

## Breast MRI and $^{18}\text{F}$ FDG PET/CT in the management of breast cancer

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**Goals:**  $^{18}\text{F}$  FDG PET/CT is used for diagnosis, staging and establishing the response to therapy in various malignancies, including breast cancer (BC). Dedicated breast MRI (BMRI) is gaining a role in the management of BC patients (pts), demonstrating high sensitivity and specificity for detection of small lesions. We were therefore prompted to review our experience with PET and BMRI in BC.

**Methods:** This is a retrospective study of 21 women with BC, 30–76 years old, who had BMRI and whole-body FDG PET/CT at our institution from Jun 2002 to May 2005. A total of 6 patients (group A) had BMRI and PET/CT in the preoperative period and 15 patients (group B) had BMRI and PET/CT after surgery. Reinterpretation of the imaging studies for accuracy and data analysis from medical records were performed. **Results:** For group A, BMRI identified breast lesions in 4 patients, while PET/CT was able to identify breast lesions in 5 patients. All these were proven to be malignancy on pathology examination. In group B, BMRI detected recurrent breast lesions in 8 patients, with 88.9% sensitivity and 83.3% specificity. In the same patient population, PET/CT was 33.3% sensitive and 91.7% specific. As a whole body examination, PET/CT revealed metastatic disease in 6 patients (100% sensitive and 90% specific). Overall, sensitivities and specificities for breast disease detection were 85.7% and 85.7% for BMRI, and 75% and 92.3% for  $^{18}\text{F}$  FDG PET/CT. **Conclusions:** As expected, BMRI is more sensitive than PET/CT in the detection of breast lesions. However, PET/CT as a whole-body examination changed the management of disease by detection of distant lesions in 6 of the 21 patients. Our study suggests that  $^{18}\text{F}$  FDG PET/CT and BMRI should be considered as complimentary imaging tools in the pre- and postoperative work-up of patients diagnosed with breast cancer.

**Key words:** breast cancer,  $^{18}\text{F}$  FDG, PET/CT, MRI

### INTRODUCTION

In the United States, breast cancer is the most common non-skin cancer and the second leading cause of cancer-related death in women. The National Cancer Institute estimates a total of 212,930 new cases of breast cancer (211,240 in women) in 2005 and 40,870 total deaths from breast cancer (40,410 in women) for the same year.<sup>1</sup>

Breast cancer strikes women of all ages, races, ethnicities, socioeconomic strata, and geographic locales.<sup>2</sup> Cancer staging is essential in determining the choice of therapy, as well as a patient's prognosis and chances for survival.<sup>3</sup>

$^{18}\text{F}$  fluoro-2-deoxyglucose (FDG) positron emission tomography (PET) fused with computed tomography (CT) provides the ability to combine functional and morphologic information in a single study, thus becoming a powerful imaging modality for diagnosis, staging and establishing the response to therapy in various malignancies, including breast cancer. Likewise, dedicated breast magnetic resonance imaging (MRI) is gaining a major role in the diagnosis and management of breast cancer patients, demonstrating high sensitivity and specificity for detection of small lesions, especially in patients at high

Received August 17, 2006, revision accepted October 3, 2006.

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risk for breast cancer. But whether to request both studies prior to therapy or opt only for one, remains a subject of debate. We were therefore prompted to review our experience with PET and MRI in breast cancer.

## MATERIALS AND METHODS

This is a retrospective study of 21 women with breast cancer, 30–76 years old (average:  $52 \pm 13.5$ ), who had breast MRI and whole-body  $^{18}\text{F}$  FDG PET/CT at our institution from June 1st, 2002 to May 31st, 2005. The study was performed with the Institutional Review Board approval. The inclusion criteria were proven diagnosis of primary breast malignancy, availability of imaging studies for review and availability of access to the patients' clinical charts. The reports of PET/CT and breast MRI were reviewed and their results were recorded. Reinterpretation of the studies by a board certified Nuclear Medicine physician and a board certified radiologist was performed for accuracy.

The PET/CT studies were acquired with a Biograph LSO PET/CT scanner (Siemens/CTI, Knoxville, TN). The system consists of a dual-slice, spiral CT (Siemens Somatom Emotion) in tandem with an ACCEL PET and is optimized for use in whole-body oncology. Data were obtained in 3D mode, with attenuation correction calculated from coregistered CT images. Images were acquired 60 minutes after i.v. injection of an average dose of 550 MBq of  $^{18}\text{F}$  FDG. The images were interpreted on a Windows NT-based computer system, with a Siemens/Syngo user interface.

