Magnetic Resonance Imaging of the Breast Prior to Biopsy

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Context Breast magnetic resonance imaging (MRI) has been shown to have high sensitivity for cancer detection and is increasingly used following mammography to evaluate suspicious breast lesions.

Objective To determine the accuracy of breast MRI in conjunction with mammography for the detection of breast cancer in patients with suspicious mammographic or clinical findings.

Design, Setting, and Patients Prospective multicenter investigation of the International Breast MR Consortium conducted at 14 university hospitals in North America and Europe from June 2, 1998, through October 31, 2001, of 821 patients referred for breast biopsy for American College of Radiology category 4 or 5 mammographic assessment or suspicious clinical or ultrasound finding.

Interventions MRI examinations performed prior to breast biopsy; MRI results were interpreted at each site, which were blinded to pathological results.

Main Outcome Measures Area under the receiver operating characteristic curve (AUC), sensitivity, and specificity of breast MRI.

Results Among the 821 patients, there were 404 malignant index lesions, of which 63 were ductal carcinoma in situ (DCIS) and 341 were invasive carcinoma. Of the 417 nonmalignant index lesions, 366 were benign, 47 showed atypical histology, and 4 were lobular carcinoma in situ. The AUC pooled over all institutions was 0.88 (95% confidence interval [CI], 0.86-0.91). MRI correctly detected cancer in 356 of 404 cancer cases (DCIS or invasive cancer), resulting in a sensitivity of 88.1% (95% CI, 84.6%-91.1%), and correctly identified as negative for cancer 281 of 417 cases without cancer, resulting in a specificity of 67.7% (95% CI, 62.7%-71.9%). MRI performance was not significantly affected by mammographic breast density, tumor histology, or menopausal status. The positive predictive values for 356 of 492 patients was 72.4% (95% CI, 68.2%-76.3%) and of mammography for 367 of 695 patients was 52.8% (95% CI, 49.0%-56.6%) ($P<.005$). Dynamic MRI did not improve the AUC compared with 3-dimensional MRI alone, but the specificity of a washout pattern for 123 of 136 patients without cancer was 90.4% (95% CI, 84%-95%).

Conclusions Breast MRI has high sensitivity but only moderate specificity independent of breast density, tumor type, and menopausal status. Although the positive predictive value of MRI is greater than mammography, MRI does not obviate the need for subsequent tissue sampling in this setting.

JAMA. 2004;292:2735-2742 www.jama.com

MAMMOGRAPHY IS THE PRIMARY imaging modality used to detect clinically occult breast cancer. However, mammography has limitations in both sensitivity and specificity that have led to exploration of other imaging techniques. Magnetic resonance imaging (MRI) has been evaluated for breast imaging because of its value for assessing soft tissues of the body. Breast MRI is performed before and after injection of a gadolinium-based contrast agent.[1,2] Additional lesions seen by MRI that are not visible on the mammogram have been reported to be present in between 27% and 37% of patients.[3,4]

For editorial comment see p 2779.

The use of MRI to evaluate women with mammographically or clinically suspicious breast lesions who are undergoing biopsy has shown high potential, with the reported sensitivities of MRI for breast cancer from larger single center studies ranging from 88% to 95%.[5-12] Thus, there has been considerable enthusiasm for breast MRI and use of the procedure for Medicare patients increased almost 3-fold between 2001 (3440 examinations) and 2003 (10115 examinations).[13] However, the reported specificity of MRI is variable, ranging from 30% to

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80%.[5,6,8,10,14,15] Interpretation of MRI is complicated by 2 fundamentally different methods for performing breast MRI that are currently used. These 2 methods characterize lesions as malignant based on 3-dimensional MRI to assess lesion morphology or dynamic MRI after bolus injection of gadolinium contrast to assess lesion enhancement.[16] The optimal imaging method (3-dimensional MRI or dynamic MRI) remains controversial and has not been subject to evaluation in large-scale trials.

To address the overall performance of 3-dimensional and dynamic MRI as an adjunct to conventional methods for breast cancer detection, the National Cancer Institute sponsored a multicenter clinical study with the aim of defining the role of MRI for breast cancer evaluation.[17] The purpose of this article is to describe the results of the International Breast Magnetic Resonance Consortium study that assessed the accuracy of 3-dimensional MRI and dynamic MRI in patients with mammographically or clinically suspicious breast lesions.

