Assessment of BI-RADS Category 4 Lesions Detected with Screening Mammography and Screening US: Utility of MR Imaging[1]

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Purpose: To investigate the utility of magnetic resonance (MR) imaging according to different types of Breast Imaging Reporting and Data System (BI-RADS) category 4 findings from screening mammography and/or screening ultrasonography (US).

Materials and Methods: This institutional review board–approved prospective study included 340 patients in whom 353 lesions were detected at screening mammography or US and were rated BI-RADS category 4 after appropriate conventional work-up. Written informed consent was obtained from all patients. Women underwent standard dynamic contrast material–enhanced MR imaging for further assessment. Women with negative or benign MR findings who did not proceed to biopsy underwent intensified follow-up for at least 18 months. Pure clustered microcalcifications were followed up for at least 24 months.

Results: Of the 353 study findings, 66 (18.7%) were finally shown to be true-positive (23 cases of ductal carcinoma in situ [DCIS], 43 invasive cancers) and 287 (81.3%) were false-positive. Assessment of MR imaging findings led to a correct diagnosis of no breast cancer in 264 of the 287 false-positive findings (92%) and helped confirm the presence of breast cancer in 63 of 66 malignancies. The false-negative rate for pure clustered microcalcifications was 12% (three of 25 cases) because of three nonenhancing low-grade DCIS cases; in turn, MR imaging depicted additional invasive cancers in three women with false-positive findings from mammography and US. For mammographic findings other than pure clustered microcalcifications, MR imaging increased the positive predictive value (PPV) from 17.5% (21 of 120 cases; 95% confidence interval [CI]: 10.7%, 24.3%) to 78% (21 of 27 cases; 95% CI: 62.1%, 93.5%), with a false-negative rate of 0%. For all US findings, MR imaging increased the PPV from 12.9% (20 of 155 cases; 95% CI: 7.6%, 18.2%) to 69% (20 of 29 cases; 95% CI: 52.2%, 85.8%), again with a false-negative rate of 0%. MR imaging resulted in false-positive findings that led to MR imaging–guided biopsy in five of the 340 patients (1.5%).

Conclusion: MR imaging is useful for the noninvasive work-up of lesions classified as BI-RADS category 4 at mammography or US and can help avoid 92% of unnecessary biopsies. The false-negative rate was 0% for all US findings and for all mammographic findings except pure clustered microcalcifications. Additional invasive cancers were identified in three women with false-positive findings from mammography and US.

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During the 1st decade of its clinical application, magnetic resonance (MR) imaging of the breast had primarily been used as a diagnostic "problem-solving" tool for further evaluation of clinical, mammographic, and ultrasonographic (US) findings (1,2). Today, breast MR imaging is more frequently used for delineating the extent of disease in patients with a new diagnosis of breast cancer and, more important, for screening (3).

One reason for this shift in clinical practice was that during the same period, minimally invasive biopsy systems became available to allow nonsurgical tissue sampling that could help clarify equivocal or suspicious findings obtained at mammography or US (4). Another reason was that it had become increasingly evident that the use of breast MR imaging could lead to additional false-positive results. As a result, current American College of Radiology practice guidelines explicitly discourage the use of MR imaging for the work-up of equivocal or suspicious findings at mammography and US (5).

Although the diagnostic accuracy of mammographic screening has improved during the past decades, on average, the published positive predictive values (PPVs) are still between 18.4% and 31% (6,7). Accordingly, seven to eight of 10 invasive breast biopsies yield benign results. With the advent of screening US, published PPVs have ranged from 6.7% to 13.2% (8,9). Conversely, published diagnostic accuracies for breast MR imaging have steadily improved during the past decade because of more advanced image acquisition and interpretation standards, such as the MR Breast Imaging Reporting and Data System (BI-RADS) lexicon and the American College of Radiology accreditation program.

Accordingly, we sought to investigate whether the current recommendation against the use of MR imaging for problem solving is still appropriate. We hypothesized that the diagnostic utility of additional MR imaging for problem solving may depend on the specific type of mammographic or US finding. Therefore, our aim was to investigate the utility of MR imaging according to different types of BI-RADS category 4 findings from screening mammography and/or screening US.

