# Cancer Yield of Mammography, MR, and US in High-Risk Women: Prospective Multi-Institution Breast Cancer Screening Study[1]

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**Purpose:** To prospectively determine cancer yield, callback and biopsy rates, and positive predictive value (PPV) of mammography, magnetic resonance (MR) imaging, and ultrasonography (US) in women at high risk for breast cancer.

**Materials and Methods:** The study was approved by the institutional review board and was HIPAA compliant, and informed consent was obtained. We conducted a prospective pilot study of screening mammography, MR, and US in asymptomatic women 25 years of age or older who were genetically at high risk, defined as *BRCA1/BRCA2* carriers or with at least a 20% probability of carrying a *BRCA1/BRCA2* mutation. All imaging modalities were performed within 90 days of each other. Data were analyzed by using exact confidence intervals (CIs) and the McNemar test.

**Results:** A total of 195 women were enrolled in this study over a 6-month period, and 171 completed all study examinations (mammography, US, and MR). Average age of the 171 participants was 46 years ± 10.2 (standard deviation). Sixteen biopsies were performed and six cancers were detected, for an overall 3.5% cancer yield. MR enabled detection of all six cancers; mammography, two; and US, one. The diagnostic yields for each test were 3.5% for MR, 0.6% for US, and 1.2% for mammography. MR, US, and mammography findings prompted biopsy in 8.2%, 2.3%, and 2.3% of patients, respectively. None of the pairwise comparisons were statistically significant. The PPV of biopsies performed as a result of MR was 43%.

**Conclusion:** Screening MR imaging had a higher biopsy rate but helped detect more cancers than either mammography or US. US had the highest false-negative rate compared with mammography and MR, enabling detection of only one in six cancers in high-risk women.



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Genetic predisposition accounts for an estimated 5%–10% of all breast cancers and leads to a minimum of 10 000 new breast cancer cases diagnosed in the United States each year (1,2). Counseling women who are at high risk for breast cancer is challenging. Although there are increasing data demonstrating that prophylactic surgery (mastectomy and oophorectomy) can reduce the risk of breast and ovarian cancer (3–8), the potential absolute benefits must be balanced against issues of body image, the impact of hormone replacement therapy, and options for enhanced surveillance and chemoprevention (9–11). Most experts suggest aggressive surveillance consisting of a mammogram and physical examination every 6–12 months beginning at age 25 to 35. However, scarce data exist to indicate that such aggressive mammographic screening of this population affects breast cancer mortality. In addition, mammographic sensitivity is lower in young women and in women with dense breast tissue. Given the younger age of onset of cancer in women at high risk (50% of women with a *BRCA1* mutation develop breast cancer by the age of 50) (12), it is worrisome that screening mammography alone may be insufficient to detect breast cancer at an early stage in this patient population.

Because of preliminary but consistent published reports from multiple investigators in the United States, Canada, and Europe supporting the added benefit of magnetic resonance (MR) imaging and ultrasonography (US) in detecting cancer in women at high risk, the American Cancer Society currently suggests that women discuss with their clinicians the potential benefits and risks of adding alternative screening methods such as US or MR to complement mammographic screening (13). In 2003, after thorough review of the literature, several third-party payers agreed to reimburse for screening MR imaging in women at high risk for breast cancer (14–16).

Few prior studies have included both US and MR for the detection of clinically and mammographically occult cancer in women at high risk, and the combined range of added cancer yield by using both modalities varies widely from less than 1% to greater than 10%. Thus, the purpose of our study was to prospectively determine cancer yield, callback and biopsy rates, and positive predictive value (PPV) of mammography, MR imaging, and US in women at high risk for breast cancer.

### Advance in Knowledge

- Screening MR allowed detection of more cancers ($n = 6$) in high-risk women compared with screening US ($n = 1$) and/or screening mammography ($n = 2$).

