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Utility of Targeted Ultrasound to Predict Malignancy Among Lesions Detected on Contrast-Enhanced Digital Mammography

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Abstract

BACKGROUND.—Targeted ultrasound (US) can be performed to characterize and potentially biopsy areas of enhancement detected on contrast-enhanced mammography (CEM).

OBJECTIVE.—The purpose of this study was to assess the utility of targeted US in predicting malignancy of lesions with indeterminate or suspicious enhancement on CEM.

METHODS.—One thousand consecutive CEM examinations with same-day targeted breast US at one institution between October 2013 and May 2018 were retrospectively reviewed. All patients with indeterminate or suspicious enhancement detected on CEM that underwent US evaluation were included. Patients with palpable or symptomatic lesions, those with suspicious findings on low-energy mammograms or images obtained with another modality, and those with less than 1 year of follow-up were excluded. Medical records, imaging, and pathology data were reviewed. Histopathologic analysis was used as the reference standard for biopsied lesions, and follow-up imaging was used for unbiopsied lesions. Associations between pathologic diagnosis, presence of a US correlate, and lesion characteristics were assessed by Fisher exact, chi-square, and Wilcoxon rank sum tests.

RESULTS.—Among 153 enhancing lesions detected on CEM in 144 patients, 47 (31%) had a US correlate. The frequency of a correlate between CEM and US was significantly higher among enhancing masses (28/43 [65%]) than among lesions exhibiting nonmass enhancement (19/110 [17%]) ($p < .001$). The likelihood of malignancy was significantly greater among lesions with a US correlate (12/47 [26%]) than among those without a US correlate (11/106 [10%]) ($p = .03$), and among mass lesions (11/43 [26%]) than among nonmass lesions (12/110 [11%]) ($p = .04$). The PPV of US-guided biopsy after CEM-directed US was 32%.

CONCLUSION.—Enhancing CEM-detected lesions that have a US correlate are more likely to be malignant and can be evaluated with US-guided biopsy to obviate additional breast MRI.

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CLINICAL IMPACT.—CEM-directed US of enhancing lesions is useful given that lesions with a US correlate are more likely to be malignant and can be used as targets for US-guided biopsy until a CEM biopsy system becomes commercially available.

Keywords

breast neoplasms; contrast media; mammography; ultrasound

Contrast-enhanced mammography (CEM) is an evolving breast imaging technique that entails use of contrast medium to detect suspicious enhancement associated with tumor angiogenesis. It is conceptually similar to contrast-enhanced breast MRI [1]. The diagnostic performance of CEM is comparable to that of MRI; the sensitivity approaches 95% and the specificity 88% [2]. Several studies [3–12] have shown that CEM may be useful for both diagnosis and screening.

Enhancing breast lesions detected on MRI may be further evaluated with a targeted ultrasound (US) examination to evaluate for a sonographic correlate before image-guided biopsy. Although MRI-guided biopsy has become an accessible modality, if a sonographic correlate to an MRI finding is identified, US-guided tissue sampling may be preferred because it is less expensive, more widely available, and more comfortable for the patient than MRI-guided biopsy [13]. However, targeted US is most reliable for identifying correlates for enhancing mass lesions and lesions larger than 1 cm [14].

The FDA recently approved a dedicated CEM biopsy system [15], but it is not yet commercially available. Therefore, suspicious enhancing lesions detected on CEM must be evaluated with US or MRI for further characterization and potential biopsy. To date and to our knowledge, the value of performing CEM-directed US has not been described in the literature. In addition, although MRI-detected lesions with US correlates are more likely to be malignant than those without US correlates [13], it is not known how the likelihood of malignancy differs among CEM-detected lesions with and without US correlates. The purpose of this study was to determine the utility of targeted US for predicting malignancy among lesions initially seen on CEM.

Methods

Patients

Institutional review board approval with a waiver of written informed consent was obtained for this retrospective study. The study was conducted in compliance with HIPAA.

Retrospective review of the Memorial Sloan Kettering Cancer Center radiology department database identified 3521 consecutive screening and diagnostic CEM examinations performed between October 2013 and May 2018. At our institution, screening CEM must be ordered by the referring physician or performed as part of a research study because CEM is currently FDA-approved only for diagnostic evaluations. Screening CEM examinations performed in our department are not batch-read, so any supplemental targeted US is performed as part of the diagnostic evaluation the same day as CEM, and results are provided to the patient at the conclusion of both examinations.

The study inclusion criteria were indeterminate or suspicious enhancing lesion detected on CEM with additional evaluation by targeted breast US. The exclusion criteria were CEM lesion correlated with a palpable or symptomatic abnormality, suspicious finding seen with another imaging modality before CEM (such as PET, ductography, or mammography from an outside institution), or suspicious finding seen on the low-energy images acquired in CEM (such as mass, distortion, or calcifications). None of the patients had a current diagnosis of breast cancer, but patients with a history of treated breast cancer were included because they are a large proportion of the screening population at our cancer center. If a patient underwent short-interval follow-up CEM during the study period, only the initial CEM examination was included. Figure 1 shows the inclusion and exclusion criteria. A total of 144 patients with 153 nonpalpable lesions constituted our study sample. Table 1 shows the patient and CEM study characteristics.

Among the 1000 patients who underwent same-day CEM and US, 68 had been included in previous studies of CEM that evaluated the performance of supplemental screening CEM compared with conventional mammography and MRI [6, 7] and radiomic analysis of cancers detected on CEM [16].

Data Collection

All CEM and targeted US examinations included in our study were performed at a breast imaging center and were interpreted by one of 17 board-certified breast imaging radiologists. A total of 13 of 17 radiologists had fellowship training in breast imaging and 5–25 years of experience; the other four did not have breast imaging fellowship training, but they had 25–37 years of experience interpreting breast imaging. For the purposes of this study, indeterminate or suspicious CEM lesions were defined as enhancing lesions seen only on recombined iodine images without a suspicious correlate on low-energy images.

