Title

Surveillance Breast MRI and Mammography: Comparison in Women with a Personal History of Breast Cancer

Journal

Radiology, 292(2)

ISSN

0033-8419

Authors

Wernli, Karen J
Ichikawa, Laura
Kerlikowske, Karla
et al.

Publication Date

2019-08-01

DOI

10.1148/radiol.2019182475

Peer reviewed

Radiology

ORIGINAL RESEARCH • BREAST IMAGING

Surveillance Breast MRI and Mammography: Comparison in Women with a Personal History of Breast Cancer

Karen J. Wernli, PhD • Laura Ichikawa, MS • Karla Kerlikowske, MD • Diana S. M. Buist, PhD • Susan D. Brandzel, MPH • Mary Bush, MS • Dianne Johnson, BA • Louise M. Henderson, PhD • Larissa Nekhlyudov, MD • Tracy Onega, PhD • Brian L. Sprague, PhD • Janie M. Lee, MD • Constance D. Lehman, MD • Diana L. Miglioretti, PhD

From the Kaiser Permanente Washington Health Research Institute, 1730 Minor Ave, Suite 1600, Seattle, WA 98101 (K.J.W., L.I., D.S.M.B., S.D.B., M.B., D.J., D.L.M.); Departments of Medicine and Epidemiology and Biostatistics, General Internal Medicine Section, Department of Veterans Affairs, University of California, San Francisco, San Francisco, Calif (K.K.); Department of Radiology, University of North Carolina, Chapel Hill, NC (L.M.H.); Department of Medicine, Brigham and Women's Hospital, Boston, Mass (L.N.); Department of Biomedical Data Science, Norris Cotton Cancer Center, Dartmouth Medical School, Hanover, NH (T.O.); Departments of Surgery and Radiology, University of Vermont, Burlington, Vt (B.L.S.); Department of Radiology, University of Washington, Seattle Cancer Care Alliance Seattle, Wash (J.M.L.); Department of Radiology, Massachusetts General Hospital, Boston, Mass (C.D.L.); Department of Public Health Sciences, University of California, Davis, Davis, Calif (D.L.M.). Received November 1, 2018; revision requested January 2, 2019; revision received April 5; accepted April 12. **Address correspondence to** K.J.W. (e-mail: *Karen.J.Wernli@kp.org*).

Study supported by Patient-Centered Outcomes Research Institute (CE-1304-6656) and the National Cancer Institute (P01 CA154292, U54 CA163303, and HHSN261201100031C).

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

See also the editorial by Newell in this issue.

Radiology 2019; 292:311–318 • https://doi.org/10.1148/radiol.2019182475 • Content codes: BR MR

Background: There is lack of consensus regarding the use of breast MRI for routine surveillance for second breast cancer events in women with a personal history of breast cancer.

Purpose: To compare performance of surveillance mammography with breast MRI.

Materials and Methods: This observational cohort study used prospectively collected data and included 13 266 women age 18 years and older (mean age, 60 years ± 13) with stage 0–III breast cancer who underwent 33 938 mammographic examinations and 2506 breast MRI examinations from 2005 to 2012 in the Breast Cancer Surveillance Consortium. Women were categorized into two groups: mammography alone (n = 11 745) or breast MRI (n = 1521). Performance measures were calculated by using end-of-day assessment and occurrence of second breast cancer events within 1 year of imaging. Logistic regression was used to compare performance for breast MRI versus mammography alone, adjusting for women, examination, and primary breast cancer characteristics. Analysis was conducted on a per-examination basis.

Results: Breast MRI was associated with younger age at diagnosis, chemotherapy, and higher education and income. Raw performance measures for breast MRI versus mammography were as follows, respectively: cancer detection rates, 10.8 (95% confidence interval [CI]: 6.7, 14.8) versus 8.2 (95% CI: 7.3, 9.2) per 1000 examinations; sensitivity, 61.4% (27 of 44; 95% CI: 46.5%, 76.2%) versus 70.3% (279 of 397; 95% CI: 65.8%, 74.8%); and biopsy rate, 10.1% (253 of 2506; 95% CI: 8.9%, 11.3%) versus 4.0% (1343 of 33 938; 95% CI: 3.7%, 4.2%). In multivariable models, breast MRI was associated with higher biopsy rate (odds ratio [OR], 2.2; 95% CI: 1.9, 2.7; $P < .001$) and cancer detection rate (OR, 1.7; 95% CI: 1.1, 2.7; $P = .03$) than mammography alone. However, there were no differences in sensitivity (OR, 1.1; 95% CI: 0.4, 2.9; $P = .84$) or interval cancer rate (OR, 1.1; 95% CI: 0.6, 2.2; $P = .70$).

Conclusion: Comparison of the performance of surveillance breast MRI with mammography must account for patient characteristics. Whereas breast MRI leads to higher biopsy and cancer detection rates, there were no significant differences in sensitivity or interval cancers compared with mammography.

Online supplemental material is available for this article.

In the United States, more than 3 000 000 women live with a personal history of breast cancer (1). Current guidelines recommend that women with prior breast cancer who are asymptomatic undergo annual mammography for surveillance of second breast cancer events (recurrence or second primary) (2–4). In observational studies, surveillance mammography is associated with a 31%–69% reduction in breast cancer mortality (5–8). Among more than 60 000 women in the Breast Cancer Surveillance Consortium (BCSC), surveillance mammography in women with previous breast cancer showed lower accuracy than screening mammography in women without breast cancer. Overall sensitivity was 65.4% in women with previous breast cancer (95% confidence interval [CI]: 61.5%, 69.0%) compared with 76.5% (95% CI: 71.7%, 80.7%) in women without breast cancer (8). Sensitivity was lowest for women who were younger than 50 years at diagnosis, had dense breasts, or who underwent chemotherapy or

Abbreviations

BCSC = Breast Cancer Surveillance Consortium, BI-RADS = Breast Imaging Reporting and Data System, CI = confidence interval, OR = odds ratio, PPV_1 = percentage of examinations with a positive end-of-day assessment that results in a second cancer diagnosis within 1 year, PPV_3 = percentage of examinations with a positive final assessment and biopsy was known to be performed that results in a second cancer diagnosis within 1 year

Summary

In the Breast Cancer Surveillance Consortium cohort, which involved more than 13 000 women with a personal history of breast cancer, surveillance breast MRI resulted in twofold higher biopsy rates than mammography alone and increased cancer detection but showed no difference in sensitivity or interval cancer rates.

