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Screening MRI in Women With a Personal History of Breast Cancer

Constance D. Lehman, Janie M. Lee, Wendy B. DeMartini, Daniel S. Hippe, Mara H. Rendi, Grace Kalish, Peggy Porter, Julie Gralow, Savannah C. Partridge

Affiliations of authors: Department of Radiology, Massachusetts General Hospital, Boston, MA (CDL); Department of Radiology, University of Washington Medical Center, Seattle, WA (JML, DSH, GK, SCP); Seattle Cancer Care Alliance, Seattle, WA (JML, SCP); Department of Radiology, University of Wisconsin-Madison, Madison, WI (WBD); Department of Pathology, University of Washington Medical Center, Seattle, WA (MHR); Fred Hutchinson Cancer Research Center, Seattle, WA, (PP, JG); Department of Medical Oncology, University of Washington Medical Center, Seattle, WA (JG).

Correspondence to: Constance D. Lehman, MD, PhD, Director of Breast Imaging, Department of Radiology, Massachusetts General Hospital, Avon Comprehensive Breast Evaluation Center, Suite 240, 55 Fruit Street, Boston, MA 02114 (e-mail: clehman@mgh.harvard.edu).

Abstract

Background: Screening MRI is recommended for individuals at high risk for breast cancer, based on genetic risk or family history (GFH); however, there is insufficient evidence to support screening MRI for women with a personal history (PH) of breast cancer. We compared screening MRI performance in women with PH vs GFH of breast cancer.

Methods: We analyzed case-series registry data, collected at time of MRI and at 12-month follow-up, from our regional Clinical Oncology Data Integration project. MRI performance was compared in women with PH with those with GFH. Chi-square testing was used to identify associations between age, prior history of MRI, and clinical indication with MRI performance; logistic regression was used to determine the combined contribution of these variables in predicting risk of a false-positive exam. All statistical tests were two-sided.

Results: Of 1521 women who underwent screening MRI from July 2004 to November 2011, 915 had PH and 606 had GFH of breast cancer. Overall, MRI sensitivity was 79.4% for all cancers and 88.5% for invasive cancers. False-positive exams were lower in the PH vs GFH groups (12.3% vs 21.6%, $P < .001$), specificity was higher (94.0% vs 86.0%, $P < .001$), and sensitivity and cancer detection rate were not statistically different ($P > .99$). Age ($P < .001$), prior MRI ($P < .001$), and clinical indication ($P < .001$) were individually associated with initial false-positive rate; age and prior MRI remained statistically significant in multivariable modeling ($P = .001$ and $P < .001$, respectively).

Conclusion: MRI performance is superior in women with PH compared with women with GFH. Screening MRI warrants consideration as an adjunct to mammography in women with a PH of breast cancer.

Guidelines for mammographic screening have been established and, when followed, have proven to result in earlier detection of breast cancer and mortality reduction (1). Women with increased risk of breast cancer may benefit from additional screening by magnetic resonance imaging (MRI). Current American Cancer Society (ACS) and National Comprehensive Cancer Network (NCCN) guidelines recommend annual breast MRI screening for women who themselves are carriers or have first-degree relatives with BRCA or other cancer susceptibility mutations, who have a greater than 20% to 25% lifetime risk of developing breast cancer based on family history, or who have had radiation to the chest (2,3). These recommendations are based on studies in which MRI, added to screening mammography, resulted in increased invasive breast cancer yield at acceptable recall and biopsy rates (4–14). Although women with a personal history of cancer have statistically significant elevated

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risk of future breast cancer events (15–18), current guidelines of the American Society of Clinical Oncology (ASCO) recommend against, and those of the ACS and NCNN recommend neither for or against, screening MRI because of insufficient performance data validating its use in this specific patient population and concerns of morbidity and costs associated with additional imaging or biopsy of benign lesions identified as suspicious for malignancy on MRI (2,3,19).

A meta-analysis of 17 randomized trials of a total 10 801 women with a personal history of breast cancer treated with breast-conserving surgery and radiation therapy reported 10-year breast cancer recurrence rates of 19.3% and 15-year breast cancer death rates of 21.4% (16). Although advances in locoregional and systemic therapy have improved, even women diagnosed with early, hormone receptor–positive breast cancer remain at statistically significant increased risk of future breast cancer events (approximately 10% and 20%, respectively, at five- and 10-year follow up) (20–24).

Despite these risks, clinical studies of breast MRI screening to date have focused on women at risk because of genetic or family history rather than personal history alone. Our study was designed to assess the diagnostic performance of MRI screening of women with a personal history of treated breast cancer compared with those with a genetic or family history of breast cancer and to inform patient and clinician decision-making regarding best methods of surveillance after successful breast cancer treatment.

Methods

Data Collection

Institutional review was performed in compliance with the Health Insurance Portability and Accountability Act (HIPAA) prior to data analysis. Data were obtained from the Consortium Oncology Data Integration (CODI) project, which is an institutional review board–approved solid tumor clinical database developed and maintained by the Fred Hutchinson Cancer Research Center in collaboration with the University of Washington. Data in CODI have been obtained in accordance with all applicable human subject laws and regulations, including any requiring informed consent. There are many sources of data for CODI, including the regional Cancer Surveillance System (CSS) tumor registry. CSS is a part of the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program and collects population-based data on the incidence, treatment, and follow-up on all newly diagnosed cancers (except nonmelanoma skin cancers) occurring in residents of the 13 counties in the western region of Washington state.

