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Impact of Surveillance Mammography Intervals Less Than One Year on Performance Measures in Women With a Personal History of Breast Cancer

Janie M. Lee[1,2], Laura E. Ichikawa[3], Karen J. Wernli[3,4], Erin J. A. Bowles[3], Jennifer M. Specht[2,5], Karla Kerlikowske[6,7,8], Diana L. Miglioretti[3,9], Kathryn P. Lowry[1,2], Anna N. A. Tosteson[10,11], Natasha K. Stout[12], Nehmat Houssami[13], Tracy Onega[10,14], Diana S. M. Buist[3,4]

[1]Department of Radiology, University of Washington School of Medicine, Seattle, WA, USA
[2]Fred Hutchinson Cancer Center, Seattle, WA, USA
[3]Kaiser Permanente Washington Health Research Institute, Seattle, WA, USA
[4]Department of Health Systems Science, Kaiser Permanente Bernard J. Tyson School of Medicine Pasadena, CA, USA
[5]Department of Medicine, University of Washington School of Medicine, Seattle, WA, USA
[6]Department of Medicine, University of California San Francisco, San Francisco, CA, USA
[7]Department of Veterans Affairs, University of California San Francisco, San Francisco, CA, USA
[8]Department of Epidemiology and Biostatistics, University of California San Francisco, San Francisco, CA, USA
[9]Division of Biostatistics, Department of Public Health Sciences, University of California Davis School of Medicine, Davis, CA, USA
[10]The Dartmouth Institute for Health Policy and Clinical Practice, Geisel School of Medicine at Dartmouth, Lebanon, NH, USA
[11]Norris Cotton Cancer Center, Geisel School of Medicine at Dartmouth, Lebanon, NH, USA
[12]Department of Population Medicine, Harvard Pilgrim Health Care Institute, Harvard Medical School, Boston, MA, USA
[13]The Daffodil Centre, University of Sydney and Cancer Council New South Wales, Kings Cross, New South Wales, Australia
[14]Huntsman Cancer Institute, University of Utah, Salt Lake City, UT, USA

Objective: When multiple surveillance mammograms are performed within an annual interval, the current guidance for one-year follow-up to determine breast cancer status results in shared follow-up periods in which a single breast cancer diagnosis can be attributed to multiple preceding examinations, posing a challenge for standardized performance assessment. We assessed the impact of using follow-up periods that eliminate the artifactual inflation of second breast cancer diagnoses.

Materials and Methods: We evaluated surveillance mammograms from 2007–2016 in women with treated breast cancer linked with tumor registry and pathology outcomes. Second breast cancers included ductal carcinoma in situ or invasive breast cancer diagnosed during one-year follow-up. The cancer detection rate, interval cancer rate, sensitivity, and specificity were compared using different follow-up periods: standard one-year follow-up per the American College of Radiology versus follow-up that was shortened at the next surveillance mammogram if less than one year (truncated follow-up). Performance measures were calculated overall and by indication (screening, evaluation for breast problem, and short interval follow-up).

Results: Of 117971 surveillance mammograms, 20% (n = 23533) were followed by another surveillance mammogram within one year. Standard follow-up identified 1597 mammograms that were associated with second breast cancers. With truncated follow-up, the breast cancer status of 179 mammograms (11.2%) was revised, resulting in 1418 mammograms associated with unique second breast cancers. The interval cancer rate decreased with truncated versus standard follow-up (3.6 versus 4.9 per 1000 mammograms, respectively), with a difference (95% confidence interval [CI]) of -1.3 (-1.6, -1.1). The overall sensitivity increased to 70.4% from 63.7%, for the truncated versus standard follow-up, with a difference (95% CI) of 6.6% (5.6%, 7.7%). The specificity remained stable at 98.1%.

Conclusion: Truncated follow-up, if less than one year to the next surveillance mammogram, enabled second breast cancers

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Corresponding author: Janie M. Lee, MD, MSc, Fred Hutchinson Cancer Center, 1144 Eastlake Ave East, LG2-200, Seattle 98109, WA, USA
• E-mail: jmlee58@uw.edu

to be associated with a single preceding mammogram and resulted in more accurate estimates of diagnostic performance for national benchmarks.
Keywords: Mammography; Diagnostic performance; Breast cancer screening; Outcome assessment

INTRODUCTION

For women with a personal history of breast cancer, annual mammography is recommended to detect early second breast cancers [1], enabling treatment to extend survival and maintain quality of life. In 2016, there were an estimated 3.5 million women with a personal history of breast cancer in the United States; by 2026, this number is expected to increase to 4.5 million women [2]. Surveillance mammograms in these women are often performed more than once per year, most frequently within the first five years after treatment [3-6]. A study of surveillance imaging patterns in United States community practice found that one-third of women underwent multiple breast imaging examinations each year within the first two years after completing treatment [4].