Key Points

- For women with a personal history of breast cancer, surveillance breast MRI in community practice resulted in higher biopsy rates (odds ratio [OR], 2.2) and cancer detection rates (OR, 1.7) for second breast cancer events compared with mammography alone.
- Breast MRI was no different than mammography alone in sensitivity (OR, 1.1) for breast cancer detection and in interval cancer rates (OR, 1.1), indicating that mammography did not miss more cancers that would become clinically detectable during the 1-year screening interval.
- Comparisons of new imaging strategies for surveillance of women with a personal history of breast cancer need to account for differences in women, incident tumor, and treatment characteristics.

endocrine therapy (8). Some of these characteristics are also associated with higher interval cancer rates (9,10).

National clinical organizations lack consensus about offering breast MRI for routine surveillance in asymptomatic women with a personal history of breast cancer (11). In 2018, the American College of Radiology recommended annual breast MRI for women with dense breasts and whose breast cancer was diagnosed before the age of 50 years. (12). However, there is limited evidence on the benefits (eg, cancers detected) and harms (eg, benign biopsies) of breast MRI in this population, although a small but growing proportion of all women who had breast cancer underwent breast MRI as an adjunct to surveillance mammography (13,14). More research about breast cancer imaging surveillance strategies is needed to understand the implications of revising the surveillance guidelines.

To understand the role of breast MRI for women with a personal history of breast cancer and to help inform surveillance imaging guidelines, we compared the performance of breast MRI to mammography alone. We used data from more than 13 000 women who were 18 years or older and who had breast cancer in a national, multi-institutional setting of community-based Breast Cancer Surveillance Consortium radiology facilities in, to our knowledge, the largest sample and most comprehensive study to date.

Materials and Methods

Setting

The BCSC is a network of breast imaging registries that link data from community-based radiology facilities to state or Surveillance, Epidemiology, and End Results cancer registries and databases of pathologic results (15). This study used data from five registries: Carolina Mammography Registry, Kaiser Permanente Washington, New Hampshire Mammography Network, San Francisco Mammography Registry, and Vermont Breast Cancer Surveillance System (16). Our research project is registered at *clinicaltrials.gov* (NCT02212834). Data were collected from women and radiologists at time of imaging performed during routine clinical care. Registries send standardized data to a Statistical Coordinating Center for pooling, linking of relevant data files, and statistical analysis.

Each registry and the Statistical Coordinating Center was granted institutional review board approval for active consent, passive permission, or a waiver of written informed consent to enroll participants, link study data, and perform analytic studies. All procedures were Health Insurance Portability and Accountability Act compliant. The study authors had all control of the data and information submitted for publication.

Study Cohort

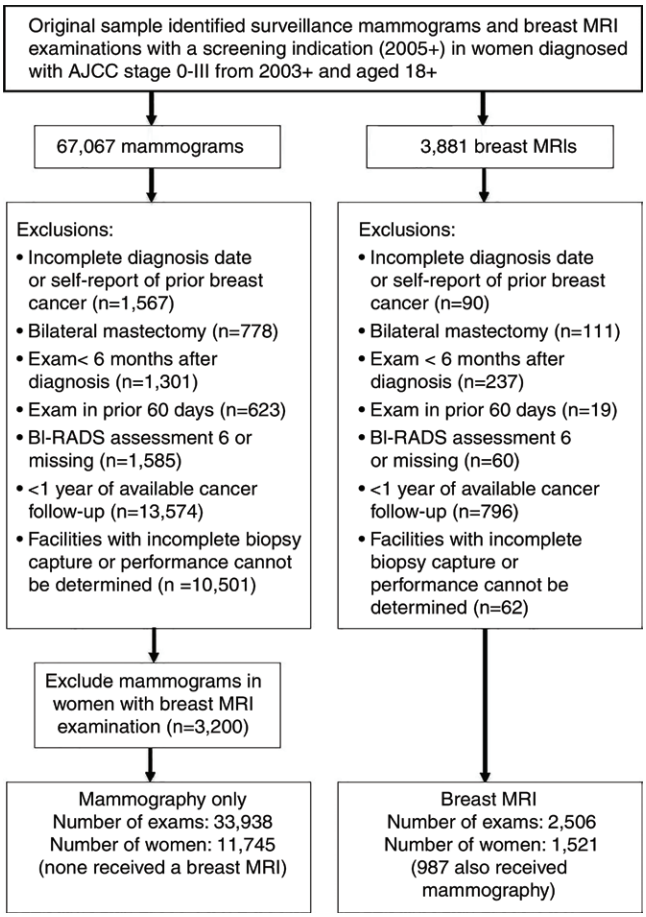
The study programmer (with >25 years of experience at the Statistical Coordinating Center) identified women with a primary incident breast cancer diagnosis of ductal carcinoma in situ or American Joint Committee on Cancer (17) stage I–III invasive cancer at age 18 years or older between January 2003 and June 2012 from Statistical Coordinating Center data files.

Breast cancer characteristics ascertained included histologic findings (invasive or ductal carcinoma in situ), American Joint Committee on Cancer stage, estrogen receptor, progesterone receptor, and tumor grade. Treatment characteristics included type of surgical procedure, chemotherapy, and/or radiation therapy. Detection mode of primary breast cancer was categorized as screen detected, interval cancer, or clinically detected (18,19). Preoperative breast MRI was defined as any MRI performed within 2 months before or 6 months after primary diagnosis date (20).