To identify women for inclusion in our study, we identified all breast MRIs conducted at our institution between July 2004 and November 2011 in women age 18 years and older who underwent screening MRI for either genetic/family history (GFH) or personal history of treated breast cancer (PH). Details of patient selection are provided in Figure 1. Exams were excluded from the study if either a metastatic diagnosis or diagnosis of a non–breast cancer malignant histology within the breast region (ie, malignant lymph node, angiosarcoma) occurred within a year of the MRI. Exams with known data errors or missing data for any key data items were also excluded. Excluded exams accounted for less than 2% (61/3019) of consecutive MRI exams performed for clinical indication of screening MRI for GFH or PH. For each woman, we selected the first eligible exam occurring during the study period as the representative examination. For each patient, cancer outcome was determined within a 12-month follow-up period using CSS and institutional pathology data in the CODI database.

MRI acquisition protocols varied during the study period, all in keeping with guidelines established by the International Breast MRI Consortium (IBMC), the American College of Radiology Imaging Network (ACRIN) MRI trials, and the American College of Radiology (ACR) Breast MRI Accreditation Program (8,25,26). MR imaging was performed on a GE LX 1.5T scanner (GE Healthcare, Waukesha, WI) from 2004 to 2009 or on a Philips Achieva 3T scanner (Philips Healthcare, Best, the Netherlands) after January 2010 using a dedicated bilateral breast coil. Our breast MRI protocols have been described in detail previously (27–29). Each protocol included a precontrast fat suppressed T2-weighted fast spin echo sequence followed by a T1-weighted dynamic contrast-enhanced (DCE) sequence with one precontrast and at least three postcontrast fat-suppressed 3D fast gradient echo acquisitions. Prior to October 2005, DCE scans were performed in the sagittal plane with a field of view (FOV) of 18 to 22 cm, depending on patient size, a slice thickness of 3 mm, and a matrix of 256 x 192. From October 2005 through June 2006, scans were performed in the axial plane with a FOV of 32 to 38 cm, slice thickness of 2.2 mm, and matrix size of 350 x 350. From June 2006 through January 2010, scans were performed in the axial plane with a FOV of 32 to 38 cm, slice thickness of 1.6 mm, and matrix size of 420 x 420. After January 2010, scans were performed in the axial plane with a FOV of 22 x 33 cm, slice thickness of 1.3 mm, and matrix size of 440 x 660.

For all protocols, initial postcontrast acquisitions were centered between 90 and 120 seconds after contrast administration, and delayed acquisitions were centered between 4.5 and 7.5 minutes after contrast administration, depending upon protocol. For all examinations, gadolinium contrast material (before November 2010: Omniscan, GE Healthcare; starting November 2010: ProHance, Bracco Diagnostics, Princeton, NJ) was power injected (0.1 mmol/kg at 2 mL/s) followed by a 20 mL saline flush.

MRI interpretations were performed by one of nine fellowship-trained breast imaging radiologists using the ACR Breast Imaging Reporting and Data System (BI-RADS) MRI lexicon (30,31). Each MRI was given a BI-RADS assessment based on lesion morphology and kinetics. Final positive MRIs were those given BI-RADS 4 or 5 assessments. Negative final MRIs were those assessed as BI-RADS 1, 2, or 3. MRIs with an initial BI-RADS 0 assessment were reclassified according to the final assessment made on the recommended follow-up study. Biopsy was performed with sonographic guidance if a sonographic correlate was present. In all other women for whom targeted ultrasound was not recommended or targeted ultrasound did not reveal a sonographic correlate to the suspicious MRI-detected lesion, MRI-guided, vacuum-assisted breast biopsy was performed.

High-risk lesions included atypical ductal hyperplasia, atypical lobular hyperplasia, lobular carcinoma in situ, and any other lesions with atypia. Final histology from lesions that were initially classified as high risk on needle biopsy was determined from histology at surgical excision. Malignant histology included ductal carcinoma in situ and/or any invasive breast carcinoma. Carcinomas in all women were reviewed by a pathologist to confirm histology, size, and staging. Available information for prior cancers in the PH group was recorded.

Statistical Analysis

To determine screening MRI performance, we followed the guidelines of the American College of Radiology Breast Imaging and Reporting Data System (ACR BI-RADS) and those of the