Dynamic contrast-enhanced breast MRI was performed on a 1.5 T magnet with multichannel capability (Siemens Symphony, Medical Solutions, Erlangen, Germany), using a standard 4 channel phased-array breast coil (Siemens coil or MRI Devices coil, Invivo, Orlando, Florida) with the patient in the prone position. A localizer sequence was obtained. This was followed by a axial TSE T2-weighted ( $\sim 4$  m; TR/TE of  $\sim 6000/90$ ; flip angle,  $180^\circ$ ; field of view  $\sim 30$ – $36$  cm; section thickness,  $<4$  mm with a 0.5 mm gap; interleaved; nex 2; matrix  $256 \times 512$ ). Then, a dynamic axial T1 3D FLASH acquisition (6 m 30 s; TR/TE of  $\sim 4.5/1.5$ ; flip angle,  $<25^\circ$ ; field of view, 30–36 cm; section thickness,  $<2$  mm; phase-encoding lateral; nex 1; matrix  $\sim 350 \times 450$ ) was obtained: a precontrast volume was acquired, followed by i.v. injection of 0.1 mmol/kg of body weight of gadopentetate dimeglumine (Magnevist; Schering, Berlin, Germany) and 20 ml of saline at a rate of 3 ml/sec with a power injector (Medrad, Indianola, Pa.) and after a 20 second delay, five post-contrast volumes were obtained. Post-processing of the dynamic sequence included subtraction and maximum intensity projection (MIP) images. The resolution of the T1 3D FLASH scans was  $<1$ – $2$  mm in all directions.

Morphologic and kinetic analysis for suspicious enhancing lesions was performed using the ACR BI-RADS

lexicon. Morphologic analysis of lesions (masses, foci, and regions) was performed assessing for size, shape, margins, and homogeneity of enhancement. Lesions that were not round or oval, with irregular borders, and heterogeneous or rim enhancement were considered more suspicious. Kinetic analysis was performed for the lesion of interest in the early (1–2 minutes after injection) and late enhancement (5–6 minutes after contrast injection). Masses ( $>5$  mm) that showed at least 50% increase in signal intensity early were considered more suspicious unless there was a benign correlate at mammography, ultrasound, or unenhanced MR imaging. Foci ( $<5$  mm) that showed at least 50% increase in signal intensity early, with washout kinetics late were also considered more suspicious. Regional enhancements with at least 50% increase in signal intensity early were considered more suspicious for malignancy. Segmental, linear, or clumped enhancement was considered suspicious for ductal carcinoma *in situ* (DCIS), regardless of kinetics. Enhancement in contiguity with the primary tumor was considered suspicious, regardless of size or morphology. Lesions that did not meet any of these kinetic or morphologic criteria were usually considered benign or probably benign.

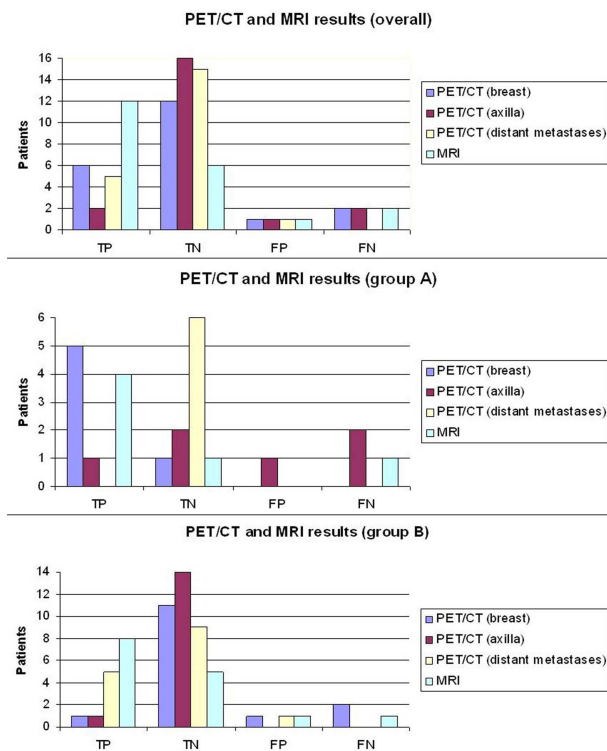
Specificities and sensitivities for breast cancer and metastases detection using PET/CT and MRI were calculated using the pathology results (17 patients) or follow-up evidence of disease progression (4 patients) as the gold standard. Confidence interval (CI) estimations were performed using the Wilson score method.

