for initial staging or when distant metastases are suspected (2-4). Whole-body hybrid FDG-PET/MRI is another modality that provides initial staging and may also improve the detection of metastases and recurrent disease (5-11). PET/MRI scanners have the potential to become an effective tool for the evaluation of oncology patients and influence patient management (12, 13). FDG-PET/MRI combines the sensitivity of molecular imaging of PET and the superior radiologic diagnostic capabilities of MRI. In addition, FDG-PET/MRI provides detailed background anatomic landmarks from MRI images.

Bone metastases are seen in 8% of all patients with breast cancer and the percentage increases with advanced disease (14-16). Tumor cells spread hematogenously and at the beginning intramedullary lesions are found in the red marrow. The lesions can be osteolytic, osteoblastic or mixed (17). Bone scintigraphy is used widely for its low cost and ability to cover whole-body (18). However, FDG-PET/CT has been shown to be an effective tool for the staging and detection of bone metastasis (19-21). Whole-body CE MRI, with its bone marrow-sensitive techniques, has been shown to have higher sensitivity than FDG-PET/CT for the detection of bone metastasis. Hence, a combination of metabolic information provided by FDG-PET/CT and the high soft tissue resolution of MRI increases the detection rate of bone metastasis.

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Materials and Methods

In our study, we retrospectively evaluated 23 patients with invasive breast cancer from August 2018 to January 2019. The Bilim University Institutional review board approved the study; the requirement of informed consent was waived because the study was a retrospective investigation. Inclusion criteria were newly diagnosed or recurrent breast cancer with clinical indication for staging and follow-up. Exclusion criteria were MRI general contraindications, pregnancy and patients with less than 12 months follow-up and no pathology reports. Six of the patients had prior FDG PET/CT and 3 of them had bone scintigraphy in other institutions. Also, 3 of the patients had CE MRI and 1 of them had FDG-PET/MRI in our institution. We extracted the results from their reports. For the rest of 10 patients, FDG-PET/MRI was the initial imaging for staging and follow-up.

All patients fasted for at least 6 hours before imaging. The blood glucose level was assessed with a blood glucose meter (OneTouch Vita; LifeScan, Milpitas, California, USA) before imaging to ensure that it was less than 140 mg/dL (7.77 mmol/L).

18F-FDG-PET/MRI was performed 60±6 minutes after the injection of FDG (mean dose, 4.54 MBq per kilogram of body weight±1; range, 370-400 MBq). The images were acquired with the patient in the supine position on a 3 Tesla Biograph mMR scanner (Siemens Healthcare, Erlangen, Germany) using a 16-channel head and neck surface coil and three 12-channel body coils. The whole-body images were obtained in five to six bed positions according to the size of the patient. PET acquisition occurred simultaneously during the whole-body MRI acquisition. In all patients, the whole-body FDG-PET/MRI covered the entire body from head to knee. PET attenuation correction was performed using four-compartment model attenuation map calculated from a Dixon-based VIBE (volumetric interpolated breath-hold examination) sequence. The MRI protocol consisted of T2-weighted single-shot echo train (HASTE) (TR/TE, 1500 msec / 87 msec) in the coronal plane, T1-weighted slice-selective Turbo Flash (TR/TE, 1600 msec / 2.5 msec) and free breath diffusion-weighted imaging using the Ecoplanar Imaging technique (EPI)(TR/TE, 12000 msec / 78 msec, b=0 s/mm^2 and b800 s/mm^2) in the axial planes. After the non-contrast enhanced (NCE) protocol was performed, a weight-adapted dose of a gadolinium-based contrast agent (was administered, and serial CE images were obtained using breath-hold 3D VIBE (TR/TE, 4.56 msec / 2.03 msec) in the arterial, portal venous, and equilibrium phases covering the upper abdomen in the axial plane. After the serial CE images were acquired, continuous breath-hold 3D VIBE images were obtained from head to knee in the axial plane. All sections were then combined, resulting in uninterrupted whole-body coverage.