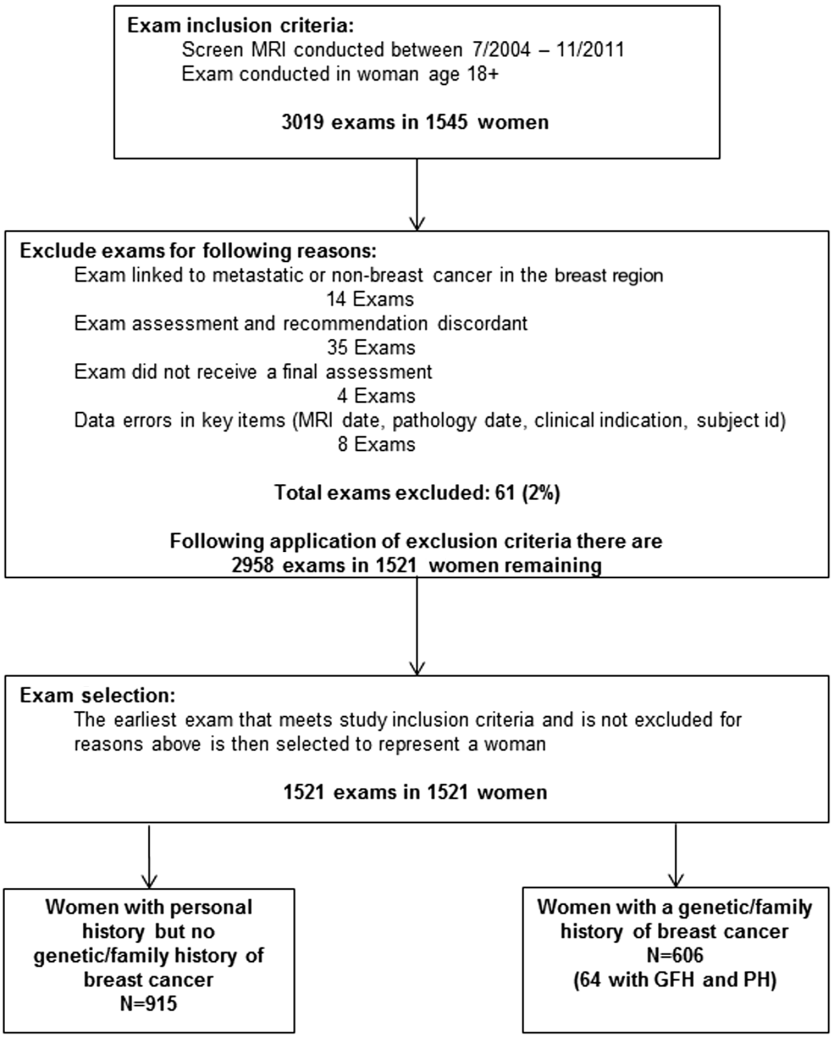

Figure 1. Study exam selection.

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Breast Cancer Surveillance Consortium (30–33). Examinations associated with a cancer were defined as those with a tissue diagnosis of ductal carcinoma in situ or invasive breast cancer within one year and before the next screening MR examination. Examinations not associated with a cancer were those without a tissue diagnosis of ductal carcinoma in situ or invasive breast cancer within one year or before the next MR screening examination, whichever occurred first. We computed initial recall percent, initial false-positive rate, cancer detection rate, positive predictive value, sensitivity, and specificity. Examinations with an initial BI-RADS assessment of 0, 3, 4, or 5 were positive for initial recall. Initial false-positive rate was computed by identifying examinations positive on initial recall (for either additional imaging or biopsy) but with no cancer. Cancer detection rate was calculated as a cancer diagnosed after an initial positive MRI and confirmed by pathology. True negatives (TN) were defined as women with a final negative MRI with verified absence of breast cancer within 12-month follow-up using CSS and institutional pathology data in the CODI database. False negatives (FN) were defined as those women with a final negative MRI and a tissue diagnosis of cancer. True positives (TP) were defined as women assessed with a final positive MRI with diagnosis of breast cancer. False positives (FP) were examinations in women with a final positive MRI with no breast cancer diagnosis. Sensitivity was defined as TP/(TP + FN), and specificity was defined as TN/(TN + FP), as per ACR BI-RADS and BCSC guidelines (30–33).

Diagnostic performance metrics were compared between the PH and GFH groups and between groups with and without prior MRI using the two-sided Chi-squared test with continuity correction. Age was compared between PH and GFH groups using the independent samples *t* test. Logistic regression was used to determine the impact of age, clinical indication of PH vs GFH, and prior history of breast MRI on the initial false-positive rate. All computations were done using SAS statistical software version 9.3 (SAS Institute, Cary, NC) and R version 3.1.1 (Vienna, Austria). A two-sided *P* value of less than .05 was considered statistically significant.

Results

A total of 1521 women age 18 years and older underwent MRI for the sole clinical indication of screening, based on either genetic family history and/or personal history during the study interval and met all study eligibility criteria. Of these, 915 women had elevated risk based on PH of breast cancer and 606 had elevated risk because of GFH of breast cancer (64 women with PH and GFH were included in the GFH group) (Figure 1).

The majority of women in both the PH and GFH groups were between age 40 and 60 years at the time of MRI although women in the PH group were older on average ($P < .001$). The distribution of mammographic density was similar across the two groups, with the majority of women having heterogeneously or extremely dense breast tissue. Of interest, a minority of women in both groups had moderate or marked MRI breast parenchymal enhancement. Women in the PH group were statistically significantly more likely to have had a prior breast MRI (54.2% vs 20.5%, $P < .001$) (Table 1).

Overall, 274 (18.0%) were recalled and 164 (10.8%) recommended for biopsy, with women in the PH group having statistically significant lower recall rates and biopsy recommendations than women in the GFH group (14.3% vs 23.6%, $P < .001$ and 7.7% vs 15.5%, $P < .001$) (Table 2). There were no statistically significant differences across the groups in cancer detection rate ($P > .99$), positive predictive value ($P = .19$), or sensitivity ($P > .99$). The PH group had a measurably higher specificity of 94.0% compared with the GFH group at 86.0% ($P < .001$). Among women screened for PH, cancer was found in 16 of 64 women who underwent biopsy (PPV = 25.0%), vs 11 cancers in 75 GFH women who underwent biopsy (PPV = 14.7%). Cancer detection rate by screening MRI was 1.7% and 1.8% in the PH and GFH groups, respectively (Table 2). All statistical conclusions reported in Table 2 were unaffected by exclusion of patients with a prior MRI (data not shown).

Multivariable analysis was conducted to further explore why the initial false-positive rate was lower in the PH group than in the GFH group (12.3 vs 21.6%, $P < .001$) (Table 2). Older age, history of prior (comparison) breast MRI, and clinical indication of PH (vs GFH) were all found to be individually associated with a woman's decreased risk of a false-positive interpretation on screening MRI (data not shown). When combined in a multiple logistic regression, both age and prior MRI history remained statistically significant predictors ($P = .001$ and $P < .001$, respectively), while clinical indication did not. A test for interaction between age and prior history was not statistically significant (data not shown).

Overall, 620 (40.8%) women had undergone prior MRI for either screening (prior to study period) or reasons other than screening, such as to evaluate extent of disease prior to surgery or to evaluate response to neoadjuvant chemotherapy. Women with a prior comparison MRI were less likely to undergo benign breast biopsy (67/620, 10.8%) compared with women without a prior MRI (185/901, 20.5%, $P < .001$). In women without a prior MRI, more cancers were diagnosed and a greater percentage of biopsies were positive compared with women with a prior MRI, though these differences did not reach statistical significance (data not shown).