The American College of Radiology's Breast Imaging Reporting and Data System (BI-RADS) [7] provides guidance to support United States regulations for all mammography facilities to analyze diagnostic performance to identify deficiencies, facilitate research, and improve outcomes. BI-RADS guidance enables standardized performance audits across facilities, and national benchmarks have been established for mammography, ultrasonography, and magnetic resonance imaging (MRI) [8]. BI-RADS recommends calculating performance using a follow-up interval for breast cancer ascertainment aligned with the recommended screening interval. The follow-up interval for surveillance mammography after breast cancer treatment is one year [1]. When multiple surveillance mammography examinations are performed within a year, the one-year follow-up period for the earlier examination extends beyond the date of the subsequent examination, resulting in shared follow-up periods. Applying the current guidance for performance assessment, a breast cancer diagnosed during these shared follow-up periods results in two mammogram-associated breast cancer diagnoses, artificially inflating the number of breast cancers in an outcome audit.

As measures of screening and surveillance effectiveness increasingly include ascertaining outcomes such as interval cancers and their characteristics, the artificial inflation of breast cancer diagnoses may lead to biased performance estimates. Using a previously published dataset of surveillance mammography in women with treated breast cancer [9], we assessed the change in performance measures using a truncated follow-up interval that eliminated shared follow-up periods compared with the standard one-year follow-up.

MATERIALS AND METHODS

Five Breast Cancer Surveillance Consortium (BCSC) [10] registries in the United States of America (Carolina Mammography Registry, Kaiser Permanente Washington Registry, New Hampshire Mammography Network, San Francisco Mammography Registry, and Vermont Breast Cancer Surveillance System) prospectively collected data through either passive consent (three registries) or a waiver of written informed consent (two registries). BCSC registries and its Statistical Coordinating Center received institutional review board approval to enroll participants and perform analyses, with a Federal Certificate of Confidentiality and other protections for participating women, physicians, and facilities. Breast cancer data were collected from state and regional tumor registries; regional Surveillance, Epidemiology, and End Results programs; and local biopsy and pathology databases. All procedures complied with the Health Insurance Portability and Accountability Act.

We included women aged ≥ 18 years with primary breast cancer diagnosed from 1988–2015 with American Joint Committee on Cancer 8th edition [11] anatomic stage 0–III who received definitive surgery (lumpectomy or mastectomy, but not bilateral mastectomy). Digital mammograms or digital breast tomosynthesis (DBT) examinations performed from 2007–2016 that occurred ≥ 6 months after primary breast cancer diagnosis were included for this analysis of mammograms that were likely performed for asymptomatic surveillance [2,6], based on indication codes for each mammogram and self-report of symptoms at the time of imaging.

The American College of Radiology [12] specifies that screening or diagnostic examination codes may be

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used for mammography performed during asymptomatic surveillance of women with treated breast cancer. In the United States, which does not have a national population-based screening and surveillance program, this guideline results in variable indication coding practices at both the woman and facility levels and across different time points during the posttreatment phase of care, making it difficult to distinguish between mammography performed in women with symptoms of breast cancer (in the index or contralateral breast) and mammography performed in asymptomatic women for surveillance. However, excluding mammograms with diagnostic indication codes may potentially bias the outcome assessment by disproportionately excluding women who received breast conservation treatment or those within the first five years after treatment [3].

We included all mammograms with indication of screening and non-screening indication codes of short-interval follow-up (SIFU) or evaluation of breast problems. Indication coding was performed at the discretion of each facility, and no effort was made to coordinate clinical operations or policies through the BCSC. Within the BCSC, the observed SIFU indication use in the surveillance setting was highest in the first year after completing breast cancer treatment, with follow-up mammograms occurring at 6 month peaks, consistent with semi-annual surveillance [3]. We subsequently excluded mammograms with self-reported symptoms, except for generalized breast pain [3,9,13-15]. We further excluded diagnostic indication mammograms completed on the same day as the screening indication mammogram, those with a prior mammogram within 90 days, and those with BI-RADS assessment category 6 (known malignancy). Mammograms with an indication code of breast problem evaluation from facilities with ≥ 25% missing self-reported symptom information were excluded to further reduce the probability of unintentionally including mammograms performed for symptoms of breast cancer recurrence. Information from questionnaires completed by women at the time of mammography and electronic health records was used to collect demographic and breast cancer risk factors, including age, race, ethnicity group, menopausal status [16], presence or absence of breast symptoms, and time since last mammogram. BI-RADS breast densities [7,17] were recorded by the interpreting radiologist.

