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Molecular Breast Imaging in Breast Cancer Screening and Problem Solving[1]

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Abbreviations: BI-RADS = Breast Imaging Reporting and Data System, BPU = background parenchymal uptake, CC = craniocaudal, DBT = digital breast tomosynthesis, ICDR = incremental cancer detection rate, IDC = invasive ductal carcinoma, LCIS = lobular carcinoma in situ, MBI = molecular breast imaging, MLO = mediolateral

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See discussion on this article by Brem (pp 1328–1329).

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SA-CME LEARNING OBJECTIVES

After completing this journal-based SA-CME activity, participants will be able to:

- Recognize the clinical role of MBI as a secondary screening modality for women with dense and/or complex mammograms.
- Describe the radiation dose associated with MBI in comparison with the radiation doses associated with other imaging procedures.
- Discuss the patient preparation procedure for MBI.

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In the United States, legislative actions in over 28 states require radiologists to notify women who undergo breast screening mammography of their breast density. This has led to increased public interest in supplemental screening, but radiologists have not come to a consensus on a supplemental screening modality. In choosing between the most common options, whole-breast ultrasonography (US) and magnetic resonance (MR) imaging, one must weigh the benefits and drawbacks of each modality, as increased cancer detection may be accompanied by increased examination costs and biopsy rates. There has been recent interest in molecular breast imaging (MBI) for supplemental screening because of its high sensitivity, as well as its high specificity. This article describes how MBI fits into clinical practice alongside digital breast tomosynthesis (DBT), targeted US, and MR imaging. The authors describe their approach to breast cancer screening, which uses DBT as the primary imaging modality. DBT is complemented by automated density calculations and supplemented with functional imaging techniques, including MR imaging or MBI, for women with dense breasts. An algorithm based on the patient's breast cancer risk is used to determine if either MR imaging or MBI for supplemental screening is appropriate. MBI is also used as a problem-solving tool for the evaluation of clinical indications following complex mammography or US, or for unexplained physical findings. This article describes aspects related to implementing MBI in clinical practice, including the clinical workflow, patient management, radioactive tracer administration, and procedure reimbursement.

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Introduction

The patient-care facility described in this article is a community breast care center that interprets approximately 35 000 screening mammograms obtained annually at several ancillary centers throughout the metro Toledo, Ohio, region. The facility is a Breast Imaging Center of Excellence, designated by the American College of Radiology, and it is fully accredited by the American College of Surgeons' National Accreditation Program for Breast Centers (NAPBC). Molecular breast imaging (MBI) was implemented in this center in 2011. At present, an average of 125 MBI scans per month are obtained.

TEACHING POINTS

- The ICDR of digital mammography and DBT (about 1.3/1000) is lower than when another high-sensitivity imaging technique, such as MBI or MR imaging, is used in conjunction with digital mammography. At our facility, an audit of the supplemental MBI screening of 1696 women, who had a less than 20% lifetime risk of developing breast cancer after primary screening with digital mammography, found an ICDR of 7.7 per 1000, which exceeds the reported ICDR of DBT over digital mammography.
- Supplemental screening modalities, notably whole-breast US, have been advocated for average-risk women with dense breasts. Published reports of clinical implementation show an increase in cancer detection rates along with corresponding increases in false positives and biopsy rates, which seem to resolve with subsequent screenings.
- In MBI, the patient's whole-body radiation dose is approximately 2.3 mSv, comparable to that of other cancer screening techniques. This radiation dose is considerably lower than the 50-mSv limit set by the U.S. federal government for annual exposure for radiation workers (eg, nuclear medicine technologists), and it is lower than the 5-mSv limit for a radiation worker during pregnancy.
- MBI is performed during the follicular phase of the menstrual cycle, between days 2 and 12, when fibroglandular tissue is not as physiologically active in premenopausal women.
- The audit of our supplemental screening MBI cases showed the baseline recall rate (the recall rate of patients who have not undergone prior MBI) to be low (8.4%). As with all modalities, the recall rates will reduce further when prior images are available for comparison.

In this article, we describe how MBI is used alongside recent technologic advances in digital breast tomosynthesis (DBT), density- and risk-assessment software, dedicated breast magnetic resonance (MR) imaging, and targeted ultrasonography (US) for breast cancer screening and problem solving. A decision algorithm used for screening populations, and for problem solving when conventional modalities are exhausted, is presented. Practical implementation issues involving patient management, radiation dose concerns, radiotracer handling, and procedure reimbursement are also described. Cases highlighting MBI's use in supplemental screening, in high-risk screening, and in diagnostic use are also presented.

Primary Screening

The value of performing screening mammography to detect and diagnose breast cancer has been validated by a number of clinical trials (1–9); however, mammographic detection of breast cancer in dense breasts presents a challenge. Parenchymal tissue in dense breasts can mask lesions such that sensitivity is substantially lower than for breasts that contain predominantly fatty tissue or have scattered density (10–12). Furthermore, density has been shown to be an independent risk factor for developing breast cancer (13,14). Thus, women with dense breasts generally have a higher risk of developing breast cancer, which is more difficult to detect at mammography. Routine supplemental screening is expected to prevent delayed diagnosis, allowing for the identification of smaller cancers and, consequently, better patient outcomes.

In January 2015, our facility converted from using two-dimensional digital mammography (Selenia Dimensions system; Hologic, Marlborough, Mass) to DBT (Genius 3D Mammography; Hologic) as the primary imaging modality for women presenting for breast cancer screenings. In a recent multisite study of nearly 450 000 examinations, DBT demonstrated reduced recall rates from 10.7% to 9.1%, while simultaneously improving cancer detection rates to 5.5 per 1000 from 4.2 per 1000 when compared with two-dimensional digital mammography (15). For this reason, all screening participants are imaged annually with the DBT system using the "C-view" software module (Hologic) in our center (16–19).

Need for Supplemental Screening after DBT

The incremental cancer detection rate (ICDR) of digital mammography and DBT (about 1.3/1000) is lower than when another high-sensitivity imaging technique, such as MBI or MR imaging, is used in conjunction with digital mammography (20–22). At our facility, an audit of the supplemental MBI screenings of 1696 women, who had a less than 20% lifetime risk of developing breast cancer after primary screening with digital mammography, found an ICDR of 7.7 per 1000, which exceeds the reported ICDR of DBT over digital mammography (23).

Furthermore, a recent multicenter analysis of DBT data as a function of density demonstrated that the cancer detection rate in extremely dense breasts is not improved by DBT (24). For these reasons, we have continued supplemental screening of women with dense breasts even after conversion to DBT for primary screening.

Supplemental Screening of High-Risk Women with Dense Breasts

MR imaging using an intravenous gadolinium contrast agent is both an anatomic and functional imaging technique that is unaffected by breast tissue density. Although breast MR imaging has performed well, with sensitivity estimates in the range of 75%–100% (25–29), it is not suitable for all patients due to its high cost and numerous contraindications. These include known claustrophobia, body habitus, renal impairment, preg-

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nancy, breast-feeding, and the presence of metallic foreign bodies or implants, such as metal clips, joint prostheses, pacemakers, insulin pumps, cochlear devices, hearing aids, and implanted cardioverter-defibrillators (30,31).

Breast MR imaging has been validated as an effective supplementary screening approach for high-risk women. A dedicated machine was integrated in our center in 2007 (32,33). Recent reports suggest that breast MR imaging may be an effective tool for screening women with a history of breast cancer and for those with strong familial and genetic risk factors, but it is not recommended for routine screenings of average-risk women (34). Guidelines support MR imaging for adjunct screening in women with a greater than 20% lifetime risk of developing breast cancer based on risk-assessment models, which factor in the patient's family history, known genetic mutations, previous radiation to the chest between the ages of 10 and 30 years, and previous lobular carcinoma in situ (LCIS) (35).

Insurance coverage of breast MR imaging is currently limited to high-risk women in many states, further restricting its use as an adjunct screening modality in women with dense breasts on mammogram. This leaves a considerable gap in the screening algorithm for average-risk women who are found to have dense or complex mammograms, and it further highlights the need for a cost-effective, safe, and sensitive supplemental modality. Moreover, high-risk women with dense tissue who present with contraindications to MR imaging are particularly underserved without an alternative modality. At our center, MBI is offered to help bridge that gap.

Supplemental Screening of Average-Risk Women with Dense Breasts

Supplemental screening modalities, notably whole-breast US, have been advocated for average-risk women with dense breasts (36,37). Published reports of clinical implementation show an increase in cancer detection rates along with corresponding increases in false positives and biopsy rates, which seem to resolve with subsequent screenings (38–40). Our center does not use whole-breast US for supplemental screening but uses MBI instead. Lesions detected at mammography, MBI, or MR imaging are confirmed with a targeted US examination before biopsy, where possible.

The conception of MBI was based on the findings that a nuclear medicine radiotracer for cardiac imaging, technetium 99m (^{99m}Tc)–sestamibi, showed a high propensity to accumulate in breast tumors. ^{99m}Tc-sestamibi allows for functional imaging, as it is metabolized by the mitochondria of active tumor cells (41) and is therefore not affected by anatomic characteristics such as density or surgical distortion. Large whole-body detectors were used to obtain functional breast images in real time, and scintimammography became an early adjunct screening method for occult breast cancers at conventional mammography (42). Effective interpretation and lesion detection were limited by the detectors' size and shape, their distance from the breast, their limited field of view, and their intrinsic spatial resolution.

The development of breast-specific gamma cameras in the late 1990s addressed some of these issues. The technique used single gamma heads and sodium iodide detectors, which improved tumor detection rates but were still restricted by limited spatial resolution and the necessity to use a high radiation dose (43).

In the mid 2000s, MBI with gamma cameras using cadmium zinc telluride semiconductor detectors and dual-head configurations for the light compression of breasts, analogous to mammography, was developed. In the initial implementation, the dose of ^{99m}Tc-sestamibi required for reliable detection was approximately 20 mCi (740 MBq), too high to be used for screening purposes (44). In recent years, the sensitivity of gamma cameras has been enhanced by modifying the collimators and by optimizing both the acquisition parameters and the imaging of a breast that is in close proximity to the camera (45,46). This reduced the prescribed dose of ^{99m}Tc-sestamibi to 8 mCi (296 MBq) (20,46), with the actual injected radiation dose ranging between 6 and 7 mCi (222–259 MBq) due to the adhesion of ^{99m}Tc-sestamibi to the plastic syringe (47).