Surveillance Imaging

The study programmer included all mammography and breast MRI performed from 2005 to 2012 with an indication for screening that included the date of examination and assessments on the basis of the Breast Imaging Reporting and Data System (BI-RADS). We did not include examinations performed from 2003 to 2004 because breast MRI use was low during this period. Assessments by interpreting radiologists at the time of the examination were recorded as part of routine data collection. The mammography-only group was restricted to examinations in women without surveillance breast MRI. The breast MRI group included women who underwent mammography (94.7% [1441 of 1521] with any mammography and 64.9% [987 of 1521] with at least one surveillance examination), but only the breast MRI examinations were included in our analysis.

Exclusion criteria for examinations was as follows (Figure): incomplete diagnosis date or self-report of previous breast cancer (1567 mammographic and 90 breast MRI examinations) or with bilateral mastectomy (778 mammographic and 111 breast MRI examinations), within 6 months of primary diagnosis (1301 mammographic and 237 breast MRI examinations), within 60



Consort diagram of study flow, Breast Cancer Surveillance Consortium, 2005–2012.

days after an examination with the same modality (623 mammographic and 19 breast MRI examinations), BI-RADS category 6 (known cancer diagnosis) or missing assessment (1585 mammographic and 60 breast MRI examinations), less than 1 year of available cancer follow-up (13 574 mammographic and 796 breast MRI examinations), or from facilities with incomplete biopsy ascertainment or performance cannot be determined (10 501 mammographic and 62 breast MRI examinations) (21). In addition, any mammographic examinations in women who underwent a breast MRI examination were excluded.

Second Breast Cancer Events

The study programmer used cancer registry and pathologic-result databases to identify second breast cancer events within the pooled data to ascertain occurrence of ductal carcinoma in situ or invasive breast cancer within 12 months of the surveillance examination. Second breast cancer events included new primary cancers (contralateral events) and recurrences (ipsilateral events). Data regarding second cancers events were ascertained irrespective to and independent from specific imaging examinations.

Performance Measures

Performance measures were calculated by using standard BCSC definitions on the basis of BI-RADS assessment and second breast cancer event (18). BI-RADS end-of-day assessment (ie, after any same-day work-up) of 1 or 2 indicated negative findings and 0, 3, 4 or 5 indicated positive findings (18,22).

The calculation of positive predictive value from biopsy (PPV_3) included examinations with final BI-RADS assessment category 4 or 5 and biopsy where the final assessment resolves examinations with BI-RADS category 0 (18,22).

Statistical Analysis

All statistical analyses were conducted by a biostatistician (L.I., with >25 years of experience with BCSC data; supervised by D.M., a professor of biostatistics). Characteristics of women with personal history of breast were described by the type of exam received. Missing data regarding cancer characteristics were imputed by using an open-source program (Imputation and Variance Estimate Software version 0.2; IVEware, Institute for Social Research, University of Michigan, Ann Arbor, Mich, *http://www.src.isr.umich.edu/software/*) (23). This software applies imputation through sequential regression models on a variable-by-variable basis rather than specifying a joint distribution to handle complex data structures with variables of different types. Five imputed data sets were created.

We calculated raw performance measures with 95% CIs by imaging modality. Logistic regression was used to compare performance measures of breast MRI to mammography alone, adjusting for age at examination, year of examination, age at diagnosis, race/ethnicity, years since previous surveillance examination, BCSC registry, American Joint Committee on Cancer stage, histologic findings, detection mode, preoperative MRI, type of surgical procedure, radiation, chemotherapy, estrogen receptor and progesterone receptor status (invasive only), grade, and breast density by using BI-RADS (22). The models were fit by using a three-step generalized estimating equation model approach with independence working correlation matrix to account for nonnested clusters of women and radiologists (23–25). In a secondary model as a sensitivity analysis, we calculated results by using a propensity score model (Appendix E1, Table E1 [online]). We also evaluated variation in performance measures by facility to assess outliers.

All analyses used commercially available software (SAS version 9.2; SAS Institute, Cary, NC) and the Mianalyze procedure was used to combine results across the five imputed data sets. Two-sided *P* values less than .05 were considered to indicate statistically significant differences.

Results

We included 33 938 surveillance mammographic examinations (in 11 745 women) and 2506 surveillance breast MRI examinations (in 1521 women) in a total of 13 266 women who had previous breast cancer (Figure). The total study population was 77.0% (10 189 of 13 226) white, non-Hispanic; 9.0% (1187 of 13 266) black, non-Hispanic; 3.2% (427 of 13 226) Hispanic; and 10.8% (1423 of 13 266) Asian, Pacific Islander, mixed, or other race/ethnicity. A majority (70.0%; 7943 of 11 342) had at least some post–high school education. Annual income was evenly distributed into quartiles from less than $47 000 to at least $86 000. Of the mammographic examinations with known type, 79.5% (26 829 of 33 728) were digital and 20.4% (6899 of 33 728) were film (data not shown).

Table 1: Study Characteristics

A: Demographics of Women with a Personal History of Breast Cancer by Mammography Alone or Breast MRI

Characteristic	Mammography Alone	MRI
No. of women	11745	1521
Age at diagnosis (y)		
18–39	353 (3.0)	157 (10.3)
40–49	2038 (17.4)	500 (32.9)
50–59	3168 (27.0)	530 (34.8)
60–69	3037 (25.9)	276 (18.1)
70–79	2172 (18.5)	53 (3.5)
≥80	977 (8.3)	5 (0.3)
Mean age at diagnosis	61 ± 13	51 ± 10
Race/ethnicity*		
White, non-Hispanic	8954 (76.5)	1235 (81.3)
Black, non-Hispanic	1132 (9.7)	55 (3.6)
Hispanic	389 (3.3)	38 (2.5)
Asian or Pacific Islander	986 (8.4)	142 (9.3)
Mixed or other	245 (2.1)	50 (3.3)
Missing	39	1
Education		
Less than high school	795 (8.0)	26 (1.8)
High school or GED	2405 (24.2)	173 (12.3)
Some college, technical	2732 (27.5)	278 (19.8)
College graduate	4004 (40.3)	929 (66.1)
Missing	1809	115
Annual income†		
<$47000	3063 (26.2)	221 (14.7)
$47000–$62999	2959 (25.3)	368 (24.5)
$63000–$85999	2967 (25.4)	358 (23.9)
≥$86000	2704 (23.1)	552 (36.8)
Missing	52	22
Median income ($)	61903	72856