Breast Cancer Outcomes Ascertainment and Performance Measures

The analysis was performed at the mammogram level, and each mammogram had 12 months of follow-up for breast cancer ascertainment. Second breast cancers were identified as ductal carcinoma in situ or invasive breast cancer diagnosed in either the ipsilateral or contralateral breast. Because surveillance mammograms had both screening and non-screening indications, performance metrics were based on the final assessment categories of the American College of Radiology BI-RADS [7]. Final assessments of 4 (suspicious) or 5 (highly suspicious) were considered positive and final assessments of 1 (negative), 2 (benign), or 3 (probably benign) were considered negative. Examinations with BI-RADS 0 (needs additional evaluation) end-of-day assessments were followed for up to 90 days for the first non-zero BI-RADS assessment. Examinations that could not be resolved to a nonzero assessment were excluded.

All examinations were classified as either true-positive (TP), false-positive (FP), true-negative (TN), or false-negative (FN) using two different approaches. The first approach used a standard one-year follow-up and the second approach used a truncated follow-up that ended at the earlier of the one year time point or the next surveillance mammogram. TP examinations (surveillance-detected cancers) were defined as examinations with positive results and breast cancer diagnosis during the follow-up period [13]. FP examinations were defined as examinations with positive results without a breast cancer diagnosis during the follow-up period. TN examinations had negative results, and no cancer was diagnosed during the follow-up period. FN examinations (interval cancers) were defined as examinations with negative results and breast cancer diagnoses during the follow-up period. Figure 1 shows how different follow-up periods affected breast cancer status.

The cancer detection rate, interval cancer rate, sensitivity, and specificity were calculated according to BI-RADS guidelines [7]. The cancer detection rate was defined as the number of examinations with a positive result and a breast cancer diagnosis within the follow-up period per 1000 examinations (TP/all examinations). The interval cancer rate was defined as the number of examinations with a negative result and breast cancer diagnosis within the follow-up period per 1000 examinations (FN/all examinations). Sensitivity was defined as the proportion of examinations with a breast cancer diagnosis during the follow-up period that had a positive result [TP/(TP + FN)] and specificity was defined as the proportion of examinations without a breast cancer diagnosis that had a negative result [TN/(TN + FP)].