In MBI, the patient's whole-body radiation dose is approximately 2.3 mSv, comparable to that of other cancer screening techniques. This radiation dose is considerably lower than the 50-mSv limit set by the U.S. federal government for annual exposure for radiation workers (eg, nuclear medicine technologists), and it is lower than the 5-mSv limit for a radiation worker during pregnancy.

Figure 1 shows the radiation dose of MBI in relation to those of other commonly performed medical procedures. Investigators who previously expressed concern about the radiation dose associated with breast-specific gamma imaging (48) published another article in which the MBI benefit-to–radiation risk ratio was recalculated, considering the new low dose for supplemental screening. The ratio was 5 for asymptomatic women 40–49 years of age, compared with 13 for mammography alone (49).

A prospective Mayo Clinic study revealed an ICDR of 8.8 per 1000 patients screened when

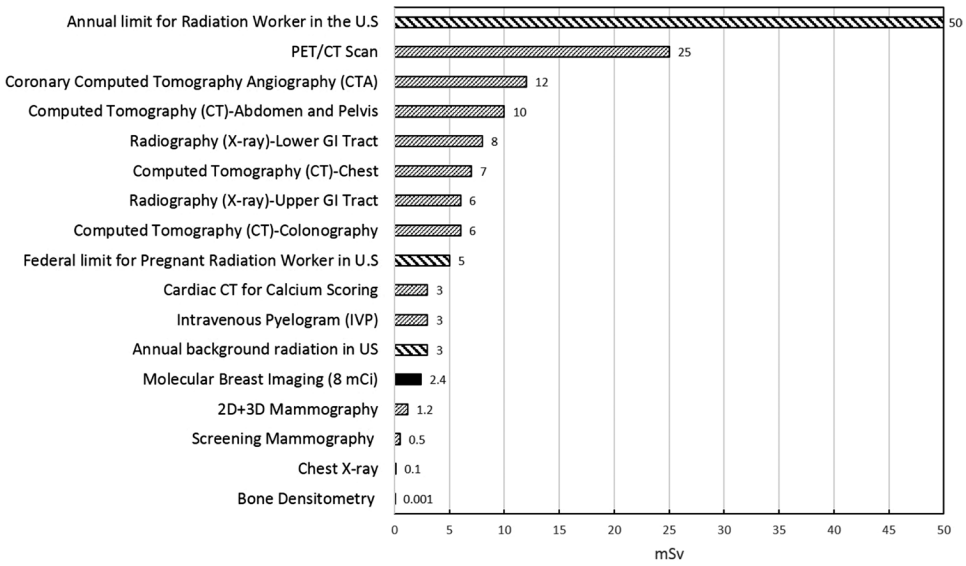


Figure 1. Chart shows the radiation dose associated with MBI compared with the radiation doses associated with other common imaging procedures, as well as the annual background radiation in the United States (*U.S.*). The U.S. federal limit for radiation workers (50 mSv) and pregnant radiation workers (5 mSv) is also shown. The radiation dose associated with MBI is far below either of these metrics. *GI* = gastrointestinal, *PET/CT* = positron emission tomography/computed tomography, *3D* = three-dimensional, *2D* = two-dimensional.

MBI was added to digital mammography versus mammography alone (20). The invasive cancer detection rate increased significantly from 1.9 to 8.8 per 1000, a relative increase of 363%, while the in situ cancer detection rate did not change significantly. Moreover, MBI substantially improved the negative and positive predictive value when added to, or compared with, mammography. Our own independent study reported similar high cancer detection rates (7.7/1000), with a baseline recall rate of 8.4%, when MBI was used for supplemental screening of women with dense breasts in routine clinical practice (23).

In many studies comparing ICDRs among multiple modalities in screening populations, the addition of each adjunct screening technique increased the cancer detection rates, but the specificity of the workflow decreased substantially with the addition of each technique (36,50). However, MBI demonstrates high sensitivity without a simultaneous increase in false-positive rates, further suggesting its suitability for screening women with dense breasts (21). This evidence led us to implement MBI in our large community-based breast imaging center for supplemental screening of non–high-risk women with dense breasts on mammogram.

Decision Algorithm for Supplemental Screening

In our facility, breast density assessment software (VolparaDensity; Volpara Solutions, Wellington, New Zealand) is used to complement the radiologist's subjective evaluation to categorize breast density on mammogram according to the American College of Radiology's Breast Imaging Reporting and Data System (BI-RADS) classifications of breast density. The breast density classifications include category A (fatty tissue), category B (scattered fibroglandular density), category C (heterogeneously dense), and category D (extremely dense) (51). It has been reported that the breast density assessment software demonstrates a moderate to strong correlation with radiologists' subjective ratings of density (52–54).

Patients with breast densities that are scored as category C or D are considered to have dense breasts. They are eligible for supplemental screening and undergo a risk-assessment test to decide between MBI or MR imaging. Each patient's lifetime risk of developing breast cancer is assessed using modified Gail and Tyrer-Cuzick models, which are embedded within the mammography management software (PenRad [version 5]; PenRad Technologies, Buffalo, Minn). The higher of the two model scores is used as the basis for recommending supplementary evaluation.

Women with dense breasts and negative screening mammograms whose lifetime risk is 20% or higher are recommended for adjunct MR imaging (Aurora Breast MRI; Aurora Imaging Technology, Danvers, Mass). Women with risk levels less than 20% are recommended for MBI (LumaGEM Molecular Breast Imaging; Gamma Medica, Salem, NH) (Fig 2).

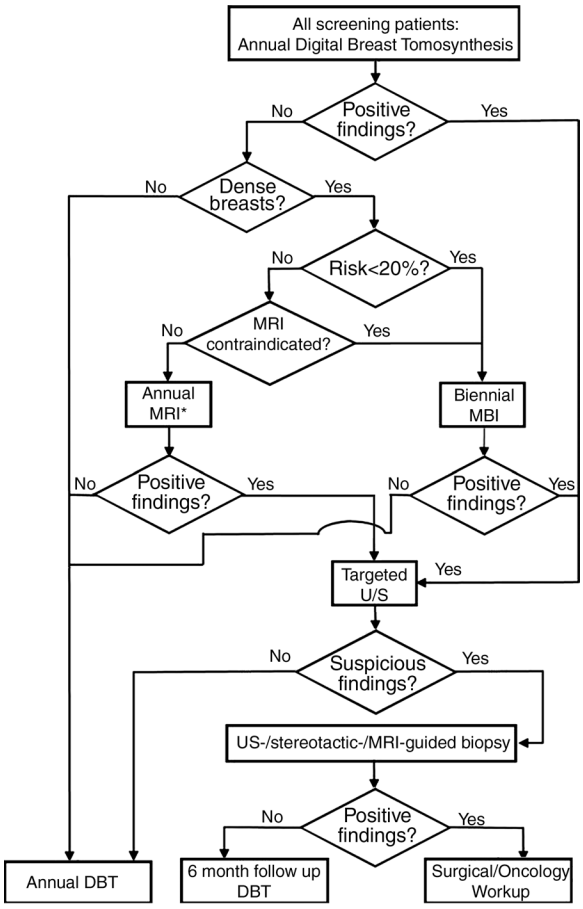


Figure 2. Flowchart shows the screening workflow, including supplemental screening for dense breast tissue, which is simplified for clarity. Targeted US examinations are performed when the lesion position is amenable. The guidance for biopsy is based on the technique in which the lesion can be clearly viewed. DBT and MR imaging are staggered so that high-risk women are imaged every 6 months (*). *MRI* = magnetic resonance imaging.

Screening Workflow and Patient Management

Women who present for breast cancer screenings at our center, which is the central hub for breast imaging for smaller satellite locations in our region, undergo DBT. The concentration of resources in our center allows the breast imagers and dedicated breast radiologists, as well as the MR imaging, US, and MBI machines, to be located under one roof. This further enhances the efficiency of our workflow and allows for the real-time reading of adjunct screening studies and additional views, as well as performing same-day targeted US examinations and biopsies.

At presentation for screening, patients are asked a series of questions by our technologists. The answers are entered into the mammography management software (PenRad), which computes breast cancer risk using models embedded in the program. DBT images are interpreted by the radiologist to assign a BI-RADS density category to the image. In addition to this subjective assessment of density, we use a breast density assessment software, which assigns an objective density score to the image and populates the results into the mammography management software. All women found to have dense tissue at mammography are notified of their density by letter, per the breast density notification legislation in Ohio. In addition, the findings, a density statement, and the recommendations for supplemental screening are communicated to the referring physician in the final mammography report.

Women with dense breasts and an increased cancer risk (>20% lifetime risk by the modified Gail and/or Tyrer-Cuzick models) are advised to undergo breast MR imaging at our breast care center. We recommend that high-risk women undergo MR imaging annually, and that this imaging be staggered with mammography to provide surveillance every 6 months.

We recommend that patients with dense breast tissue with a risk of less than 20% on the Tyrer-Cuzick and/or modified Gail models undergo MBI to supplement the mammography. The patient receives a letter by mail, and the referring physician receives the mammography report, which documents the density findings and recommendation to undergo MBI as supplemental screening.

Additionally, patients who undergo diagnostic mammography for correlation of clinical symptoms and are found to have dense breast tissue are recommended for MBI. In those cases, we follow the written communication with a phone call to the patient to schedule the MBI. Two dedicated schedulers assist patients with verifying their insurance coverage for the test, if necessary. We contact the insurance carriers directly, many of which do not require precertification. We provide our patients with the *International Classification of Diseases, Tenth Revision* (ICD-10) code and *Current Procedural Terminology* (CPT) billing code for the examination and diagnosis. We advise patients to verify their own coverage. In the United States, CPT code 78800 (radiopharmaceutical localization of tumor or distribution of radiopharmaceutical agent[s]; limited area) is used for MBI. In the United States, the average reimbursement from private insurance companies and Medicare is approximately $330.

MBI is performed during the follicular phase of the menstrual cycle, between days 2 and 12, when fibroglandular tissue is not as physiologically active in premenopausal women. The patients are required to fast for 3 hours prior to the study (but they may consume diet soda, coffee without cream, or water), and they are provided with a warming blanket on arrival. These measures have been suggested to enhance uptake of the tracer in pathologic lesions.

The patient receives 6–8 mCi (222–296 MBq) of ^{99m}Tc-sestamibi intravenously, which is administered by a nuclear medicine technologist (47). There is no wait time between the radiotracer administration and the beginning of imaging, as the uptake time of ^{99m}Tc-sestamibi is less than 5 minutes.