Table 1 *(continues)*

Table 1: *(continued)* Study Characteristics

B: Primary Breast Cancer Characteristics of Women with a Personal History of Breast Cancer by Mammography Alone or Breast MRI

Characteristic	Mammography Alone	MRI
Year of diagnosis		
2003–2004	2920 (24.9)	249 (16.4)
2005–2006	3036 (25.8)	428 (28.1)
2007–2008	2751 (23.4)	474 (31.2)
2009–2010	2232 (19.0)	279 (18.3)
2011–2012	806 (6.9)	91 (6.0)
Mode of detection		
Screen detected	6228 (66.1)	553 (47.8)
Interval detected	2300 (24.4)	474 (41.0)
Clinically detected	887 (9.4)	130 (11.2)
Missing	2330	364
AJCC stage		
0	2614 (22.3)	250 (16.4)
I	5170 (44.0)	657 (43.2)
IIa	2035 (17.3)	308 (20.2)
IIb	1066 (9.1)	146 (9.6)
III (a–c)	860 (7.3)	160 (10.5)
Histologic findings		
DCIS	2614 (22.3)	250 (16.4)
Invasive ductal	7741 (65.9)	978 (64.3)
Invasive lobular	611 (5.2)	151 (9.9)
Invasive ductal & lobular	749 (6.4)	134 (8.8)
Invasive other	30 (0.3)	8 (0.5)
Preoperative MRI‡		
Yes	1574 (13.4)	670 (44.0)
No	10171 (86.6)	851 (56.0)
Surgical procedure		
None	180 (1.5)	20 (1.3)
Breast conserving therapy	8298 (70.9)	1085 (71.5)
Unilateral mastectomy	3229 (27.6)	413 (27.2)
Missing	38	3
Radiation therapy		
Yes	6613 (58.4)	961 (64.7)
No	4702 (41.6)	524 (35.3)
Missing	430	36
Chemotherapy		
Yes	3463 (30.5)	703 (47.7)
No	7878 (69.5)	770 (52.3)
Missing	404	48
ER/PR for invasive cancer only		
ER− and PR−	1546 (17.6)	223 (18.1)
ER+ or PR+	7245 (82.4)	1008 (81.9)
Missing	2954	290
Grade		
1	2279 (20.9)	301 (21.2)
2	4758 (43.7)	626 (44.0)
3	3856 (35.4)	496 (34.9)
Missing	852	98

Table 1 *(continues)*

Characteristics of women, her primary breast cancer, and examination differed by imaging modality. Characteristics associated with use of breast MRI included the following: younger age at diagnosis (<50 years), more white non-Hispanic women, higher education level (college graduate), residence in a higher-income area, more recent breast cancer diagnosis (after 2008), interval- versus screen-detected primary breast cancer, diagnosis of invasive carcinoma and higher stage (>IIb), preoperative breast MRI for primary breast cancer diagnosis, chemotherapy for primary breast cancer, and dense breasts (Table 1A–1C). Almost half (48.2%; 1207 of 2506) of surveillance MRIs were performed within 1 year of a previous surveillance examination of any type compared with 12.1% (4119 of 33938) in the mammography-only group (Table 1C).

Among the 33938 surveillance mammographic examinations, 397 second breast cancer events occurred within 1 year of the examination, and 279 were detected at mammography (Table 2). Among 2506 surveillance breast MRI examinations, there were 44 second breast cancer events, and 27 were detected at MRI.

Table 1: *(continued)* Study Characteristics

C: Surveillance Imaging Examination Characteristics by Mammography Alone or Breast MRI

Characteristic	Mammography Alone	MRI
No. of examinations	33938	2506
Year of examination		
2005–2006	3778 (11.1)	137 (5.5)
2007–2008	7248 (21.4)	449 (17.9)
2009–2010	10780 (31.8)	819 (32.7)
2011–2012	12132 (35.7)	1101 (43.9)
BI-RADS breast density[§]		
Almost entirely fat	3278 (9.8)	57 (2.4)
Scattered	16490 (49.5)	777 (32.9)
Heterogeneously dense	12100 (36.4)	1144 (48.4)
Extremely dense	1413 (4.2)	387 (16.4)
Missing	657	141
Time since primary breast cancer diagnosis (y)		
<1	4463 (13.2)	265 (10.6)
1 to <2	6692 (19.7)	558 (22.3)
2 to <3	6033 (17.8)	489 (19.5)
3 to <4	4879 (14.4)	408 (16.3)
4 to <5	3949 (11.6)	306 (12.2)
≥5	7922 (23.3)	480 (19.2)
Time since prior surveillance examination (y)		
No prior examination	11488 (33.8)	715 (28.5)
<1	4119 (12.1)	1207 (48.2)
1 to <2	16642 (49.0)	478 (19.1)
2 to <3	1273 (3.8)	75 (3.0)
≥3	416 (1.2)	31 (1.2)

Note.—Unless otherwise indicated, data in A and B are numbers of women and data in C are examinations. Data in parentheses are percentages. Mean data are ± standard deviation. This study included 13266 women (age at diagnosis, ≥18 years; mean age, 60 years ± 13) in the Breast Cancer Surveillance Consortium from 2003 to 2012. AJCC = American Joint Committee on Cancer, BI-RADS = Breast Imaging Reporting and Data System, DCIS = ductal carcinoma in situ, ER = estrogen receptor, GED = general equivalency diploma, PR = progesterone receptor.

