

# Breast Lesions Detected via Molecular Breast Imaging: Physiological Parameters Affecting Interpretation

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**Rationale and Objectives:** To evaluate correlations between molecular breast imaging (MBI) descriptor characteristics and positive predictive value (PPV) in detecting breast cancer.

**Materials and Methods:** A retrospective review was performed on 193 suspicious findings from 153 women (31–81 years) with positive MBI examinations. We assessed associations between (i) lesion pattern (mass vs. nonmass) and PPV; (ii) lesion pattern and suspected likelihood of cancer (low vs. moderate vs. high); (iii) background parenchymal uptake (BPU) (homogeneous vs. heterogeneous) and PPV; (iv) breast density (dense vs. non-dense) and PPV; and (v) BPU and density.

**Results:** One hundred ten of 153 patients were diagnosed with malignancy or high-risk pathology (PPV1 = 71.9%), and 130/193 biopsies resulted in malignant or high-risk lesions (PPV3 = 67.4%). Biopsies of mass vs. nonmass findings had comparable PPV3 (71.7% vs. 61.3%;  $P = .0717$ ). Mass findings were correlated with higher suspicion for cancer than nonmass findings ( $P < .001$ ). There was no significant difference in PPV3 when comparing biopsies from homogeneous vs. heterogeneous BPU (72.5% vs. 60.7%;  $P = .103$ ). No association was found between patients' BPU and diagnosed cancer or high-risk lesions ( $P = .513$ ). Biopsies from nondense breasts demonstrated higher PPV3 than biopsies from dense breasts (85.4% vs. 60.6%;  $P = .0025$ ); patients with nondense breasts were more likely to be diagnosed with cancer or high-risk pathology (PPV1 = 87.8% vs. 66.0%;  $P = .00844$ ). Dense breasts had a greater association with heterogeneous BPU ( $P = .0844$ ).

**Conclusion:** Neither variability in mass or nonmass positive MBI findings, nor variability in BPU on MBI were significant determinants for the probability of malignancy. Dense breasts were associated with lower predictability and heterogeneous BPU on MBI.

**Key Words:** Breast cancer; molecular breast imaging; background parenchymal enhancement; homogeneous; heterogeneous; density; mass lesion; nonmass; breast specific gamma imaging; scintimammography.

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## INTRODUCTION

Molecular breast imaging (MBI), also known as breast-specific gamma imaging, is increasingly being used as an adjunct imaging modality in the detection of breast cancer. In recent years, breast-optimized gamma detectors have been noted to reliably detect tumors less than

1 cm in size (1–3). A meta-analysis in 2013 from 8 studies, including 2183 lesions, showed that the sensitivity and specificity of MBI were 95% and 80%, respectively (4). In addition to demonstrating a sensitivity and specificity in diagnosing breast cancer comparable to that of magnetic resonance imaging (MRI), MBI also has many advantages for clinical use (5–7). While mammography is affected by breast density, MBI has been shown to be reliable irrespective of breast density (8–11). MBI is also a feasible screening alternative for women who refuse to undergo MRI due to claustrophobia, which may hinder up to about 25% of women, including those at high breast cancer risk (12).

Currently accepted clinical and research indications of MBI include, but are not limited to, the extent of disease/preoperative staging in newly diagnosed breast cancer, the evaluation of response to neoadjuvant chemotherapy, the detection of local breast cancer recurrence, the evaluation for primary breast cancer in women with metastases or metastatic axillary lymphadenopathy of unknown primary, breast cancer screening, an adjunct to conventional breast imaging for problem solving in indeterminate cases, technically difficult

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breast imaging, and patients for whom breast MRI would be indicated but is not possible due to renal insufficiency, implanted devices, body habitus, or claustrophobia (13–15).

One MBI lexicon by Conners et al. illustrates that as a physiological imaging modality, images obtained with MBI have been noted to present with highly variable distributions of radiotracer uptake and are often influenced by hormonal factors (15). The lexicon categorized such distributions into measures of background uptake intensity and lesion uptake intensity. For example, background parenchymal uptake (BPU) intensity was assessed visually relative to subcutaneous fat uptake as either photopenic (less than that of fat tissue), mild (equal or slightly greater than fat tissue), moderate (more than mild but less than twice that of fat tissue), or marked (at least twice that of fat tissue). Homogeneous BPU was defined as having either “photopenic” or “mild” breast glandular tissue uptake, and heterogeneous BPU was defined as having either “moderate” or “marked” breast glandular tissue uptake. Similarly, the intensity of lesions was described as being photopenic, mild, moderate, or marked relative to subcutaneous fat and was also further characterized as being either mass patterned or non-mass patterned (15).

