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Diagnostic Workup and Costs of a Single Supplemental Molecular Breast Imaging Screen of Mammographically Dense Breasts

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Abstract

OBJECTIVE—The purpose of this study was to examine additional diagnostic workup and costs generated by addition of a single molecular breast imaging (MBI) examination to screening mammography for women with dense breasts.

SUBJECTS AND METHODS—Women with mammographically dense breasts presenting for screening mammography underwent adjunct MBI performed with 300 MBq ^{99m}Tc-sestamibi and a direct-conversion cadmium-zinc-telluride dual-head gamma camera. All subsequent imaging tests and biopsies were tracked for a minimum of 1 year. The positive predictive value of biopsies performed (PPV3), benign biopsy rate, cost per patient screened, and cost per cancer detected were determined.

RESULTS—A total of 1651 women enrolled in the study. Among the 1585 participants with complete reference standard, screening mammography alone prompted diagnostic workup of 175 (11.0%) patients and biopsy of 20 (1.3%) and yielded five malignancies (PPV3, 25%). Results of combined screening mammography plus MBI prompted diagnostic workup of 279 patients (17.6%) and biopsy of 67 (4.2%) and yielded 19 malignancies (PPV3, 28.4%). The benign biopsy rates were 0.9% (15 of 1585) for screening mammography alone and 3.0% (48 of 1585) for the combination ($p < 0.001$). The addition of MBI increased the cost per patient screened from \$176 for mammography alone to \$571 for the combination. However, cost per cancer detected was lower for the combination (\$47,597) than for mammography alone (\$55,851).

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Supplemental Data

Available online at www.ajronline.org.

CONCLUSION—The addition of MBI to screening mammography of women with dense breasts increased the overall costs and benign biopsy rate but also increased the cancer detection rate, which resulted in a lower cost per cancer detected than with screening mammography alone.

Keywords

benign biopsy rate; breast density; costs; molecular breast imaging; supplemental screening

Because screening mammography has decreased sensitivity in women with dense breast parenchyma, several techniques are under consideration for supplemental screening of this population, including whole-breast screening ultrasound, MRI, digital tomosynthesis, and molecular breast imaging (MBI) [1–7]. Although supplemental screening can improve cancer detection rates by revealing mammographically occult cancers, the generation of additional recalls and benign biopsy results, and associated costs are major concerns [8, 9]. In this era of health care cost containment, with recent reductions in Centers for Medicare and Medicaid Services reimbursement for breast imaging, consideration of the economic implications of additional breast screening tests is increasingly important [10, 11].

Nuclear medicine–based breast imaging techniques, including both single photon and positron emission systems, depict mammographically occult breast cancer in dense breasts [5, 12–16]. The evaluation of these techniques in the screening environment has been limited, partly because of concerns about radiation dose [17]. The use of low-radiation-dose MBI for supplemental screening of women with mammographically dense breasts has been reported [6]. Adding MBI to mammography increased the cancer yield from 3.2 per 1000 with mammography alone to 12.0 per 1000 ($p < 0.001$). However, the recall rate increased from 11% to 18%, and the biopsy rate increased from 1.3% to 4.2% (both $p < 0.001$) [6]. During that trial, we tracked the diagnostic imaging tests and biopsies generated by the screening approach of mammography with supplemental MBI versus that generated by screening mammography alone. The purpose of the current study was to examine the additional diagnostic workup and costs generated by the addition of a single MBI examination to screening mammography of women with dense breasts.

Materials and Methods

Participants

The subjects in this study were participants in a single-institution prospective trial in which the performance of screening mammography with adjunct MBI was compared with the performance of screening mammography alone in women with dense breasts [6]. MBI was performed with injection of 300 MBq (8 mCi) ^{99m}Tc -sestamibi and a dual-head cadmium-zinc-telluride gamma camera (Discovery NM 750b, GE Healthcare, or LumaGem, Gamma Medica). The study protocol was approved by our institutional review board and was HIPAA compliant; participants provided written informed consent. Participants had no symptoms, presented for routine screening mammography, and had a BI-RADS density of either heterogeneously dense or extremely dense breasts on their most recent previous mammogram [18].

Screening Test Assessments

Mammograms and MBI studies were interpreted independently by different radiologists without knowledge of the results of the other imaging test [6]. The study was designed such that diagnostic workup of the screening mammographic findings was performed according to the standard of care, and positive MBI findings (see later) were allowed to generate additional workup but were not allowed to alter the recommended workup of mammographic findings.