* Race/ethnicity from self-report with missing information filled in from cancer registry.

† Annual income was on the basis of median at census block group level or zip code if census block group was not available.

‡ Preoperative MRI defined as any MRI within 2 months before or 6 months after diagnosis.

§ Breast density is from mammography data; missing information is filled in from closest mammographic examination at least 6 months after primary cancer diagnosis.

Ductal carcinoma in situ (American Joint Committee on Cancer stage 0) or stage 1 invasive breast cancer accounted for 79.2% (236 of 298) of second cancer events in the mammography-only group and 79% (26 of 33) of second cancer events in women with breast MRI and known stage. Bilateral cancers were detected on 7.9% of mammograms only (30 of 380) and at 5% of breast MRI examinations (two of 40) with known laterality. Of the 17 cancers missed at breast MRI, one was subsequently diagnosed at screening mammography, seven were detected at diagnostic mammography (either short interval follow-up or evaluation of a breast problem), one was detected at subsequent breast MRI, and eight underwent no additional imaging with a positive finding observed subsequent to the surveillance breast MRI (data not shown).

Raw measures of performance of breast MRI versus mammography included the following, respectively: cancer detection rates, 10.8 (95% CI: 6.7, 14.8) versus 8.2 (95% CI: 7.3, 9.2) per 1000 examinations; sensitivity, 61.4% (95% CI: 46.5%, 76.2%) versus 70.3% (95% CI: 65.8%, 74.8%); specificity, 88.2% (95% CI: 86.9%, 89.5%) versus 88.5% (95% CI: 88.1%, 88.8%); and biopsy rate, 10.1% (95% CI: 8.9%, 11.3%) versus 4.0% (95% CI: 3.7%, 4.2%) (Table 3).

In fully adjusted models, breast MRI versus mammography resulted in higher cancer detection rate (odds ratio [OR], 1.7; 95% CI: 1.1, 2.7; $P = .03$) and more than two-fold higher biopsy rate (OR, 2.2; 95% CI: 1.9, 2.7; $P < .001$), with no difference in sensitivity (OR, 1.1; 95% CI: 0.4, 2.9; $P = .84$) or interval cancer rate (OR, 1.1; 95% CI: 0.6, 2.2; $P = .70$) (Table 4). Although not statistically significant, the percentage of examinations with a positive end-of-day assessment that resulted in a second cancer diagnosis within 1 year (PPV_1) was higher for breast MRI relative to mammography alone. This suggested an increased proportion of examinations with interpretation of abnormal findings that resulted in a second cancer event (OR, 1.6; 95% CI: 0.9, 2.8; $P = .10$). However, the proportion of examinations with a second cancer event in women who had undergone biopsy favored mammography alone compared with breast MRI (OR, 0.6; 95% CI: 0.3, 1.2; $P = .15$). Biopsy rates were highest in women at first examination regardless of imaging modality compared with subsequent examinations. At first examinations, biopsy rates were 5.2% in women who underwent mammography and 11.9% in women who underwent breast MRI. At subsequent examinations, biopsy rates were 3.3% in women who underwent mammography and 7.3% in women who underwent breast MRI (data not shown).

In our sensitivity analysis with propensity score matching, models included at least 82% of women in the breast MRI group except PPV_3, which included 75% of women. The ORs in these models provide a comparison of results if women in the mammography-only group had undergone breast MRI. Results from the propensity score analysis remained similar to our fully adjusted model for performance measures with attenuated CIs (Table E1 [online]). Further, by evaluating facility differences, we found increased use of BI-RADS assessment category 3 at mammography at one practice (with two facilities) in the first 3 years after cancer diagnosis per surveillance guidelines at this practice. After recoding this subset of examinations from positive findings to negative findings at sensitivity analysis, there was decreased specificity for breast MRI compared with mammography (adjusted model OR, 0.7; 95% CI: 0.5, 0.9). Therefore, we cannot be certain that there is no difference for specificity between imaging examinations.

Table 2: Characteristics of Second Breast Cancer Events Detected at Mammography Alone or at Breast MRI within 1 Year of Surveillance Imaging Examination

Characteristic	Mammography Alone	MRI
No. of cancers	397	44
No. of cancers detected	279	27
Cancer histologic analysis		
Invasive	286 (72.6)	30 (69.8)
DCIS	108 (27.4)	13 (30.2)
Unknown	3	1
AJCC stage		
0	108 (36.2)	13 (39.4)
I	128 (43.0)	13 (39.4)
IIa	33 (11.1)	4 (12.1)
IIb	9 (3.0)	3 (9.1)
III (a–c)	13 (4.4)	0 (0.0)
IV	7 (2.3)	0 (0.0)
Missing	99	11
Tumor size		
≤10 mm	101 (46.3)	9 (42.9)
11–15 mm	42 (19.3)	4 (19.0)
16–20 mm	32 (14.7)	2 (9.5)
>20 mm	43 (19.7)	6 (28.6)
Missing	179	23
Laterality		
Contralateral	163 (42.9)	16 (40.0)
Ipsilateral	187 (49.2)	22 (55.0)
Bilateral	30 (7.9)	2 (5.0)
Missing	17	4

Note.—Data are number of second breast cancers; data in parentheses are percentages. AJCC = American Joint Committee on Cancer, DCIS = ductal carcinoma in situ.

Discussion

Use of surveillance breast MRI resulted in increased biopsy and subsequent cancer detection rate relative to the use of mammography alone, as measured by odds ratios (ORs) adjusted for relevant confounders. However, there was no difference in the interpretation of breast MRI for second cancers compared with mammography (ie, sensitivity, OR, 1.1) or in interval cancer rate (ie, rate of false-negative findings, OR, 1.1). Therefore, the radiologic interpretation of mammography does not appear to miss more second cancer events that would become clinically detectable during the screening interval of 12 months compared with the radiologic interpretation of breast MRI. Our raw measure of sensitivity (70.3%) in our sample was higher than previous Breast Cancer Surveillance Consortium (BCSC) results (65.4%) on the basis of film mammography in women with a personal history of breast cancer (8). However, sensitivity remained lower than the greater-than-80% benchmark standard for mammography screening (26), which reinforced the need for improved surveillance strategies.