Advances in Knowledge

- MR imaging helped increase the positive predictive value of Breast Imaging Reporting and Data System (BI-RADS) category 4 findings from screening mammography and US from 18.7% (66 of 353 cases; 95% confidence interval [CI]: 14.6%, 22.8%) to 73% (63 of 86 cases; 95% CI: 63.9%, 82.7%).
- MR imaging work-up of US BI-RADS 4 findings helped avoid unnecessary benign biopsies in 126 of 135 study participants without cancer (93.3%) and was associated with a false-negative rate of 0% (zero of 20 cases).
- MR imaging work-up of mammographic BI-RADS 4 findings other than pure clustered microcalcifications (without accompanying mass) helped avoid unnecessary benign biopsies in 93 of 99 study participants without cancer (94%) and was associated with a false-negative rate of 0% (zero of 21 cases).
- MR imaging work-up of mammographic findings of pure clustered microcalcifications (without accompanying mass) was associated with a false-negative rate of 12% (three of 25 cases) because three low-grade ductal carcinomas in situ were not considered suspicious at MR imaging.
- MR imaging work-up helped depict three additional invasive breast cancers in women whose BI-RADS category 4 lesions had been false-positive (benign) and resulted in five additional false-positive findings.

Implication for Patient Care

- MR imaging appears to be a reliable method for demonstrating the absence and helping confirm the presence of breast cancer in women with possibly malignant findings at screening mammography and/or screening US, at least for findings not due to pure clustered microcalcifications.

Materials and Methods

Study Design and Inclusion Criteria

The institutional review board approved this prospective cohort study. Patients were recruited between June 2010 and January 2013. All patients provided written informed consent.

We included consecutive women who were clinically asymptomatic but had suspicious findings at screening mammography or screening US and in whom appropriate work-up with mammography or US yielded a BI-RADS category 4 diagnosis. Patients underwent the same type of assessment regardless of whether a suspicious finding was first obtained at screening US or screening mammography. This assessment consisted of additional mammographic views or magnification views and/or coned-down views where appropriate, as well as additional US studies of the questionable area. For the targeted US examination, a breast radiologist (C.K.K., S.S., or K.S., with 20,

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Abbreviations:
BI-RADS = Breast Imaging Reporting and Data System
CI = confidence interval
DCIS = ductal carcinoma in situ
PPV = positive predictive value

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Conflicts of interest are listed at the end of this article.

8, and 5 years of experience in breast imaging, respectively) performed high-spatial-resolution US with a 15-MHz linear probe along with further US techniques, such as three-dimensional US, color Doppler US, and shear-wave elastography. Patients were included in our study if, after this assessment, the lesion was classified as BI-RADS category 4 (ie, a finding that, according to current practice guidelines, would lead to surgical or core biopsy).

Women with imaging findings classified as BI-RADS category 5 and those with histologically proved cancers (BI-RADS category 6) were excluded.

Table 1

MR Imaging Technique

Parameter	T2-weighted Imaging	Dynamic Imaging
Type of examination	2D turbo spin echo	2D multisection gradient echo
Repetition time (msec)	≤4000	≤260
Echo time (msec)	80–110	4.6
Fractional anisotropy (degrees)	90	90
SENSE factor	1.6	1.5–1.8
Image orientation	Axial	Axial
Anatomic coverage	Bilateral	Bilateral
In-plane spatial resolution (mm)	0.56–0.68	0.56–0.68
Section thickness (mm)	≤3	≤3
Acquisition matrix	512 × 512	512 × 512
Field of view (mm)	290–350	290–350
Acquisition time (sec)	140	55–70 (per dynamic acquisition)
No. of precontrast acquisitions	1	1
No. of postcontrast acquisitions	…	4
Postprocessing	…	Subtraction of all dynamic frames

Note.—SENSE = sensitivity-encoding scheme, 2D = two-dimensional.

Imaging Technique

Screening mammography was conducted, and results were read in accordance with national practice and quality assurance guidelines. Bilateral digital full-field mammography was performed in two standard planes (craniocaudal and mediolateral oblique) (Selenia Dimensions; Hologic, Bedford, Mass). As explained earlier, additional views and spot compression were performed where appropriate for further assessment. Computer-assisted detection was used for assessment (ImageChecker Digital; Hologic). Independent double reading by two radiologists who specialized in breast imaging (C.K.K., S.S.) was performed for all mammograms.