## RESULTS

A total of 6 patients (group A) had breast MRI and PET/CT in the preoperative period (3–78 days, average: 25 days) and 15 patients (group B) had breast MRI and PET/CT as follow-up after surgery (4–175 days, average: 51.3 days). The interval between the PET/CT and breast MRI ranged 2–188 days (average: 52.7 days). The age at diagnosis ranged 30–72 years (average:  $52 \pm 17$ ) in group A and 38–76 years (average:  $52 \pm 19$ ) in group B. This difference has no statistical significance ( $p$  values of 1.0).

For group A (imaging studies prior to surgery), MRI identified breast lesions in 4 patients, while PET/CT was able to identify breast lesions in 5 patients. All these were proven to be malignancy on pathology examination. In the same group,  $^{18}\text{F}$  FDG PET/CT detected axillary metastases in 1 patient, but missed them in another, with sensitivity of 33.3% and specificity of 66.7%. There were no patients with distant metastases noted on the whole-body PET/CT exam.

In group B, breast MRI detected recurrent breast lesions in 8 patients, with 88.9% sensitivity (95% CI: 56.5–98) and 83.3% specificity (95% CI: 43.6–96.9). In the same patient population, PET/CT was 33.3% sensitive and 91.7% specific. Axillary lymph nodes metastases were seen on PET/CT in a single patient. As a whole-body

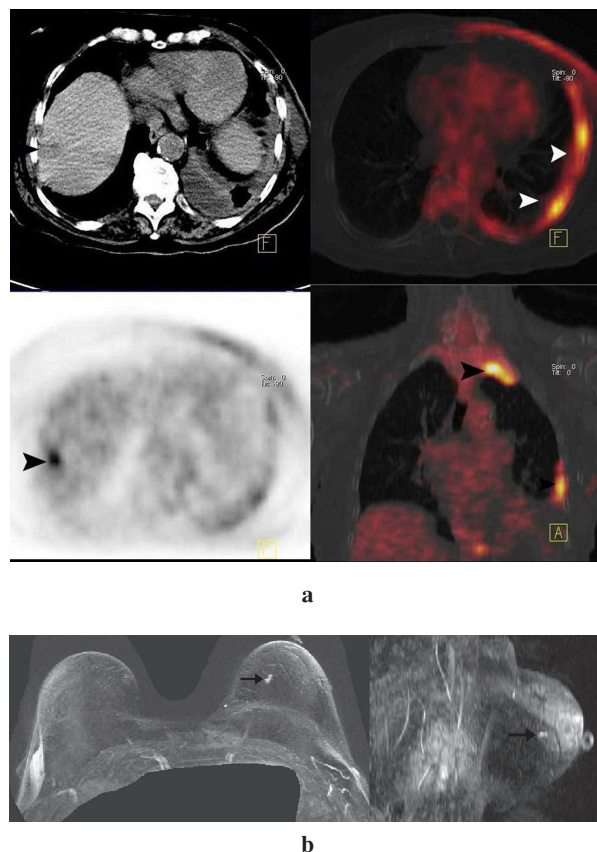


**Fig. 1** Analysis of PET/CT and MRI results in the studied population (TP = true positive; TN = true negative; FP = false positive; FN = false negative).

examination, PET/CT revealed metastatic disease in 6 patients (100% sensitive and 90% specific), thus altering the management of disease in these cases.

Overall, sensitivities and specificities for breast disease detection were 85.7% (95% CI: 60.1–95.9) and 85.7% (95% CI: 48.7–97.4) for breast MRI, and 75% (95% CI: 40.9–92.8) and 92.3% (95% CI: 66.7–98.6) for  $^{18}\text{F}$  FDG PET/CT. As a whole-body examination,  $^{18}\text{F}$  FDG PET/CT was 50% sensitive (95% CI: 15–85) and 94.1% specific (95% CI: 73–98.9) for axillary disease, 100% sensitive (95% CI: 56.5–100) and 93.7% specific (95% CI: 71.7–98.9) for distant metastases. A detailed analysis of these results is presented in Figure 1.