Previous studies have suggested that breast MRI might be relevant in expanding multimodality surveillance imaging, often on the basis of sensitivity measures of breast MRI. However, our results indicated that breast MRI sensitivity was 61.4%, which is both lower than the 75%–100% sensitivity in previous surveillance breast MRI studies (27–32) and not statistically different from mammography. Our measure of breast MRI sensitivity may differ from previous studies for several reasons. First, our results represent diverse, community-based breast imaging settings, where radiologists may be more variable (33) than in single-institution or academic environments. However, BCSC radiologists achieved quality standards and met screening breast MRI benchmarks in women both with and without breast cancer (21). Second, previous studies in women with a personal history of breast cancer may not have identified all false-negative results, so previous sensitivity measures could be overestimates (27–32). Cancer registries do not report ipsilateral second cancer events, which is a challenge for studying women with prior breast cancer. Our study used pathologic-results databases maintained by BCSC registries to ascertain second breast cancer events. We excluded facilities with low biopsy data ascertainment to avoid missing breast cancer diagnoses. It is uncertain from other studies whether they evaluated cancer outcomes up to 1 year from examination because the time frame of evaluation was not specified. Finally, because breast MRI is used as an adjunct to mammography, multimodality breast imaging may lead to more false-negative findings at breast MRI if the cancer event was detected at mammography. We did not observe a high proportion of missed cancers depicted at subsequent screening mammography. Furthermore, previous observational studies (27–32) did not incorporate the effect of mammography in their performance measures. Finally, our results also indicated no difference in the interval cancer rate on the basis of adjusted models.

Previous studies of breast MRI performance did not consider differences according to characteristics of women, primary cancer diagnosis, and treatment. Women who underwent surveillance breast MRI were more educated and lived in wealthier neighborhoods, consistent with disparities in access to screening breast MRI for women without breast cancer (34). BCSC data on women with a less than 20% lifetime risk of breast cancer and without breast cancer showed that white women and college graduates are 1.7 to 3.0 times more likely to undergo screening breast MRI. Compared with women who underwent mammography alone, women who underwent breast MRI had higher-stage primary cancers and higher likelihood of chemotherapy, which suggested a greater risk of second breast cancer events. Therefore, understanding the effect of the latest imaging tests for surveillance of second breast cancer events requires an understanding of the baseline cancer rate in the evaluated population and characteristics in women to obtain accurate performance estimates.

The effect of additional and potentially unnecessary biopsies should be considered in evaluating modifications to surveillance strategies in women with a personal history of breast cancer. On a population level, the universal use of breast MRI for surveillance could have a profound effect; if all 235 020 US women diagnosed with stage 0–III breast cancer in 2018 underwent one MRI, an estimated 14 336 more would undergo biopsy than if they had undergone mammography alone. On an individual level, our previous work (35) in the BCSC determined that

Table 3: Mammography and Breast MRI Performance in Women with a Personal History of Breast Cancer

Performance Measure	Mammography Alone	Breast MRI
Cancer rate*	11.7 (10.6, 12.8) [397/33 938]	17.6 (12.4, 22.7) [44/2506]
Cancer detection rate*	8.2 (7.3, 9.2) [279/33 938]	10.8 (6.7, 14.8) [27/2506]
Interval cancer rate*	3.5 (2.9, 4.1) [118/33 938]	6.8 (3.6, 10.0) [17/2506]
Biopsy within 1 year (%)	4.0 (3.7, 4.2) [1343/33 938]	10.1 (8.9, 11.3) [253/2506]
Sensitivity (%)	70.3 (65.8, 74.8) [279/397]	61.4 (46.5, 76.2) [27/44]
Specificity (%)	88.5 (88.1, 88.8) [29 669/33 541]	88.2 (86.9, 89.5) [2172/2462]
Recall (%)	12.2 (11.9, 12.6) [4151/33 938]	12.6 (11.3, 14.0) [317/2506]
PPV_1 (%)	6.7 (6.0, 7.5) [279/4151]	8.5 (5.4, 11.6) [27/317]
PPV_3 (%)	30.5 (27.0, 34.0) [202/663]	19.5 (12.3, 26.7) [23/118]

Note.—Data are from the Breast Cancer Surveillance Consortium (2005–2012). Data in parentheses are 95% confidence intervals; data in brackets are numerator/denominator. PPV_1 = percentage of examinations with a positive end-of-day assessment that results in a second cancer diagnosis within 1 year, PPV_3 = percentage of examinations with a positive final assessment and biopsy was known to be performed that results in a second cancer diagnosis within 1 year.

* Unit of measure was per 1000 examinations.

Table 4: Logistic Regression Results Comparing Performance of Breast MRI Relative to Mammography Alone in Fully Adjusted Models

Measure	No. of Examinations	OR*	*P* Value
Cancer rate	36 444	1.5 (1.0, 2.1)	.03
Cancer detection rate	36 444	1.7 (1.1, 2.7)	.03
Interval cancer rate†	36 444	1.1 (0.6, 2.2)	.70
Biopsy within 1 year	36 444	2.2 (1.9, 2.7)	<.001
Sensitivity†	441	1.1 (0.4, 2.9)	.84
Specificity	36 003	1.2 (0.7, 2.0)	.49
PPV_1	4468	1.6 (0.9, 2.8)	.10
PPV_3	781	0.6 (0.3, 1.2)	.15

Note.—Data in parentheses are 95% confidence intervals. *P* values less than .05 were considered to indicate statistical significance. AJCC = American Joint Committee on Cancer, CI = confidence interval, OR = odds ratio, PPV_1 = percentage of examinations with a positive end-of-day assessment that results in a second cancer diagnosis within 1 year, PPV_3 = percentage of examinations with a positive final assessment and biopsy was known to be performed that results in a second cancer diagnosis within 1 year.