## Materials and Methods

### The International Breast MRI Consortium and Cancer Genetics Network

This study was conducted by the International Breast MRI Consortium (IBMC) in collaboration with the Cancer Genetics Network (CGN). The IBMC was developed and supported by the National Cancer Institute and the Office of Women's Health to evaluate the role of MR in breast cancer. Since its inception, the consortium has conducted two large multicenter studies. Research institutions and community hospitals and clinics from the United States, Canada, and Europe participate. The CGN is a national network of centers specializing in the study of inherited predisposition to developing cancer (17). CGN supports studies on the genetic basis of human cancer susceptibility and the integration of this information into medical practice. The gadolinium-based contrast agents used in the study were provided by GE Healthcare (Waukesha, Wis) and Bracco Diagnostics (Milan, Italy). The authors had full control of the data and information submitted for publication.

### Implications for Patient Care

- Women at high risk for breast cancer can benefit from screening MR imaging.
- Women at high risk for breast cancer who undergo MR do not show benefit from screening US.
- In counseling high-risk women who are considering screening MR, the benefits include a predicted added cancer yield of 23 cancers per 1000 women screened with MR, and the risk of false-positives includes less than 5% of women undergoing biopsy resulting in a benign outcome.

### Study Participants

Six facilities located throughout the United States participated in this IBMC/CGN study. All facilities obtained approval to participate from their institutional review boards, and written informed consent was obtained from all participants prior to entering the study. The study was Health Insurance Portability and Accountability Act compliant. Women were deemed eligible to participate in the study if they were 25 years of age or older and identified as genetically high risk. A woman was determined to be high risk if she met any of the following criteria:

1. Tested positive for *BRCA1/BRCA2* mutation or had a first- or second-degree relative who tested positive for either mutation;

2. The probability of carrying a *BRCA1/BRCA2* mutation (given family

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**Abbreviations:**
CGN = Cancer Genetics Network
CI = confidence interval
IBMC = International Breast MRI Consortium
PPV = positive predictive value

**Author contributions:**
Guarantor of integrity of entire study, C.D.L.; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; approval of final version of submitted manuscript, all authors; literature research, C.D.L., C.I., M.D.S., C.G.; clinical studies, C.D.L., C.I., M.D.S., E.D.P., S.M.A., P.T.W., D.A.B., P.K.M., D.K.A., S.M.D., G.T.; experimental studies, M.D.S.; statistical analysis, S.J.S., C.G.; and manuscript editing, C.D.L., C.I., M.D.S., E.D.P., S.M.A., P.T.W., D.J.B., D.K.A., S.M.D., C.G.

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history of breast and ovarian cancer) was found to exceed 20%, as determined with BRCAPRO (18);

3. The family contained at least two instances of ovarian or breast cancer among the participant and first- or second-degree relatives within the same lineage (multiple primary cancers within same person met criteria); or

4. The woman was of Ashkenazi Jewish ethnicity with one first- or two second-degree relatives with breast or ovarian cancer or was Ashkenazi Jewish and had breast cancer. Where breast cancer was required to meet criteria, participant age of diagnosis of at least one of the breast cancers must have been premenopausal or less than 50 years old.

Women were excluded on the basis of the following criteria:

1. Known contraindication to MR: pregnancy, pacemaker, magnetic aneurysm clip or other implanted magnetic device, or severe claustrophobia;

2. Current palpable or mammographic-actionable finding known at time of enrollment assessment (benign findings at mammography or physical examination allowed);

3. Prior biopsy in the study breast within the past 6 months (including fine-needle aspiration);

4. Received adjuvant chemotherapy or radiation therapy within 6 months of study entry (may have been receiving tamoxifen or aromatase inhibitor either as adjuvant hormonal therapy or for preventive measures);

5. A first- or second-degree relative with a *BRCA1/BRCA2* mutation and the potential participant tested negative for the same mutation;

6. Current untreated malignancy (other than nonmelanoma skin cancer);

7. Metastatic malignancy within the past 5 years; and

8. A psychiatric condition preventing fully informed consent.

## Data Collection

All sites collected data by using study forms and submitted the data by means of Web site entry to the American College of Radiology. Quality-control procedures included review of each submission to identify critical missing forms or data. The American College of Radiology provided routine reports to each participating institution to identify participants with missing information and to clarify inconsistencies in information.