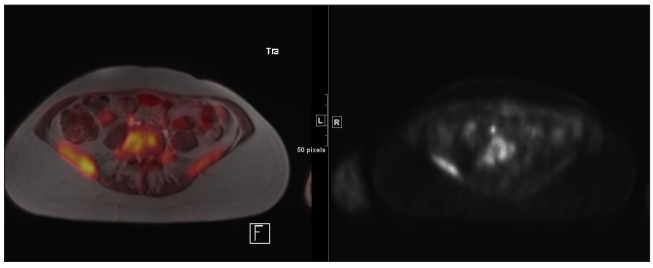

Figure 1. a, b. PET/MR (a, b) of a 37-year-old patient with grade 3 invasive ductal carcinoma. The axial plane PET/MR fusion image (a) shows bilateral iliac and vertebral body metastatic lesions; the corresponding PET image does not show the left iliac metastatic lesion

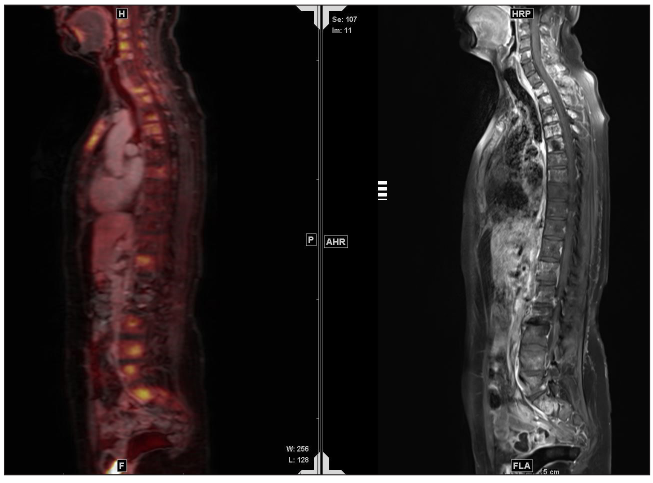

Figure 2. a, b. A 35-year-old patient with grade 3 invasive ductal carcinoma of the left breast. Fused PET/MR and sagittal Dixon T1W MR images (a, b) both show similar metastatic lesions

Images were evaluated by a radiologist with 10 years' experience in body MRI reading and 5 years' experience in hybrid imaging. The data were analyzed on a dedicated workstation (Syngo Via; Siemens Healthcare, Erlangen, Germany). The number of bone metastasis was recorded for each patient.

Statistical analyses were performed using Statistical Package for Social Sciences for Windows software version 25 (IBM Corp.; Armonk, NY, USA). The variables were investigated using the Kolmogorov-Smirnov test to determine whether the distribution was normal. Due to the fact that most variables except for age were not normally distributed, Friedman's test was conducted to evaluate whether there was a significant change in the total number of detected bone metastasis among the different sequences. Pairwise comparisons were performed using the Wilcoxon signed-rank test. A p-value of less than or equal to 0.05 was accepted as statistically significant.

Results

Twenty-three women with pathologically confirmed breast cancer were included in our study. The women were aged between 23-80 (mean ± standard deviation, 47.7±12.9) years. All patients included in the study were stage 3 or higher at the time of diagnosis. Eight of the 23 patients had bone metastasis (26%). Bone metastases were dominantly localized in the spine (63%) and pelvis (25%).

Breast carcinoma was histopathologically confirmed in surgical specimen or using a tru-cut biopsy for every patient. Three patients (13%) were determined to have bone metastases after histopathologic confirmation through surgery and Tru-cut biopsy. The other 20 (87%) patients had prior 18F-FDG-PET/CT, bone scintigraphy, CE MRI, 18F-FDG-PET/MRI for follow-up and the metastases were recorded as malignant after a comparison of these modalities. For cases without pathology results the mean follow up period was 18.5 months (range: 12–36 months) and was used as the standard of reference. The number of metastases detected using 18F-FDG-PET/MRI (mean 3.57; median 0; range, 0-2) was significantly higher than in the PET component only (mean 2.87, median 0; range, 0-1) (p=0.026) (Figure 1). There was no statistical difference between the bone metastases detected with FDG-PET/MRI (mean 3.57; median 0; range 0-2) and CE MRI