All study participants underwent either screening or targeted breast US as part of the work-up of mammographic findings. Examinations were performed by a dedicated breast radiologist using a dedicated breast US unit with a high-spatial-resolution linear 15-MHz probe (Aixplorer; Supersonic Imagine, Aix-en-Provence, France). Screening US was performed in accordance with national practice guidelines. At the discretion of the radiologist, Doppler US, shear-wave elastography, and three-dimensional US were used to further classify findings obtained at two-dimensional imaging. US findings were described and categorized in accordance with the current US BI-RADS lexicon (10).

All breast MR imaging examinations were performed with a 1.5-T unit (Achieva; Philips, Best, the Netherlands) and a four-channel breast coil (Invivo PMS, Gainesville, Fla) by using breast immobilization in the craniocaudal direction (CC-Fixation for Invivo OBC; Noras, Höchberg, Germany) with a standardized protocol (Table 1).

Image Interpretation

The individual imaging finding that led to the classification of a patient's screening mammogram or US scan as showing a BI-RADS category 4 lesion is referred to as the "study finding."

All MR imaging studies were reviewed by one of two breast radiologists (C.K.K. or S.S.). Readers searched the MR images for a possible correlate of the respective study finding. To do so, readers carefully compared the location (by considering different patient positioning during MR imaging vs that during mammography and US), size, and morphologic features of possible imaging correlates. Readers then provided an MR imaging BI-RADS category for the area of the study finding. Thereafter, readers reviewed the entire breast MR imaging study and made their BI-RADS diagnosis for possible incidental findings in the same breast and in the contralateral breast. Accordingly, for every study participant, BI-RADS categories were assigned for *(a)* the area that prompted MR imaging, *(b)* the remaining parts of the same breast, and *(c)* findings obtained in the contralateral breast.

Data Analysis

The unit of analysis was the individual study finding. Study findings were classified according to the imaging method with which the finding was first obtained (ie, if a patient underwent screening mammography resulting in a BI-RADS category 4 diagnosis and targeted US was performed for work-up, with the finding finally classified as BI-RADS category 4 at US, the lesion was categorized as a mammographic study finding even if there was a US correlate).

In accordance with the current BI-RADS lexicon descriptors (11), mammographic findings were classified as follows: masses with or without microcalcifications (referred to as "masses" herein), asymmetric densities, architectural distortions, and pure clustered microcalcifications without accompanying mass. For US, findings were classified as masses and nonmass lesions. The latter included such US findings as suspected intraductal pathologic abnormalities, focal acoustic shadowing without

detectable mass, and architectural distortions at three-dimensional US.

All lesions classified as BI-RADS category 1–3 with MR imaging were considered "test negative," and all lesions classified BI-RADS category 4 or 5 were considered "test positive."

Data Validation

All patients with study findings and possible incidental findings finally categorized as BI-RADS category 4 or 5 at MR imaging underwent biopsy. Histologic sampling was performed with core or vacuum-assisted biopsy in accordance with national practice guidelines and under US, mammographic, or MR imaging guidance depending on which method was best suited to locate and access the lesion. All tissue samples were examined in consensus by two certified breast pathologists with 26 and 9 years of experience in the pathologic assessment of breast lesions.

For study findings classified as BI-RADS category 1–3 at MR imaging, further management depended on the type of study finding (pure clustered microcalcifications vs all other study finding types).

Vacuum biopsy was recommended for women with pure clustered microcalcifications irrespective of the final MR imaging categorization. Some women, however, declined to undergo biopsy if the MR imaging result was negative. These women were monitored for at least 24 months with mammography, US, and MR imaging to check *(a)* the stability of calcifications on coned-down magnification views and *(b)* possible signs of breast cancer at the site of the pure clustered microcalcifications without accompanying mass. For women whose pure clustered microcalcifications remained stable and who had no evidence of breast cancer or ductal carcinoma in situ (DCIS) at US and MR imaging during follow-up, a negative validation result was accepted.

Women with all other study findings (ie, those without pure clustered microcalcifications) and BI-RADS category 1 or 2 lesions at MR imaging did not proceed to biopsy but underwent systematic clinical, mammographic, US, and MR imaging follow-up for at least 18 months. If during this follow-up the study finding regressed or remained stable, absence of breast cancer was accepted and a negative validation result was assumed.

Statistical Analysis

Invasive breast cancers and DCIS were considered malignant diagnoses and as having positive validation results. All other histologic diagnoses and uneventful follow-up were accepted as proof of absence of breast cancer and, accordingly, as having a negative validation result.

Results

Patient Cohort

We recruited 340 patients with a total of 353 study findings. The mean patient age was 53.9 years (median age, 53 years; range, 23–81 years). Table 2 provides demographic details for the patient cohort.