*Clinical history.*—Study participants were seen in a cancer risk evaluation program where a pertinent history and physical examination were performed prior to study entry. Demographic information and a thorough medical history, including genetic testing, hormonal medications, family and personal history of breast disease, obstetric history, phase of menstrual cycle, and results of prior breast cancer screening, were collected.

*Study procedures.*—All patients underwent a clinical breast examination, mammography, US, and MR imaging as part of the study. Study protocol specified all examinations be performed within 90 days of each other. Because the radiologists conducting US had direct contact with the patient during the examination, US was performed prior to the MR and the study mammographic examinations to reduce potential contamination of the US examination with information from the mammogram or MR images. The MR, mammographic, and US images were interpreted without knowledge of the results of the other modalities at the host institution. Separate readers were assigned for each examination to ensure blinded readings. Study protocol required all suspicious findings to be acted on. Fifteen readers participated in the study. All mammographers and US readers were Mammography Quality Standards Act certified. All MR image readers were trained in imaging and qualitative kinetic features and had at least 2 years experience interpreting MR images prior to participating in this study.

All study participants underwent a two-view mammographic study of each

**Figure 1**

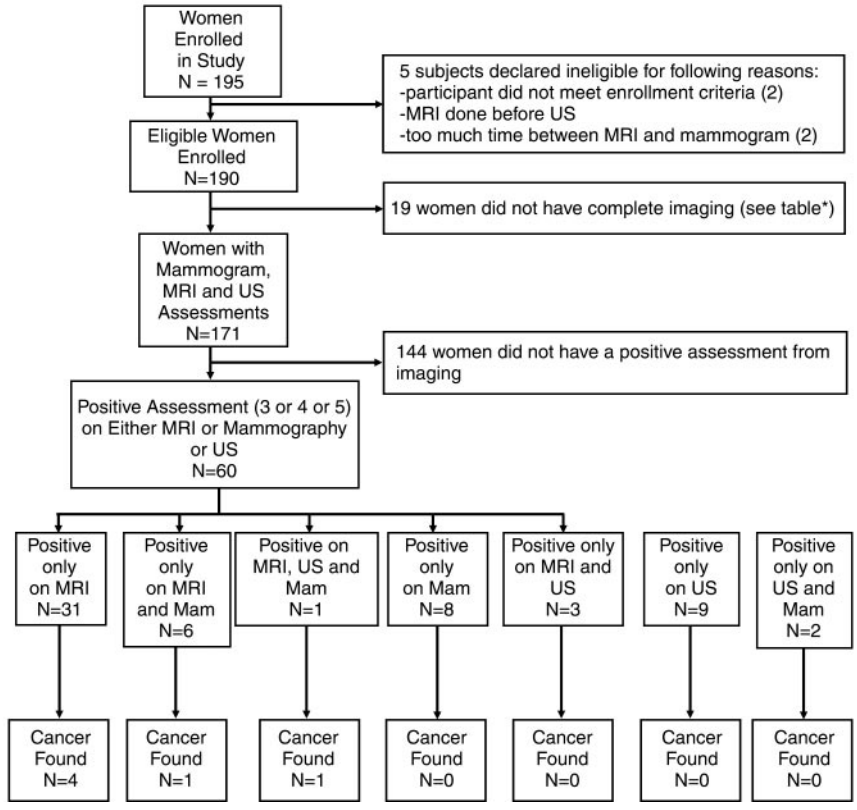


**Figure 1:** Flow chart shows enrollment, eligibility, and study findings.

breast consisting of a craniocaudal and a mediolateral oblique view. Spot magnification was used as needed. All mammograms were coded according to the American College of Radiology Breast Imaging and Reporting Data System (ACR BI-RADS) lexicon, including breast composition, findings, and overall assessment (19). The overall assessment was performed according to a five-point scale as indicated in the ACR BI-RADS lexicon (1 = negative, 2 = benign, 3 = probably benign, 4 = suspicious abnormality, 5 = highly suggestive of malignancy).