Findings from the CEM and targeted US examinations were reported together with a single overall BI-RADS assessment. When a US correlate of the CEM lesion was not identified, the radiologist recommended either breast MRI or 6-month follow-up CEM based on their level of suspicion. The mean time between CEM and MRI was 10 days (range, 0–127 days). When an MRI correlate was not identified, 6-month follow-up CEM was recommended. When a suspicious US or MRI correlate was identified, US- or MRI-guided, , core needle biopsy was performed, respectively. One patient who had a gadolinium allergy and could not undergo MRI underwent stereotactic biopsy instead, in which anatomic landmarks were used to localize and target the suspicious enhancing CEM lesion.

For this study, a single radiologist with fellowship training in breast imaging and 6 years of experience (K.C.) reviewed all histopathology reports and imaging (CEM, US, MRI). Patient medical records were reviewed for age and history of prior treated breast cancer. The following were recorded from the CEM reports: indication for CEM examination, breast tissue density, background parenchymal enhancement, number of breast lesions, lesion size, and lesion type (mass or nonmass enhancement). Breast density was determined on low-energy-exposure images and classified according to the BI-RADS mammography lexicon [17]. CEM background parenchymal enhancement was classified according to the BI-RADS MRI lexicon (minimal, mild, moderate, or marked), because there is no formal lexicon for

CEM. The following were recorded from the MRI reports: lesion size and type (mass or nonmass enhancement). If lesion size was not included in the CEM report, the radiologist, blinded to outcome, measured the enhancing lesion on the recombined image.

Reference Standard

Histopathologic analysis was used as the reference standard for 75 biopsied lesions (72 patients). Three patients underwent two biopsies each. Thirty-seven US-guided core biopsies were performed with a variety of 12- to 14-gauge vacuum-assisted and spring-loaded needle biopsy devices, according to radiologist preference. Thirty-seven MRI-guided and one stereotactic core biopsies were performed with 9-gauge vacuum-suction biopsy systems. All image-guided biopsies were performed by the same group of 17 breast imaging radiologists. The postbiopsy mammograms for all 75 biopsies were reviewed to confirm correlation with the original CEM finding.

Follow-up imaging served as the reference standard for 78 lesions (72 patients) that were not biopsied. Six-month follow-up CEM was performed unless an MRI correlate was identified, in which case 6-month follow-up MRI was performed. All 78 unsampled CEM lesions were followed for at least 1 year with either CEM or MRI until stability or resolution on follow-up imaging allowed the lesion to be diagnosed as benign.

Imaging Technique

Dual-energy contrast-enhanced mammography——Dual-energy CEM was performed at our institution with a digital mammography unit (SenoBright, GE Healthcare). IV administration of iohexol (Omnipaque 350, GE Healthcare) at a dose of 1.5 mL/kg body weight was performed with a power injector at an injection rate of 3 mL/s. The first mammogram was obtained approximately 2.5 minutes after injection, and a total of four images (craniocaudal and mediolateral oblique views of each breast) were obtained within 10 minutes after injection. A low-energy-exposure image (26–30 kVp) and a high-energy-exposure image (45–49 kVp) around the k-edge of iodine were acquired for each view. A proprietary algorithm was used to generate a recombined iodine image from the low- and high-energy exposures to highlight areas of contrast enhancement. Enhancement seen on the recombined iodine image was directly correlated with the low-energy image. Additional 2D spot compression or magnification images were acquired when clinically indicated.

Breast ultrasound——Breast US examinations were performed with an 11–15 MHz linear transducer (Logiq E9, GE Healthcare; Acuson, Siemens Healthineers) with the patient supine or in the supine oblique position. All examinations were performed by a US technologist trained and certified in breast imaging. Both gray-scale and color Doppler images were acquired. CEM studies were available to the interpreting radiologist for reference at the US examination, allowing targeted evaluation of the areas of enhancement based on the position, size, and shape of the lesion. The interpreting radiologist directed the US technologist to the expected location of the CEM lesion and reviewed all imaging. The interpreting radiologists also had the opportunity to perform the scans themselves if needed.

Breast MRI——Breast MRI examinations were performed with a 1.5-T or 3-T commercially available system (3-T GE Discovery MR750 or 1.5-T Signa Artist 450, GE Healthcare) and a dedicated surface breast coil with the patient prone. The standard examination included a localizing sequence followed by axial fat-suppressed T2-weighted and T1-weighted sequences. An axial T1-weighted 3D fat-suppressed fast-spoiled gradient-echo sequence was performed before and three times after IV administration of a gadolinium-based contrast agent at a dose of 0.1 mL/kg body weight and injection rate of 2 mL/s. Subtraction images were generated by subtracting the unenhanced images from the contrast-enhanced images. CEM studies were available to the interpreting radiologists for reference at the MRI examination, allowing direct correlation of the areas of enhancement based on the position, size, and shape of the lesion.

Statistical Analysis

Statistical analyses were performed with R software (version 4.0.2, R Core Team). The chi-square, Fisher exact, and Wilcoxon rank sum tests were used to assess associations between pathologic diagnosis, presence of a US correlate, lesion type, and lesion size on CEM and MRI. Pearson correlation, Bland-Altman plots (defining the limits of agreement as 2 SD above and below the mean of differences of the two imaging techniques), and Passing-Bablok regression were used to assess the level of agreement between the measurement of lesion size on CEM and MRI. Median size was reported. The McNemar test for paired proportions was used to assess agreement between lesion types on CEM and MRI. Statistical significance was evaluated at $p < .05$. The PPV of biopsies performed was also calculated.

Results

Recommendations After Contrast-Enhanced Mammography–Directed Ultrasound

Figure 2 summarizes the recommendations made after the CEM and targeted US examinations. A US correlate was identified in 31% (47/153) of the CEM-detected lesions. Of these 47 lesions, 79% (37/47) were suspicious on US and evaluated with US-guided biopsy (Figs. 3 and 4). The other 21% (10/47) had either a benign (3/10) or probably benign (7/10) sonographic appearance and were confirmed as benign on follow-up CEM.