Among the 353 study findings, 66 (in 66 individual participants) were finally shown to be malignant (43 invasive cancers and 23 DCIS cases), for a malignancy rate of 18.7%. In addition, MR imaging depicted three invasive cancers in three patients. Thus, cancer was found in 69 of the 340 patients (20.3%; 95% confidence interval [CI]: 16.0%, 24.6%) (Table 3). The remaining 287 study findings (81.3%; 95% CI: 77.2%, 85.4%) were finally classified as benign.

Types of Validation

All 69 malignant diagnoses were established with imaging studies conducted during the trial; none of the malignant diagnoses were established with follow-up imaging studies.

One hundred thirty-five of the 353 study findings (38.2%) were finally clarified with imaging-guided biopsy. Fifty-eight of the 78 women with pure clustered microcalcifications as the study finding (74%) underwent vacuum biopsy. DCIS or invasive cancer was confirmed in 25 of the 78 patients (32%), and nonmalignant tissue changes were seen in 33 (42%) (Figure). The remaining 20 women (26%) underwent follow-up for at least 24 months (mean follow-up, 30.3 months; range, 24–44 months). None of the patients exhibited a change from the mammographic assessment (eg, change in configuration or number of calcifications, development of an accompanying mass at follow-up, or change in US or MR imaging findings that prompted biopsy).

In addition to the 135 study findings clarified with biopsy, the incidental MR imaging findings in eight patients (three in the same breast as the study finding

Table 2

Demographic Data

Characteristic	Value
Age (y)	
Mean	53.9
Median	53
Range	23–81
Menopausal status	
Premenopausal	133/340 (39.1)
Postmenopausal	207/340 (60.9)
Indication for the initial imaging study	
Screening	298/340 (87.6)
Routine follow-up after breast cancer	42/340 (12.4)
Previous breast biopsies	
Yes, benign result	79/340 (23.2)
Yes, malignant result	42/340 (12.4)
None	219/340 (64.4)
Familial risk of breast cancer	
Lifetime risk >20%*	7/340 (2.1)
Lifetime risk <20%*	121/340 (35.6)
No family history of breast cancer	212/340 (62.4)
Mammographic breast density†	
1	19/198 (9.6)
2	72/198 (36.4)
3	77/198 (38.9)
4	30/198 (15.2)

Note.—Unless otherwise noted, data are numbers of patients. Numbers in parentheses are percentages.

* According to the criteria for high familial risk as defined by the Consortium on Familial Breast and Ovarian Cancer of the German Cancer Aid (12).

† American College of Radiology breast density categories were used.

Table 3

Histologic Findings and Tumor Stages in 143 Biopsies Performed in 140 Patients

Parameter	No. of Study Findings	No. of Incidental MR Imaging Findings	Total
Histologic type of breast cancers*			
Total no. of cancers	66	3	69
DCIS	23 (35)	0	23 (33)
IDC	21 (32)	1 (33)	22 (32)
IDC plus DCIS	14 (21)	0	14 (20)
ILC	8 (12)	2 (67)	10 (14)
Breast cancer stage			
pTis	23 (35)	0	23 (33)
pT1a	6 (9.1)	2 (67)	8 (12)
pT1b	11 (17)	1 (33)	12 (17)
pT1c	16 (24)	0	16 (23)
pT2	8 (12)	0	8 (12)
pT3	2 (3.0)	0	2 (2.9)
Grade of DCIS			
Low grade	6 (26)	0	6 (26)
Intermediate grade	10 (43)	0	10 (43)
High grade	7 (30)	0	7 (30)
Grade of invasive breast cancers			
Low grade/well differentiated	4 (9.3)	2 (67)	6 (13)
Intermediate grade/moderately differentiated	27 (63)	1 (33)	28 (61)
High grade/poorly differentiated	12 (28)		12 (26)
Histologic diagnosis of benign findings			
Total no. of benign findings	69	5	74
Benign lesion	50 (72)	2 (40)	52 (70)
Lesion with uncertain malignant potential	19 (28)	3 (60)	22 (30)

Note.—Data are numbers of biopsies, with percentages in parentheses.

* IDC = invasive ductal carcinoma, ILC = invasive lobular carcinoma.

and five in the contralateral breast) prompted MR imaging–guided biopsy.