METHODS

Entrance Criteria

Women self-classified in all races and ethnic groups between the ages of 18 and 80 years were eligible for the study. Patients were eligible for enrollment if they were referred for breast biopsy because a mammogram was classified as American College of Radiology (ACR) category 4 or 5 (suspicious abnormality, highly suggestive of malignancy, respectively) or if the patient had a suspicious clinical or ultrasound finding without associated benign mammographic features. All patients were required to have a mammogram within 2 months of the MRI examination. An *index lesion* was defined as the palpable, ultrasonographic or mammographic lesion that was the basis for the referral for breast biopsy. Patients were enrolled at 1 of 14 university centers in North America and Europe that had documented experience in breast MRI.

Patients were excluded if (1) a prior excisional or core biopsy of the affected breast was performed less than 6 months before enrollment, (2) there was a contraindication to MRI (eg, pacemaker, ferromagnetic aneurysm clip), (3) there was prior breast cancer in the affected breast, or (4) the patient was pregnant. The institutional review board at each participating site approved the study. Written informed consent was obtained from patients prior to any study-related procedure.

Mammography

Mammograms were performed in accordance with ACR standards, and consisted of craniocaudal and mediolateral oblique views. Spot views with magnification were performed as needed.

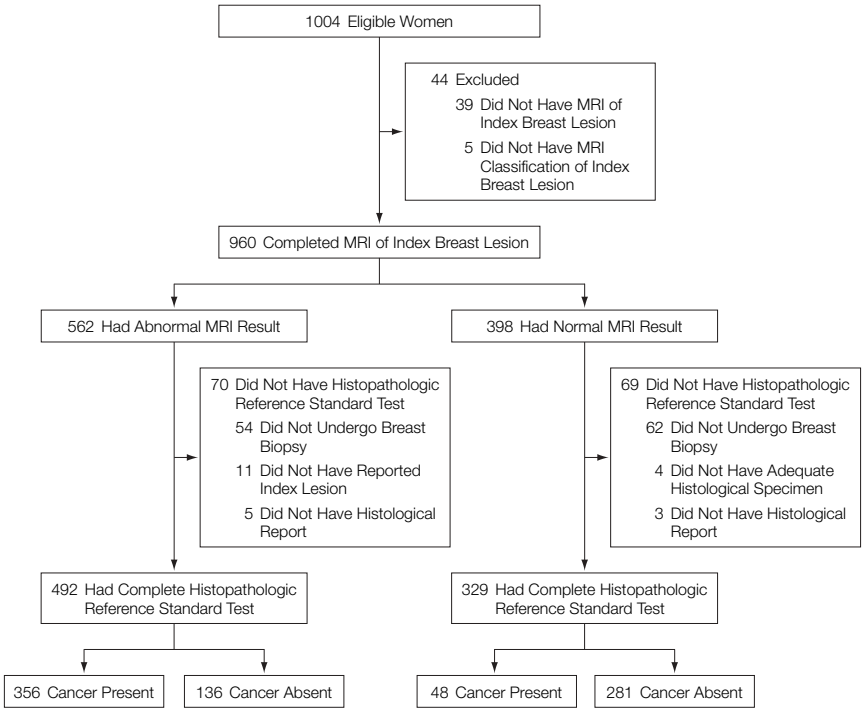
Mammograms were prospectively interpreted with knowledge of the original clinical findings but without knowledge of pathologic or MRI findings. Mammograms were coded using the ordered categories of the ACR breast imaging reporting and data system (BI-RADS) lexicon (category 1, negative; 2, benign finding; 3, probably benign; 4, suspicious finding; 5, highly suggestive of malignancy).

Magnetic Resonance Imaging

All women underwent high resolution 3-dimensional MRI of the breast to assess the suspicious lesion. Patients with enhancing abnormalities were asked to return for dynamic MRI no sooner than 18 hours later. All MRI examinations were performed at 1.5 T using a dedicated breast coil. A single breast was imaged to maximize the spatial resolution of the MRI.

High-Resolution 3-Dimensional MRI. T2-weighted images (slice thickness ≤4 mm and time to repetition of 4000 milliseconds and time to echo of 90 milliseconds) were obtained to identify cystic breast lesions. This was followed by a 3-dimensional T1-weighted set of images taken immediately prior to and after the intravenous administration of 0.1 mmol/kg of gadolinium che-

Figure 1. Patient Flowchart for Breast MRI



MRI indicates magnetic resonance imaging.

late.[18,19] The gadolinium chelate was injected over 10 seconds through a 20- or 22-gauge intravenous catheter followed by a 20-mL saline flush. Imaging began after gadolinium injection but before the saline flush. The 3-dimensional T1-weighted parameters were time to repetition of 20 milliseconds or less, time to echo of 4.5 milliseconds or less, and flip angle of 45°. Chemical shift fat suppression was used. The field of view was 16 to 18 cm. The image matrix was greater than or equal to 256×128 and the slice thickness was 3 mm or less. Total imaging time was less than 4 minutes for the 3-dimensional MRI.