Screening mammograms were interpreted by breast radiologists in the course of routine clinical practice. Assessments were assigned according to BI-RADS categories [18]. Categories 1 and 2 were considered test negative, and category 0 was considered test positive. For 1582 of 1585 (99.8%) participants, previous mammograms were available for comparison.

Images from the MBI examinations were interpreted by one of four breast radiologists with 3–14 years in practice after a breast fellowship. MBI was first interpreted in isolation, and an assessment was assigned on a 1–5 scale paralleling BI-RADS [18, 19]. Category 1 or 2 was considered test negative, and categories 3, 4, and 5 were considered test positive, in keeping with the outcomes monitoring chapter of BI-RADS, fifth edition [20]. Test-positive MBI studies were reviewed with the current screening mammogram and with access to all relevant clinical information to rule out benign explanations of MBI uptake. A previous MBI examination performed within 3 years before the study MBI was available for comparison for 37 of 1585 (2.3%) participants. Clinical management was based on the integrated interpretation of mammography plus MBI.

Diagnostic Workup of Screening Findings

Test-negative findings of both mammography and MBI led to a recommendation of routine screening mammography in 1 year. If mammography was test positive, diagnostic workup was performed according to the standard of care, which may have included diagnostic mammography, targeted ultrasound, biopsy, short-interval follow-up imaging, or a combination of these techniques.

Test-positive MBI findings that correlated with test-positive screening mammographic findings were worked up according to the standard of care for test-positive mammograms described earlier. If comparison with the mammogram and history explained the MBI finding as benign (e.g., uptake in a biopsy-proven benign lesion), the combined assessment of MBI plus mammography was test negative, and routine screening mammography in 1 year was recommended. If MBI showed a finding that could not be categorized as benign on a mammogram, subsequent workup was performed according to the previously presented diagnostic algorithm [5] described as follows.

A combined MBI plus mammographic assessment of category 3 or greater triggered diagnostic mammography, targeted ultrasound, or both. Suspicious findings at this diagnostic imaging led to biopsy. If MBI uptake was not explained by the diagnostic mammographic or ultrasound findings, further workup was performed according to the level of suspicion. An MBI assessment of category 3 led to follow-up MBI in 6 months (with

further evaluation if the uptake was unchanged or increased, as opposed to returning to annual screening if the uptake was diminished). An MBI assessment of category 4 or 5 led to immediate MRI. A benign MRI finding led to classification of the MBI result as false-positive, whereas a suspicious MRI finding led to biopsy under either MRI or ultrasound guidance. In some instances, patients with suspicious lesions at MBI that had benign findings at MRI were given recommendations by the radiologist to undergo further follow-up with MBI at 6-month intervals to confirm benignity.

Assignment of Generated Tests and Procedures

The diagnostic imaging studies and biopsy procedures generated from positive findings on screening mammogram, adjunct screening MBI, or both were followed for 1 year after study imaging was complete. Breast cancer status in both malignant and nonmalignant cases was verified through the combination of histopathologic findings, negative findings at next annual screening, or medical record review or patient interview at least 1 year after study imaging, as previously detailed [6]. Cancer status was reported on the per-participant level; the most severe histopathologic finding was reported for each patient. Malignancy was classified as any finding of invasive cancer or ductal carcinoma in situ (DCIS).

On the basis of correct localization of imaging findings with subsequent diagnostic workup by an expert reconciler (breast radiologist with 5 years postfellowship experience), each imaging test and biopsy procedure was assigned to have been generated by findings on either a screening mammogram alone or the combination of a screening mammogram with adjunct MBI. Assignment of induced testing from the combination of mammography and MBI was based on the assessment from integrated interpretation of both tests.

For screening mammography alone and for adjunct MBI, positive predictive value 3 (PPV3), that is, the number of malignancies diagnosed per biopsies performed, was calculated at both the per-lesion and the per-participant levels as the number of malignancies per biopsy performed. Benign biopsy rates were calculated at the per-participant level as the number of women who underwent a biopsy revealing benign findings per number of women screened.