Within the PH group, the influence of a prior MRI on performance of screening MRI was demonstrated by reduced false positives and higher specificity. Twenty percent of women in the PH group with no prior MRI received an initial recall, while 9.5% in PH women with prior MRIs were recalled ($P < .001$) (Table 3). Cancer detection rate, positive predictive value, and sensitivity did not vary statistically significantly across the prior/no prior groups within the PH women, although specificity was found to

Table 1. Characteristics of study population by clinical indication for screening MRI*

Characteristic	Personal history (n = 915) No. (%)	Genetic/ family history (n = 606) No. (%)
Age, y		
<40	104 (11.4)	170 (28.1)
40–49	278 (30.4)	207 (34.2)
50–59	317 (34.6)	148 (24.4)
60–69	178 (19.5)	72 (11.9)
70+	38 (4.2)	9 (1.5)
Mammographic breast density		
Fatty/scattered	162 (17.7)	89 (14.7)
Heterogeneous/ extremely dense	395 (43.2)	290 (47.9)
Missing data	358 (39.1)	227 (37.5)
Breast parenchymal enhancement		
None/minimal	334 (36.5)	165 (27.2)
Mild	180 (19.7)	174 (28.7)
Moderate	59 (6.4)	85 (14.0)
Marked	18 (2.0)	63 (10.4)
Missing data	324 (35.4)	119 (19.6)
Prior breast MRI		
No	419 (45.8)	482 (79.5)
Yes	496 (54.2)	124 (20.5)

* MRI = magnetic resonance imaging.

Table 2. Performance of screening breast MRI

Performance statistic	Total (n = 1521) No. (%)	Personal history (n = 915) No. (%)	Genetic/family history (n = 606) No. (%)	Difference (95% CI), %	P*
Initial recall (assessment 0, 3, 4, or 5)	274/1521 (18.0)	131/915 (14.3)	143/606 (23.6)	-9.3 (-13 to 5)	<.001
Final positive (assessment 4 or 5)	164/1521 (10.8)	70/915 (7.7)	94/606 (15.5)	-7.9 (-11 to 4)	<.001
Initial false-positive rate	244/1521 (16.0)	113/915 (12.3)	131/606 (21.6)	-9.3 (-13 to 5)	<.001
Cancer detection rate†	30/1521 (1.8)	18/915 (1.7)	12/606 (1.8)	-0.1 (-1 to 1)	>.99
Positive predictive value‡	27/139 (19.4)	16/64 (25.0)	11/75 (14.7)	10.3 (-4 to 25)	.19
Sensitivity§	27/34 (79.4)	16/20 (80.0)	11/14 (78.6)	1.4 (-28 to 31)	>.99
Specificity§	1350/1487 (90.8)	841/895 (94.0)	509/592 (86.0)	8.0 (5 to 11)	<.001

* Based on two-sided Chi-square test with continuity correction. CI = confidence interval; MRI = magnetic resonance imaging.
† Based on initial positive assessment of 0, 3, 4, 5.
‡ Positive predictive value for biopsies recommended and performed (Breast Imaging Reporting and Data System positive predictive value$_3$).
§ Sensitivity and specificity computed using final assessment.

Table 3. MRI performance in women with a personal history of breast cancer: impact of prior MRI

Performance statistic	Prior MRI: No (n = 419) No. (%)	Prior MRI: Yes (n = 496) No. (%)	Difference (95% CI), %	P*
Initial recall (assessment = 0, 3, 4, or 5)	84/419 (20.0)	47/496 (9.5)	10.6 (6 to 15)	<.001
Final positive (assessment = 4 or 5)	41/419 (9.8)	29/496 (5.8)	3.9 (0 to 8)	.04
Initial false-positive rate	75/419 (17.9)	38/496 (7.7)	10.2 (6 to 15)	<.001
Cancer detection rate†	9/419 (1.9)	9/496 (1.6)	0.3 (-2 to 2)	.93
Positive predictive value‡	8/38 (21.1)	8/26 (30.8)	-9.7 (-35 to 15)	.56
Sensitivity§	8/9 (88.9)	8/11 (72.7)	16.2 (-27 to 60)	.74
Specificity§	377/410 (92.0)	464/485 (95.7)	-3.7 (-7 to -0)	.03

* Based on two-sided Chi-square test with continuity correction. CI = confidence interval; MRI = magnetic resonance imaging.
† Based on initial positive assessment of 0, 3, 4, 5.
‡ Positive predictive value for biopsies recommended and performed (Breast Imaging Reporting and Data System positive predictive value).
§ Sensitivity and specificity computed using final assessment.

be statistically significantly higher in women with a prior MRI experience (95.7% vs 92.0%, P = .03) (Table 3).

Thirty-four of the 1521 women in our study were diagnosed with breast cancer, 27 after a positive MRI and seven after a negative MRI (overall sensitivity of 79.4%) (Table 2). Histologic findings of the 27 women diagnosed with cancer by MRI screening included ductal carcinoma in situ (DCIS) as the most severe histology in four women and invasive disease in the remaining 23 (sensitivity for invasive cancers was 88.5%). Four of seven FN exams were cases of DCIS, which presented as calcifications on mammography within one year of a negative MRI (three of these were mammograms performed on the same day as the MRI, and one was a mammogram performed four months following the negative MRI). The remaining three FN cases were assessed on MRI as BI-RADS 3, with invasive cancer diagnosed within one year (Tables 4 and 5).