Images are acquired using light breast compression (about 5 lbs [2.3 kg]) for 7 minutes per view, for a total of approximately 28 minutes. Eight images in the craniocaudal (CC) and mediolateral oblique (MLO) views are generated during a standard bilateral study and are immediately available to the interpreting radiologist on site. The total interpretation time per study is about 30 seconds, in most cases. In generating a report, the first documented consideration is the reference to the comparative mammogram, followed by the degree of background parenchymal uptake (BPU) of the tracer, which is classified as none, mild, moderate, or marked (if symmetric). The pathologic uptake is described as mass-like or non–mass-like and is classified as a mild, moderate, or intense accumulation compared with BPU.

To facilitate standardized interpretation of MBI examinations, a lexicon for MBI has been developed using a BI-RADS–like structure (55). Some nonmalignant processes, such as lymph nodes, fibroadenomas, and fat necrosis, may result in false-positive examinations, so MBI images are interpreted alongside the corresponding mammograms and US images. Focal uptake that corresponds with a known physiologic process, previously shown on mammogram or US image, is noted as such. Representative clinical cases illustrating these types of situations are presented in the case studies section of this article.

Following the examination, the patient is invited to the reading room to review the MBI results with the radiologist. Patients have anecdotally reported that this reduces their anxiety and improves their overall experience, because they do not have to wait for results. In the case of negative results, women are recommended to continue annual mammography. To minimize radiation exposure, we currently recommend biennial MBI as supplemental screening in non–high-risk women.

Positive findings at MBI are evaluated immediately with targeted US examination. The majority of MBI-identified lesions are found with US, which allows for same-day biopsy. In the rare case that lesions cannot be located with US, the patient is scheduled for MR imaging. Biopsies are primarily US-guided, but stereotactic core-needle or MR imaging–guided biopsies are performed in women with lesions not visible at US. An examination with a false-positive result confirmed by pathologic analysis is recommended for a short-term follow-up mammography to establish new baseline mammographic images.

Implementing MBI in Clinical Practice

At our facility, the integration of MBI into clinical practice has proven to be straightforward and seamless. The equipment fits into a 10 × 12-ft (3.0 × 3.7-m) room that does not need to be radiation-shielded. It is necessary that the facility has access to a physicist to obtain and maintain a radioactive materials license, a physician with a nuclear medicine license, a state-licensed nuclear technician to perform injections, and a radiation safety officer (who can be the physicist or a physician with a nuclear medicine license). We benefit from being connected to a tertiary hospital, which facilitates many of these requirements. At our center, we employ nuclear medicine and mammogram technologists who collaborate on each patient study, view the images in real time, and optimize positioning before recording images to ensure the highest-quality result.

Communication has been an integral component in the implementation and success of our MBI program. Education of our colleagues, referring physicians, and insurance companies by way of phone calls, letters, and lectures has been crucial for the maintenance and continuation of the program. MBI is now well accepted by our community physicians and continues to be readily reimbursed by insurance companies.

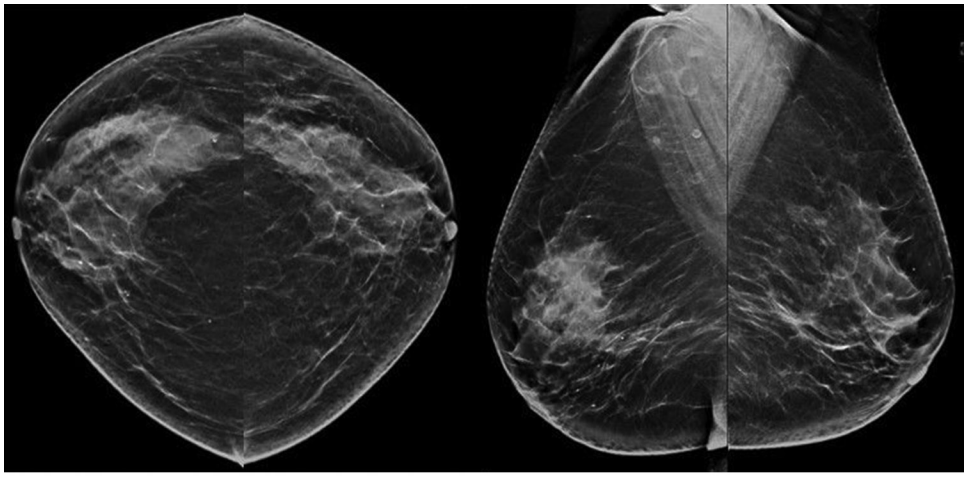
Case Studies

In this section, we present several cases that illustrate the use of MBI in supplemental screening and problem solving.

Supplemental Screening for Dense/Complex Mammograms

Case 1.—A 55-year-old asymptomatic woman presented for a routine screening and was imaged with DBT. The DBT C-view images were interpreted as negative by the reading radiologist (Fig 3). The breast density algorithm assessment of heterogeneously dense breasts correlated with the radiologist's assessment. The risk-assessment software showed a lifetime risk below 20%, and the patient was recommended for supplemental screening with MBI.

MBI of the right breast demonstrated focal uptake in an area of density seen on mammograms, as seen in Figure 3b. A targeted US examination helped confirm a solid irregular



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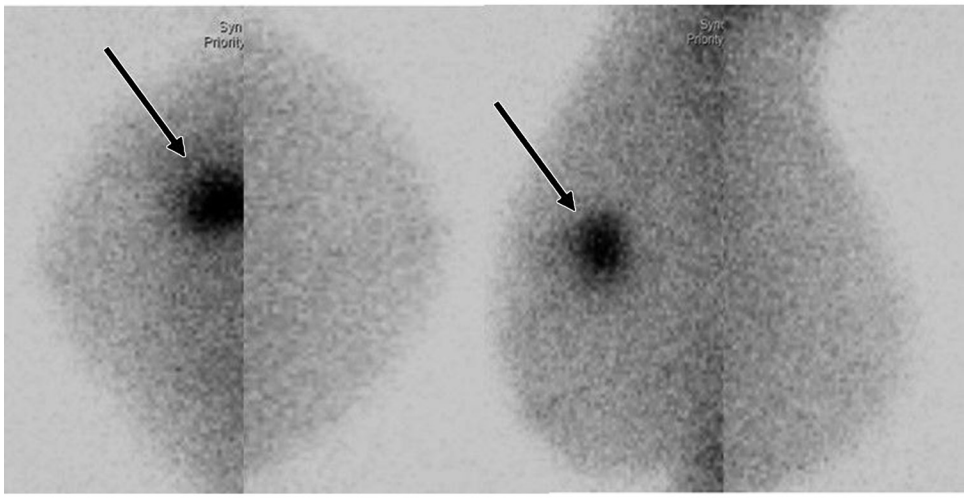

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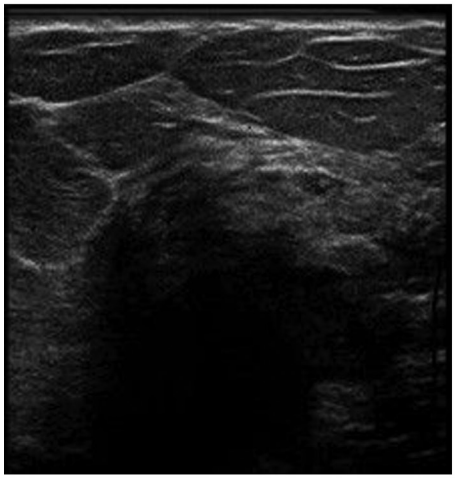

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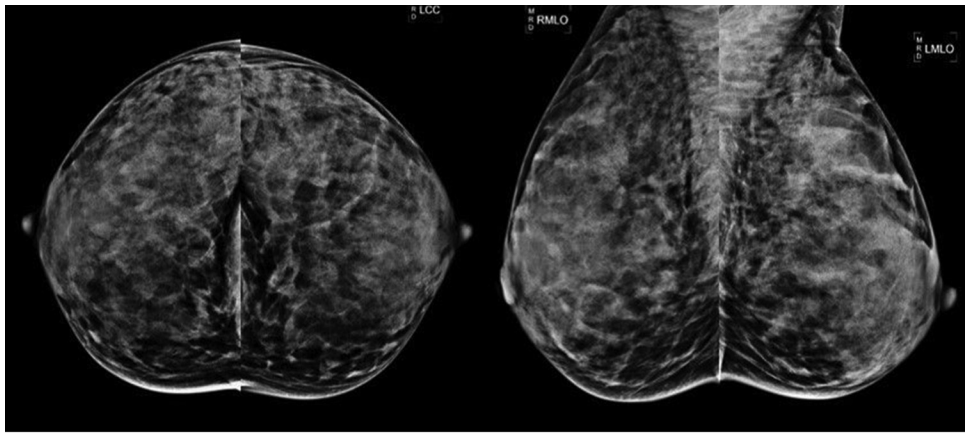
Figure 3. Case 1. A woman with heterogeneously dense breasts. **(a)** Bilateral CC (left) and MLO (right) DBT mammograms were interpreted as negative. **(b)** Supplemental CC (left) and MLO (right) molecular breast images show focal uptake (arrows) in an area of density seen on mammograms in the right breast. **(c)** Transverse targeted US image depicts a solid mass at the 10-o'clock position and at mid depth. The results of a US-guided biopsy confirmed invasive ductal carcinoma (IDC).

mass (Fig 3c). The results of a US-guided biopsy confirmed invasive ductal carcinoma (IDC).

Case 2.—Figure 4 shows the DBT C-view images of an extremely dense mammogram. The subsequent supplemental MBI was negative. The audit of our supplemental screening MBI cases showed the baseline recall rate (the recall rate of patients who have not undergone prior MBI) to be low (8.4%). As with all modalities, the recall rates will reduce further when prior images are available for comparison. The high negative predictive value of MBI, previously reported at 99.7% (20), is reassuring to both radiologists and patients at our center in cases in which a mammogram is too dense for accurate interpretation and MBI is clearly negative.