US examinations were conducted by using high-frequency high-resolution techniques with 8-mHz or greater transducers. The entire breast was scanned in two planes by an experienced radiologist. Special emphasis was directed toward areas in the breast periphery that often are not well-studied with mammography, including the regions of the inframammary fold, medial breast, far lateral breast, and infraclavicular portions of the breast. The ACR BI-RADS lexicon for US was used to report findings.

The MR examination protocol included 1.5-T magnet strength, a dedicated breast coil, and the following sequences: precontrast sagittal T2-weighted (repetition time msec/echo time msec, 4000/80; matrix, 256 × 256) fast spin echo images with fat suppression, and both pre- and postcontrast sagittal T1-weighted (<50/<4.5; matrix, 256 × 128; sections, 32–60) three-dimensional gradient-echo images with a 60° flip angle. Field of view was restricted to 16–18 cm over the breast depending on patient size, and sections were 3 mm thick or less. T1-weighted images were acquired prior to and immediately following bolus injection of contrast–enhanced material (0.1 mmol/kg gadolinium [0.1 mmol/kg = 0.2 mL/kg] gadolinium).

Any suspicious MR-enhanced lesions were described based on lesion shape, borders, distribution, kinetics, and internal architecture. The final MR assessment was classified on a five-point scale (1 = negative, 2 = benign, 3 = probably benign, 4 = suspicious abnormality, 5 = highly suggestive of malignancy). Examinations given an initial assessment of incomplete or 0 received a final MR assessment of 1–5 based on results of follow-up procedures. A lesion was identified as suspicious 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 one quadrant. Benign lesions were identified as having smooth or lobulated margins with internal septations, or if the mass was cystic. Reference standard information about cancer status was obtained for cases that had a positive result in one of the modalities under investigation and went on to have a biopsy performed. Because the primary outcomes of this study were cancer yield, callback and biopsy rates, and PPV of biopsies performed, the study design did not include additional follow-up (eg, 12- or 24-month follow-up) information about the patients.

**Figure 2**

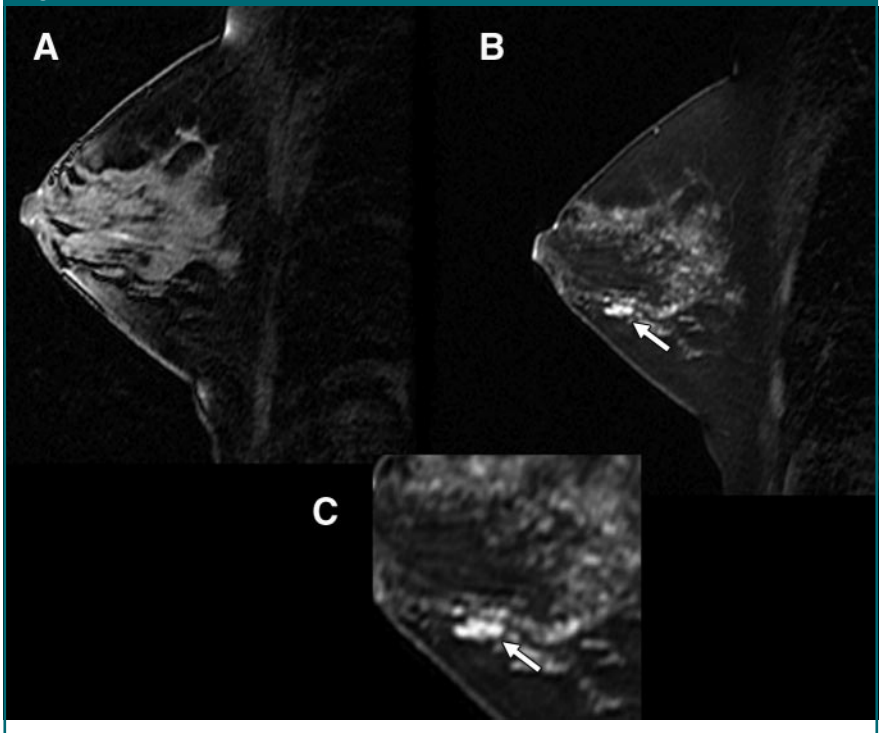


**Figure 2:** Negative screening mammogram and US of 46-year-old woman. Sagittal precontrast (*A*, T2-weighted fast spin-echo with fat suppression) and postcontrast (*B*, T1-weighted gradient-echo with fat suppression) images demonstrate 8 × 3 × 3 linear focus of enhancement in left breast *(C)* (arrow). Pathologic report proved infiltrating ductal carcinoma.