Dynamic MRI. Patients with focal abnormalities on 3-dimensional MRI were asked to return for a dynamic MRI with an additional injection of gadolinium contrast. Two-dimensional, T1-weighted images centered on the focal abnormality were acquired at 15-second intervals after the administration of 0.1 mmol/kg of gadolinium chelate administered over 10 seconds, followed by a 20-mL saline flush. Imaging began at the same time as the gadolinium injection. Imaging parameters were time to repetition of 100 milliseconds, time to echo of 4 to 5 milliseconds, and flip angle of 90°. The image acquisition matrix was 256×128 and the slice thickness was 4 mm. Dynamic images were repeatedly acquired every 15 seconds for a total duration of 5 minutes.

A single reader at each site prospectively interpreted the MRI and was blinded to the pathological findings. The likelihood of malignancy was classified as definitely benign (category 1), probably benign (category 2), indeterminate (category 3), probably malignant (category 4), or definitely malignant (category 5). Enhancement of the lesion on 3-dimensional MRI was classified as malignant if there was a focal mass with irregular or spiculated margins, if enhancement was in a ductal distribution, if a solid lesion showed rim enhancement, or if there was intense regional enhancement in less than 1 quadrant. Enhancement of the lesion was classified as benign if a focal mass showed smooth or lobulated margins with internal septations, or if the mass was cystic. Breast lesions not fitting criteria of either malignant or benign were considered indeterminate.

For dynamic MRI, lesion enhancement was classified by the reader as a washout, plateau, delayed, or indeterminate enhancement curve.[15] The likelihood of malignancy was also classified by the MRI reader on a 5-category scale, as described earlier.

Breast Biopsy

Pathology reports and representative slides from core needle biopsies and excision specimens were sent to a reference pathologist for confirmation of the final diagnosis. Specimens were classified as benign, atypical, in situ cancer, or invasive cancer. Patients with negative needle biopsies that did not yield specific benign diagnoses (eg, fibroadenoma, papilloma) and who did not undergo subsequent excisional biopsy underwent clinical and mammographic follow-up after 1 year to ensure stability of the suspicious lesion.

Statistical Analysis

The primary measure of diagnostic performance in the analysis was the area under the receiver operating characteristic curve (AUC). The receiver operating characteristic curves and their corresponding AUCs were estimated using a binormal model for categorical data.[20,21] The comparison of AUC estimates took into account correlations when necessary. The results of the primary receiver operating characteristic curve analysis using the binormal model were

Table 1. Patient Demographics*

	Eligible Patients (n = 1004)	Enrolled Patients (n = 821)
Age, mean (SD), y	53.0 (11.6)	53.2 (11.6)
Race		
White	764 (76.1)	624 (76.0)
Hispanic or Latino	24 (2.4)	23 (2.8)
Black	168 (16.7)	136 (16.6)
Pacific Islander	2 (0.2)	2 (0.2)
Asian	24 (2.4)	20 (2.4)
Other	6 (0.6)	4 (0.5)
Unknown	16 (1.6)	12 (1.5)
Menopausal status		
Premenopause	359 (35.8)	297 (36.2)
Surgical menopause	195 (19.4)	161 (19.6)
Postmenopause	383 (38.1)	313 (38.1)
Perimenopause	61 (6.1)	49 (6.0)
Unknown	1 (0.1)	1 (0.1)
Missing	5 (0.5)	0
Family history of breast cancer		
No	589 (58.7)	496 (60.4)
Yes	397 (39.5)	315 (38.4)
First-degree relative	214 (21.3)	170 (20.7)
Other relative	183 (18.2)	145 (17.7)
Unknown	11 (1.1)	9 (1.1)
Missing	7 (0.7)	1 (0.1)
Prior hormone use		
No	226 (22.5)	184 (22.4)
Yes	768 (76.5)	632 (77.0)
Missing	10 (1.0)	5 (0.6)
Prior benign breast biopsy		
No	792 (78.9)	649 (79.0)
Yes	200 (19.9)	167 (20.3)
Missing	12 (1.2)	5 (0.6)

*Values are expressed as number (percentage) unless otherwise indicated.

compared and corroborated using a *U* statistic, nonparametric approach.[22] For expository purposes, a secondary analysis was conducted in which test results were treated as binary and estimates of sensitivity, specificity, and predictive value were derived. For this analysis, MRI and mammography results in categories 1 through 3 were classified as negative and results in categories 4 or 5 were classified as positive for malignancy. Invasive cancer or ductal carcinoma in situ (DCIS) were classified as malignant; all others were not malignant. In a secondary analysis, only invasive cancers comprised the malignant category. Exact confidence intervals (CIs) were computed for dichotomized test performance. Correlations were taken into account in the comparisons of positive predictive values estimated from paired test data.[23] All analyses of diagnostic performance were based on data pooled across sites. Variation across sites was assessed using hierarchical models,[24] fitted with the WinBUGS software.[25]