For women in the PH group in whom a new cancer was detected, average age at the time of the prior, original cancer diagnosis was 48 years (range = 33–65). The following information was obtained regarding the original tumor: mean tumor size was 16 mm (range = 2–30 mm), and 36.0% were node negative. Of the 14 prior cancers with detailed receptor status available, 57.0% were estrogen receptor (ER)/progesterone receptor (PR) positive and HER2 negative, 7.0% were ER/HER2 positive and PR negative, 7.0% were HER2 positive (ER/PR negative), and 29.0% were triple negative (ER/PR/HER2 negative) (Table 4). Breast conservation surgery with radiation was performed to treat the prior breast cancer in 91.0% of women, and mastectomy was performed in 9.0%.

Average age at time of secondary breast cancer diagnosis was 53 years (range = 36–69). The second breast cancer event was observed within two years in 14.0% of women; in 57.0% of women, more than five years had elapsed since their original cancer diagnosis. Of the women treated with breast conservation who had a second breast cancer event, six were diagnosed with cancer in the ipsilateral breast on screening MRI (60.0%), and four were diagnosed with cancer in the contralateral breast (40.0%). Of the invasive cancers diagnosed by MRI in the PH group, the average tumor size was 9 mm (range = 1–18 mm), and all were node negative (Table 4). Of the 16 PH women diagnosed with cancer by screening MRI, 13 had a recent mammogram at our institution, all of which were negative.

Discussion

The current recommendations by ASCO, the ACS, and the NCCN for women with a PH of breast cancer are mammographic and clinical surveillance after treatment (2,3,19). Although the use of MRI is supported by the ACS and NCCN to screen women with greater than 20% risk of breast cancer based on familial and genetic models, their current guidelines recommend neither for nor against MRI surveillance in women with a PH of breast cancer based on lack of published scientific evidence, and those of ASCO recommend against MRI surveillance (2,3,19). Our study comprises the largest cohort published to date of screening MRI in women with a personal but no known genetic or family history of breast cancer. We found significantly lower rates of biopsy recommendations in our patients with a personal history of breast cancer and equally high cancer detection rates compared with patients with a genetic or family history of breast cancer.

There are several possible explanations for the lower false-positive rate of MRI in patients with a PH compared with GFH of breast cancer. While a prior MRI reduced false positives in both groups and patients with a personal history of MRI are more likely to have a comparison MRI if obtained during the pre-operative staging period, the statistically significantly lower false-positive rates in the PH group we identified were maintained when we assessed only those patients without prior MR exams for comparison. It is also possible that the treatment (whether mastectomy, radiation, or hormonal therapy) could render the MRI in the patient with a personal history of breast cancer easier to interpret. For example, in a patient with mastectomy there might be fewer "lesions" available to raise concern. In addition, benign breast parenchymal enhancement can be challenging to distinguish from suspicious areas of enhancement, and both radiation treatment and hormonal treatment (such as tamoxifen or aromatase inhibitors) decrease breast parenchymal enhancement. Alternatively, these changes after treatment could raise more challenges for the interpreting radiologist as in the mastectomy patient the natural internal control to compare the breasts for symmetry in enhancement is gone, as is the case with unilateral radiation treatment. Finally, the impact of hormonal therapy on parenchymal enhancement is variable and can create fluctuations in enhancement patterns depending on dosing, compliance, and individual responses to the therapy.

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Table 4. Characteristics of cancers diagnosed in women with a personal history of breast cancer (n = 20)

				Subsequent breast cancer								Primary breast cancer					
Study ID	Age at MRI, y	BI-RADS assessment	Outcome	Histology	TNM	Size, mm	ER	PR	HER2	Prior cancer ipsi or contra	Time in y between prior and index cancer	Histology	TNM	Size, mm	ER	PR	HER2
1	63	5	TP	IDC; DCIS	T1cN0M0	18	neg	neg	neg	I	9.0	IDC	T1N2M0	2	neg	neg	pos
2	56	5	TP	IDC	—	—	pos	pos	neg	C	9.4	IDC	T1cN0M0	15	pos	pos	neg
3	47	5	TP	IDC	T1cN0M0	11	—	—	—	I	1.2	IDC	T2N2M0	30	neg	neg	neg
4	36	4	TP	IDC; DCIS	T1aN0M0	1	neg	—	—	I	3.0	IDC	T1cN0M0	12	pos	neg	pos
5	66	4	TP	DCIS	TisN0M0	—	—	—	—	I	16.0	IDC	—	—	—	—	—
6	63	4	TP	IDC; DCIS	T1aN0M0	2	pos	neg	neg	I	12.5	IDC	—	—	pos	pos	neg
7	50	4	TP	IDC; DCIS	T1aN0M0	2	neg	neg	neg	I	1.5	IDC	T1bN2M0	10	neg	neg	neg
8	67	4	TP	IDC	T1bN0M0	6	pos	pos	neg	I	7.1	IDC	T2N1M0	21	pos	pos	neg
9	39	4	TP	IDC	T1bN0M0	7	neg	neg	neg	C	1.0	IDC	T1cN1aM0	15	neg	neg	neg
10	43	4	TP	IDC	T1bN0M0	6	pos	pos	neg	C	10.0	IDC	T2N0M0	30	pos	pos	neg
11	59	4	TP	IDC; ILC	T1cN0M0	15	pos	pos	neg	C	3.8	IDC	T1aN0M0	2	pos	pos	neg
12	50	4	TP	DCIS	TisN0M0	5	pos	—	—	I	5.0	IDC	T1bN0M0	10	pos	pos	neg
13	47	4	TP	IDC; DCIS	T1bN0M0	10	neg	pos	neg	C	6.2	IDC	T1cN0M0	15	neg	neg	neg
14	45	4	TP	IDC	—	—	pos	pos	neg	—	—	—	—	—	—	—	—
15	37	4	TP	IDC; ILC	T1cN0M0	17	pos	neg	neg	—	—	—	—	—	—	—	—
16	63	4	TP	IDC; DCIS	T1cN0M0	18	neg	neg	neg	C	13.2	IDC	T2N0M0	30	pos	pos	neg
17	69	3	FN	Invasive, NOS	T1bN1aM0	7	pos	pos	neg	C	4.7	IDC	T1cNXM0	20	pos	pos	neg
18	55	3	FN	IDC; DCIS	T1bN0M0	9	pos	pos	neg	C	—	—	—	—	—	—	—
19	60	2*	FN	DCIS	TisN0M0	—	—	—	—	—	7.5	DCIS	TisN0M0	6	—	—	—
20	46	2*	FN	DCIS	TisN0M0	2	pos	—	—	—	—	—	—	—	—	—	—