### Statistical Analysis

Data were analyzed under the direction of the Center for Statistical Sciences at Brown University, which served as the Biostatistics Center for all IBMC trials. Data were prospectively monitored in a collaborative effort with IBMC data management located at the American College of Radiology. Statistical software SAS (version 8.0; SAS, Cary, NC) and Stata (version 7.0; Stata, College Station, Tex) were used to process the data and facilitate statistical analyses.

For purposes of computing the diagnostic yield of an imaging modality, test results were dichotomized as negative (category 1 or 2) or positive (categories 3, 4, or 5). Invasive cancer and ductal carcinoma in situ were classified as malignant; all other pathologic findings were classified as not malignant. For this study, callback or positive examination rates were computed as the percentages of participants who had a test

result in category 3, 4, or 5. Biopsy rates based on a positive examination were computed as the percentages of participants who had a biopsy performed based on a positive examination. PPVs of biopsies performed were computed as the percentage of participants diagnosed with cancer after a biopsy.

Exact confidence intervals (CIs) were computed for each test performance measure. Rates were compared using the McNemar test to account for the paired nature of the design. CIs for rate differences were obtained by inverting the McNemar test results. A *P* value of .05 was utilized to define statistical significance. Computations were performed using SAS and Stata subroutines.

## Results

### Participants

One hundred ninety-five women were enrolled in this study during a 6-month period from November 2002 to April 2003. Two women were later found to not meet eligibility criteria, one underwent screening US after MR, and two were found ineligible because the length of time between study procedures was greater than 90 days. Of the remaining 190 women, seven did not undergo mammography, 11 did not undergo MR, and one withdrew her consent. The remaining 171 had evaluable assessments for all examinations and comprised the analysis group for this study (Fig 1). Patient characteristics of the 190 eligible women and the 171 women included in analysis showed no substantial differences between the two groups (Table 1).

**Table 1**

**Patient Characteristics**

| Characteristic | All Eligible Women ($n = 190$) | Women Included in Analysis Set ($n = 171$) |
|---|---|---|
| Age (mean ± SD) | 45.4 ± 10.3 | 45.6 ± 10.2 |
| Genetic risk | | |
| Family member *BRCA1/BRCA2*-positive | 51 (26.8) | 49 (28.7) |
| Participant had genetic testing | 99 (52.1) | 91 (53.2) |
| Confirmed *BRCA1*-positive | 41 (21.6) | 37 (21.6) |
| Confirmed *BRCA2*-positive | 39 (20.5) | 36 (21.1) |
| Menopause status | | |
| Premenopausal | 88 (46.3) | 78 (45.6) |
| Surgically induced menopause | 56 (29.5) | 52 (30.4) |
| Postmenopausal | 40 (21.1) | 36 (21.1) |
| Perimenopausal | 5 (2.6) | 5 (2.9) |
| History of hormone use | 160 (84.2) | 145 (84.8) |
| Breast density | | |
| Mostly fat: <10% | 16 (8.4) | 14 (8.2) |
| Scattered fibroglandular tissue: 11–50% | 45 (23.7) | 43 (25.2) |
| Heterogeneously dense: 51–90% | 88 (46.3) | 83 (48.5) |
| Extremely dense: >90% | 32 (16.8) | 31 (18.1) |
| Prior benign biopsy | 72 (37.9) | 64 (37.4) |
| Prior diagnosis of breast cancer | 47 (24.7) | 44 (25.7) |

Note.—Numbers in parentheses are percentages.