Cost Analysis

The costs of imaging tests and procedures performed as a result of screening with mammography and screening with mammography plus MBI were estimated with the 2014 national average Medicare reimbursement rates [21]. Because there is currently no reimbursement for MBI screening, the codes for diagnostic tumor imaging with scintimammography were used as a surrogate. Costs for the following tests were included: screening digital mammography with computer-aided detection; screening MBI studies; diagnostic imaging workup with diagnostic mammography, targeted ultrasound, or MRI; follow-up mammography, ultrasound, MBI, or MRI at 6 months and 12 months; and biopsy procedures, including costs of imaging guidance, marker placement, postprocedure mammography, and pathologic processing. In cases in which patients underwent breast biopsy of more than one lesion, charges for both the primary and the additional lesion were considered if biopsies were performed at the same visit under the same imaging guidance. Charges for a separate procedure were considered if biopsies were performed at separate

visits or under separate imaging guidance, in accordance with 2014 Centers for Medicare and Medicaid Services coding procedures. The average cost per patient screened and the cost per cancer detected were determined for screening mammography alone and for the combination of screening mammography and adjunct MBI.

Results

A total of 1651 women enrolled. The analysis set comprised 1585 women who met eligibility criteria, completed both screening mammography and MBI, and had verified cancer status. Among the 1585 participants, 279 (17.6%) were recalled for diagnostic imaging workup, including 175 (11.0%) patients recalled because of a positive screening mammographic finding (category 0). An additional 104 patients were recalled because of positive findings (categories 3–5) at adjunct MBI (Fig. 1). In 11 patients with positive findings with both modalities, MBI showed a lesion separate from that identified at mammography, prompting additional workup. Thus, a total of 115 of 1585 (7.2%) patients underwent additional workup because of findings at adjunct screening with MBI.

Diagnostic Workup Generated by Screening Mammographic Findings Alone

Among 175 patients recalled because of positive screening mammographic findings (Fig. 2), 174 underwent immediate diagnostic imaging with diagnostic mammography, targeted ultrasound, or both. Diagnostic mammography was recommended to the other patient, but the patient did not follow the recommendation. Her cancer status was considered negative on the basis of negative findings on the next annual screening mammogram. No MRI examinations were performed for primary diagnostic evaluation of screening mammographic findings.

After immediate diagnostic imaging, findings were resolved as benign in 149 patients; 18 underwent immediate biopsy; and seven underwent follow-up imaging at 6 months. In the seven patients who underwent 6-month follow-up imaging, the findings were resolved as benign in four, biopsy was performed in two, and one patient underwent another follow-up ultrasound examination at 12 months, in which the findings were ultimately resolved as benign.

Diagnostic Workup Generated by Findings at Adjunct Molecular Breast Imaging Screening

MBI was test positive at initial blinded interpretation in 173 of 1585 (11.0%) patients. Figure 3 details the workup performed for these patients. After comparison of positive MBI studies with the current screening mammogram and clinical history, 54 patients had findings explained as benign, four patients had a suspicious lesion identified at MBI that corresponded to a test-positive screening mammographic finding. The other 115 of 1585 (7.2%) patients underwent diagnostic workup for the finding seen only at MBI. Seven of the 115 underwent diagnostic mammography and targeted ultrasound simultaneously for evaluation of a separate finding detected on the screening mammogram. Thus, the MBI findings generated additional diagnostic imaging beyond that already generated by mammographic findings for 108 patients. Considering all workup performed to resolve MBI findings (Fig. 3), the addition of MBI for 1585 patients generated the following additional

tests: 100 diagnostic mammographic examinations, 110 targeted ultrasound examinations (which included two MRI-directed ultrasound examinations), 19 MRI examinations, 66 6-month follow-up MBI examinations, and 50 biopsies (38 ultrasound guided and 12 MRI guided) in 47 patients.

Molecular Breast Imaging Studies Resolved by Comparison With Screening Mammograms

The MBI studies that were downgraded from test positive to test negative after comparison with screening mammogram of 54 patients accounted for the following conditions: uptake within an axillary or intramammary lymph node with benign mammographic features in 22 patients (Fig. 4); background parenchymal uptake corresponding to mammographically stable fibroglandular tissue in 20; uptake in a previously biopsied benign lesion in five (four fibroadenomas, one fibrocystic change), in a mammographically stable mass in two, and in a skin lesion in one patient; benign nipple uptake in one patient; uptake attributed to postoperative change in two patients; and uptake that decreased compared with previous MBI findings in one patient.