Few studies have documented how characterizations in background uptake and lesion uptake may affect the interpretation of MBI images. The objective of this study was to retrospectively evaluate MBI’s positive predictive value (PPV) for detecting breast cancer, in relation to predictive factors based on the character of radiotracer uptake in suspected lesions and on the BPU of images. We assessed the associations between (i) lesion pattern characteristic (mass vs. nonmass) and PPV; (ii) lesion pattern characteristic and suspected likelihood of cancer by the radiologist (low vs. moderate vs. high); (iii) background parenchymal uptake (BPU; homogeneous vs. heterogeneous) and PPV; (iv) density (dense vs. nondense) and PPV; and (v) BPU and density. Significant correlations between descriptor characteristics and PPV may affect how guidelines for the interpretation of MBI images are being implemented and practiced.

## MATERIALS AND METHODS

### Patients

All women who had an MBI examination between October 2010 and October 2011 were retrospectively reviewed. Patients were included whose MBI was positive, and pathological correlation of the lesion of suspicion was recorded. In patients who had more than one MBI examination during this time period, only the first positive exam was included, as repeat exams are not always independent events. Our analysis included MBI images from 153 women with a total of 193 suspicious findings leading to pathological diagnosis by biopsy or subsequent surgical excision. Patients ranged in age from 31 to 81 years (mean age = 57 years).

Clinical indications for MBI included, but were not limited to, a palpable lesion with no mammographic correlation; screen-

ing for multicentric and/or multifocal tumors in women with biopsy-proven cancer; asymmetric density seen on mammography with no corresponding ultrasound (US), MRI, or clinical finding; patients for whom breast MRI should be indicated but was not performed; and screening of women with a personal or family history of breast cancer.

### MBI Technique and Interpretation

A high-resolution small-field-of-view breast-specific gamma camera (6800; Dilon Technologies, Newport News, VA) was used to obtain images. Patients received an intravenous injection of 16–27 mCi of Tc-99m-sestamibi radiotracer in the antecubital vein. Craniocaudal and mediolateral oblique projections were obtained at 7–10 minutes per image, with additional views performed as necessary without additional radiotracer injection. Of note, since the completion of this study, we now use a dose of 5–10 mCi as this results in an equal image quality with a reduced dose to the patient (16).

MBI examinations were interpreted in 2010–2011 by radiologists with 2–15 years of experience in the clinical setting with access to patient history and adjunct imaging studies. Gamma images were categorized for focal radiotracer uptake using the Breast Imaging Reporting and Data System (BI-RADS) as one of the following: incomplete (score of 0), with additional imaging needed; normal (score of 1), with no focal or diffuse uptake; benign (score of 2), with minimal patchy uptake; probably benign (score of 3), with minimal patchy uptake with some areas of more focal uptake; probably abnormal (score of 4), with mild focal radiotracer uptake; abnormal (score of 5), with marked focal radiotracer uptake; and biopsy-proven malignancy (score of 6) (15). Any exam for which additional workup was needed was considered positive, which included BI-RADS scores 0 ( $n = 82$ ), 3 ( $n = 1$ ), 4 ( $n = 12$ ), 5 ( $n = 9$ ), and 6 ( $n = 49$ ). Meanwhile, completely normal exams were negative and not considered in our study (BI-RADS scores 1 and 2).

Additional classifications were made in 2016–2017 by a radiologist with 16 years of experience in MBI interpretation at the time, without prior knowledge of the patient characteristics and MBI reports made in 2010–2011. These include classifications of each lesion by (i) character as mass or nonmass and (ii) the likelihood of cancer on a subjective 1–3 scale (e.g., 1 = low likelihood of cancer, 2 = moderate likelihood, 3 = high likelihood). Images were classified by surrounding BPU, as either homogeneous or heterogeneous uptake of glandular tissue in relation to uptake of subcutaneous fat, in accordance with the MBI lexicon by Conners et al. (15) (Fig 1).

Breast density at the time of last screening mammogram (within 12 months prior to MBI) was determined for 144 patients (mean age = 57 years) and classified utilizing the American College of Radiology BIRADS version 5 density characterization: A = almost entirely fatty, B = scattered areas of fibroglandular density, C = moderately dense, and D = extremely dense (17,18). In our analysis, A ( $n = 4$ ) and B ( $n = 37$ ) represented nondense breasts, and C ( $n = 85$ ) and D ( $n = 18$ ) represented dense breasts. Histologic findings,

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