RESULTS

Patient Description

There were 1004 women who met all eligibility criteria enrolled at 1 of 14 enrolling institutions from June 2, 1998, through October 31, 2001 (FIGURE 1). A total of 821 women (81.8%) had complete MRI examinations and had a histopathologic reference standard test. The basis for entry into the trial was an abnormal mammogram in 695 (84.7%) of 821 patients, a palpable breast abnormality without a lesion on the mammogram in 96 (11.7%) of 821 patients, an abnormal ultrasound without a lesion on the mammogram in 15 (1.8%) of 821 patients and other physical examination findings (eg, nipple discharge) in 15 (1.8%) of 821 patients. There were no significant differences in demographic or clinical characteristics between eligible patients and patients who completed the MRI examination and histopathologic reference standard test (TABLE 1).

There were 404 malignant index lesions, of which 63 (15.6%) were DCIS and 341 (84.4%) were invasive carcinoma. Of the remaining index lesions,

Table 2. MRI Assessment of the Index Lesion*

Group	No. of Patients	No. of Cancer Cases	Sensitivity, % (95% CI)	Specificity, % (95% CI)	PPV, % (95% CI)	NPV, % (95% CI)	AUC (95% CI)
Overall†	821	404	88.1 (84.6-91.1)	67.4 (62.7-71.9)	72.4 (68.2-76.3)	85.4 (81.1-89.0)	0.88 (0.86-0.91)
Menopausal status							
Premenopause or perimenopause	346	144	85.4 (78.6-90.7)	66.3 (59.4-72.8)	64.4 (57.2-71.2)	86.5 (80.0-91.4)	0.85 (0.81-0.90)
Surgical/postmenopause	474	260	89.6 (85.3-93.0)	68.2 (61.5-74.4)	77.4 (72.3-82.0)	84.4 (78.1-89.5)	0.91 (0.88-0.93)
Palpable lesion							
Present	345	213	91.1 (86.4-94.5)	61.4 (52.5-69.7)	79.2 (73.6-84.1)	81.0 (71.9-88.2)	0.90 (0.86-0.93)
Absent	474	191	84.8 (78.9-89.6)	70.0 (64.3-75.2)	65.6 (59.3-71.5)	87.2 (82.2-91.3)	0.86 (0.83-0.90)
Microcalcifications (by mammography)							
Present	300	127	83.5 (75.8-89.5)	75.7 (68.6-81.9)	71.6 (63.6-78.7)	86.2 (79.7-91.2)	0.88 (0.84-0.93)
Absent	470	257	90.3 (86.0-93.6)	60.6 (53.7-67.2)	73.4 (68.2-78.2)	83.8 (77.0-89.2)	0.88 (0.85-0.91)
Palpability and microcalcification status							
Palpable							
Calcification	63	46	95.7 (85.2-99.5)	64.7 (38.3-85.8)	88.0 (75.7-95.5)	84.6 (54.6-98.1)	0.95 (0.90-0.99)
No calcification	254	155	90.3 (84.5-94.5)	59.6 (49.3-69.3)	77.8 (71.0-83.6)	79.7 (68.8-88.2)	0.85 (0.80-0.90)
Nonpalpable							
Calcification	236	81	76.5 (65.8-85.2)	76.8 (69.3-83.2)	63.3 (52.9-72.8)	86.2 (79.3-91.5)	0.81 (0.75-0.87)
No calcification	216	102	90.2 (82.7-95.2)	61.4 (51.8-70.4)	67.6 (59.1-75.4)	87.5 (78.2-93.8)	0.86 (0.81-0.91)
Family history of breast cancer							
First-degree relative	170	94	86.2 (77.5-92.4)	69.7 (58.1-79.8)	77.9 (68.7-85.4)	80.3 (68.7-89.1)	0.86 (0.80-0.92)
Other relative	145	66	90.9 (81.3-96.6)	59.5 (47.9-70.4)	65.2 (54.6-74.9)	88.7 (77.0-95.7)	0.88 (0.82-0.94)
None	496	243	88.5 (83.8-92.2)	68.8 (62.7-74.4)	73.1 (67.7-78.1)	86.1 (80.6-90.6)	0.90 (0.87-0.93)
Prior hormonal therapy							
Yes	632	303	87.8 (83.6-91.3)	68.1 (62.7-73.1)	71.7 (66.8-76.2)	85.8 (81.0-89.8)	0.88 (0.86-0.91)
No	184	100	90.0 (82.4-95.1)	64.3 (53.1-74.4)	75.0 (66.3-82.5)	84.4 (73.1-92.2)	0.88 (0.83-0.93)
Breast density (by mammography)							
Mostly fat	106	54	90.7 (79.7-96.9)	51.9 (37.6-66.0)	66.2 (54.3-76.8)	84.4 (67.2-94.7)	0.90 (0.83-0.96)
Scattered	235	119	90.8 (84.1-95.3)	71.6 (62.4-79.5)	76.6 (68.7-83.3)	88.3 (80.0-94.0)	0.91 (0.87-0.95)
Heterogeneous	369	184	86.4 (80.6-91.0)	69.7 (62.6-76.3)	74.0 (67.5-79.7)	83.8 (77.0-89.2)	0.87 (0.83-0.91)
Dense	79	37	86.5 (71.2-95.5)	59.5 (43.3-74.4)	65.3 (50.4-78.3)	83.3 (65.3-94.4)	0.84 (0.74-0.93)