Of the 106 lesions without a US correlate, 86% (91/106) were further evaluated with MRI of 86 patients. An MRI correlate was identified for 62% (56/91) of lesions. Of these, 66% (37/56) were suspicious and evaluated with MRI-guided biopsy (Fig. 5), and 34% (19/56) had either a benign (15/19) or probably benign (4/19) MRI appearance and were confirmed as benign on CEM or MRI follow-up. All 35 lesions that did not have an MRI correlate were confirmed to be benign on short-interval follow-up CEM. Among the 14% (15/106) of lesions without a US correlate that were not further evaluated with MRI, one lesion was in a patient with a gadolinium allergy who could not undergo MRI and instead underwent stereotactic biopsy, in which anatomic landmarks were used to target the CEM lesion, and the results were benign. Fourteen lesions were confirmed to be benign in short-interval follow-up CEM (Fig. 6).

All 78 presumed benign CEM-detected lesions not evaluated with histopathologic sampling were stable or had resolved on CEM or MRI during a follow-up period of at least 1 year (mean, 29.9 months; range 12–60 months). Follow-up lasted 2-years or more for 74% (58/78) of lesions and 1–2 years for 26% (20/78) of lesions. All lesions were downgraded to benign at follow-up with a recommendation for annual screening mammography (Fig. 6). An interval cancer developed in two patients during the follow-up period; one was diagnosed 3.3 years after CEM of the contralateral breast, and the other was diagnosed 4.1 years after CEM of a different quadrant of the ipsilateral breast.

Contrast-Enhanced Mammography Lesion Characteristics and Correlation With Ultrasound and MRI

Table 2 shows the characteristics of the 153 CEM-detected lesions. A total of 28% (43/153) were mass lesions, and 72% (110/153) were nonmass lesions. The median lesion size was 0.7 cm, and lesion size was slightly larger for nonmass lesions than for mass lesions (0.8 cm vs 0.7 cm; $p = .01$). A US correlate was found in 65% (28/43) of mass lesions and in 17% (19/110) of nonmass lesions ($p < .001$). Lesion size was not significantly different between lesions with a US correlate and those without a US correlate (0.7 cm vs 0.8 cm; $p = .13$).

As shown in Table 3, malignancy was present in 26% (12/47) of CEM lesions with a US correlate versus 10% (11/106) of lesions without a US correlate ($p = .03$) and in 26% (11/43) of mass lesions versus 11% (12/110) of nonmass lesions ($p = .04$). Lesion size measured on CEM was not significantly different between benign and malignant lesions (0.8 cm vs 0.7 cm; $p = .90$).

Table 4 shows the characteristics and outcomes for the 37 CEM-detected lesions that had an MRI correlate and were evaluated by MRI-guided biopsy. The frequency of malignancy was not significantly different between mass (7/15) and nonmass (4/22) lesions ($p = .08$) or lesion sizes ($p = .90$) on MRI. Lesion size measured on CEM and MRI showed strong correlation ($r = 0.83$). The Bland-Altman plot indicated that more than 95% of data points lay within the limits of agreement of the two imaging techniques for lesion size. Passing-Bablok regression showed no evidence of systematic or proportional differences in lesion size between the modalities (95% CI for the intercept contains 0 [−0.27, 0.14] and the slope for the equation contains 1 [0.86, 1.33]). However, lesion type was significantly different between CEM and MRI: 24% (9/37) of lesions were characterized as nonmass enhancement on CEM and mass on MRI ($p = .008$). For the other 76% (28/37) of lesions, lesion type was concordant between CEM and MRI: 6 of 28 were characterized with both modalities as masses, and 22 of 28 were characterized as nonmass lesions with both modalities.

Histopathologic Results

Table 5 shows the histopathologic results for the 75 biopsied CEM lesions: 31% (23/75) in 21 women were malignant, and 69% in 52 women (52/75) were benign. Malignancy was detected in 12 of 37 suspicious US correlates for which US-guided biopsy was performed (PPV, 32%), and in 11 of 37 suspicious MRI correlates for which MRI-guided biopsy was performed (PPV, 30%). The 12 cancers seen with US were found in 7% (10/144) of patients. The 11 sonographically occult cancers seen with MRI were found in 8% (11/144)

of patients and represented 48% of the total 23 CEM-detected cancers. For two patients who had a cancer initially seen on CEM and diagnosed with MRI-guided biopsy, an additional multicentric cancer was diagnosed with MRI, giving a total of two CEM-occult cancers. Review of all 75 postbiopsy mammograms confirmed adequate targeting of the CEM lesion based on biopsy marker position.

All 52 benign histopathologic results were concordant with imaging findings (Fig. 6) and were often a combination of benign pathologic findings. Diagnoses included fibroadenoma, stromal fibrosis, pseudoangiomatous stromal hyperplasia, fat necrosis, sclerosing adenosis, posttreatment changes, hemangioma, atypical lobular hyperplasia, periductal inflammation, atypical ductal hyperplasia (ADH), radial scar, intraductal papilloma, and classic type lobular carcinoma in situ. All high-risk lesions subsequently surgically excised (two ADH, one papilloma, one radial scar) were confirmed to be benign at surgical pathologic examination. One ADH lesion bordered on low-grade ductal carcinoma in situ but was benign through 3 years of follow-up. One radial scar lesion was not surgically excised because it was incidental and completely removed in the biopsy specimen.

Discussion

Our study shows the utility of performing a CEM-directed US to identify a correlate for indeterminate or suspicious enhancement initially seen on CEM. We observed a 31% frequency of a correlate between CEM and US, which is within the wide range of reported correlates between MRI and US (23–89%) [13, 14, 18–25].