### Genetic Testing, Cancers

Ninety-one of 171 women included in the analysis group had genetic testing for possible familial cancer risk. Thirty-seven women were found to be positive for a *BRCA1* mutation and 36 were positive for a *BRCA2* mutation. The mean age of the patients was 46 years; nearly one-half (45.6%) were premenopausal while another 52 (30.4%) entered into menopause due to surgery. The majority (84.8%) of the participants reported some history of hormone use. Over 65% of the women had heterogeneously or extremely dense breasts. More than one-third of the study participants had prior benign biopsy and one-fourth had a prior diagnosis of breast cancer.

Six cancers were detected among the 171 study participants. Of these, mammography enabled detection of two (33%) cancers; US, one (17%); and MR, six (100%). All six cancers were infiltrating ductal carcinomas (Table 2). One-half of the participants with a detected cancer were positive for *BRCA1/BRCA2*. Two of six (33%) participants diagnosed with cancer had scattered fibroglandular breast density, three (50%) had heterogeneously dense breast tissue, and one (17%) had extremely dense breast tissue. The four cancers in women with heterogeneously dense and extremely dense breast tissue were only detected at MR (Table 2, Fig 2).

### MR, US, and Mammography

MR resulted in more patients being recalled for additional imaging or biopsy (24%) compared with mammography (10%) or US (9%) alone (Table 3). MR resulted in 8.2% of women undergoing biopsy compared with 2.3% for mammography and 2.3% for US. The PPVs of biopsies obtained by using MR (43%) and mammography (50%) were higher than those of US (25%). Of the four cancers identified by MR alone, one was removed for biopsy under MR guidance and three under targeted US guidance. The three lesions identified only at MR were removed for biopsy under US guidance. These lesions were not seen prospectively at screening US. Overall, 16 biopsies were performed as the result of a positive examination and produced a cancer yield of 3.5%. Although the estimated yield of MR was higher than the other two modalities (the estimated yield of MR was almost three times that of mammography and five times that of US), none of the pairwise comparisons was statistically significant (95% CIs were MR-US, −0.002%, 0.06%; MR-mammography, −0.005%, 0.052%; and US-mammography, −0.011%, 0.023%).

## Discussion

Our prospective study of 171 women screened with mammographic, US, and

MR imaging led to the detection of six cancers. All cancers were detected with MR, 33% with mammographic, and 17% with US imaging. The added cancer yield was associated with a higher biopsy rate with MR (8.2%) compared with mammographic (2.3%), and US (2.3%) imaging.

Our findings are similar to those reported by Kriege et al (20), and by other prior screening studies comparing MR with mammography in a high-risk population (Table 4) (20–27). Overall, all studies demonstrate that MR has higher sensitivity in cancer detection at the cost of a higher biopsy rate. The recent reports from the Netherlands (20) and the United Kingdom (21) lend further support to MR as an effective screening tool in this patient population. In the Netherlands study, 45 cancers were diagnosed in 1909 (2.4%) women at high risk. The respective sensitivities of clinical breast examination, mammography, and MR were 17.9%, 33.3%, and 79.5%. One-half of the cancers were identified by using MR alone. Although the specificity of MR was lower than that of mammography or clinical breast examination (89.8%, 95.0%, and 98.1%, respectively), the overall accuracy of MR was significantly higher ($P < .05$). The two control groups of women at high risk that did not undergo any form of screening had more than double the incidence of positive nodes and micrometastases ($P < .001$). Similarly, in the UK study, MR resulted in an additional cancer yield of 2.9% and found the sensitivity of MR to be significantly higher (77%) when compared with mammography (40%) in high-risk women (21). The highest sensitivity (94%) was accomplished with a combination of MR and mammography, although this came at the cost of lower specificity (77%). Neither the Netherlands nor the UK study included US to screen the women enrolled.

In our study, US did not identify cancers missed at mammography. The one cancer that was prospectively identified by using US was also detected at mammography and MR. The lower yield of US compared with MR is consistent with prior studies that have evaluated both MR and US in a single-patient cohort (22–24). However, other studies have reported increased cancer yield by using US compared with mammography alone in women with dense breast tissue (28,29).