Types of Study Findings

Of the 353 study findings, 198 (56.1%) were obtained with mammography and 155 (43.9%) were obtained with US. Seventy-one of the 198 mammographic findings (35.9%) were masses, 34 (17.2%) were asymmetric densities, 15 (7.6%) were architectural distortions, and 78 (39.4%) were clustered microcalcifications. One hundred fifteen of the 155 findings obtained with US were masses (74.2%) and 40 were nonmass lesions (25.8%).

MR Imaging at the Site of the Study Finding

MR imaging yielded true-positive results for all mammographic study findings that were caused by invasive breast cancer (Table 4). MR imaging had true-positive results for 18 of the 21 mammographic study findings that showed DCIS; the three false-negative DCIS cases were low-grade DCIS (size of 6, 7, and 11 mm, respectively). MR imaging yielded true-negative results for all remaining mammographic study findings that were ultimately validated as being free of cancer.

MR imaging had true-positive results for all 18 US study findings that were caused by invasive breast cancer and for two that showed pure DCIS. MR imaging yielded true-negative results for all remaining US study findings.

PPV before and after MR Imaging Assessment

Overall, MR imaging assessment reduced the number of false-positive diagnoses from 287 to 23 (92% reduction [264 of 287 findings]): from 152 false-positive mammographic study findings before MR imaging to 14 after MR imaging (90.8% reduction [138 of 152 findings]) and from 135 false-positive US study findings to nine (93.4% reduction [126 of 135 findings]) (Table 5).

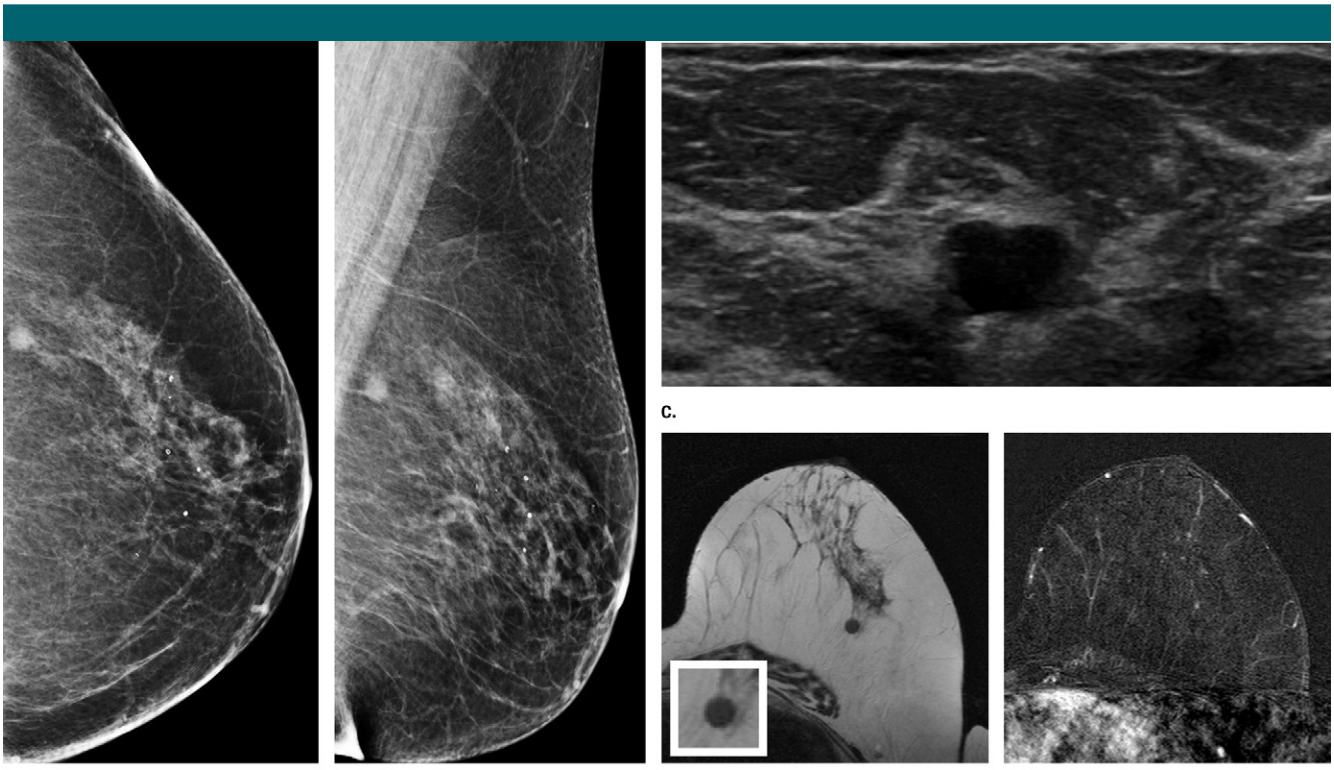
MR imaging exhibited a negative predictive value of 100% (91 of 91 findings and 35 of 35 findings) and a false-negative rate of 0% (zero of 275 findings) for both types of US study findings (masses and nonmass lesions) and for all types of mammographic study findings except pure clustered microcalcifications without accompanying mass. For pure clustered microcalcifications, the negative predictive value was 94% (45 of 48 findings [95% CI: 87.0%, 100%]), yielding a false-negative rate of 12% (three of 25 findings [95% CI: 0%, 24.7%]).