The importance of identifying a US correlate is threefold. First, identification of a suspicious sonographic correlate can allow US-guided biopsy, which is the least expensive, most accessible, and best-tolerated approach for histopathologic sampling. The FDA recently approved a dedicated CEM biopsy system, but it is not yet commercially available. Therefore, patients with suspicious CEM lesions without a correlate on low-energy or US images need MRI evaluation for potential biopsy, which is an expensive and time-consuming modality [13]. Second, we found that enhancing CEM lesions with a US correlate were statistically more likely to be malignant than those without a US correlate (26% vs 10%); the PPV was 32% for lesions evaluated by US-guided biopsy. This finding is consistent with those of prior MRI studies showing higher malignancy rates among MRI-detected lesions identified with targeted US [13, 14, 19, 20, 22, 25, 26]. Third, identification of a benign or probably benign US correlate may obviate supplemental MRI. In our study, 21% of the US correlates had a benign or probably benign sonographic appearance and did not require MRI for further characterization; 7 of 10 such lesions were probably benign and evaluated by short-interval follow-up CEM and US, wherein the benign impression was confirmed (mean follow-up period, 26.3 months).

The frequency of a correlate between CEM and US was significantly greater for enhancing masses than for nonmass enhancement (65% vs 17%). This finding is supported by prior MRI studies that have similarly shown higher US correlation rates among mass lesions than among nonmass lesions [13, 14, 19, 20, 23–25]. Our data suggest that MRI may be particularly helpful as a next step in the diagnostic workup of nonmass enhancement seen on

CEM of patients with negative US findings, given that a US correlate was less often found for these types of lesions.

In our study, breast MRI was performed to further evaluate 86% of CEM lesions in 86 patients who did not have a US correlate. Although MRI is more expensive and less accessible than US, it has high sensitivity, approaching 100%, and an NPV of 98% [27–29]. Eleven cancers in 11 patients that were occult on US were diagnosed with MRI, accounting for 48% of total cancers detected on CEM. Furthermore, two additional CEM-occult cancers were detected on MRI, representing a site of multicentric disease in two patients. The PPV of MRI-guided biopsy after a negative US finding was 30%. These results suggest that MRI is valuable for further evaluation of suspicious CEM lesions despite a negative US finding. For the 37 CEM lesions that had an MRI correlate and were evaluated with MRI-guided biopsy, lesion size measured on CEM and on MRI correlated strongly, although size was not predictive of malignancy in either analysis. Interestingly, we observed significant disagreement between CEM and MRI lesion type (mass vs nonmass). This disagreement may reflect interreader inconsistency in using CEM descriptors owing to the lack of a BI-RADS lexicon for CEM lesions.

Enhancing CEM lesions with suspicious findings on low-energy mammograms were excluded from our study. Nonetheless, one patient in our study (who could not undergo MRI because of a gadolinium allergy) successfully underwent a tomosynthesis-guided biopsy in which anatomic landmarks were used to localize and target the enhancing lesion, which was benign. The lesion was confirmed with an accurately positioned clip on the postbiopsy mammogram and over 3 years of CEM follow-up with benign results. Thus, tomosynthesis may have value in localizing CEM lesions that are occult on low-energy images, US, and MRI; this warrants further investigation.

Limitations

Our study had several limitations. First, it was performed at a single institution, and our sample size was limited to 153 lesions in 144 patients. Second, 26% of unbiopsied lesions did not have 2-year follow-up findings, although all had at least 1-year of follow-up. Third, although all US examinations were performed by technologists and radiologists with expertise in breast imaging, US is inherently an operator-dependent modality with potential for interoperator variability. Fourth, there could have been patients who did not undergo the targeted US evaluation on the same day as the CEM examination (if they, for example, could not stay for US) and were therefore excluded from our sample. However, we expect this number to be very low because it is standard practice at our institution that all CEM be interpreted on the same day as the imaging examination with results conveyed to the patient after a complete CEM and US evaluation.

Last, the decision to recommend MRI after negative US was made at the discretion of the interpreting radiologist rather than according to a standard protocol. However, 86% of lesions without a US correlate were further evaluated with MRI, and if the MRI findings were negative, 6-month follow-up CEM was performed. MRI was not recommended by the radiologist for 14% of lesions either because the patient had a gadolinium contrast allergy (1 patient) or because the level of suspicion was low enough (< 2%) to safely follow the

lesion with CEM (14 patients). Examples of cases in our study in which MRI was not recommended after a negative US finding included baseline CEM examinations in which the enhancement was believed to represent background parenchymal enhancement and first CEM examinations after surgery in which the enhancement was believed to represent postsurgical change. All of these cases were confirmed to be benign at short-interval follow-up CEM for at least 1 year. A standardized protocol for when to recommend MRI after CEM when the US findings are negative would be of value and could be investigated further.

At our institution, aside from research studies, screening CEM is performed for patients at intermediate risk of breast cancer as determined by the ordering physician. Growing literature supports the use of CEM for screening of patients at intermediate risk who may not qualify for screening MRI and for those who may be at intermediate or high risk of breast cancer and have limited access to MRI [6, 8]. In our study, 12 cancers in 7% of patients were detected on CEM and US alone (MRI was not performed). As the adoption of CEM continues to grow in the radiology community, CEM-directed US may be useful for further characterizing CEM lesions detected on screening and for potential biopsy planning, especially when MRI is not readily available.

Conclusion

A US correlate was found for 31% of enhancing lesions seen on CEM. Lesions with a US correlate were significantly more likely to be malignant than lesions without a US correlate. The likelihood of identifying a US correlate was significantly greater among mass lesions than among nonmass lesions. Patients with suspicious enhancing CEM lesions, particularly nonmass enhancement, may benefit from MRI to exclude malignancy despite having negative US results given the high sensitivity and NPV of MRI. CEM-directed US is clinically useful given that a sonographic correlate can serve as a potential biopsy target and may obviate breast MRI if adequately characterized with US.

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HIGHLIGHTS

Key Finding

- Among enhancing lesions detected on contrast-enhanced mammography (CEM), 31% had an ultrasound (US) correlate. The likelihood of malignancy was significantly higher among enhancing lesions with a US correlate than lesions without a US correlate (26% vs 10%; p = .03). The PPV of US-guided biopsy after CEM-directed US was 32%.

Importance

- CEM-directed US may help identify targets for US-guided biopsy and may obviate further evaluation with contrast-enhanced breast MRI.