Biopsy Procedures and Pathologic Findings

Screening mammography alone prompted a total of 21 biopsies in 20 patients (1.3%): 13 ultrasound-guided biopsies (one patient had two lesions), six stereotactic biopsies, and two ultrasound-guided cyst aspirations (Fig. 2). Cancer was diagnosed in six lesions in five patients, resulting in a lesion-level PPV3 of 28.6% (6 of 21) and participant-level PPV3 of 25% (5 of 20) for mammography alone.

Adjunct MBI prompted biopsy of an additional 50 lesions in 47 patients. In the absence of an MBI-guided biopsy system at the time of this study, MBI-prompted biopsies were performed under ultrasound guidance (38 lesions in 36 patients) or MRI guidance (12 lesions in 12 patients, where one of these patients underwent both ultrasound-guided biopsy and MRI-guided biopsy of separate lesions). Of the additional biopsies prompted by adjunct MBI findings, cancer was diagnosed in 15 of 50 lesions and 14 of 47 patients. Therefore, the combination of mammography and MBI resulted in a lesion-level PPV3 of 29.6% (21 of 71) and participant-level PPV3 of 28.4% (19 of 67). Example cases of MBI-prompted biopsies are shown in Figures 5 and 6.

The five cancers detected at screening mammography included three invasive ductal cancers (two of three node negative) and two DCIS lesions. The 14 cancers detected only with adjunct MBI included 11 invasive cancers (nine ductal, two lobular) with a median size of 0.9 cm (range, 0.5–4.1 cm), of which 9 of 11 were node negative, and three DCIS lesions. Two patients with cancer detected only with MBI had bilateral disease. Further details of cancers detected are provided elsewhere [6].

The benign biopsy rate increased from 0.9% (15 of 1585) for screening mammography alone to 3.0% (48 of 1585) for the combination of mammography and adjunct MBI ($p < 0.001$). Of the 115 patients with new findings identified with adjunct MBI, the MBI assessment before the start of workup with diagnostic mammography or targeted ultrasound was category 3 (probably benign) in 79 patients and category 4 (suspicious) in 36 patients.

No category 5 assessments were assigned. The malignancy rate for category 3 findings was 4 of 79 (5.1%) and for category 4 findings was 10 of 36 (27.8%).

Costs of Tests and Procedures

The costs of all imaging tests and biopsy procedures generated by findings at screening mammography with adjunct MBI compared with the costs of screening mammography alone are shown in Table 1 (Table S1, which shows results of a detailed analysis with procedure codes, can be viewed in the *AJR* electronic supplement to this article, available at www.ajronline.org.) In terms of national average Medicare reimbursement rates, the total cost of performing screening mammography and the subsequent diagnostic imaging tests and biopsies in this cohort of 1585 women with mammographically dense breasts was \$279,256, resulting in detection of breast cancer in five patients. Adding MBI to this group cost an additional \$625,095, resulting in detection of breast cancer in an additional 14 patients. The total cost of the combination of screening mammography with adjunct MBI was \$904,351, yielding detection of breast cancer in 19 patients.

The cost per patient screened was \$176 for mammography alone and \$571 for the combination. The cost per cancer detected was \$55,851 for mammography alone and \$47,597 for the combination. Screening with a combination of mammography and MBI resulted in savings in cost per cancer detected of \$8254 compared with the cost of mammography alone.

Discussion

The combination of screening mammography and adjunct MBI of dense breasts was associated with an almost fourfold increase in the number of cancers detected compared with the number detected with screening mammography alone while a favorable benign biopsy rate and PPV3 for additional findings were maintained. The additional cancers detected with MBI came at a price of a 3.2-fold increase in total costs in this study.

Adding a single MBI examination to mammography for women with dense breasts increased the benign biopsy rate 2.1% (33 of 1585) compared with the rate for mammography alone. A higher benign biopsy rate was reported for supplemental ultrasound in the American College of Radiologic Imaging Network (ACRIN) 6666 trial, which included women at elevated breast cancer risk who also had a least one dense breast quadrant. The addition of physician-performed screening ultrasound to mammography increased the benign biopsy rate 7.3% (193 of 2659) after a single screen and 4.7% (224 of 4814) in years 2 and 3 of annual screening [1]. In two reports of supplemental screening ultrasound performed for women with dense breasts and normal mammographic findings, the benign biopsy rate was 0.9% (83 of 9157) in an Italian study using physician-performed ultrasound [22] and 6.4% (60 of 935) in a Connecticut study using technologist-performed ultrasound [2].