Incidental Findings at MR Imaging

Incidental findings at MR imaging classified as BI-RADS category 4 or 5 were noted in eight of the 340 patients (2.4%). In five of these 340 patients (1.5%), histologic features were benign or borderline (sclerosing adenosis in two patients, atypical ductal hyperplasia in one patient, and papilloma with atypia in two patients). In the remaining three patients with incidental findings (three of 340 patients [0.9%]), MR imaging depicted small invasive breast cancers that were occult with mammography and/or US. The three incidental breast cancers seen only at MR imaging were identified in women whose study findings were ultimately shown to be false positive (benign). All other MR imaging BI-RADS diagnoses outside the area of the study finding were classified as BI-RADS category 2; there were no BI-RADS category 3 findings with MR imaging.

Discussion

In this prospective study, 353 BI-RADS category 4 lesions were diagnosed in 340 women after extensive conventional imaging work-up with full-field digital mammography or



Images in 69-year-old postmenopausal woman who had undergone mammographic screening. **(a, b)** Screening mammograms (left craniocaudal and left mediolateral oblique views, respectively) show a mass with ill-defined margins in posterior third of left breast at 1 o'clock position. **(c)** B-mode US scan shows hypoechoic mass with ill-defined margins in left breast at 1 o'clock position. **(d)** T2-weighted turbo spin-echo MR image and magnification view show a round mass as the correlate of the mammographic finding at 1 o'clock position in left breast. The mass is isointense with discrete internal septations. **(e)** Subtracted T1-weighted gradient-echo MR image obtained after administration of contrast material shows no enhancement of lesion. US-guided core needle biopsy was performed, and histologic examination showed a sclerosed fibroadenoma.

high-frequency US. We found that MR imaging was a powerful tool for further assessment of such possibly malignant findings.

Overall, MR imaging helped increase the PPV from 18.7% (66 of 353 findings) to 73% (63 of 86 findings). MR imaging helped detect a benign correlate for as many as 264 of the 287 BI-RADS category 4 findings that were ultimately shown to be benign (92%) and helped accurately diagnose all 43 invasive breast cancers and 20 of the 23 DCIS cases. MR imaging did not help diagnose three low-grade DCIS cases in women with pure clustered calcifications at mammography, but it did help establish a new diagnosis of invasive breast cancer in three women whose BI-RADS category 4 study findings were ultimately determined to be false-positive (benign).

Table 4

BI-RADS Categories with MR Imaging

Parameter	No. of Study Findings	BI-RADS Category 1	2	3	4	5
All study findings	353	97 (27.5)	157 (44.5)	12 (3.4)	37 (10.5)	50 (14.2)
Mammographic study findings						
All findings	198	65 (32.8)	70 (35.4)	6 (3.0)	24 (12.1)	33 (16.7)
Mass	71	7 (9.9)	45 (63)	2 (2.8)	1 (1.4)	16 (22)
Asymmetric density	34	16 (47)	14 (41)	1 (2.9)	1 (2.9)	2 (5.9)
Architectural distortion	15	6 (40)	2 (13)	0 (0.0)	4 (27)	3 (20)
PCM*	78	36 (46)	9 (11)	3 (3.8)	18 (23)	12 (15)
US study findings						
All findings	155	32 (20.6)	87 (56.1)	6 (3.9)	13 (8.4)	17 (11.0)
Mass	115	14 (12.2)	71 (61.7)	5 (4.3)	10 (8.7)	15 (13.0)
Nonmass lesions	40	18 (45)	16 (40)	1 (2.5)	3 (7.5)	2 (5.0)
MR imaging–only findings	8	NA	NA	NA	5 (62)	3 (37)

Note.—Data are numbers of findings, with percentages in parentheses. NA = not applicable.