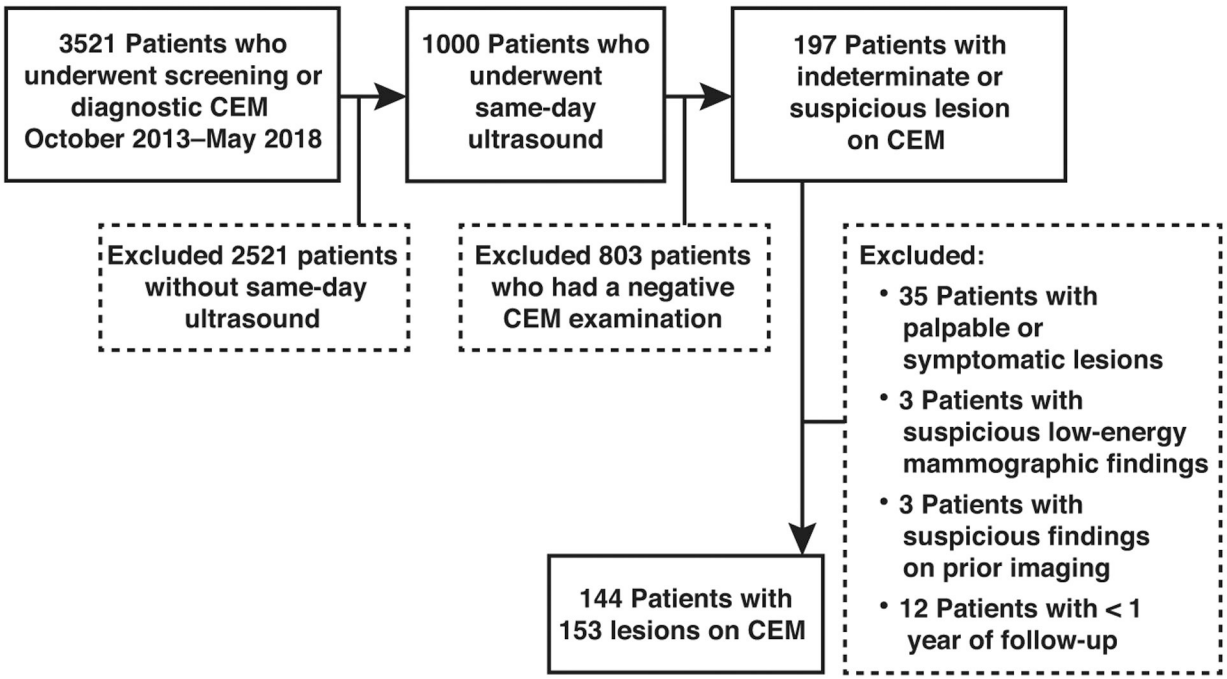

Fig. 1—.
Flowchart shows patient inclusion and exclusion. CEM = contrast-enhanced mammography.

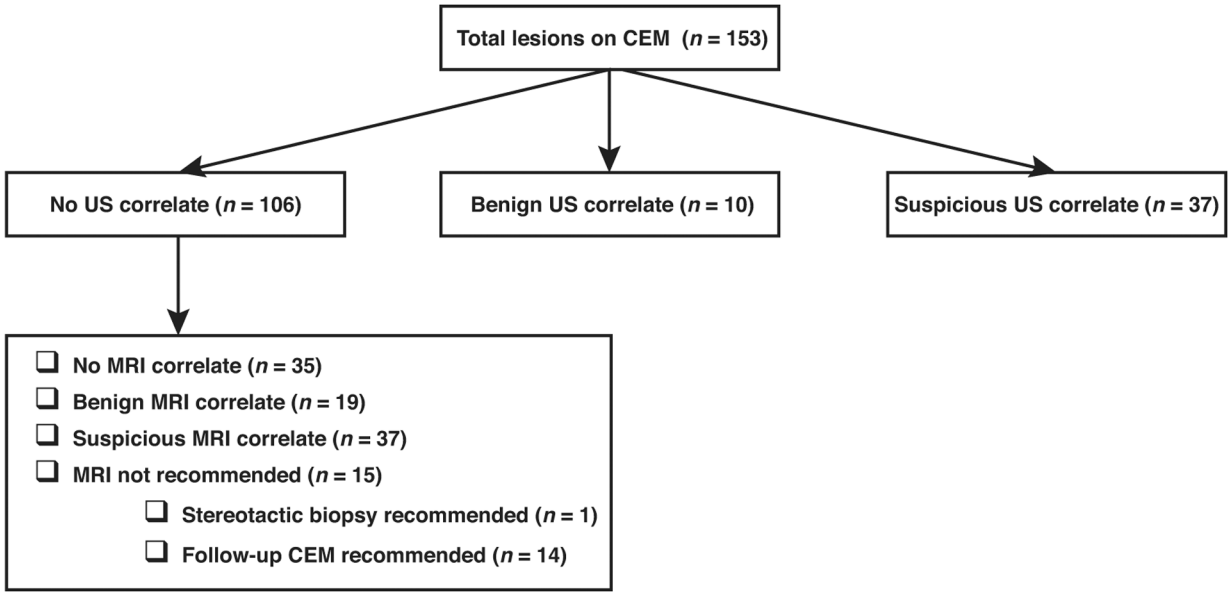

Fig. 2—.
Chart shows recommendations after contrast-enhanced mammography (CEM)-directed ultrasound (US).