In this case, the BPU was reduced in regions corresponding to higher mammographic breast density. There is no correlation between breast density in mammograms and the BPU in MBI. The BPU shown in this case is categorized as



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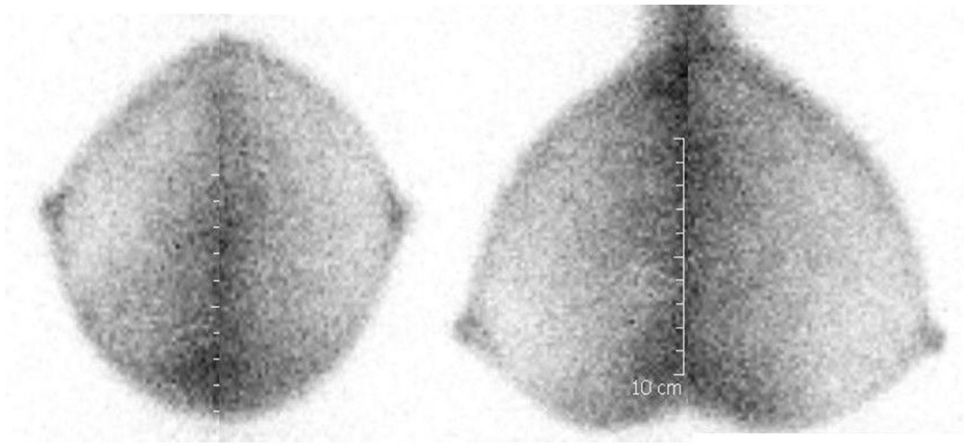

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Figure 4. Case 2. A woman with extremely dense breasts. **(a)** Bilateral CC (left) and MLO (right) DBT C-view mammograms. **(b)** Supplemental bilateral CC (left) and MLO (right) molecular breast images do not show an area of increased uptake and illustrate uniform background uptake of the tracer, which is considered to be physiologic. No further workup was required. In comparing the DBT mammograms and molecular breast images, it is clear that BPU is not tied to density.

photopenic (56), with the BPU response categorized as uniform. Researchers at the Mayo Clinic have shown preliminary evidence that MBI BPU may be an independent risk factor for breast cancer, with the risk increasing with increased BPU (57).

Case 3.—A 52-year-old woman was recommended for supplemental screening due to extremely dense tissue on mammograms (Fig 5a). At MBI, the left breast exhibited mass-like accumulation corresponding to a previously biopsy-proven fibroadenoma. An additional mass-like uptake at the 11-o'clock position in the right breast was also appreciated. A targeted US examination showed an irregular hypoechoic mass, and the biopsy results confirmed IDC.

Case 4.—We present a case in which a patient was scheduled for same-day screening mammography and MBI due to known dense breast tissue (Fig 6). A 67-year-old woman presented with no breast concerns, and mammograms were interpreted as negative. MBI revealed uptake at the 12-o'clock position in the left breast. A targeted US examination was immediately performed and helped confirm a 1.1-cm solid mass. The results from a same-day US-guided biopsy confirmed IDC.

High-Risk Screening and MR Imaging Contraindications

Case 5.— This case presents an example of a high-risk patient who could not undergo MR imaging due to the presence of a pacemaker (Fig 7). A 63-year-old woman received breast implants following a previous breast cancer surgery. The encapsulation of the left implant prevented displacement and meaningful mammography views (Fig 7a). The patient underwent supplemental screening with MBI, which showed focal mass-like uptake in the left breast. A targeted US examination demonstrated a 0.8-cm lobulated solid mass, and the results from a US-guided biopsy confirmed IDC.

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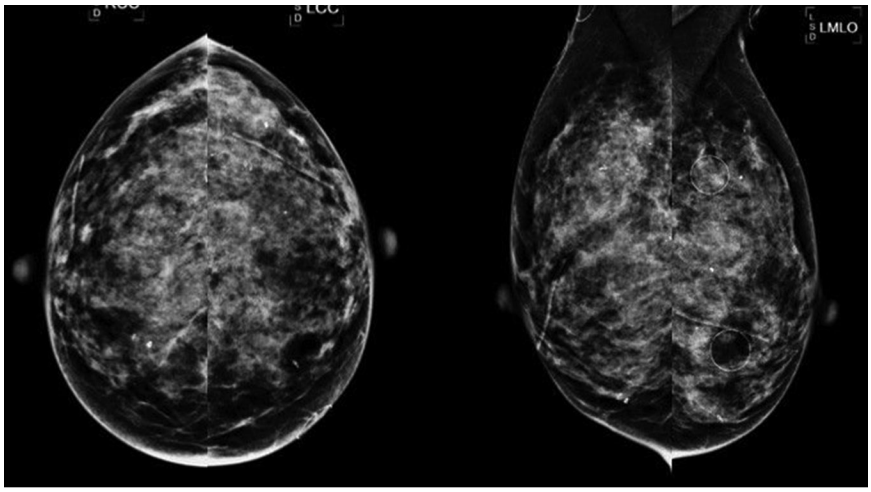

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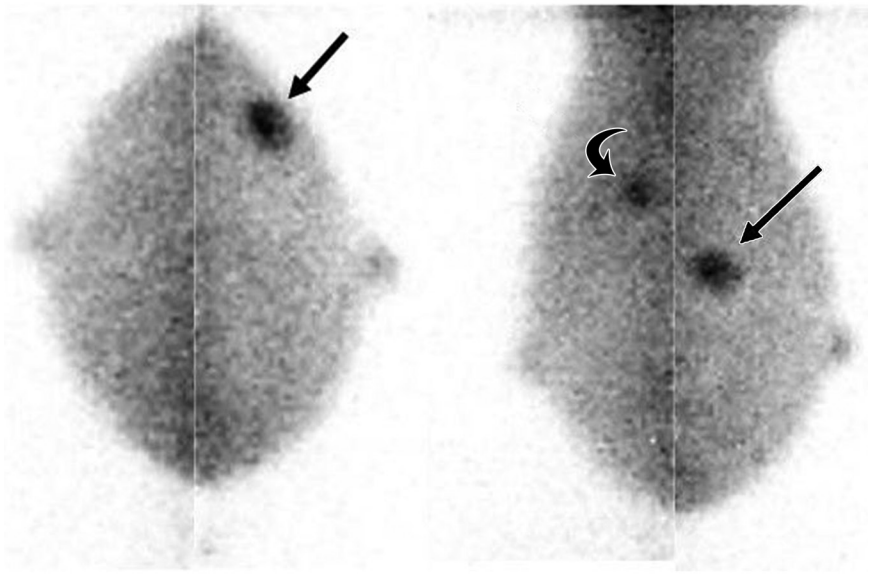

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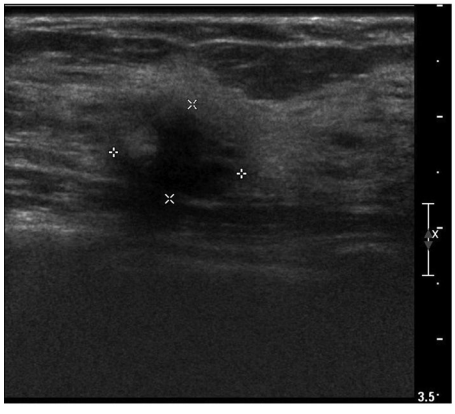

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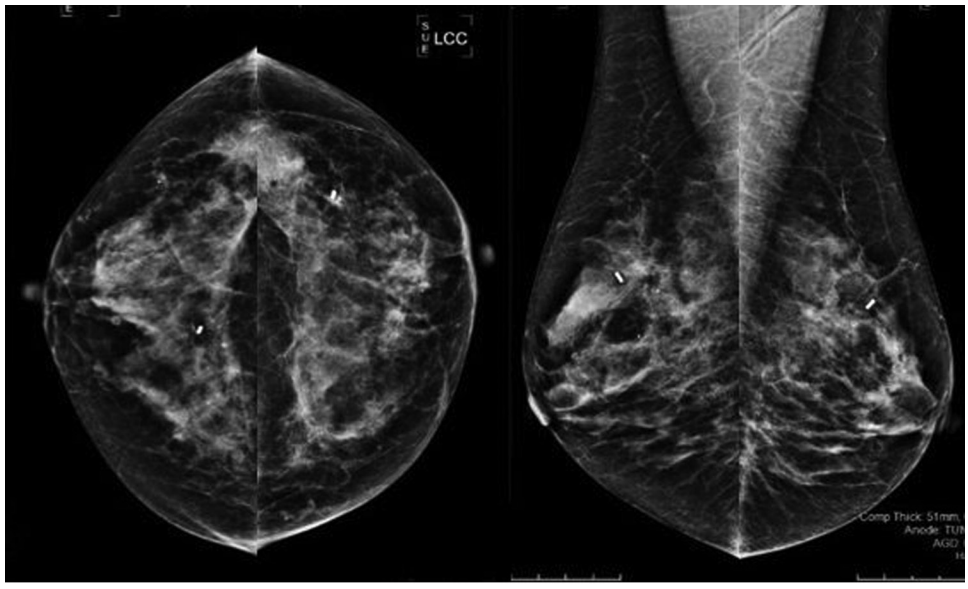
Figure 5. Case 3. Extremely dense tissue in a 52-year-old woman. **(a)** Bilateral CC (left) and MLO (right) mammograms show extremely dense tissue. **(b)** Supplemental CC (left) and MLO (right) molecular breast images show a mass-like accumulation (straight arrows) corresponding to a known fibroadenoma at the 3-o'clock position. Additional mass-like uptake (curved arrow) at the 11-o'clock position in the right breast is also seen on the MLO view. **(c)** Sagittal targeted US image shows a vague irregular hypoechoic mass at posterior depth. The US-guided biopsy results confirmed IDC.

Case 6.—MBI is useful when a high-risk patient cannot undergo MR imaging, and it may also be used as an adjunct for preoperative planning in such patients. A 60-year-old patient, who was unable to tolerate MR imaging, underwent MBI for presurgical planning to excise an atypical ductal hyperplasia in the left breast, which had been confirmed by the results of a stereotactic core-needle biopsy (Fig 8). MBI showed a subcentimeter area of uptake in the right breast. A targeted US examination helped confirm that the suspicious mass was solid, and the results of the biopsy confirmed IDC.

MBI Diagnostic Use for Problem Solving

In addition to the uses of MBI in the cases previously described, we have found MBI to be an excellent "problem solver" to help direct management, particularly when multiple findings of unknown significance are present or after conventional imaging has been exhausted.