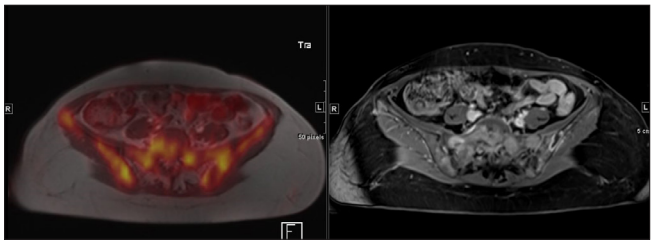

Figure 3. a, b. PET/MR (a, b) of the same patient with grade 3 invasive ductal carcinoma. The axial plane PET/MR fusion image (a) shows bilateral iliac, sacral and vertebral body metastases and the corresponding axial Dixon T1W MR shows similar metastatic lesions

(Figure 2, 3) (mean 3.43; median 0; range 0-2) (p=0.083). CE MRI superior to PET for the detection of bone metastasis, but the statistical significance was not as high as with FDG-PET/MRI (p=0.042).

Discussion and Conclusion

The presence of bone metastasis has an important effect on morbidity and mortality (22). Early stage breast cancer incidence is increasing with improved screening techniques and diagnosis of cancer at in situ stage increases survival. Therefore, optimal assessment for treatment planning may avoid unnecessary chemotherapy and early detection enables accurate staging and management of therapy (23, 24). 18FDG-PET/MRI is a new and promising tool in oncologic imaging and may improve the detection of early bone marrow infiltration and increase diagnostic confidence in the assessment of bone metastasis (25).

Our data showed that the combined evaluation of PET and MRI with post-contrast VIBE images increased the detection rate of bone metastases. Previous studies have shown that CE MRI and DWI have similar sensitivities for the assessment of bone metastases (26), but only FDG-PET/CT has lower sensitivity than these modalities. FDG-PET is not sensitive for hypometabolic metastasis and increased bone marrow activity after chemotherapy (27-29). Therefore, in PET/MRI, even in cases of low FDG activity , the likelihood of correct detection and staging seems to be higher than PET/CT. (30).

The metabolic information from PET data together with the diagnostic accuracy of CE whole-body MRI without radiation exposure may increase the sensitivity of detection. FDG-PET/MRI showed superior lesion detection than only PET component in our study and this may reflect the superiority of PET/MRI over PET/CT with its ability to assess early infiltration of bone marrow with malignant tissue, as mentioned in the literature (31). However, we found no significant difference between CE MRI and FDG-PET/MRI, probably because of the absence of hypometabolic metastases in our study group.

Diagnostic ability of the various radiopharmaceuticals depends on the type of the metastases. 18F-FDG is superior to other tracers in the detection of osteolytic pattern, while sclerotic lesions show low glycolytic activity are well identified by 18F-NaF PET and bone scintigraphy. The low specificity and planar resolution of planar scintigraphy and SPECT are the limitations that may decrease the ability of these techniques to identify early bone infiltration. 18F-NaF PET and other bone-seeking radiopharmaceuticals identify osteoblastic reaction around the metastatic lesion of the bone and is not tumor specific (32-34). Sonni et al. (35) found that the ability of Na[18F]F/[18F]FDG PET/MRI is superior than ^{99m}Tc-MDP WBBS and Na[18F]F/[18F] FDG PET/MRI is a promising tool for the evaluation of metastatic and extra-skeletal lesions.

Our study has limitations, including the limited number of patients and lack of histopathologic confirmation for every lesion. The results should be considered as preliminary and larger studies are needed to show the potential of FDG-PET/MR.

In conclusion, our results showed that FDG-PET/MRI may be beneficial over PET/CT and bone scintigraphy in breast cancer patients with only few early bone metastasis without radiation exposure.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of Bilim University Institutional Review Board (No. 28.06.2016/51-06).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Conflict of Interest: The authors have no conflicts of interest to declare.

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