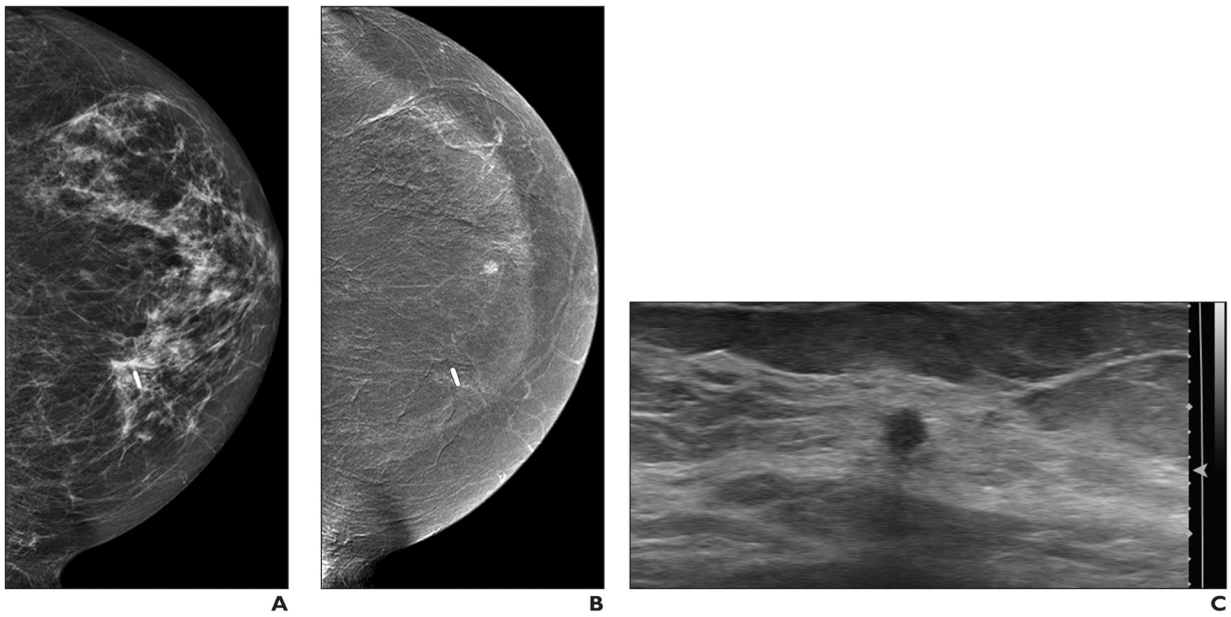

Fig. 3—.

57-year-old woman with history of left breast excision for lobular carcinoma in situ who underwent contrast-enhanced mammography.

A, Low-energy mammogram shows no abnormality.

B, Recombined mammogram shows enhancing 0.4-cm mass in 6-o'clock axis of left breast. Mass was evident only on recombined images.

C, Image obtained during targeted ultrasound-guided core biopsy shows ultrasound correlate. Pathology result was invasive lobular carcinoma.

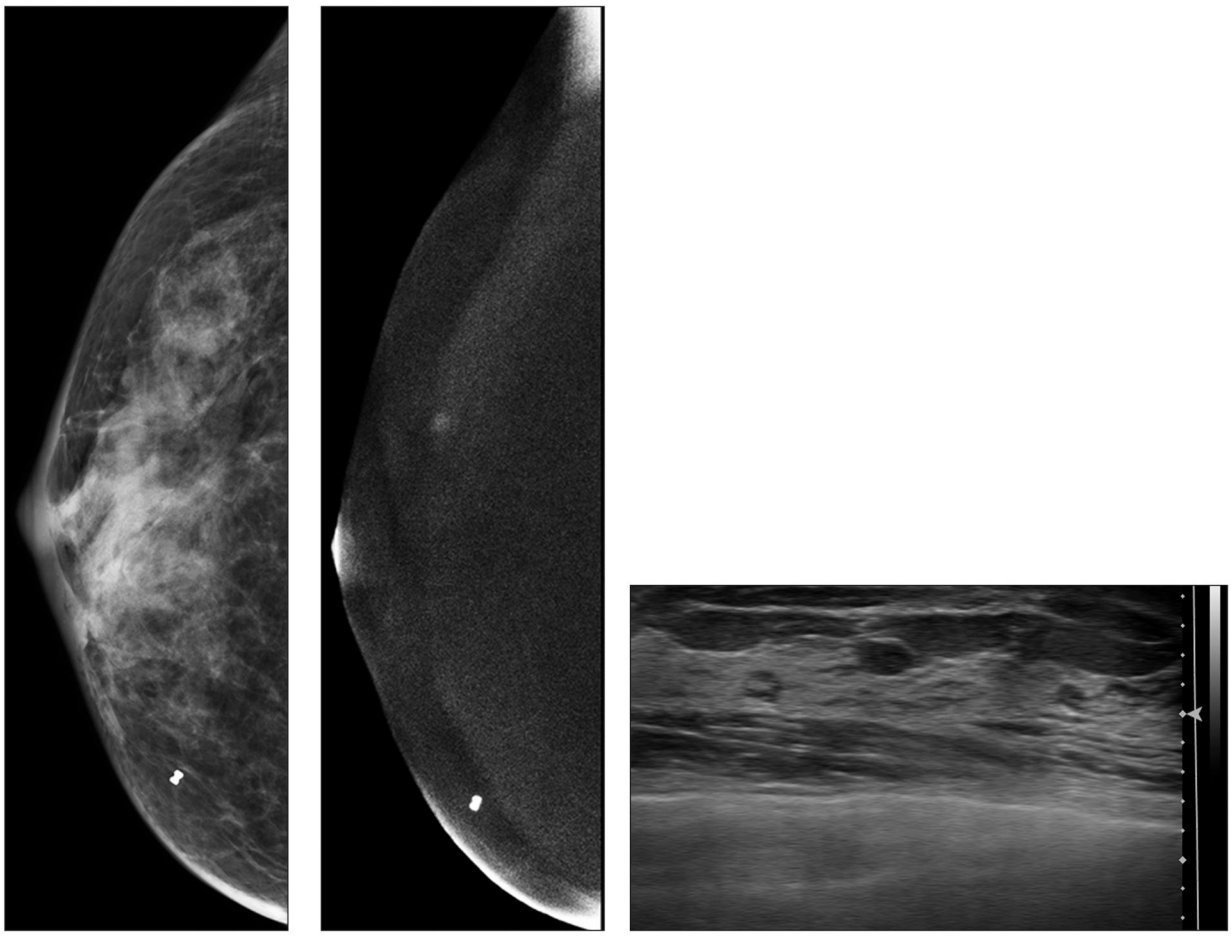

Fig. 4—.