* Odds ratios adjusted for age at diagnosis, Breast Cancer Surveillance Consortium registry, AJCC stage, histologic findings, mode of detection, preoperative MRI, surgical procedure, radiation therapy, chemotherapy, estrogen receptor and progesterone receptor status (invasive only), grade, breast density, age at examination, year of examination, years since prior surveillance examination, and race/ethnicity.

† Because of convergence issues with interval cancer rate and sensitivity, we used a reduced model, which did not adjust for surgical procedure, radiation, year of examination, or race/ethnicity.

women with a personal history of breast cancer had mixed responses to additional biopsy. In our qualitative study with more than 40 women in focus group discussions, we found that some women perceive biopsies with negative results as assurance that cancer was not missed. However, other women want to avoid additional work-up, anxiety, and false-positive work-up costs (35). Patient preferences balanced by population health needs may guide the consideration of multimodality surveillance strategies.

Our study had limitations, including an inability to adjust for other confounders such as 5-year breast cancer risk, human epidermal growth factor receptor 2 tumor biology, and referral reason for breast MRI order. However, we adjusted for the most relevant confounders, including stage and treatment, and minimized residual confounding (36). Our analysis did not specifically identify subgroups of women in whom breast MRI might be more effective than mammography for surveillance because of the limited number of second breast cancer events and limited power.

In conclusion, for women with a personal history of breast cancer, the potential benefits and harms, specifically the effect of increased biopsies, should be carefully considered when incorporating breast MRI into surveillance imaging strategies. Further research may identify subgroups of women who benefit from undergoing breast MRI, especially in minimizing the effect of unnecessary benign biopsies.

Acknowledgments: This work was supported through a Patient-Centered Outcomes Research Institute (PCORI) Project Program Award (CE-1304–6656-Comparative effectiveness of surveillance imaging modalities in breast cancer survivors) and the National Cancer Institute-funded Breast Cancer Surveillance Consortium (BCSC; P01 CA154292, U54 CA163303, and HHSN261201100031C). The collection of cancer data used in this study was supported in part by several state public health departments and cancer registries throughout the United States. For a full description of the BCSC, please see *http://www.bcsc-research.org/*. The design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication is solely the responsibility of the authors and does not necessarily represent the official views of the Patient-Centered Outcomes Research Institute, the National Cancer Institute, or the National Institutes of Health. We thank the participating women, mammography facilities, and radiologists for the data they provided for this study. Further, we thank the study Patient Advisory Board and Stakeholder Panel for their ongoing support of this research project. A list of the BCSC investigators and procedures for requesting BCSC data for research purposes are provided at *http://www.bcsc-research.org/*. The authors thank Drs Natasha Stout and Rebecca Hubbard for their perspectives of this manuscript.

Author contributions: Guarantors of integrity of entire study, K.J.W., S.D.B., L.M.H., T.O.; 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; agrees to ensure any questions related to the work are appropriately resolved, all authors; literature research, K.J.W., K.K., D.S.M.B., L.M.H., L.N., J.M.L., C.D.L. clinical studies, K.K., T.O.; statistical analysis, K.J.W., L.I., L.M.H., D.L.M.; and manuscript editing, K.J.W., L.I., K.K., D.S.M.B., S.D.B., M.B., D.J., L.M.H., L.N., T.O., J.M.L., C.D.L., D.L.M.

Disclosures of Conflicts of Interest: **K.J.W.** disclosed no relevant relationships. **L.I.** disclosed no relevant relationships. **K.K.** Activities related to the present article: disclosed no relevant relationships. Activities not related to the present article: disclosed money paid to author's institution for a grant from Google Sciences; disclosed travel funds from the Breast Cancer Research Foundation and the American Cancer Society. Other relationships: disclosed no relevant relationships. **D.S.M.B.** Activities related to the present article: disclosed no relevant relationships. Activities not related to the present article: disclosed money paid to author for board membership from Concure Oncology; money paid to author's institution for travel expenses from GRAIL; money paid to author for Data Safety Monitoring Board membership from University of California, San Francisco. Other relationships: disclosed no relevant relationships. **S.D.B.** disclosed no relevant relationships. **M.B.** Activities related to the present article: disclosed compensation as a patient partner from Patient-Centered Outcomes Research Institute. Activities not related to the present article: disclosed no relevant relationships. Other relationships: disclosed no relevant relationships. **D.J.** disclosed no relevant relationships. **L.M.H.** disclosed no relevant relationships. **L.N.** disclosed no relevant relationships. **T.O.** disclosed no relevant relationships. **B.L.S.** disclosed no relevant relationships. **J.M.L.** Activities related to the present article: disclosed no relevant relationships. Activities not related to the present article: disclosed money paid to author for consultancy from GE Healthcare; disclosed money to author's institution for grants/grants pending from GE Healthcare. Other relationships: disclosed no relevant relationships. **C.D.L.** Activities related to the present article: disclosed no relevant relationships. Activities not related to the present article: disclosed money paid to author for consultancy from GE Healthcare; disclosed money to author's institution for grants/grants pending from GE Healthcare. Other relationships: disclosed no relevant relationships. **D.L.M.** Activities related to the present article: disclosed no relevant relationships. Activities not related to the present article: disclosed money paid to author for consultancy from Hologic; disclosed money to author's institution for royalties from Elsevier. Other relationships: disclosed no relevant relationships.