Prior studies aimed at screening women with dense breast tissue by using US have not included MR. In a recent study of over 6000 asymptomatic women with dense breasts and normal mammograms, 23 (cancer yield of 0.3%) malignancies were detected in 21 patients by using US (30). In that study, the sensitivity of US for the detection of malignancy was 100% but the specificity was low at 35%. A more recent study of 1517 women with dense breast tissue

**Table 2**

**Characteristics of Cancers Detected**

| | Patient Characteristics | | | | Examination Results | | | Pathologic Results | |
|---|---|---|---|---|---|---|---|---|---|
| Patient No. | Age | *BRCA* Status | Menopause Status | Breast Density | Mammography | US | MR | Histology | TNM Stage |
| 1 | 52 | *BRCA1* | Surgical | Heterogeneously | − | − | + | IDC | T1 N0 M0 |
| 2 | 46 | *BRCA2* | Surgical | Heterogeneously | − | − | + | IDC | NA |
| 3 | 46 | Unknown | Premenopausal | Extremely | − | − | + | IDC | T0 N0 M0 |
| 4 | 55 | *BRCA1* | Postmenopausal | Heterogeneously | − | − | + | IDC | T1 N0 M0 |
| 5 | 40 | Unknown | Surgical | Scattered fibroglandular | + | − | + | IDC | T1 N0 M0 |
| 6 | 50 | Unknown | Surgical | Scattered fibroglandular | + | + | + | IDC | T2 N1 M0 |

Note.—IDC = infiltrating ductal carcinoma, NA = not available, TNM = tumor-node-metastasis, + = positive, − = negative.

**Table 3**

**Performance Rates of Mammography, US, and MR**

| Examination | Positive Exam Rates* | Biopsies Performed Based on Positive Examination† | PPV of Biopsies Performed | Diagnostic Yield (%) | Additional Cancer Yield‡ |
|---|---|---|---|---|---|
| Mammography | 17/171 (10) [6%, 15%] | 4/171 (2.3) | 2/4 (50) | 2/171 (1.2) [0, 4] | 0/171 (0) |
| US | 15/171 (9) [5%, 14%] | 4/171 (2.3) | 1/4 (25) | 1/171 (0.6) [0, 3] | 0/171 (0) |
| MR | 41/171 (24) [18%, 31%] | 14/171 (8.2) | 6/14 (43) | 6/171 (3.5) [1, 7] | 4/171 (2.3) |

Note.—Numbers in parentheses are percentages, numbers in square brackets are confidence intervals.

* As classified by using BI-RADS 3, 4, or 5.

† Not mutually exclusive. Total biopsies performed as the result of at least one positive exam is 16.

‡ Additional yield is defined as all cancers detected by this examination that were not detected by any other examination.

and normal mammograms reported an additional seven (cancer yield of 0.46%) cancers diagnosed by using US (31).

Four cancers were detected in high-risk women and three in women with average risk. Thus, the added cancer yield of US in the high-risk group was 1.3%. This study did not include MR. A large-scale study is currently being conducted through the American College of Radiology Imaging Network (ACRIN study 6666, *http://www.acrin.org*) to assess the performance of screening US in women at high risk with dense breast tissue. That study should provide more definitive information on the cancer yield by using US alone in this subgroup (those with dense breast tissue) of women at high risk for breast cancer.

There are a few possible explanations for our failure to identify cancers at US that were occult at mammography. First, since MR was not included in the listed US trials, the sensitivity of US had no reference standard for comparison, in essence acting as its own reference standard. Likewise, in our study, MR had the highest sensitivity (100%) because no independent reference standard is possible in these trial designs. Breast density has little effect on MR sensitivity, and may have performed better than US in this regard, as US is challenged in women with fatty breast tissue (32). In addition, the numbers in all prior studies are small and the CIs are wide. Our study included women with fatty breast tissue and scattered fibroglandular breast density. Most prior US screening studies excluded these women as it is unlikely US will help confirm occult cancers in women with fatty breast tissue. It is unlikely that the quality of equipment was lower in our study, as the requirements are in keeping with prior studies. It is extremely unlikely that the performance of the US examinations or interpretive skills of the participating radiologists were lower in our study compared with prior studies as all sites are high-volume breast imaging centers with many years of experience in high-quality breast US.