57-year-old woman with family history of breast cancer and personal history of excised lobular carcinoma in situ in right breast who underwent screening contrast-enhanced mammography.

A, Low-energy mammogram shows no abnormality.

B, Recombined mammogram shows enhancing 0.5-cm mass in 9-o'clock axis of right breast. Mass was evident only on recombined images.

C, Image obtained during targeted ultrasound-guided core biopsy shows ultrasound correlate. Pathology result was benign fibroadenoma.

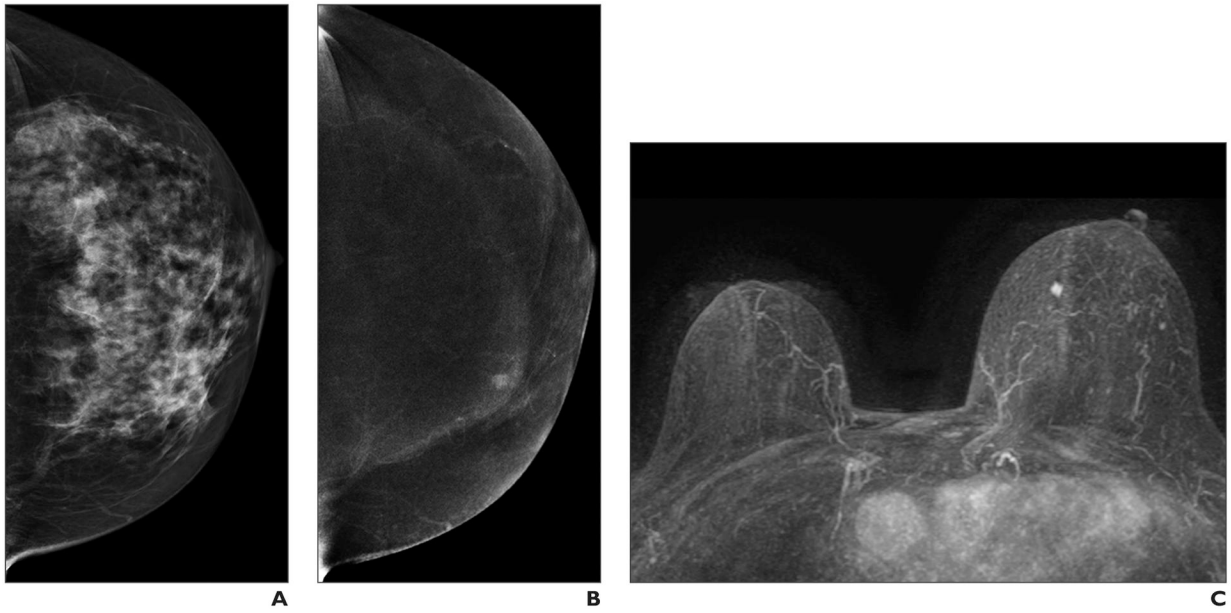

Fig. 5—.

43-year-old woman with history of right breast cancer after conservation treatment who underwent screening contrast-enhanced mammography.

A, Low-energy mammogram shows no abnormality.

B, Recombined mammogram shows enhancing 0.8-cm mass in 8-o'clock axis of left breast. Mass was evident only on recombined images. No ultrasound correlate was identified.

C, Image obtained during targeted MRI-guided core biopsy shows MRI correlate. Pathology result was invasive ductal carcinoma.