* Ductal carcinoma in situ diagnosed by calcifications on mammography performed after benign breast magnetic resonance imaging. — = data was not available in institutional Consortium Oncology Data Integration or regional Cancer Surveillance System databases; BI-RADS = Breast Imaging Reporting and Data System; C = contralateral; DCIS = ductal carcinoma in situ; ER = estrogen receptor; FN = false negative; HER2 = human epidermal growth factor receptor 2; I = ipsilateral; IDC = invasive ductal carcinoma; ILC = invasive lobular carcinoma; MRI = magnetic resonance imaging; neg = negative; NOS = not otherwise specified; pos = positive; PR = progesterone receptor; TP = true positive.

Table 5. Characteristics of cancers diagnosed in women with a genetic/family history of breast cancer (n = 14)

Study ID	Age at MR	BI-RADS assessment	Outcome	Histology	TNM	Size, mm	ER	PR	HER2
1	66	5	TP	IDC; DCIS	T2N1aM0	29	pos	pos	neg
2	58	5	TP	IDC	T1cN0M0	11	pos	pos	neg
3	46	4	TP	IDC	T1bN0M0	7	neg	pos	neg
4	68	4	TP	IDC	T1aN0M0	3	pos	pos	—
5	54	4	TP	IDC; DCIS	T2N0M0	27	neg	neg	pos
6	60	4	TP	DCIS	TisN0M0	120	neg	—	—
7	31	4	TP	IDC	T2N0M0	25	pos	pos	neg
8	31	4	TP	DCIS	TisN0M0	7	pos	—	—
9	53	4	TP	IDC	T1aN0M0	4	pos	pos	neg
10	59	4	TP	IDC; DCIS	T1bN0M0	7	pos	neg	neg
11	44	4	TP	IDC	T1bN0M0	8	pos	pos	pos
12	49	3	FN	IDC	—	—	neg	neg	neg
13	40	2*	FN	DCIS	TisN0M0	2	pos	—	—
14	45	2*	FN	DCIS	TisN0M0	—	—	—	—

* Ductal carcinoma in situ diagnosed by calcifications on mammography performed after benign breast magnetic resonance imaging. — = data was not available in institutional Consortium Oncology Data Integration or regional Cancer Surveillance System databases; BI-RADS = Breast Imaging Reporting and Data System; DCIS = ductal carcinoma in situ; ER = estrogen receptor; FN = false negative; HER2 = human epidermal growth factor receptor 2; IDC = invasive ductal carcinoma; ILC = invasive lobular carcinoma; MRI = magnetic resonance imaging; neg = negative; NOS = not otherwise specified; pos = positive; PR = progesterone receptor; TP = true positive.

A limitation of our study is that we did not have detailed treatment history on all patients, nor sufficient numbers to compare smaller subgroups within the personal history cohort. These areas are important topics for further study.

As in our study, prior reports have found similar increased cancer detection rates with MRI in patients with a personal history of breast cancer (34–37). Gweon et al. studied 932 surveillance breast MRI examinations in 607 women in Korea after breast conservation therapy (36). Ninety-two percent of women in their study had undergone pre-operative breast MRI. The cancer detection rate for prevalence imaging was 18 per 1000 women (95% CI = 16 to 21 per 1000 women). Geiss et al evaluated 1194 MRI examinations in 691 women with a personal history of breast cancer, in which 12 second breast cancers were detected by MRI surveillance (35). The cancer detection rate for MRI was 17 per 1000 women, and the average time from primary breast cancer diagnosis to second breast cancer detection was 6.2 years (range = 1–23 years). Neither study compared performance of MRI in women with a personal history compared with women with genetic or family history.

Schacht et al. compared MRI screening in 208 patients with a personal history of breast cancer to 345 who had a family history as the sole risk factor (37). They found the relative risk of breast cancer detection by MRI given a personal history was 1.42 (95% CI = 0.48 to 4.17) compared with family history.

In their report of 144 women with prior breast cancer but no family history of breast cancer, Brennan et al. reported higher biopsy rates (31%) and higher cancer detection rates (12%) compared with our study (34). These differences may be explained by differences in study design and patient populations. For example, the Brennan study was less restrictive in identifying cancers to calculate cancer detection rate: Any cancers in the breast (eg, sarcoma) were included, as were multiple years and exams, in including cancer rates in the cohort. In our study, only breast histology cancers were included in our performance measures and only cancers identified within the year of the first MRI were included to calculate rates of detection after a single breast MR exam. In our study, patients with a known genetic mutation were excluded from the personal history cohort; this was not reported in the study by Brennan et al.