Abbreviations: AUC, area under the receiver operating characteristic curve; CI, confidence interval; MRI, magnetic resonance imaging; NPV, negative predictive value; PPV, positive predictive value.
*Positive MRI result for malignancy is defined as having index lesion classified as 4 (probably malignant) or 5 (definitely malignant).
†Percentages for overall were derived from 356 of 404 cases for sensitivity; 281 of 417 for specificity; 356 of 492 for PPV; and 281 of 329 for NPV.

366 (98.8%) of 417 were benign, 47 (11.3%) of 417 showed atypical histology, and 4 (1.0%) 417 were lobular carcinoma in situ. A total of 117 patients with benign tissue by core needle biopsy had follow-up clinical and mammographic examination at 1 year. All cases confirmed the original core needle biopsy diagnosis of benign tissue.

Mammographic Findings

Of 821 patients who completed the MRI, 491 (59.8%) had a mammographic ACR BI-RADS category 4 (suspicious abnormality) index lesion and 204 (24.8%) had a category 5 (highly suggestive of malignancy) index lesion. The remainder of the patients had lesions that were clinically suspicious (eg, palpable) but had mammograms that had benign findings (42/821; 5.1%), no findings (59/821; 7.2%), or no reported results (25/821; 3.1%). Of 695 patients with a mammogram positive for maligancy (BI-RADS category 4 or 5), 367 patients had DCIS or invasive cancer, resulting in a positive predictive value for mammography of 52.8% (95% CI, 49.0%-56.6%). There was no significant difference in frequency of ACR BI-RADS category or positive predictive value in the eligible patients compared with the patients who completed the MRI.

MRI Findings

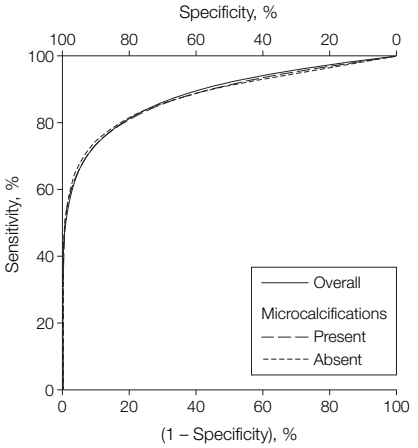
Of 404 patients with DCIS or invasive carcinoma, MRI identified 356 as malignant, resulting in a sensitivity of 88.1% (95% CI, 84.6%-91.1%). Of 417 patients without DCIS or invasive cancer, MRI was negative for maligancy in 281, resulting in a specificity of 67.4% (95% CI, 62.7%-71.9%) (TABLE 2). Of 492 patients with a positive MRI for malignancy, 356 patients had DCIS or invasive cancer, resulting in a positive predictive value of 72.4% (95% CI, 68.2%-76.3%), which was significantly higher than that of mammography ($P<.005$). Of 329 patients with a negative MRI for malignancy, 281 patients had no evidence of DCIS or invasive cancer, resulting in a negative predictive value of 85.4% (95% CI, 81.1%-89.0%). The AUC was 0.88 (95% CI, 0.86-0.91; FIGURE 2). There was no significant difference in the AUC for patients with mammographically detected microcalcifications compared with those without microcalcifications ($P>.50$).