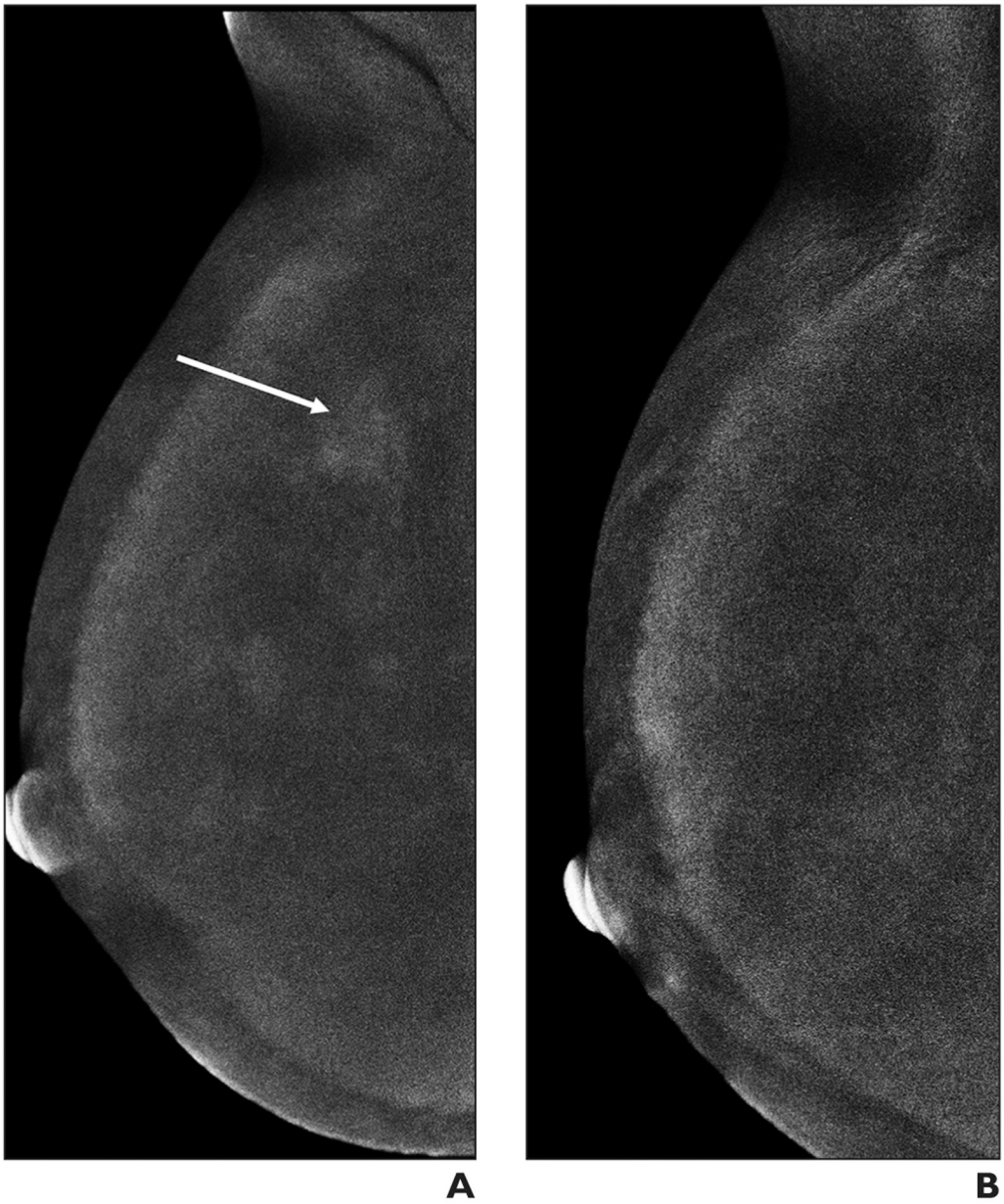

Fig. 6—.

43-year-old woman with history of left breast cancer after mastectomy who underwent baseline screening contrast-enhanced mammography.

A, Mediolateral oblique implant-displaced recombined mammogram shows focal nonmass enhancement (*arrow*) measuring 1.9 cm in superior aspect of right breast. Finding was evident only in this view. No correlate was identified on low-energy mammograms, targeted ultrasound, or MR images.

B, Short-interval (6-month) follow-up contrast-enhanced mammogram shows enhancement has resolved. Enhancement was stable at 2-year follow-up contrast-enhanced mammography, consistent with benign background parenchymal enhancement.

TABLE 1:

Patient Characteristics

Characteristic	No. of Patients (*n* = 144)
Age (y)	
Mean	52.7
Range	39–68
History of breast cancer	55 (38)
Contrast-enhanced mammography	
Bilateral	131 (91)
Left	8 (6)
Right	5 (3)
Breast density	
Predominantly fatty	0 (0)
Scattered fibroglandular tissue	16 (11)
Heterogeneously dense	109 (76)
Extremely dense	19 (13)
Background parenchymal enhancement	
Minimal	36 (25)
Mild	63 (44)
Moderate	40 (28)
Marked	5 (3)
No. of lesions per patient	
One	135 (94)
Two	9 (6)[a]

Note—Except for age, values are numbers of patients with percentages in parentheses.

[a]Six of nine patients had one lesion in each breast; three of nine had two lesions in the same breast.

TABLE 2:

Contrast-Enhanced Mammography (CEM) Lesion Characteristics and Frequency of Ultrasound (US) Correlation

CEM Lesion Characteristic (*n* = 153)	All	Comparison				
		Mass	NME	Lesions With US Correlates (*n* = 47)	Lesions Without US Correlates (*n* = 106)	*p* [a]
Size (cm)[b]						
By type	0.7 (0.5–1.3)	0.7 (0.5–0.8)	0.8 (0.5–1.5)			.01
By US correlation				0.7 (0.5–1.0)	0.8 (0.5–1.3)	.13
Type[c]						< .001
Mass (*n* = 43)				28 (65)	15 (35)	
NME (*n* = 110)				19 (17)	91 (83)	

Note—NME = nonmass enhancement.

[a]Chi-square test of independence and Wilcoxon rank sum test.

[b]Median with interquartile range in parentheses.

[c]Number with percentage in parentheses.

TABLE 3:

Frequency of Malignancy of 153 Lesions Detected With Contrast-Enhanced Mammography (CEM)

Comparison	Malignant Lesions (*n* = 23)	Benign Lesions (*n* = 130)	*p* [a]
Ultrasound correlate			.03
Present (*n* = 47)	12 (26)	35 (74)	
Absent (*n* = 106)	11 (10)	95 (90)	
CEM lesion type			.04
Mass (*n* = 43)	11 (26)	32 (74)	
Nonmass (*n* = 110)	12 (11)	98 (89)	
CEM lesion size (cm)	0.7 (0.6–1.0)	0.8 (0.5–0.3)	.90

Note—Except for lesion size (median and interquartile range), values are number with percentage in parentheses.

[a]Chi-square test of independence and Wilcoxon rank sum test.

TABLE 4:

Outcomes of 37 Lesions Biopsied With MRI Guidance

MRI Lesion Characteristic	Overall (*n* = 37)	Malignant (*n* = 11)	Benign (*n* = 26)	*p* [a]
Type				.08
Mass	15 (41)	7 (64)	8 (31)	
Nonmass	22 (59)	4 (36)	18 (69)	
Size (cm)	0.8 (0.6–1.4)	0.8 (0.7–0.9)	0.8 (0.6–1.4)	.90

Note—Except for lesion size (median and interquartile range), values are number with percentage in parentheses.

[a]Fisher exact test and Wilcoxon rank sum test.

TABLE 5:

Histopathology Results for 75 Biopsied Lesions Detected With Contrast-Enhanced Mammography

Histopathologic Finding	No.	Ultrasound-Guided Biopsy Correlate Present (*n* = 37)	Ultrasound Correlate Absent (*n* = 38)	
			MRI-Guided Biopsy (*n* = 37)	Stereotactic Biopsy (*n* = 1)
Benign	52	25 (68)	26 (70)	1 (100)
Malignant	23	12 (32)	11 (30)	0
Ductal carcinoma in situ	5	0	5	
Invasive	18	12	6	
Ductal	15	11	4	
Lobular	2	1	1	
Adenosquamous	1	0	1	
PPV (%)		32	30	0

Note—Values in parentheses are percentages.