Case 7.—This case describes how MBI is used to guide management (Fig 9). A 42-year-old patient presented with focal pain in the left breast. Diagnostic mammography was interpreted as inconclusive, and the US findings at the



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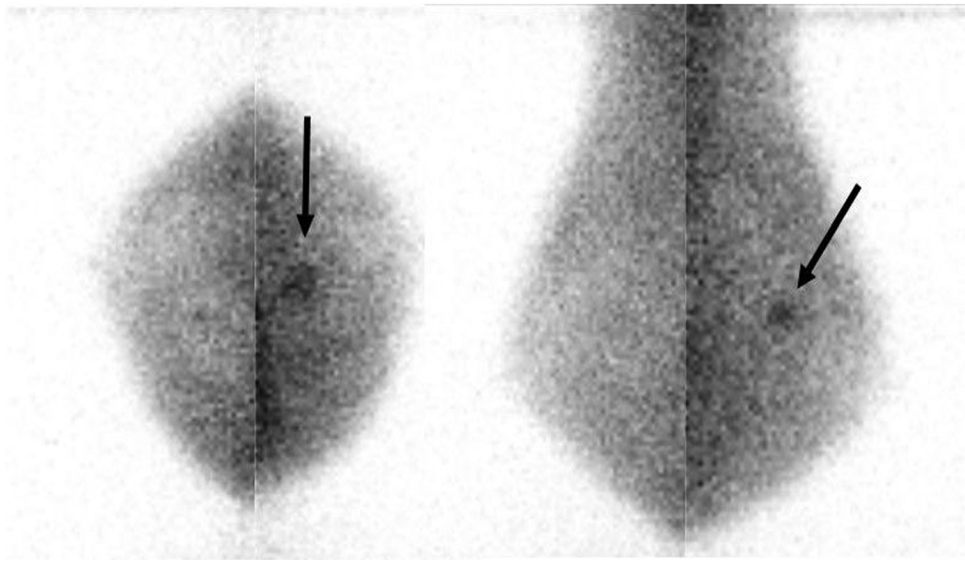

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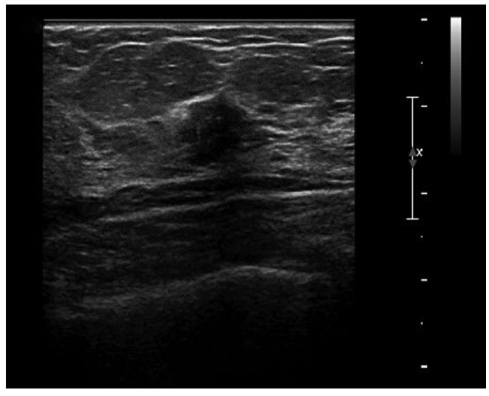

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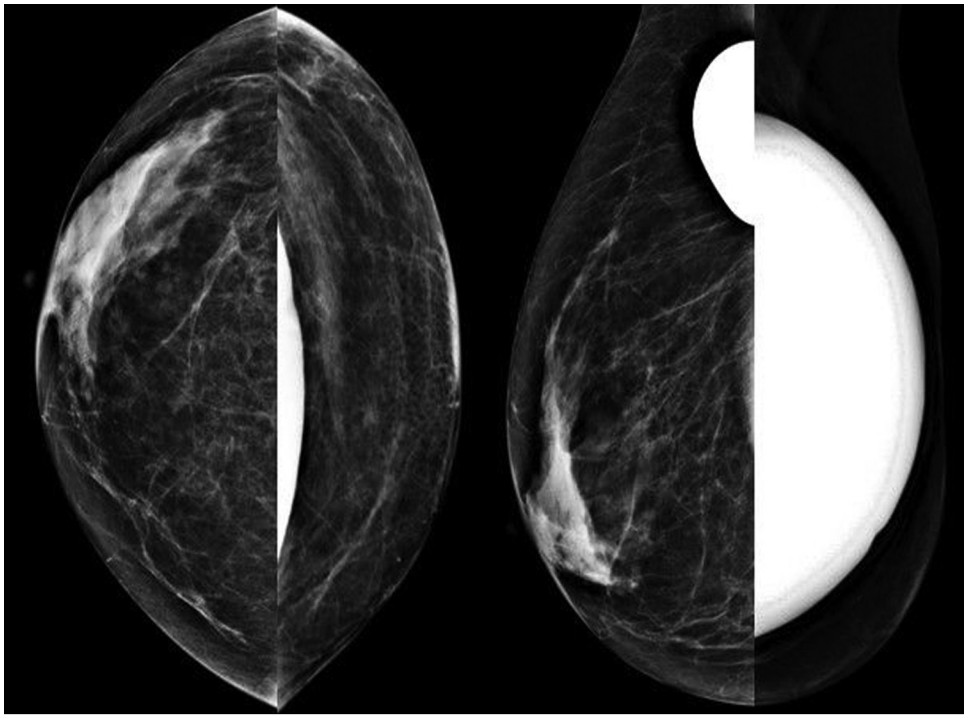
Figure 6. Case 4. A 67-year-old woman with no breast concerns. **(a)** Bilateral CC (left) and MLO (right) mammograms were interpreted as negative. MBI was performed as adjunct screening due to the density of the tissue. **(b)** Bilateral CC (left) and MLO (right) molecular breast images show uptake (arrows) at the 12-o'clock position in the left breast. **(c)** Transverse targeted US image shows a 1.1-cm solid mass at the 12-o'clock position at mid depth. Same-day US-guided biopsy revealed IDC.

8–9-o'clock position were of uncertain importance. MBI revealed two areas of focal uptake around the 1-o'clock position with no uptake at the 8–9-o'clock position; therefore, US findings in that location were assumed to be benign. A second-look US examination showed hypoechoic solid masses corresponding to the MBI uptake. The results of a biopsy confirmed two adjacent tumors, both IDC. The surgical pathology analysis after mastectomy confirmed multifocal ductal carcinoma in situ (DCIS), multifocal and multicentric IDC, fibroadenoma, and LCIS.

RadioGraphics

Figure 7. Case 5. A high-risk woman with dense breasts who could not undergo MR imaging due to the presence of a pacemaker. **(a)** Bilateral CC (left) and MLO (right) mammograms show the encapsulation of an implant (which was present after reconstruction following surgery for a previous cancer) that prevented displacement and meaningful mammography views. The patient underwent supplemental screening with MBI. **(b)** Bilateral CC (left) and MLO (right) molecular breast images show a mass-like uptake (arrows) at the 3-o'clock position in the left breast. **(c)** Sagittal targeted US image helps confirm a 0.8-cm lobulated solid mass at mid depth. The results of the biopsy confirmed IDC.



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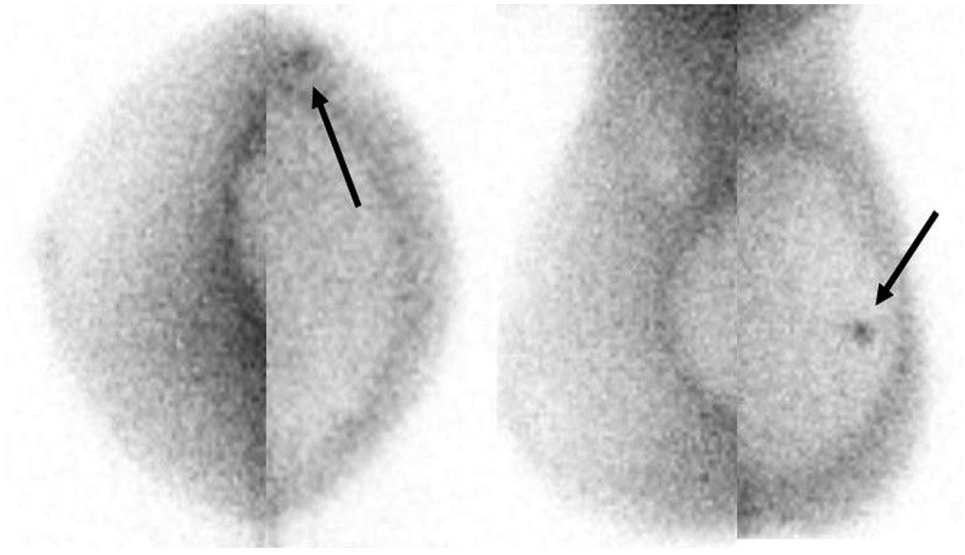

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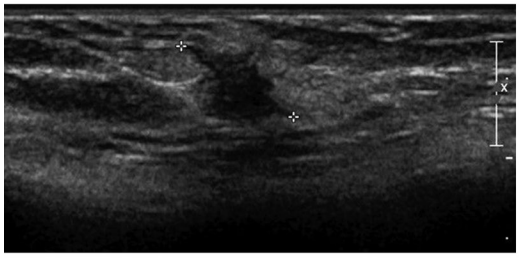

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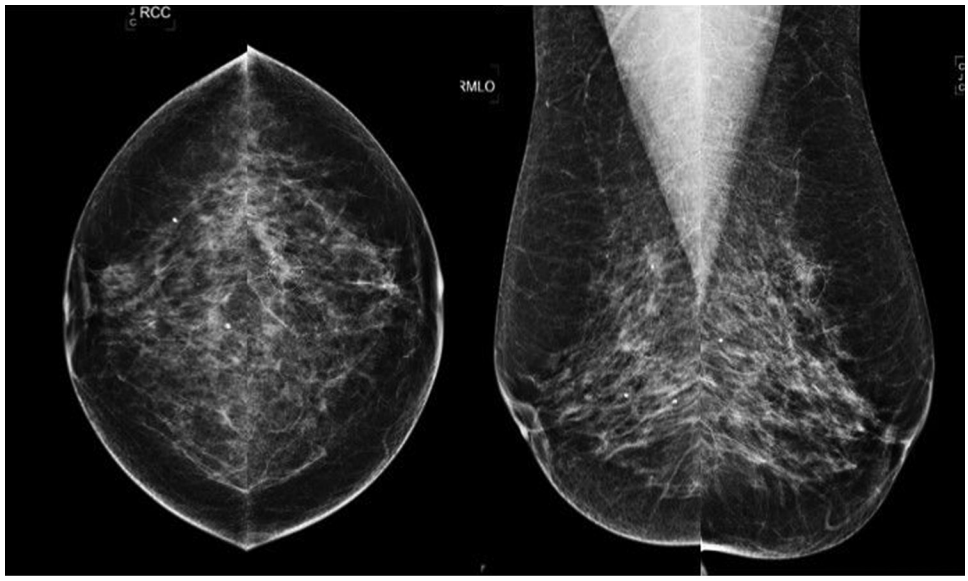