Ductal carcinoma in situ was identified by MRI in 46 of these 63 patients, resulting in a sensitivity of 73% (95% CI, 60.3%-83.4%). Of 341 patients with invasive cancer, MRI identified cancer in 309, resulting in a sensitivity of 90.9% (95% CI, 87.3%-93.7%). The AUC for invasive tumors (0.91; 95% CI, 0.89-0.93) was greater than that of DCIS (0.76; 95% CI, 0.68-0.83).

The mean (SD) size of malignant lesions was 23 (17) mm. The sensitivity of MRI as a function of tumor size is shown in TABLE 3 for both DCIS and invasive cancer. The detection rates by tumor size show higher detection rates for invasive tumor compared with DCIS but the 95% CIs overlap because of the small number of DCIS lesions for each size category. Overall, the sensitivity, AUC, and positive predictive value of MRI for invasive cancer was significantly greater than that for DCIS (TABLE 4).

FIGURE 3 shows receiver operating characteristic curves for MRI as a function of breast density. Sensitivity was greatest in patients with mostly fat (90.7%) or scattered fibroglandular tissue (90.8%) and was least in patients with heterogeneous (86.4%) or dense breasts (86.5%) (Table 2). However, differences in sensitivity and AUC between groups were not statistically significant (all P values $>.14$).

Figure 2. Area Under the Receiver Operating Characteristic Curve for MRI for All Patients



The area under the receiver operating characteristic curve is 0.88 (95% confidence interval [CI], 0.86-0.91) for overall; 0.88 (95% CI, 0.84-0.93) for microcalcifications present; and 0.88 (95% CI, 0.85-0.91) for microcalcifications absent. MRI indicates magnetic resonance imaging.

Table 3. MRI Sensitivity as a Function of Tumor Size

	DCIS		Invasive Cancer	
Tumor Size, mm	Tumors Detected/Total No. of Cancer Cases	Sensitivity, % (95% CI)	Tumors Detected/Total No. of Cancer Cases	Sensitivity, % (95% CI)
1-5	0/4	0	3/4	75.0 (19.4-99.4)
6-10	9/10	90 (55.5-99.7)	41/49	83.7 (70.3-92.7)
11-15	11/14	78.6 (49.2-95.3)	68/74	91.9 (83.2-97.0)
16-20	6/8	75.0 (34.9-96.8)	60/67	89.6 (79.7-95.7)
≥21	13/18	72.2 (46.5-90.3)	130/138	94.2 (88.9-97.5)

Abbreviations: CI, confidence interval; DCIS, ductal carcinoma in situ; MRI, magnetic resonance imaging.

Table 4. MRI Sensitivity Comparing Invasive Cancer With Ductal Carcinoma In Situ

	Invasive Cancer	DCIS
Sensitivity, % (95% CI)	90.9 (87.3-93.7)	73.0 (60.3-83.4)
Specificity, % (95% CI)	67.4 (62.7-71.9)	67.4 (62.7-71.9)
PPV, % (95% CI)	69.5 (65.0-73.7)	25.3 (19.1-32.2)
NPV, % (95% CI)	90.1 (86.2-93.1)	94.3 (91.0-96.6)
AUC (95% CI)	0.91 (0.89-0.93)	0.76 (0.68-0.83)

Abbreviations: AUC, area under the receiver operating characteristic curve; CI, confidence interval; DCIS, ductal carcinoma in situ; MRI, magnetic resonance imaging; NPV, negative predictive value; PPV, positive predictive value.

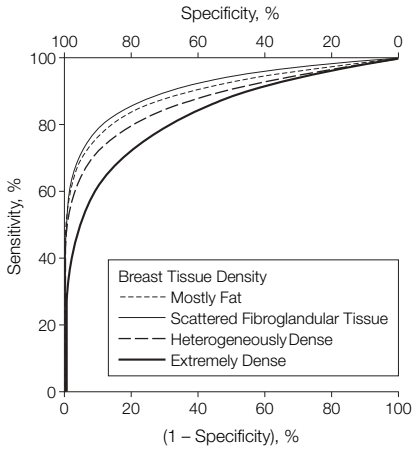
Dynamic MRI

Of 821 patients, 345 (42.0%) had dynamic MRI of a focal lesion that was detected by 3-dimensional MRI (TABLE 5). There were no significant differences in demographic characteristics between the group who received dynamic MRI and the group who received 3-dimensional MRI alone. However, 209 (60.6%) of 345 patients who had dynamic MRI had DCIS or invasive cancer compared with 404 (49.2%) of 821 patients who had 3-dimensional MRI alone.