The PPV3 for additional biopsies prompted by supplemental MBI in this study was 30.0% (14 of 47), higher than that reported for supplemental ultrasound. In ACRIN 6666, the PPV3 for additional biopsies prompted by ultrasound was 5.8% (12 of 207) for a single screening ultrasound and 7.4% (18 of 242) for years 2 and 3 of screening ultrasound [1]. In an

overview of studies evaluating technologist-performed adjunct screening ultrasound of dense breasts [23], the overall PPV3 for ultrasound findings was 5.8%. The reported average cancer detection rates for prevalent screening ultrasound are 2.5 per 1000 for technologist-performed examinations [23] and 4.3 per 1000 for physician-performed examinations [1, 22], considerably lower than the 12.0 per 1000 supplemental cancer detection rate found for prevalent MBI in our study.

The addition of a single MRI examination to mammography in ACRIN 6666 led to additional benign biopsies in 6.2% (38 of 612) of participants, higher than the rate of additional benign biopsies prompted by MBI in our study (2.1%). The PPV3 for additional biopsies prompted by MRI findings was 20.4% (10 of 49), somewhat lower than that observed with MBI (30.0%). Notably, the supplemental cancer detection rate of MRI in this population at elevated risk and with dense breasts was 18.0 per 1000, higher than that observed with MBI (12.0 per 1000) in our cohort recruited solely on the basis of having dense breasts.

Our results show the importance of comparison of adjunct MBI studies with a recent screening mammogram and review of the clinical history. In our study, comparison with screening mammograms explained the MBI findings as benign in 31.2% (54 of 173) of patients with initially positive MBI findings, which substantially lowered its false-positive rate. As has been seen with other breast imaging modalities [24], we expect the specificity of MBI to improve in the incidence screening setting with the benefit of previous images to review, though we also expect the cancer detection rate to decrease.

Our results also show the importance of performing a thorough diagnostic workup of all MBI-detected lesions regardless of the assessment category assigned. The malignancy rate for probably benign (category 3) findings at adjunct MBI, after comparison with mammograms, was 5.1%, which is substantially higher than the less than 2% malignancy rate observed with probably benign assessments with mammography and ultrasound [18, 25, 26]. An analysis of probably benign (BI-RADS 3) findings at supplemental ultrasound showed a low malignancy rate of 0.8% [18, 27]. The malignancy rate for BI-RADS 3 lesions detected with MRI in recent years has ranged from 0.6% to 1.8% [28].

We conducted this study in the absence of MBI-guided biopsy capability; therefore, we relied on other modalities for diagnostic evaluation and localization. Although biopsy capability exists for other nuclear medicine breast imaging technologies, including positron emission mammography (PEM) and single-head breast-specific gamma imaging cameras, a biopsy system compatible with the dual-head MBI gamma camera used in this study is under development [29, 30]. Biopsy, when indicated, was performed under ultrasound guidance whenever possible. For 19 of 1585 (1.2%) patients, however, MRI was performed for imaging evaluation, and for 12 of 1585 (0.7%) patients, MRI-guided biopsy was necessary. Future availability of direct biopsy guidance for MBI may decrease the need to use MRI in diagnostic workup and thus reduce the cost associated with adjunct MBI. However, direct MBI guidance is needed because not all patients can tolerate MRI. An important observation in this study was that for any MBI finding that was not resolved with mammography or ultrasound, a corresponding finding was obtained with MRI. This is

different from reported findings with PEM performed with ^{18}F -FDG, in which different findings were seen at MRI and PEM, and direct PEM-guided biopsy was necessary [15, 31].

Although additional costs were incurred with supplemental MBI screening, the cost per cancer detected for the combination of techniques was lower than that for screening mammography alone because of the increased cancer yield. One potential criticism of this approach is that the additional cancers detected may represent overdiagnosis, defined as the diagnosis of a breast cancer as a result of screening that would not have been clinically diagnosed in the woman's lifetime had screening not taken place. However, the cancers detected only with adjunct MBI had features of clinical importance: 2 of 14 occurred in patients with bilateral mammographically occult disease, and 11 of 14 were invasive cancers with a median size of 0.9 cm.