There are limitations to our study. Our results are from a single center, where breast MRI surveillance in women with a personal history of breast cancer is used based on individual discussions of patients with their care providers. At our institution, decisions regarding MR surveillance are made on a case-by-case basis and after discussion of potential benefits and harms. In general, MRI tends to be offered more to women with dense breast tissue who are young and whose primary breast cancer was mammographically occult, but the decisions vary based on provider and patient-shared decision-making. Currently, given the equivocal recommendations by organizations with guidelines for surveillance of women following treatment, there is likely variation in practice of surveillance MRI after successful breast cancer treatment both within and outside of our center. At our institution, surveillance MRI may be more common, while at other institutions MRI may be reserved for those considered at the very highest risk for recurrence (ie, patients with prior high-risk cancers or patients who did not receive radiation after breast-conserving surgery or who did not complete recommended hormonal therapy).

In the PH group, we found a wide range in the interval between the first and second diagnoses of breast cancers. However, most (57%) of the second breast cancer diagnoses occurred more than five years after initial diagnosis and 21% occurred after 10 years of initial diagnosis. This finding is in keeping with previously published studies showing that breast cancer recurrences occur well beyond the first five post-treatment years, even in women who receive adjuvant treatment (15–18).

In our study, the majority (88%) of cancers identified by screening MRI in women with a personal history of breast cancer were invasive, all were node negative, and all were less than 2 cm. It is beyond the scope of our study to measure the impact of MRI on quality-adjusted life-years in women with a personal history of breast cancer or to analyze cost-effectiveness of screening MRI in this population. Our results can help inform those modeling studies by providing test performance measures in a large cohort of women with a personal history of breast cancer. Prior studies have found MRI cost-effective in patients with BRCA mutations and other high-risk women (38–40).

In conclusion, our study shows that the diagnostic performance of screening MRI is superior for women with PH of breast cancer

compared with women with GFH. The cancers detected by MRI were predominantly invasive carcinomas, and more than half were detected more than five years after treatment. Our findings suggest that MRI can enhance surveillance in women with a personal history of breast cancer by detecting mammographically occult invasive breast cancers while they are small and node negative.