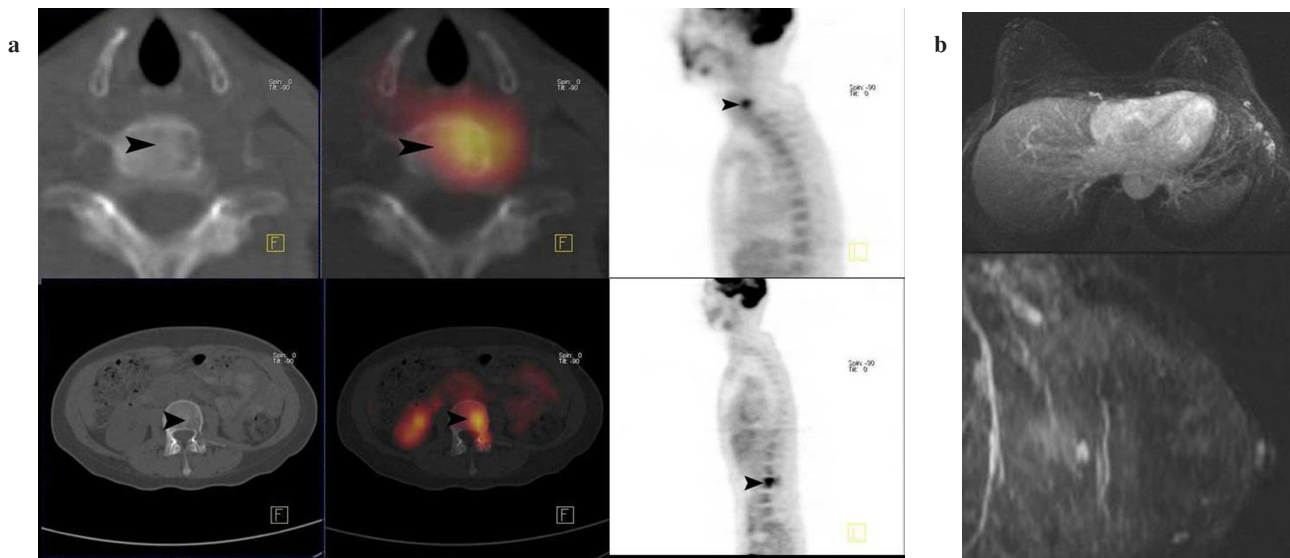
Figure 2 shows distant hepatic and pleural metastases in a 75-year-old patient that had prior breast MRI indicating the lesion. Identification of distant metastases with PET/CT changed the management of disease in this case. Figure 3 shows cervical and lumbar vertebral metastases in a 43-year-old woman with history of breast cancer. Her follow-up breast MRI was negative for recurrent disease, but the findings on PET/CT prompted institution of an altered therapeutic regimen. Left breast carcinoma with left internal mammary lymph node metastasis is seen in another patient on PET/CT and breast MRI (Fig. 4).



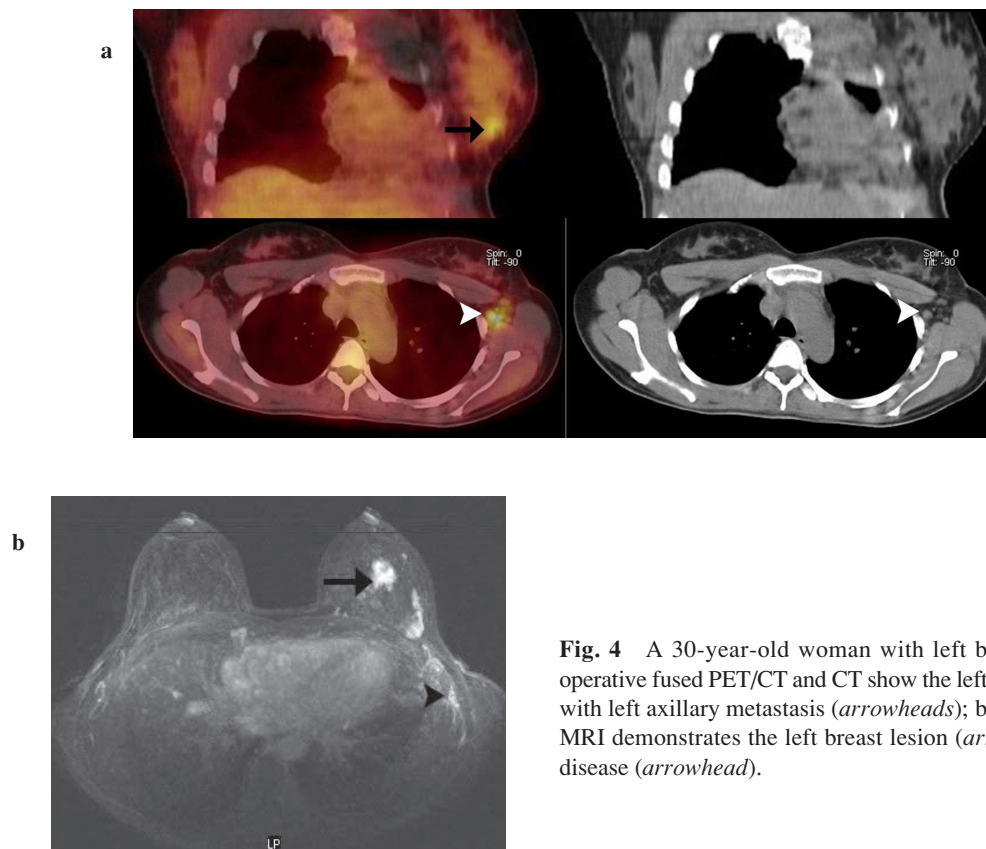
**Fig. 2** A 75-year-old woman with breast cancer. a) Post-operative CT, PET and fused PET/CT show liver and pleural metastases (arrowheads); b) Pre-operative breast MRI identifies the left breast lesion (arrows).