* PCM = pure clustered microcalcifications without accompanying mass.

Table 5

Findings before and after MR Imaging

Parameter	No. of Biopsy Findings*	Before MR Imaging			After MR Imaging							
		No. of TP Findings	No. of FP Findings	PPV (%)	No. of TP Findings	No. of FP Findings	No. of TN Findings	No. of FN Findings	PPV (%)	NPV (%)	Sensitivity (%)	Specificity (%)	FNR (%)
All study findings	353 (100.0)	66	287	18.7 (14.6, 22.8)	63	23	264	3	73.3 (63.9, 82.7)	98.9 (97.6, 100)	95.5 (90.5, 100)	92.0 (88.9, 95.1)	4.5 (0, 9.5)
Mammographic study findings													
Overall	198 (100.0)	46	152	23.2 (17.3, 29.1)	43	14	138	3	75.4 (64.2, 86.6)	97.9 (95.5, 100)	93.5 (86.4, 100)	90.8 (86.2, 95.4)	6.5 (0, 13.6)
Mass	71 (35.9)	16	55	22.5 (12.8, 32.2)	16	1	54	0	94.1 (82.9, 100)	100.0 (100)	100.0 (100)	98.2 (94.7, 100)	0.0 (0)
Asymmetric density	34 (17.2)	2	32	5.9 (0, 13.8)	2	1	31	0	66.7 (13.4, 100)	100.0 (100)	100.0 (100)	96.9 (90.9, 100)	0.0 (0)
Architectural distortion	15 (7.6)	3	12	20.0 (0, 40.2)	3	4	8	0	42.9 (6.2, 79.6)	100.0 (100)	100.0 (100)	66.7 (40.0, 93.4)	0.0 (0)
PCM	78 (39.4)	25	53	32.1 (21.7, 42.5)	22	8	45	3	73.3 (57.5, 89.1)	93.8 (87.0, 100)	88.0 (75.3, 100)	84.9 (75.3, 94.5)	12.0 (0, 24.7)
US study findings													
Overall	155 (100.0)	20	135	12.9 (7.6, 18.2)	20	9	126	0	69.0 (52.2, 85.8)	100.0 (100)	100.0 (100)	93.3 (89.1, 97.5)	0.0 (0)
Mass	115 (74.2)	18	97	15.7 (9.1, 22.3)	18	6	91	0	75.0 (57.7, 92.3)	100.0 (100)	100.0 (100)	93.8 (89.0, 98.6)	0.0 (0)
Nonmass lesions	40 (25.8)	2	38	5.0 (0, 11.8)	2	3	35	0	40.0 (0, 82.9)	100.0 (100)	100.0 (100)	92.1 (83.5, 100.0)	0.0 (0)
MR imaging–only findings	8	NA	NA	…	3	5	NA	NA	…	…	…	…	…

Note.—Except where indicated, numbers in parentheses are 95% CIs. FN = false-negative, FNR = false-negative rate, FP = false-positive, NA = not applicable, NPV = negative predictive value, PCM = pure clustered microcalcifications without accompanying mass, TN = true-negative, TP = true-positive.

* Numbers in parentheses are percentages.

The use of imaging to resolve equivocal breast imaging findings has become a delicate task with the advent of minimally invasive biopsy. Imaging-guided biopsy, especially with vacuum assistance, offers high accuracy. The reported false-negative rate for imaging-guided biopsy is low overall but can be as high as 9% for 14-gauge core biopsy (13). The high diagnostic accuracy that is achievable with core biopsy, together with the widespread availability of such procedures, means that there is little tolerance for false-negative results of the work-up of possibly malignant screening findings.

It is well known, however, that imaging findings classified as BI-RADS category 4 cover a wide range of malignancy rates; the current BI-RADS lexicon specifies a likelihood of malignancy of greater than 2% to less than 95% and recommends tissue sampling as the single acceptable management option (10). In the worst-case scenario (ie, findings that reflect the lower boundary of this range), this means that invasive tissue sampling may be recommended for a patient even though the likelihood of a benign result could be as high as 97%.