This study had limitations. Although the study clearly demonstrates the feasibility of a multisite screening study in-

**Table 4**

**Comparative Sensitivity of Screening Mammography, US, and MR in Women at Increased Risk for Breast Cancer**

| Author, Location | Study Design* | Follow-up (in Months) | Mean Age in Years (Range) | Cancer (%) | Sensitivity (%) | | | Cancer Yield from MR Alone† | Biopsies Recommended as a Result of MR | PPV of Biopsies Performed Based on MR (%) |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Mammography | MR | US | | | |
| Kuhl, Germany (24) | P | 12 | 39 (18–65) | 4.7 (9/192) | 33 (3/9) | 100 (9/9) | 33 (3/9) | 6/192 (3.1) [0.9, 6.0] | 14/192 (7.3%) | 64 |
| Warner, Canada (25) | P | 36 | 47 (26–65) | 9.3 (22/236) | 36 (8/22) | 77 (17/22) | 33 (7/21) | 7/236 (3.0)‡ [1.7, 7.1] | 37/236 (15.7%) | 46 |
| Italian Multi-Center Project (26) | P | 24 | 46 (25–77) | 7.6 (8/105) | 13 (1/8) | 100 (8/8) | 13 (1/8) | 7/105 (6.7) [2.7, 13.3] | 9/105 (8.6%) | 89 |
| Tilanus-Linthorst, Netherlands (27) | P | 12 | 42 (22–68) | 2.8 (3/109) | 0 | 100 (3/3) | — | 3/109 (2.8) [0.6, 7.8] | 5/109 (4.6%) | 60 |
| Morris, USA (28) | R | None | 50§ (23–82) | 3.8 (14/367) | NA | NA | NA | 14/367 (3.8) [2.1, 6.3] | 59/367 (15.8%) | 24 |
| MRI Screening Study Group, Netherlands (22) | P | 33 | 40 (19–72) | 2.4 (45/1909) | 40 (18/45) | 71 (32/45) | — | 22/1909 (1.2) [1.1, 2.4] | 56/1909 (2.9%) | 57 |
| IBMC, International (29) | P | None | 45 (26–86) | 1.1 (4/367) | NA | NA | NA | 3/367 (0.8) [0.2, 2.4] | 23/367 (6.3%) | 17 |
| MARIBS, UK (33) | P | Varied 0–72 | 40 (31–55) | 5.1 (33/649) | 40 (14/35)‖ | 77 (27/35) | — | 19/649 (2.9) [1.7, 4.5] | — | 25 |
| This Study, USA | P | None | 46 (25–72) | 3.5 (6/171) | NA | NA | NA | 4/171 (2.3) [0.6, 6] | 14/171 (8.2%) | 42 |

* P = prospective, R = retrospective, NA = sensitivity and specificity not performed as one-year follow-up was not performed.

† Numbers in parentheses are percentages, numbers in square brackets are confidence intervals.

‡ One patient in this study did not undergo US.

§ Reported median.

‖ Two cancers in this study were identified as "interval" and not detected by either screening examination.

corporating MR, US, and mammographic imaging in a one-patient cohort, the population is small for a screening study. The small participant number may also explain why there were no cases of dual carcinoma in situ detected during the study. The study did not include long-term follow-up, and consequently did not provide reference standard information on participants with negative MR results. Thus, the variables of callback and biopsy rates, biopsy PPVs, and cancer yields are emphasized rather than sensitivity and specificity measures, which would be subject to verification bias in this study setting. Our study performed a single round of screening. This can bias our results by reporting prevalent malignancies for an examination that has been previously used by participants (mammography) and comparing them with incident malignancies found during an examination that is new to participants (US and MR).

In conclusion, our multi-institutional study further supports MR as an important complement to mammography in screening women at high risk for breast cancer. At this time, further studies are needed to more clearly address the potential role of US in this patient population before it can be promoted as a reasonable alternative to MR for screening women at high risk.

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