References

1. Cancer Surveillance System: Cancer Surveillance System: Surveillance, Epidemiology, and End Results (SEER) Program. http://www.fhcrc.org/en/labs/phs/projects/cancer-surveillance-system.html. Accessed September 25, 2013.
2. Runowicz CD, Leach CR, Henry NL, et al. American Cancer Society/American Society of Clinical Oncology breast cancer survivorship care guideline. J Clin Oncol 2016;34(6):611–635.
3. National Comprehsenive Cancer Network. National Comprehensive Cancer Network: NCCN guidelines. http://www.nccn.org/professionals/physician_gls/f_guidelines.asp. Published 2013. Accessed May 12, 2012.
4. 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.
5. Lash TL, Fox MP, Buist DS, et al. Mammography surveillance and mortality in older breast cancer survivors. J Clin Oncol 2007;25(21):3001–3006.
6. Lu W, Schaapveld M, Jansen L, et al. The value of surveillance mammography of the contralateral breast in patients with a history of breast cancer. Eur J Cancer 2009;45(17):3000–3007.
7. Houssami N, Ciatto S, Martinelli F, Bonardi R, Duffy SW. Early detection of second breast cancers improves prognosis in breast cancer survivors. Ann Oncol 2009;20(9):1505–1510.
8. Houssami N, Abraham LA, Miglioretti DL, et al. Accuracy and outcomes of screening mammography in women with a personal history of early-stage breast cancer. JAMA 2011;305(8):790–799.
9. Buist DS, Abraham LA, Barlow WE, et al. Diagnosis of second breast cancer events after initial diagnosis of early stage breast cancer. Breast Cancer Res Treat 2010;124(3):863–873.
10. Lee JM, Buist DS, Houssami N, et al. Five-year risk of interval-invasive second breast cancer. J Natl Cancer Inst 2015;107(7):djv109.
11. Lam DL, Houssami N, Lee JM. Imaging surveillance after primary breast cancer treatment. AJR Am J Roentgenol 2017;208(3):676–686.
12. Monticciolo DL, Newell MS, Moy L, Niell B, Monsees B, Sickles EA. Breast cancer screening in women at higher-than-average risk: recommendations from the ACR. J Am Coll Radiol 2018;15(3 Pt A):408–414.
13. Stout NK, Nekhlyudov L, Li L, et al. Rapid increase in breast magnetic resonance imaging use: trends from 2000 to 2011. JAMA Intern Med 2014;174(1):114–121.
14. Wernli KJ, DeMartini WB, Ichikawa L, et al. Patterns of breast magnetic resonance imaging use in community practice. JAMA Intern Med 2014;174(1):125–132.
15. Breast Cancer Surveillance Consortium Web site. http://www.bcsc-research.org/.
16. Ballard-Barbash R, Taplin SH, Yankaskas BC, et al. Breast Cancer Surveillance Consortium: a national mammography screening and outcomes database. AJR Am J Roentgenol 1997;169(4):1001–1008.
17. Edge SB, Byrd DR, Compton CC, Fritz AG, Greene FL, Trotti A. AJCC cancer staging manual. New York, NY: Springer-Verlag, 2009; 646.
18. Breast Cancer Surveillance Consortium. Breast Cancer Surveillance Consortium Glossary of Terms, Version 2. http://www.bcsc-research.org/data/bcsc_data_definitions_version2_final__2017.pdf. Published 2017. Accessed April 28, 2017.
19. Mandelblatt JS, Near AM, Miglioretti DL, et al. Common model inputs used in CISNET collaborative breast cancer modeling. Med Decis Making 2018;38(1_suppl):9S–23S.
20. Goodrich ME, Weiss J, Onega T, et al. The role of preoperative magnetic resonance imaging in the assessment and surgical treatment of interval and screen-detected breast cancer in older women. Breast J 2016;22(6):616–622.
21. Lee JM, Ichikawa L, Valencia E, et al. Performance benchmarks for screening breast MR imaging in community practice. Radiology 2017;285(1):44–52.
22. D'Orsi C, Mendelson E, Ikeda D, et al. ACR BI-RADS Atlas, Breast Imaging Reporting and Data System. 4th ed. Reston, Va: American College of Radiology, 2013.
23. Miglioretti DL, Heagerty PJ. Marginal modeling of multilevel binary data with time-varying covariates. Biostatistics 2004;5(3):381–398.
24. Miglioretti DL, Heagerty PJ. Marginal modeling of nonnested multilevel data using standard software. Am J Epidemiol 2007;165(4):453–463.
25. Liang KY, Zeger SL. Longitudinal data analysis using generalized linear models. Biometrika 1986;73(1):13–22.
26. Lehman CD, Arao RF, Sprague BL, et al. National performance benchmarks for modern screening digital mammography: update from the Breast Cancer Surveillance Consortium. Radiology 2017;283(1):49–58.
27. Cho N, Han W, Han BK, et al. Breast cancer screening with mammography plus ultrasonography or Magnetic Resonance Imaging in women 50 years or younger at diagnosis and treated with breast conservation therapy. JAMA Oncol 2017;3(11):1495–1502.
28. Berg WA, Zhang Z, Lehrer D, et al. Detection of breast cancer with addition of annual screening ultrasound or a single screening MRI to mammography in women with elevated breast cancer risk. JAMA 2012;307(13):1394–1404.
29. 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):1331–1337.
30. 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.
31. Lehman CD, Lee JM, DeMartini WB, et al. Screening MRI in women with a personal history of breast cancer. J Natl Cancer Inst 2016;108(3):djv349.
32. Weinstock C, Campassi C, Goloubeva O, et al. Breast magnetic resonance imaging (MRI) surveillance in breast cancer survivors. Springerplus 2015;4(1):459.
33. Elmore JG, Jackson SL, Abraham L, et al. Variability in interpretive performance at screening mammography and radiologists' characteristics associated with accuracy. Radiology 2009;253(3):641–651.
34. Haas JS, Hill DA, Wellman RD, et al. Disparities in the use of screening magnetic resonance imaging of the breast in community practice by race, ethnicity, and socioeconomic status. Cancer 2016;122(4):611–617.
35. Brandzel S, Rosenberg DE, Johnson D, et al. Women's experiences and preferences regarding breast imaging after completing breast cancer treatment. Patient Prefer Adherence 2017;11:199–204.
36. Greenland S, Pearl J, Robins JM. Causal diagrams for epidemiologic research. Epidemiology 1999;10(1):37–48.