## DISCUSSION

Breast MRI and whole-body PET/CT scanning are becoming important imaging studies for diagnosis, monitoring of treatment response, and detection of recurrence or metastasis in breast cancer patients.<sup>4</sup> MRI has demonstrated excellent sensitivity in screening at-risk populations, in detecting extent of known cancers, and in evaluating for response to therapy and recurrent cancers.<sup>5–9</sup> In a recent review, Lehman and Schnall conclude that breast MRI is highly sensitive, with an acceptable specificity compared with other imaging modalities.<sup>10</sup> Although PET has a limited role in the diagnosis of breast cancer, it can be important in detecting distant disease, in helping to plan surgical and medical treatment, in monitoring response to treatment and recurrence.<sup>9,11–16</sup> PET also has the potential to evaluate novel treatment agents rapidly by detecting their effects on specific receptors.<sup>9</sup> Our data supports prior observation showing that MRI is more sensitive in detecting breast disease, while PET is important for identifying disease outside of the breast and axilla. In our study, the reduced overall sensitivity of PET/CT for detection of axillary disease (50%, 95% CI: 15–85) is



**Fig. 3** A 43-year-old woman with breast cancer. a) Post-operative CT, fused PET/CT and PET show cervical and lumbar spine metastases (*arrowheads*); b) Post-operative breast MRI is negative for suspicious lesions.



**Fig. 4** A 30-year-old woman with left breast cancer. a) Pre-operative fused PET/CT and CT show the left breast cancer (*arrow*) with left axillary metastasis (*arrowheads*); b) Pre-operative breast MRI demonstrates the left breast lesion (*arrow*) and left axillary disease (*arrowhead*).



probably due to the small size of these lesions (below the spatial resolution of PET) and to the presence of micro-metastases detected on histopathologic examination of the surgical specimens.

Although our study is limited by the small population of patients that fits the inclusion criteria, the data suggests that  $^{18}\text{F}$  FDG PET/CT might actually have similar sensitivity to MRI in detecting primary or locally recurrent lesions during the pre- and postoperative period. In our study, PET detected 1 more breast lesion than MRI did in group A. Some authors consider  $^{18}\text{F}$  FDG PET/CT and MR imaging complementary modalities for detecting local-regional breast cancer recurrence, with PET confirming the diagnosis in cases in which MR imaging is indeterminate due to non-specific findings.<sup>17</sup> However, MRI has been shown to be able to pick up smaller lesions, less than 10 mm in size and those that conventional mammography and PET scanning may miss.<sup>16,18</sup> It has been reported to have better correlation with pathology than physical exam, mammography, and sonography.<sup>19,20</sup> PET, however, is more specific in detecting local-regional breast cancer recurrence, with PET again able to detect additional metastases outside of the field of view of MRI. A combination of the two modalities has been suggested to result in sensitivity and specificity near 95%.<sup>21</sup> Walter et al. agree, but suggest MR mammography first and PET if differentiation of benign vs. malignant is needed, to avoid the high costs of both of these examinations.<sup>22</sup>

Evaluation of a larger patient population with prospective studies, with the addition of mammography and breast ultrasound is needed to further determine the precise role and timing of each imaging modality in breast cancer evaluation. Availability of dedicated breast PET units with improved spatial resolution will improve breast cancer detection and their role will need to be ascertained. Our study suggests that currently a combination of anatomic and metabolic approach is needed in breast cancer identification.

## CONCLUSION

As expected, breast MRI is more sensitive than PET/CT in the detection of breast lesions, particularly in the postoperative patients, probably due to higher resolution. However, PET/CT as a whole body examination changed the management of disease by detection of distant lesions in 6 of the 21 patients (100% sensitive and 90% specific). Additional larger prospective studies, with the addition of dedicated breast PET units and possibly dual time imaging<sup>23</sup> are warranted to define the appropriate sequence of studies during initial work-up. Our study suggests that  $^{18}\text{F}$  FDG PET/CT and breast MRI should be considered as complimentary imaging tools in the pre- and postoperative work-up of patients diagnosed with breast cancer and at high risk due to tumor histology or symptomatology.

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