References

1. Lee CH, Dershaw DD, Kopans D, et al. Breast cancer screening with imaging: recommendations from the Society of Breast Imaging and the ACR on the use of mammography, breast MRI, breast ultrasound, and other technologies for the detection of clinically occult breast cancer. *J Am Coll Radiol*. 2010;7(1):18–27.
2. Bevers TB, Anderson BO, Bonaccio E, et al. NCNN clinical practice guidelines in oncology: breast cancer screening and diagnosis. *J Natl Compr Canc Netw*. 2009;7(10):1060–1096.
3. Saslow D, Boetes C, Burke W, et al. American Cancer Society guidelines for breast screening with MRI as an adjunct to mammography. *CA CancerJ Clin*. 2007;57(2):75–89.
4. Kriege M, Brekelmans CT, Boetes C, et al. Efficacy of MRI and mammography for breast-cancer screening in women with a familial or genetic predisposition. *New Engl J Med*. 2004;351(5):427–437.
5. Kuhl C, Weigel S, Schrading S, et al. Prospective multicenter cohort study to refine management recommendations for women at elevated familial risk of breast cancer: the EVA trial. *J Clin Oncol*. 2010;28(9):1450–1457.
6. Kuhl CK, Schrading S, Leutner CC, et al. Mammography, breast ultrasound, and magnetic resonance imaging for surveillance of women at high familial risk for breast cancer. *J Clin Oncol*. 2005;23(33):8469–8476.
7. Leach MO, Boggis CR, Dixon AK, et al. Screening with magnetic resonance imaging and mammography of a UK population at high familial risk of breast cancer: a prospective multicentre cohort study (MARIBS). *Lancet*. 2005;365(9473):1769–1778.
8. Lehman CD, Blume JD, Weatherall P, et al. Screening women at high risk for breast cancer with mammography and magnetic resonance imaging. *Cancer*. 2005;103(9):1898–1905.
9. Podo F, Sardanelli F, Canese R, et al. The Italian multi-centre project on evaluation of MRI and other imaging modalities in early detection of breast cancer in subjects at high genetic risk. *J Exp Clin Cancer Res*. 2002;21(3 Suppl):115–124.
10. Sardanelli F, Podo F. Breast MR imaging in women at high-risk of breast cancer. Is something changing in early breast cancer detection? *Eur Radiol*. 2007;17(4):873–887.
11. Sardanelli F, Podo F, D'Agnolo G, et al. Multicenter comparative multimodality surveillance of women at genetic-familial high risk for breast cancer (HIBCRIT study): interim results. *Radiology*. 2007;242(3):698–715.
12. Sardanelli F, Podo F, Santoro F, et al. Multicenter surveillance of women at high genetic breast cancer risk using mammography, ultrasonography, and contrast-enhanced magnetic resonance imaging (the high breast cancer risk italian 1 study): final results. *Invest Radiol*. 2011;46(2):94–105.
13. Tilanus-Linthorst MM, Bartels CC, Obdeijn AI, Oudkerk M. Earlier detection of breast cancer by surveillance of women at familial risk. *Eur J Cancer*. 2000;36(4):514–519.
14. Warner E, Plewes DB, Hill KA, et al. Surveillance of BRCA1 and BRCA2 mutation carriers with magnetic resonance imaging, ultrasound, mammography, and clinical breast examination. *JAMA*. 2004;292(11):1317–1325.
15. Clarke M, Collins R, Darby S, et al. Effects of radiotherapy and of differences in the extent of surgery for early breast cancer on local recurrence and 15-year survival: an overview of the randomised trials. *Lancet*. 2005;366(9503):2087–2106.
16. Early Breast Cancer Trialists' Collaborative Group, Darby S, McGale P, et al. Effect of radiotherapy after breast-conserving surgery on 10-year recurrence and 15-year breast cancer death: meta-analysis of individual patient data for 10,801 women in 17 randomised trials. *Lancet*. 2011;378(9804):1707–1716.
17. Poggi MM, Danforth DN, Sciuto LC, et al. Eighteen-year results in the treatment of early breast carcinoma with mastectomy versus breast conservation therapy: the National Cancer Institute Randomized Trial. *Cancer*. 2003;98(4):697–702.
18. Veronesi U, Cascinelli N, Mariani L, et al. Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. *New Engl J Med*. 2002;347(16):1227–1232.
19. Khatcheressian JL, Hurley P, Bantug E, et al. Breast cancer follow-up and management after primary treatment: American Society of Clinical Oncology clinical practice guideline update. *J Clin Oncol*. 2013;31(7):961–965.
20. Bliss JM, Kilburn LS, Coleman RE, et al. Disease-related outcomes with long-term follow-up: an updated analysis of the intergroup exemestane study. *J Clin Oncol*. 2012;30(7):709–717.
21. Cuzick J, Sestak I, Baum M, et al. Effect of anastrozole and tamoxifen as adjuvant treatment for early-stage breast cancer: 10-year analysis of the ATAC trial. *Lancet Oncol*. 2010;11(12):1135–1141.
22. Dubsky PC, Jakesz R, Mlineritsch B, et al. Tamoxifen and anastrozole as a sequencing strategy: a randomized controlled trial in postmenopausal patients with endocrine-responsive early breast cancer from the Austrian Breast and Colorectal Cancer Study Group. *J Clin Oncol*. 2012;30(7):722–728.
23. Jin H, Tu D, Zhao N, Shepherd LE, Goss PE. Longer-term outcomes of letrozole versus placebo after 5 years of tamoxifen in the NCIC CTG MA.17 trial: analyses adjusting for treatment crossover. *J Clin Oncol*. 2012;30(7):718–721.
24. Regan MM, Neven P, Giobbie-Hurder A, et al. Assessment of letrozole and tamoxifen alone and in sequence for postmenopausal women with steroid hormone receptor-positive breast cancer: the BIG 1–98 randomised clinical trial at 8.1 years median follow-up. *Lancet Oncol*. 2011;12(12):1101–1108.
25. Breast Magnetic Resonance Imaging (MRI) Accreditation Program Requirements. American College of Radiology Web Site; updated July 3, 2013. http://www.acr.org/~/media/ACR/Documents/Accreditation/BreastMRI/Requirements.pdf.
26. Lehman CD, Gatsonis C, Kuhl CK, et al. MRI evaluation of the contralateral breast in women with recently diagnosed breast cancer. *New Engl J Med*. 2007;356(13):1295–1303.
27. Dontchos BN, Rahbar H, Partridge SC, et al. Are Qualitative Assessments of Background Parenchymal Enhancement, Amount of Fibroglandular Tissue on MR Images, and Mammographic Density Associated with Breast Cancer Risk? *Radiology*. 2015;276(2):371–380.
28. Gutierrez RL, Strigel RM, Partridge SC, et al. Dynamic breast MRI: does lower temporal resolution negatively affect clinical kinetic analysis? *Am J Roentgenol*. 2012;199(3):703–708.
29. Wang LC, DeMartini WB, Partridge SC, Peacock S, Lehman CD. MRI-detected suspicious breast lesions: predictive values of kinetic features measured by computer-aided evaluation. *Am J Roentgenol*. 2009;193(3):826–831.
30. (ACR) ACoR. ACR BI-RADS - Magnetic Resonance Imaging In: *ACR Breast Imaging Reporting and Data System, Breast Imaging Atlas*. 3rd *ed*. Reston, VA: American College of Radiology; 2003.
31. Morris EA CC, Lee CH, et al. ACR BI-RADS Magnetic Resonance Imaging In: *ACR Breast Imaging Reporting and Data System*. 5th *ed*. Reston, VA: American College of Radiology; 2013.
32. Performance measures for 1,838,372 screening mammography examinations from 2004–2008 by age & time (months) since previous mammography - based on BCSC data through 2009. National Cancer Institute; updated July 9, 2014. http://breastscreening.cancer.gov/statistics/performance/screening/2009/perf_age_time.html#f8.
33. Yankaskas BC, Taplin SH, Ichikawa L, et al. Association between mammography timing and measures of screening performance in the United States. *Radiology*. 2005;234(2):363–373.
34. Brennan S, Liberman L, Dershaw DD, Morris E. Breast MRI screening of women with a personal history of breast cancer. *Am J Roentgenol*. 2010;195(2):510–516.
35. Giess CS, Poole PS, Chikarmane SA, Sippo DA, Birdwell RL. Screening Breast MRI in Patients Previously Treated for Breast Cancer: Diagnostic Yield for Cancer and Abnormal Interpretation Rate. *Acad Radiol*. 2015;22(11):1331-1137.
36. Gweon HM, Cho N, Han W, et al. Breast MR imaging screening in women with a history of breast conservation therapy. *Radiology*. 2014;272(2):366–373.
37. Schacht DV, Yamaguchi K, Lai J, Kulkarni K, Sennett CA, Abe H. Importance of a personal history of breast cancer as a risk factor for the development of subsequent breast cancer: results from screening breast MRI. *Am J Roentgenol*. 2014;202(2):289–292.
38. Cott Chubiz JE, Lee JM, Gilmore ME, et al. Cost-effectiveness of alternating magnetic resonance imaging and digital mammography screening in BRCA1 and BRCA2 gene mutation carriers. *Cancer*. 2013;119(6):1266–1276.
39. Evans DG, Kesavan N, Lim Y, et al. MRI breast screening in high-risk women: cancer detection and survival analysis. *Breast Cancer Res Treat*. 2014;145(3):663–672.
40. Taneja C, Edelsberg J, Weycker D, Guo A, Oster G, Weinreb J. Cost effectiveness of breast cancer screening with contrast-enhanced MRI in high-risk women. *J Am Coll Radiol*. 2009;6(3):171–179.

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