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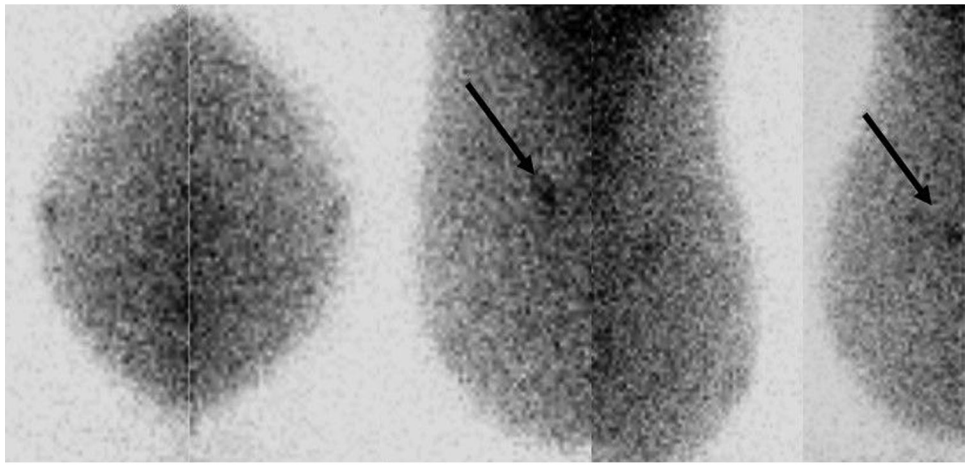

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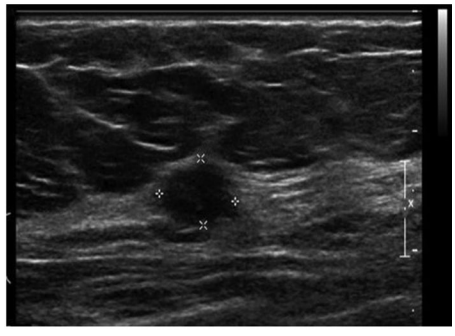

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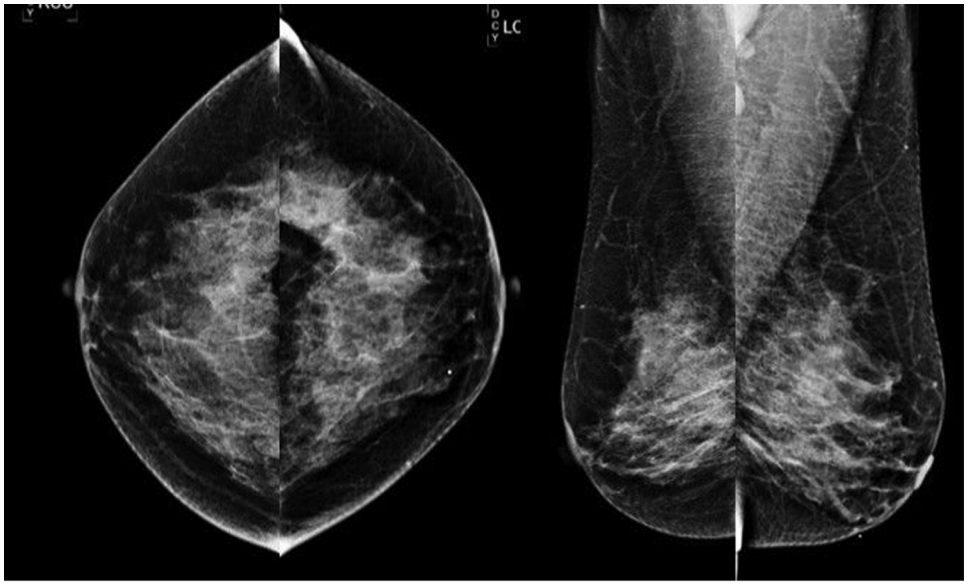
Figure 8. Case 6. A 60-year-old patient who could not tolerate MR imaging underwent MBI for presurgical planning to treat an atypical ductal hyperplasia in the left breast. **(a)** Bilateral CC (left) and MLO (right) mammograms are shown for comparison. **(b)** Bilateral CC (left) and MLO (center, right) molecular breast images show a subcentimeter area of uptake (arrows) in the right breast, most easily seen on the right MLO image. **(c)** Sagittal targeted US image helps confirm that the mass at the 10-o'clock position at posterior depth is solid. The results of the biopsy confirmed IDC.

Case 8.—Figure 10 shows the images obtained from a 38-year-old patient seen at our center for the evaluation of a lump in the right breast. Diagnostic mammograms and targeted US images demonstrated that the lump correlated with a cyst, which was interpreted as benign. MBI was recommended due to a complex dense mammogram. The focal uptake of the radiotracer prompted a repeat US examination, and it was discovered that the original study used improper gain. A solid mass was revealed, and the results of a biopsy confirmed IDC.

Case 9.—A 47-year-old patient presented to the center with contraction and hardening of the right breast and a vague lump. The initial mammogram showed new asymmetry in the size of the right breast, but the targeted US examination with color power Doppler vocal fremitus US was indeterminate, as shown in Figure 11. MBI was performed to guide management and showed focal uptake. A second-look US of the area of tracer



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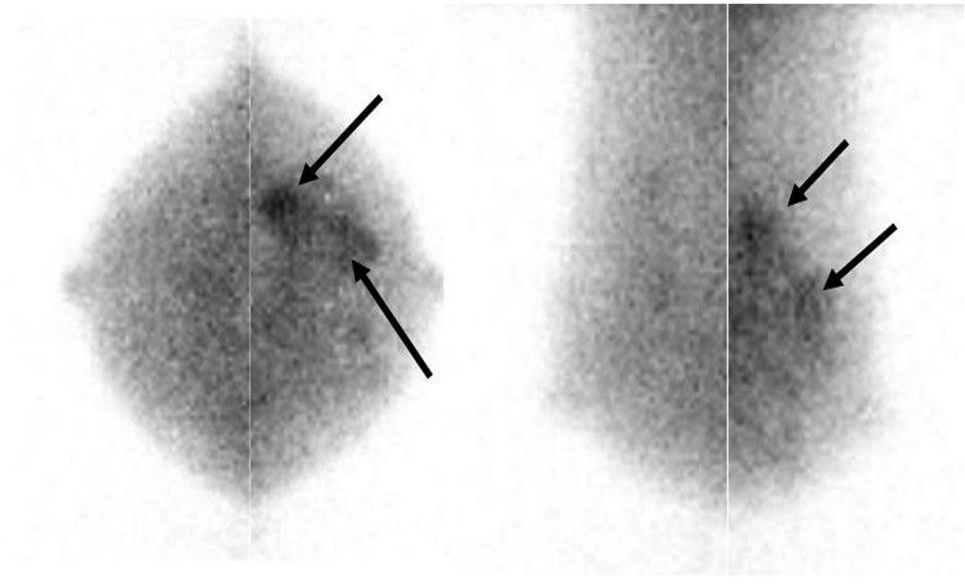

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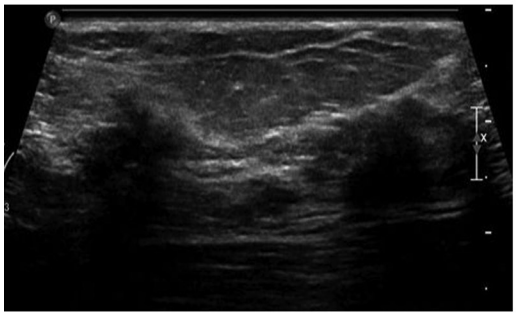

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Figure 9. Case 7. MBI used as a problem solver after mammography was indeterminate and a targeted US image showed findings of unknown importance in a 42-year-old patient with focal pain in the left breast. **(a)** Bilateral CC (left) and MLO (right) mammograms did not correlate with the location of focal pain and were inconclusive. Targeted US image showed a lobulated hypoechoic mass at the 9-o'clock position (not shown). **(b)** Bilateral CC (left) and MLO (right) molecular breast images show two areas of focal uptake (arrows) surrounding the 1-o'clock position, while no accumulation was noted at the 8–9-o'clock position (assumed benign). **(c)** Transverse second-look US image shows two adjacent hypoechoic solid masses: a 1.4-cm mass in the posterior position and a 1.0-cm mass in the anterior position. Results from a US-guided biopsy confirmed adjacent IDC.

accumulation showed some heterogeneity to the breast echo pattern at the 11–12-o'clock position at posterior depth, which warranted a US-guided biopsy. A pathologic analysis confirmed invasive lobular carcinoma (ILC).

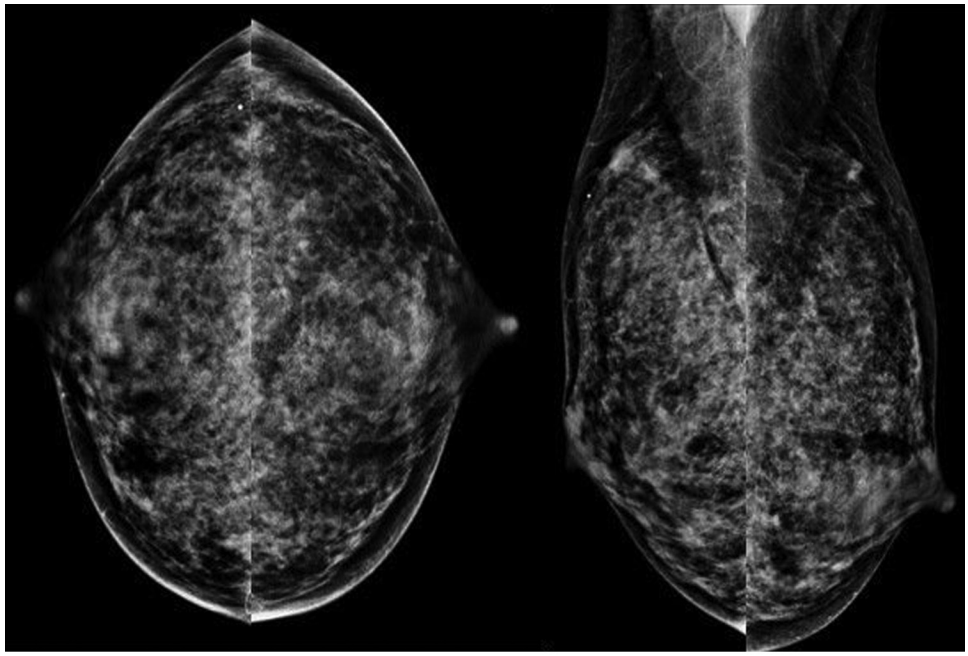
False Positives

Case 10.—Figure 12 shows the images obtained in a 36-year-old woman with dense tissue and a history of seat belt trauma to the breast. MBI showed focal uptake in the left breast. A second-look US examination (Fig 12c) was performed, and the area of uptake corresponded to findings indicative of fat necrosis and oil cysts (false positive).