Data on the actual costs of supplemental screening of women with dense breasts are limited. Hooley et al. [2] reported the cost per additional cancer detected with handheld screening ultrasound performed by technologists in women with dense breasts who had normal screening mammograms as \$60,267 (2012 Connecticut Medicare reimbursement rates) [2]. A review of six Connecticut radiology practices that offered technologist-performed handheld screening ultrasound [32] estimated a cost per cancer detected of \$50,000 using average insurance reimbursement for 2009–2010. Our results compare favorably with these, because the cost per additional cancer detected with MBI was \$44,650 (\$625,095 divided by 14). Although the cost of supplemental MRI screening of dense breasts has yet to be evaluated, the cost-effectiveness of MRI screening of women who are *BRCA1* or *BRCA2* mutation carriers has been found to vary widely depending on patient age [33]. For the estimated 50% of screening-eligible U.S. women who have dense breasts [34], the cost of MRI combined with a lower incidence of cancer than the *BRCA*-positive population is likely to make MRI too expensive to use in this setting.

Reimbursement for supplemental screening when dense breast tissue is the only indication varies from state to state and between insurance providers. Cost saving per cancer detected with supplemental screening MBI is compelling evidence for future coverage of screening MBI of women with dense breasts.

There were limitations to our cost analysis. First, we considered costs of imaging tests and biopsies but did not consider costs beyond those of cancer detection. There could be potential cost savings associated with relative lead time, that is, the amount of time the breast cancer diagnosis is advanced by adding MBI compared with relying on mammographic or clinical detection. Because earlier detection may reduce the costs (in dollars and lost productivity) associated with treatments of advanced disease, the magnitude of the cost benefit for supplemental screening with MBI may be considerably higher. Second, sestamibi, which is commonly available as a myocardial perfusion agent, is off patent so may be available at a lower cost than we report. If so, the future cost of adding MBI to screening mammography in this cohort is likely overestimated. Third, we did not explicitly measure important factors in evaluation of costs, including the complexity of the examination and time of radiologist's interpretation. High interreader and intrareader agreement of MBI interpretations after a 2-hour radiologist training session has been found

[19, 35]. In our experience, a full bilateral dual-head MBI study can be rapidly assessed, with interpretation times consistently less than for concomitant mammography.

Compared with other imaging modalities under consideration for supplemental screening of women with dense breasts, MBI is associated with a relatively low benign biopsy rate and relatively high PPV for additional findings. Considering the costs of screening examinations, subsequent diagnostic imaging, and biopsies that were generated, the addition of MBI to mammography screening of dense breasts results in a high enough supplemental cancer yield to result in a lower cost per cancer detected than for mammography alone.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Fig. 1.

Flowchart shows numbers of patients recalled because of findings at screening mammography (MG) or adjunct molecular breast imaging (MBI).

Fig. 2.

Flowchart shows steps in diagnostic workup prompted by screening mammography alone. One patient had two separate lesions biopsied under ultrasound guidance. MG = mammography, US = ultrasound.

Fig. 3.

Flowchart shows additional diagnostic workup prompted by adjunct screening with molecular breast imaging (MBI) beyond that prompted by screening mammography. Two patients each had two separate lesions biopsied under ultrasound guidance. One patient who underwent MRI-guided biopsy also underwent separate ultrasound-guided biopsy. Two patients who underwent ultrasound-guided biopsy after MRI also underwent MRI-directed targeted ultrasound, and two also underwent second-look targeted ultrasound examination. MG = mammography, US = ultrasound.

Fig. 4.

63-year-old woman with lesion in left breast.

A, Mediolateral oblique screening molecular breast image (MBI) (300 MBq ^{99m}Tc -labeled sestamibi, dual-head cadmium-zinc-telluride gamma camera) shows focal area of radiotracer uptake in upper left aspect of breast (*arrow*). Initial blinded interpretation was test positive (category 3, probably benign).

B, Mediolateral oblique view screening mammogram shows correlation of uptake in **A** with mammographically stable axillary lymph node (*arrow*). Integrated assessment of mammography and MBI was test negative (category 2, benign), and no further workup was performed.

Fig. 5.

69-year-old woman with normal mammographic findings and lesion detected at molecular breast imaging (MBI).

A, Craniocaudal mammogram of left breast interpreted as negative.