Table 5 shows the dynamic MRI enhancement pattern for malignant and benign lesions. A washout curve was present in 43 of 209 patients with DCIS or invasive cancer, resulting in a sensitivity of 20.5% (95% CI, 15%-27%). A washout curve was absent in 123 of 136 patients without DCIS or invasive carcinoma, resulting in a specificity of 90.4% (95% CI, 84%-95%). A plateau curve was present in 89 of 203 patients with DCIS or invasive cancer, resulting in a sensitivity of 42.6% (95% CI, 36%-50%). A plateau curve was absent in 102 of 136 patients without DCIS or invasive cancer, resulting in a specificity of 75% (95% CI, 67%-82%). Using either plateau or washout curve as an indicator of malignancy yielded a sensitivity of 63.2% (95% CI, 56.2%-69.7%) and a specificity of 65.4% (95% CI, 56.8%-73.4%). The sensitivity and specificity of a persistent enhancement curve to indicate a benign lesion were 52.2% (95% CI, 43%-61%) and 71% (95% CI, 64%-77%), respectively.

The overall interpretation of dynamic MRI data was also classified by readers for receiver operating characteristic curve analysis. The AUC for dynamic MRI alone was 0.73 (95% CI, 0.67-0.78). This was significantly less than the AUC for 3-dimensional MRI ($P<.001$).

Figure 3. Area Under the Receiver Operating Characteristic Curve for MRI as a Function of Breast Tissue Density



The area under the receiver operating characteristic curve is 0.90 (95% confidence interval [CI], 0.83-0.96) for mostly fat; 0.91 (95% CI, 0.87-0.95) for scattered fibroglandular tissue; 0.87 (95% CI, 0.83-0.91) for heterogeneously dense; and 0.84 (95% CI, 0.74-0.93) for extremely dense. MRI indicates magnetic resonance imaging.

Combination of Dynamic MRI and 3-Dimensional MRI

Dynamic and 3-dimensional MRI results were combined by using the higher of the 2 interpretations as the final score. The AUC for this combined score was 0.86 (95% CI, 0.82-0.86). The combined score was not significantly different than the AUC obtained from 3-dimensional MRI alone. By using the lower of the 2 interpretation scores as the final score, the AUC decreased to 0.76 (95% CI, 0.71-0.81).

Variation of Results by Institution

Hierarchical model-based estimates of the AUC for each institution ranged from 0.78 (SE, 0.03) to 0.91 (SE, 0.02). Variation between sites was not significantly related to the following characteristics: prevalence of malignant disease, breast density, palpability of breast tumors, or breast calcifications. The average tumor size showed a trend toward significance, with increasing tumor size modestly correlating with increased AUC.

COMMENT

This article describes the performance of MRI in conjunction with mammography in the largest multicenter study to date (821 patients). For patients with suspicious lesions identified prior to planned breast biopsy, breast MRI has high accuracy as measured by the AUC of 0.88. The overall sensitivity of MRI was high (88.1%), but the specificity was only moderate (67.4%). The positive predictive value for malignancy for MRI (72.4%) was significantly higher than that of mammography (52.8%). The use of dynamic MRI did not improve the AUC compared with high resolution 3-dimensional MRI alone.

The overall sensitivity of MRI in this 14-site investigation was within the range reported for large, single-center studies (range, 88%-95%),[5-10,14,15] albeit at the lower end of the spectrum. A multicenter study of 463 patients reported a sensitivity of 86% to 97% depending on the interpretation criteria that were used.[26] We detected a trend toward improved MRI performance at centers that evaluated larger breast lesions, but other measures of patient selection criteria showed no significant relationship to MRI performance. Taken as a whole, however, there is consistent evidence that breast MRI sensitivity is high, and that results from multicenter studies are generally consistent with prior single-center data.

The specificity of MRI that has been reported in the literature varies widely (range, 30%-83%).[5,6,8,10,14,15,26] Our results indicate that the specificity of MRI is only moderate (67.4%). To improve

Table 5. Dynamic MRI Assessment of Malignancy

	No. (%) of Patients With Dynamic MRI		
Enhancement Pattern	Benign or Atypical	DCIS or Invasive Cancer	Total
Persistent	71 (20.6)	61 (17.7)	**132** (38.3)
Plateau	34 (9.9)	89 (25.8)	**123** (35.7)
Washout	13 (3.8)	43 (12.5)	**56** (16.2)
Indeterminate	18 (5.2)	16 (4.6)	**34** (9.8)
Total	**136** (39.4)	**209** (60.6)	**345** (100)

Abbreviations: DCIS, ductal carcinoma in situ; MRI, magnetic resonance imaging.

specificity, radiologists rely on either lesion morphology (eg, irregular compared smooth lesion borders) using 3-dimensional MRI[12,27-30] and/or the rate and extent of lesion enhancement depicted by dynamic MRI.[2,15,31-35] This study provides important insight to the relative importance of dynamic compared with high resolution 3-dimensional MRI. The dynamic MRI has potential in some situations to improve specificity; in particular a washout curve was associated with a specificity of 90.4%. Other patterns of the dynamic enhancement curves had substantially lower specificity than the washout pattern. Further analysis of dynamic MRI for certain lesion types or quantitation of enhancement curves may lead to further methods to improve specificity.[26,31] These approaches are under investigation.