Case 11.—An asymptomatic 42-year-old woman with a history of stereotactic core-needle breast biopsy for evaluation of calcifications (confirmed usual ductal hyperplasia [DHU] and fibrocystic changes [FC]) and previous MBI with symmetric physiologic tracer uptake presented for screening DBT. Due to heterogeneously dense tissue, supplemental screening was recommended. MBI showed

RadioGraphics

Figure 10. Case 8. A 38-year-old woman presented with a lump in the right breast. **(a)** Bilateral CC (left) and MLO (right) diagnostic mammograms were interpreted as inconclusive and required additional imaging. Targeted US image (with later discovered improper gain) suggested the lump correlated with a cyst and was interpreted as negative (not shown). **(b)** Bilateral CC (left) and MLO (right) molecular breast images show focal uptake (arrows) of radiotracer, which prompted a second-look US examination. **(c)** Transverse second-look US image shows a solid mass, and the results of a US-guided biopsy confirmed IDC.



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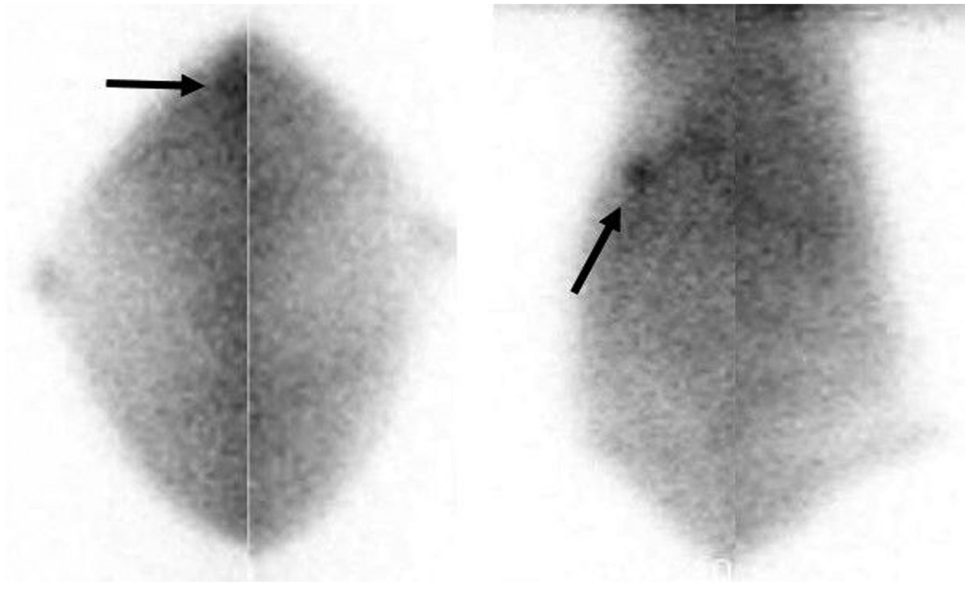

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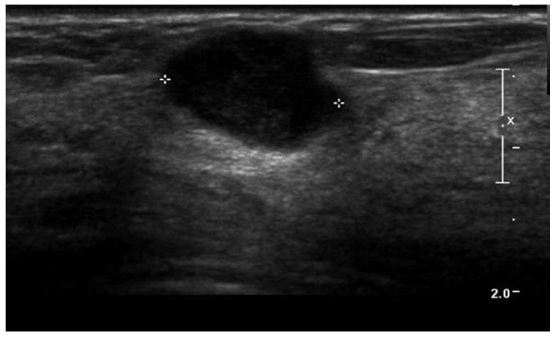

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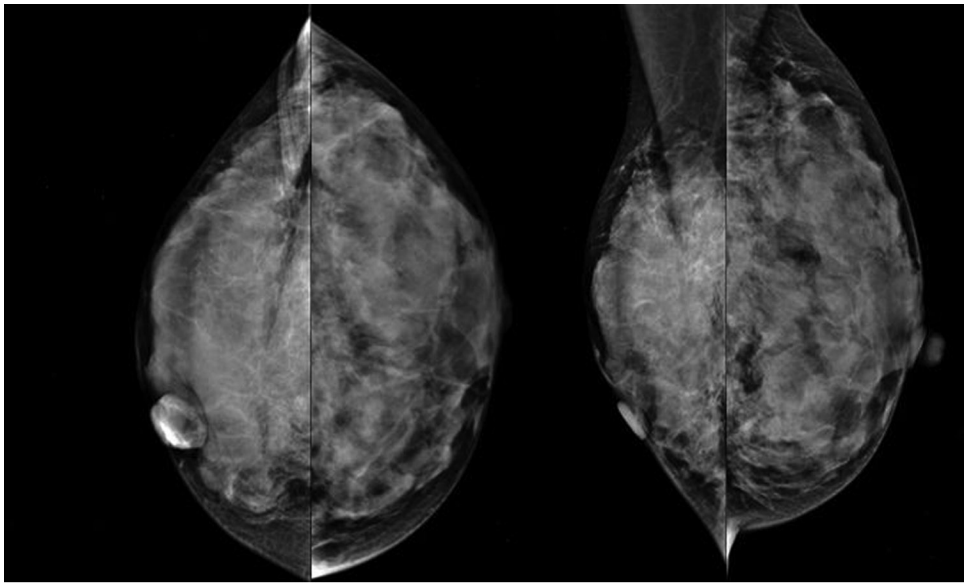
Figure 11. Case 9. A 47-year-old patient with contraction of the right breast. **(a)** Bilateral CC (left) and MLO (right) DBT mammograms help confirm size asymmetry of the right breast. **(b)** Sagittal targeted US image was indeterminate, requiring MBI for further evaluation. **(c)** CC (left) and MLO (right) molecular breast images show focal uptake at the 11–12-o'clock position (arrows). The results of a US-guided biopsy confirmed invasive lobular carcinoma (ILC).



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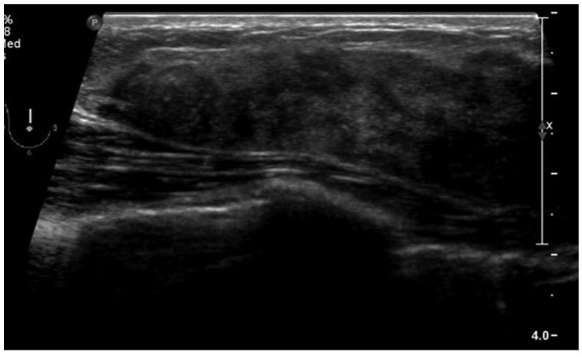

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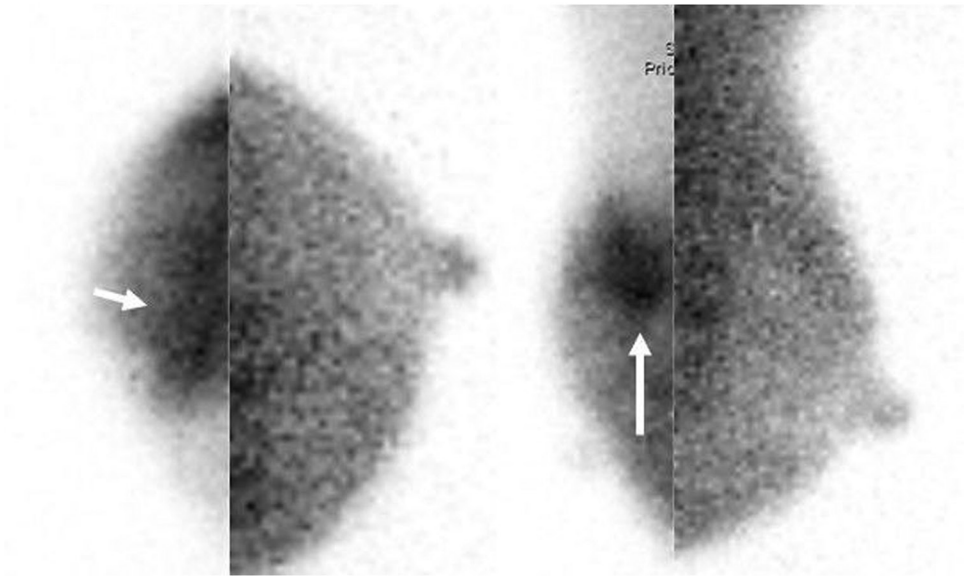

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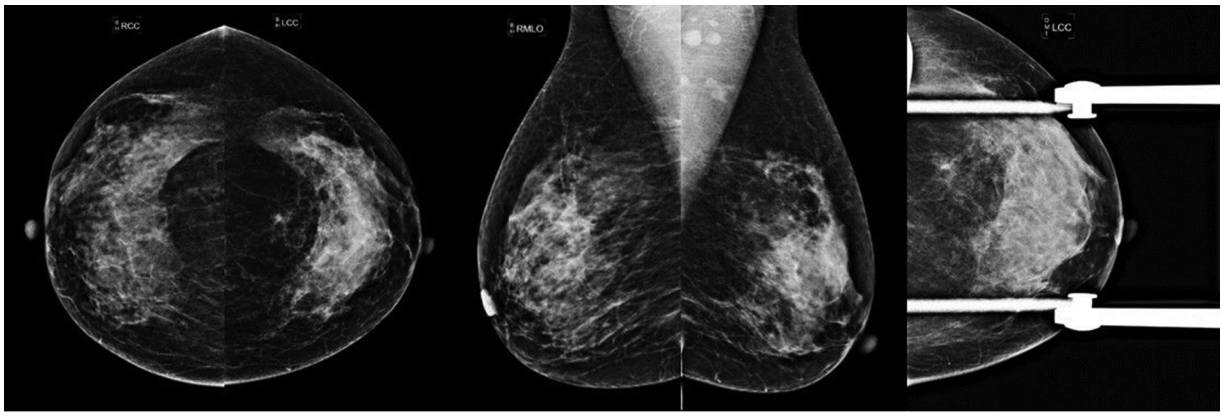