B, Craniocaudal image from adjunct screening MBI of left breast (300 MBq ^{99m}Tc -labeled sestamibi, dual-head, cadmium-zinc-telluride gamma camera) shows moderate-intensity focal area of radiotracer uptake (*arrow*). Integrated assessment of mammography and MBI was category 4, suspicious.

C, Diagnostic mammogram shows punctate calcifications in area of concern (*arrows*).

D, Targeted ultrasound image shows 10-mm circumscribed oval hypoechoic mass. Color Doppler examination (not shown) revealed internal vascularity. Result of ultrasound-guided biopsy was fibroadenoma.

Fig. 6.

75-year-old woman with normal mammographic findings and lesion detected at molecular breast imaging (MBI).

A, Craniocaudal mammogram of right breast interpreted as negative.

B, Craniocaudal image of right breast from adjunct screening MBI (300 MBq ^{99m}Tc -labeled sestamibi, dual-head, cadmium-zinc-telluride gamma camera), shows 4-cm area of regional mild uptake in upper outer quadrant (*arrow*). Integrated assessment of mammography and MBI was category 3, probably benign.

C, Diagnostic mammogram shows normal findings.

D, Targeted ultrasound image shows normal findings.

E, Craniocaudal image of right breast from short-interval follow-up MBI performed at 6 months shows two focal areas of uptake (*arrows*) that have increased in intensity.

F, Contrast-enhanced MR image of right breast shows 0.7-cm mass correlating with anterior lesion and area of nonmasslike enhancement correlating with posterior lesion (*arrows*) in **E**. MRI-guided biopsy showed malignancy at both sites. Surgical pathologic result was multiple foci of invasive ductal carcinoma (grade 3) over 6.2-cm ill-defined area with largest focus measuring 0.7 cm.

TABLE 1

Cost of Diagnostic Workup and Biopsies From Screening With Mammography Alone and Mammography Combined With Molecular Breast Imaging

Imaging Test or Procedure	Cost From Screening Mammography Alone		Costs From Combined Screening Mammography and Molecular Breast Imaging		Cost Difference (US\$)
	No. of Patients (%)	Cost (US\$)	No. of Patients (%)	Cost (US\$)	
Screening tests					
Mammography	1585/1585 (100)	230,507	1585/1585 (100)	230,507	0
Molecular breast imaging	0/1585 (0)	—	1585/1585 (100)	520,593	520,593
Immediate workup					
Diagnostic mammography	171/1585 (10.8)	22,174	269/1585 (17.0)	34,881	12,708
Targeted ultrasound	83/1585 (5.2)	8295	189/1585 (11.9)	18,889	10,594
MRI	0/1585 (0)	—	13/1585 (0.8)	7588	7588
Follow-up studies					
Diagnostic mammography	6/1585 (0.4)	778	8/1585 (0.5)	1037	259
Targeted ultrasound ^a	5/1585 (0.3)	500	9/1585 (0.6)	899	400
MRI	0/1585 (0)	—	6/1585 (0.4)	3502	3502
Molecular breast imaging	0/1585 (0)	—	66/1585 (4.2)	21,678	21,678
Biopsy ^b					
Ultrasound-guided, first lesion	12/1585 (0.8)	10,532	48/1585 (3.0)	42,127	31,595
Ultrasound-guided, additional lesion	1/1585 (0.1)	543	3/1585 (0.2)	1630	1087
Stereotactic	6/1585 (0.4)	5294	6/1585 (0.4)	5294	—
Cyst aspiration	2/1585 (0.1)	634	2/1585 (0.1)	634	—
MRI guided	0/1585 (0)	—	12/1585 (0.8)	15,091	15,091
Total cost		279,256		904,351	625,095
No. of patients with cancer detected	5		19		14
Cost per cancer detected		55,851		47,597	(8254)

Note—Detailed costs with procedure codes are shown in Supplemental Table 1 [36–38]. Except for cost difference, values in parentheses are percentages. Dash (—) indicates not applicable.

^aIn two patients with new findings at molecular breast imaging, MRI-directed ultrasound was performed to evaluate the feasibility of performing ultrasound-guided biopsy; these two ultrasound examinations are included in follow-up studies.^bA total of 67 biopsies were performed on 71 patients; screening mammography prompted 21 biopsies in 20 patients and combined screening mammography and MBI prompted 50 biopsies in 47 patients.