There appears to be no major effect of breast density on the performance of MRI for patients with ACR BI-RADS 1, 2, or 3 mammograms. For extremely dense breasts, MRI sensitivity as well as AUC were slightly lower but not significantly different than the other ACR BI-RADS density categories. The corresponding sensitivity of mammography was not determined in this study (because the entrance criteria was an abnormal mammogram, the number of falsely negative mammograms was not known), but mammography sensitivity has been well documented previously. Mammography has previously been shown to have decreased sensitivity in patients with dense breast tissue[36] while cancer risk increases with increasing breast density.[37] Bird et al[38] reported that 77 (24%) of 320 cancerous tumors were missed primarily due to dense breast tissue obscuring an underlying lesion. Leconte et al[39] reported a study of 4236 patients showing mammogram detection rates were 80% for patients with ACR BI-RADS densities of 1 (mostly fat) or 2 (scattered fibroglandular tissue), but only 56% for densities of 3 (heterogeneously dense) or 4 (extremely dense). MRI performance was also independent of menopausal status and tumor histology. These factors support a role for MRI in breast cancer detection in patients with mammographically dense breasts. Indeed, studies of patients at high risk for breast cancer, who are frequently younger and have dense breast tissue, have shown that MRI detects cancer that is mammographically occult.[40]

The purpose of this study was to determine breast MRI performance as an adjunct to mammography. As such, a direct comparison of mammography and MRI was not performed because the mammography results were used as enrollment criteria. Some comparisons of the 2 modalities, however, are available within the study design. For example, MRI had a significantly higher positive predictive value (72.4%) than mammography (52.8%). Although MRI performance exceeded mammography in this regard, these findings are balanced by a negative predictive value of MRI of 85.4%. This negative predictive value is not sufficiently high in most circumstances to use MRI as an alternative to proceeding directly to breast biopsy for suspicious lesions.[16] Other various roles of breast MRI such as determining lesion extent, identifying additional lesions,[3,4] or evaluating the postoperative or scarred breast[41] remain promising.

There are several limitations to this study. The positive predictive value of mammography was relatively high (52.8%) compared with reported values in the literature of 15% to 30%.[42,43] This suggests that patients with more advanced breast lesions were referred into the trial. Assessments of the effects of patient characteristics (such as breast density) were not the primary aim of the study, and subsequent studies will be needed to confirm these findings. Finally, despite initial training and interpretation guidelines that were used in the trial as well as selection of participating sites on the basis of experience with breast MRI, there was variability in AUC at the 14 participating institutions. These results point to the importance of multicenter trials to develop true estimates of the performance of new imaging technologists compared with single-center studies.

In conclusion, MRI shows high sensitivity and moderate specificity for breast cancer. However, for lesions that are mammographically or clinically suspicious, tissue sampling of the breast may not be avoided with the use of MRI. Because MRI appears to be only mildly affected by breast density, a role for MRI in evaluating patients with dense breast tissue is suggested.

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Author Contributions: Dr Schnall had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
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Statistical analysis: Gatsonis, Chen.
Obtained funding: Gatsonis, Schnall.
Administrative, technical, or material support: Bluemke, Gatsonis, DeAngelis, Harms, Hylton, Kuhl, Lehman, Pisano, Causer, Smazal, Weatherall, Schnall.
Study supervision: Bluemke, Gatsonis, DeAngelis, Heywang-Köbrunner, Weatherall, Schnall.
Financial Disclosure: Dr Weatherall has received a research grant from Philips Medical Systems. Dr Schnall has received a research grant from Siemens Medical Systems and has a royalty agreement with USA Instruments.

Funding/Support: This study was funded by grants UO1-CA74696 and UO1-CA74680 from the National Cancer Institute. Gadolinium contrast agents were provided by Amersham Health, Berlex Laboratories, and Bracco Diagnostics.
Role of the Sponsor: The National Cancer Institute's project officer had input into the study design and monitored ongoing study progress including recruitment rates. No other sponsor had any role in the study design, conduct, collection, management, analysis, or intrepretation of the data, or preparation, review, or approval of the manuscript.
Acknowledgment: We thank Paul Stomper, MD, of Roswell Park Cancer Center and Carl D'Orsi, MD, of the Emory Clinic for central review of mammograms.

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