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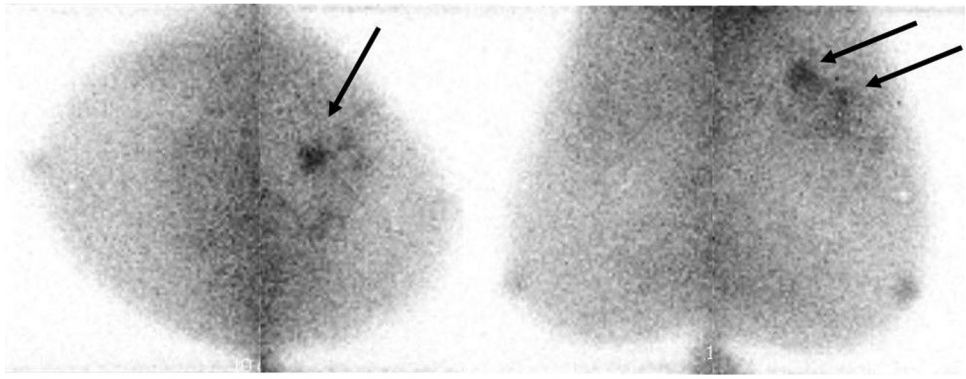

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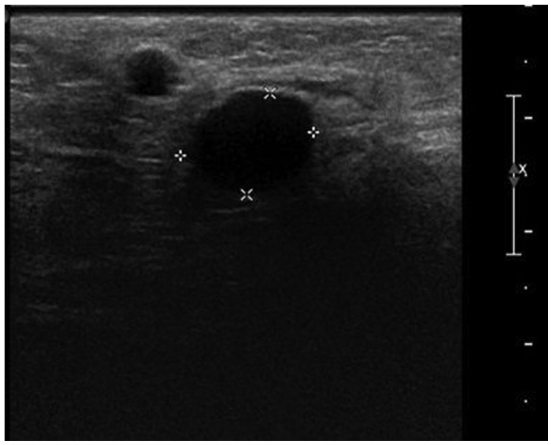

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Figure 12. Case 10. A 36-year-old woman with dense tissue and a history of seat belt trauma to the breast. **(a)** Inconclusive screening mammograms prompted bilateral diagnostic CC (left, right) and MLO (center) mammograms; initial targeted US images were interpreted as negative. **(b)** Bilateral CC (left) and MLO (right) molecular breast images show focal uptake in the left breast (arrows). **(c)** Transverse second-look US image shows that the uptake in **b** corresponds to findings indicative of fat necrosis and oil cysts.

focal uptake at the 10-o'clock position, which was immediately evaluated with targeted US (Fig 13). A 2-cm solid hypoechoic mass was located at posterior depth in this position, prompting a US-guided biopsy. A pathologic analysis of the tissue indicated pseudoangiomatous stromal hyperplasia (PASH), in addition to previously noted DHU and FC. No further workup was required.

Case 12.—The images shown in Figure 14 demonstrate another case where a physiologic process resulted in a false-positive examination. A 61-year-old woman presented for supplemental screening with MBI after a negative mammography examination. Focal asymmetric tracer accumulation was noted in the left breast on CC projections at the 3-o'clock position. A targeted US examination demonstrated an incidental intramammary lymph node accounting for tracer accumulation, which color osteography helped to confirm. The examination was rated as negative, and the patient was recommended to continue biennial MBI screening.

Conclusion

Overall, we have integrated an efficient workflow that includes adjunct screening for women who are not particularly well served by anatomic techniques, such as digital mammography or DBT alone. In addition, we have presented the logistics for implementation of a new screening

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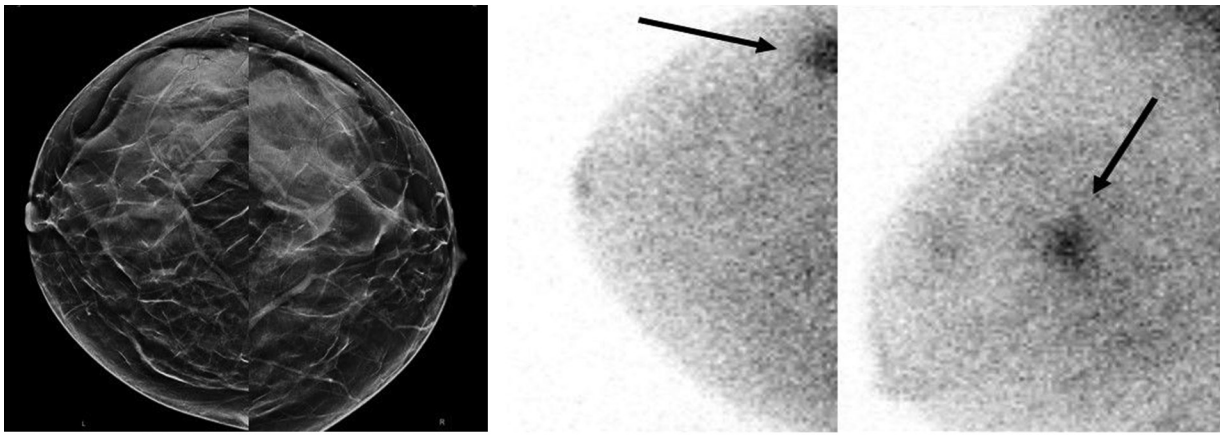

Figure 13. Case 11. A patient recommended to undergo MBI due to heterogeneously dense tissue. **(a)** Bilateral DBT CC images show negative screening results. **(b)** Unilateral CC (left) and MLO (right) molecular breast images show asymmetric uptake (arrows) at the 10-o'clock position in the right breast. **(c)** Sagittal targeted US image shows a 2-cm solid mass-like area at posterior depth, which prompted biopsy. Pseudoangiomatous stromal hyperplasia (PASH) was identified with pathologic analysis as the explanation for the uptake.

technique for average-risk women with dense breasts. This modality has been easy to implement, has had high patient satisfaction, and—with proper education and communication—has been easily reimbursable. Our experience has proven it effective in a screening population of women with dense breasts, and its integration has covered a gap in the screening techniques available to women with dense breasts.

***Disclosures of Conflicts of Interest.*—R.B.S.** *Activities related to the present article:* reports to and is a member of the Gamma Medical Clinical Advisory Board. *Activities not related to the present article:* disclosed no relevant relationships. *Other activities:* disclosed no relevant relationships.

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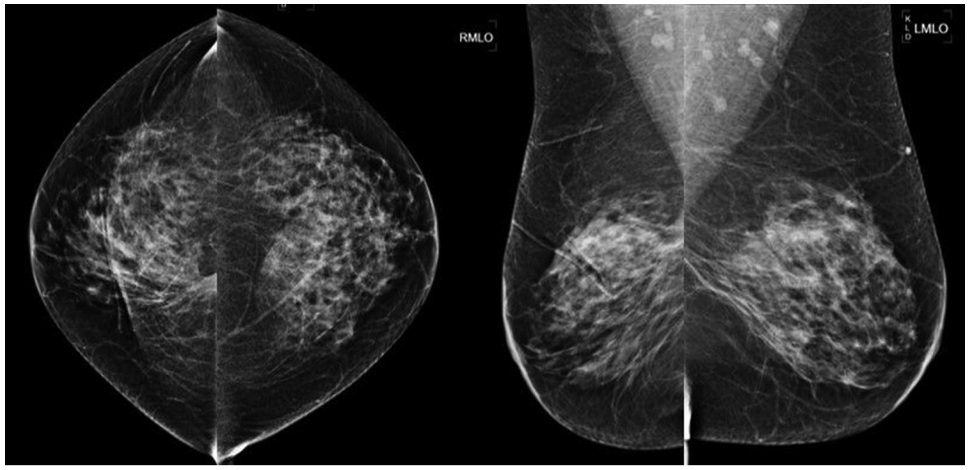

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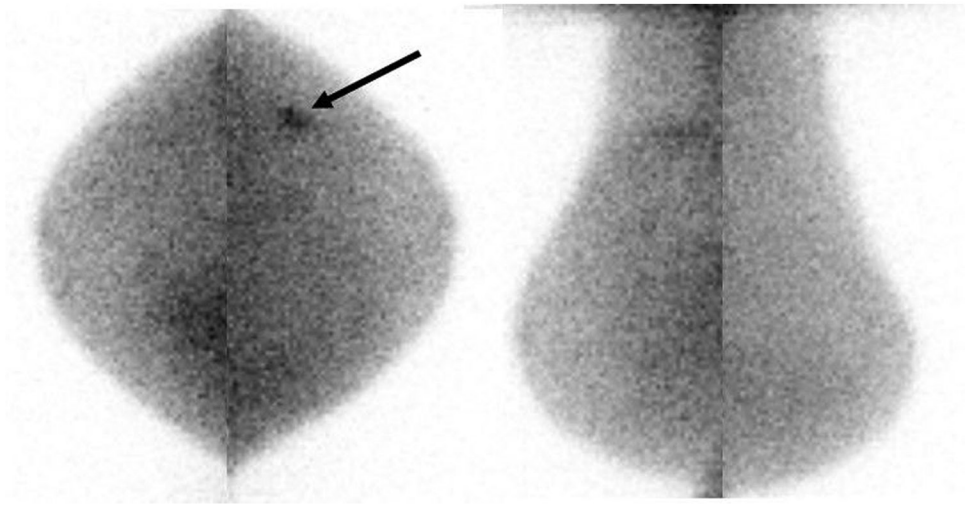

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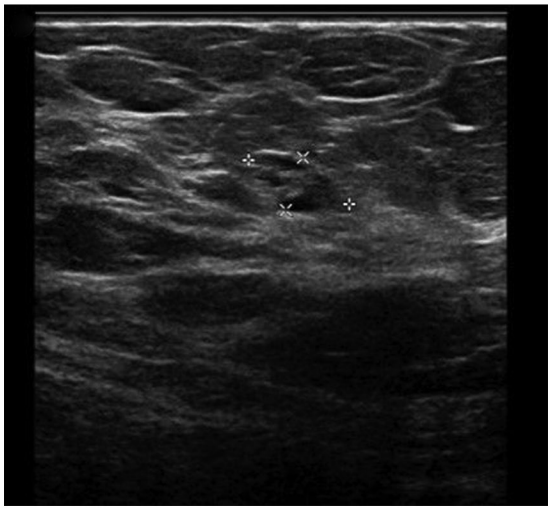

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Figure 14. Case 12. **(a)** Bilateral CC (left) and MLO (right) mammograms, interpreted as negative, show dense and complex tissue. **(b)** Bilateral CC (left) and MLO (right) molecular breast images were obtained for adjunct screening. The CC image shows focal uptake (arrow) at the 3-o'clock position. **(c)** Transverse targeted US image indicates an intramammary lymph node, which was correlated with the mammographic findings on the CC view (arrow in **b**). The examination results were negative, and no further workup was required.

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