The reservations against the use of MR imaging for problem solving were shaped during a time when breast MR imaging was still evolving and the radiologic community was still learning how to appropriately image the breast with MR imaging and how to interpret the respective findings. The first multi-institutional trial on the use of MR imaging for problem solving (14), published in 2004, found a sensitivity of MR imaging of just over 88%—which is low by today's standards. The major issue at that time, however, was the limited specificity, which was as low as 67.7%. Meanwhile, the increasing expertise in breast MR imaging, as well as the availability of MR imaging–guided biopsy, has greatly improved our understanding of the natural appearance of the breast and the MR imaging manifestations of benign and malignant changes. Our results reflect this growing knowledge and demonstrate that, with adequate reader expertise, breast MR imaging

was indeed suitable to alleviate indications to biopsy. This was true for all types of US findings and for all mammographic findings except pure clustered microcalcifications; in these types of BI-RADS category 4 findings, MR imaging offered a negative predictive value of 100% and a false-negative rate of 0%. Accordingly, we propose to accept diagnostic MR imaging, instead of tissue sampling, as an alternate assessment tool for such types of BI-RADS category 4 findings.

For mammographic findings consisting of pure clustered microcalcifications, the false-negative rate was as high as 12% (three of 25 findings)—which arguably is too high to be used to discourage performing a biopsy on the basis of a negative MR imaging finding. Does this mean that MR imaging is altogether worthless in women with BI-RADS category 4 microcalcifications? We believe that this may be too narrow an interpretation of our findings. One should consider that in 45 of the 78 women with pure clustered microcalcifications (58%), MR imaging could have been used to correctly avoid vacuum biopsy. In addition, in the 22 women in whom MR imaging results were positive for DCIS, MR imaging was useful for upgrading the mammographic finding to BI-RADS category 5. In these 22 women, the MR imaging study was not only useful for work-up but could also aid in treatment planning (ie, help define resection margins and rule out or demonstrate possible invasive components within a DCIS).

The three women with pure clustered microcalcifications who received a false-negative MR imaging diagnosis each had low-grade DCIS. The false-negative MR imaging diagnosis could have led to a late diagnosis of DCIS or even invasive breast cancer. However, it is also conceivable—and on pathophysiologic grounds, there is good reason to assume—that these three nonenhancing low-grade DCIS cases may have indeed corresponded to biologically unimportant disease (15). Ongoing prospective trials on the prognostic implications of the different MR imaging phenotypes of DCIS will help elucidate whether nonenhancing low-grade DCIS must be considered a direct precursor of invasive breast cancer that requires immediate action. In the patient with prostate cancer, such paradigms are already put to practice, and the MR imaging phenotype of (even invasive) prostate cancer is used to help stratify patients according to different treatment strategies (eg, active surveillance vs surgical or radiation treatment) (16).

Another concern with regard to the use of MR imaging for problem solving has been the observation that, even if MR imaging were useful for resolving a given diagnostic problem, it may cause additional false-positive findings of its own. In our study, however, such additional MR imaging findings occurred in only 2.3% of patients (eight of 340 patients) and were associated with a high PPV: Three of these eight additional "MR imaging–only" findings corresponded to invasive breast cancer, which was identified in women whose actual study findings had proved to be benign; another three women had high-risk lesions (atypical ductal hyperplasia, papilloma).

A limitation of our study is that 20 women with calcifications classified as BI-RADS category 4 and negative MR imaging findings decided against the recommended biopsy. Instead, they were treated with long-term follow-up, including mammographic and MR imaging controls, for more than 24 months. Long-term follow-up was uneventful in each of these women, and study findings remained completely stable. This result suggests that we were dealing with benign changes or, if indeed these women harbored low-grade DCIS, that their DCIS did not progress (on the basis of clinical and conventional or MR imaging grounds) during the 2-year follow-up. Our study was performed in a single institution. Multicenter trials are needed before recommendations for BI-RADS category 4 findings can be revised.

In summary, MR imaging for the work-up of BI-RADS category 4 lesions detected with screening mammography or US was associated with a negative predictive value and false-negative rate that were equivalent to those afforded by invasive breast biopsy. For the time being, MR imaging cannot be used to discourage biopsy in women with pure clustered calcifications. However, we expect that, with increasing understanding of the predictive implications of the MR imaging phenotype of DCIS, this will probably change. Our results provide initial evidence for the fact that it is clinically acceptable not to act on BI-RADS category 4 calcifications that are negative at MR imaging.

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