Performance measures were calculated overall and

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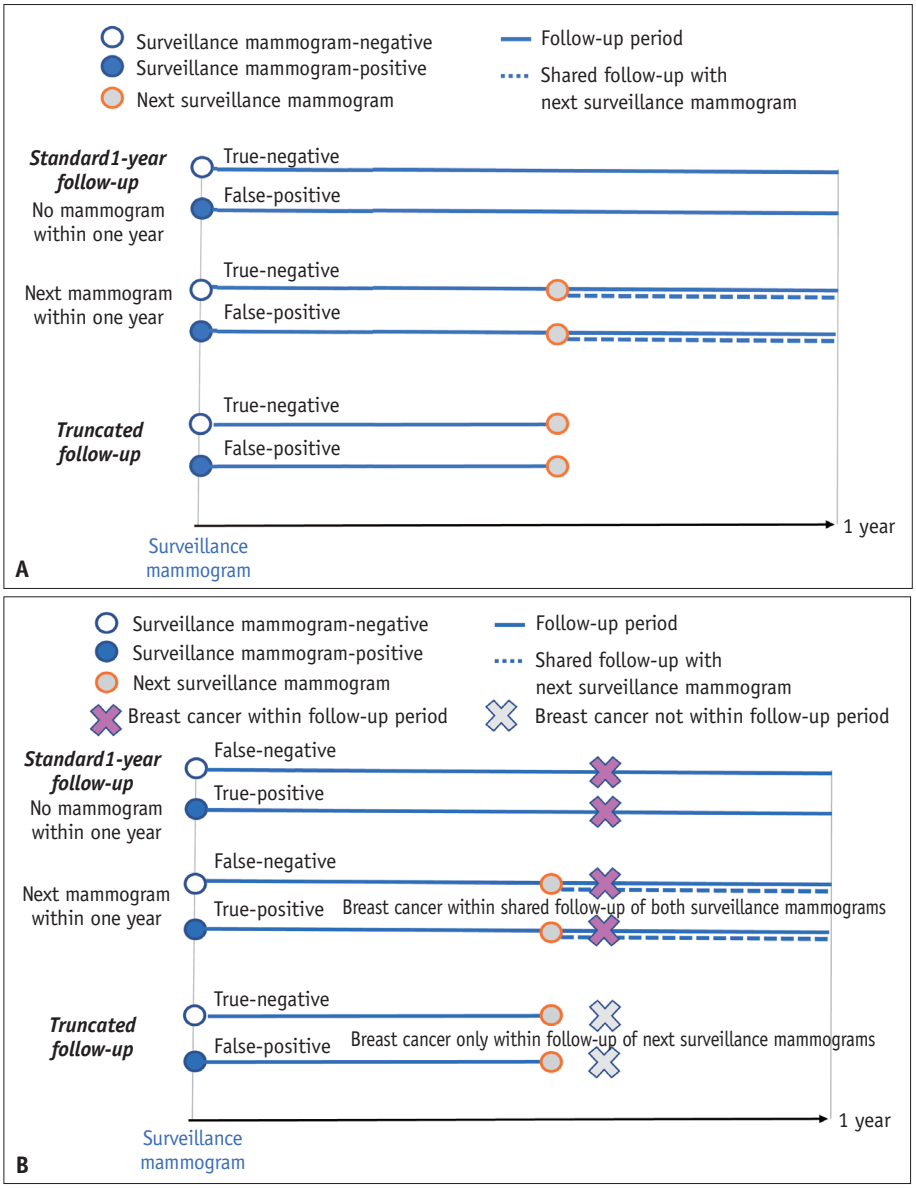

Fig. 1. Breast cancer status with standard one-year versus truncated follow-up. **A:** No breast cancer diagnosis within one year. No change in examination classification occurs when follow-up is truncated at the next surveillance mammogram within one year, and the shared follow-up period required by standard one-year follow-up is eliminated. **B:** Breast cancer diagnosis within one year. For a breast cancer diagnosis that occurs within one-year of the index mammogram and during the shared follow-up period of two mammograms performed within one year, two breast cancers are recorded and attributed to both preceding mammograms. With truncated follow-up, if the next surveillance mammogram occurred before the breast cancer diagnosis, a false-negative index mammogram with one-year follow-up would be reclassified as a true-negative mammogram at the time of follow-up truncation, since no breast cancer was diagnosed during its follow-up period. Similarly, an index mammogram classified as true-positive with one year follow-up would be reclassified to false-positive with truncated follow-up at the next mammogram. The breast cancer diagnosis that occurred after the next mammogram is attributed only once to the immediately preceding mammogram.

stratified by indication for standard one-year follow-up versus truncated follow-up periods. With both approaches, breast cancer status was based on whether a breast cancer diagnosis occurred during the follow-up period.

Statistical Analysis

Crude differences in performance using standard one-year and truncated follow-up were calculated; 95% confidence intervals were estimated using generalized estimating equations, assuming an independent working correlation structure to account for multiple examinations per woman [18].

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RESULTS

Characteristics of Surveillance Mammograms

Of 117971 surveillance mammograms that met the inclusion and exclusion criteria (Table 1), 112269 (95%) were digital mammograms and 5702 (5%) were DBT examinations. Most were performed for screening indications (73%, n = 86624), followed by evaluation of breast problems (17%, n = 19638), and SIFU (10%, n = 11709) indications. The mean age at mammography was 65 years (standard deviation: 11 years) and 39% (41977/106662) of the mammograms were classified as having dense breasts (heterogeneously or extremely dense). The mammograms were obtained from 32331 women with the following distribution of race and ethnicity: white, non-Hispanic (79.0%, n = 25509); black, non-Hispanic (7%, n = 2263); Hispanic (3%, n = 1005); Asian or Pacific Islander (10%, n = 3127); and other (1%, n = 399). The mean age at first cancer diagnosis was 59 years (standard deviation: 12 years), and there were 1418 unique second breast cancer events.

Table 1. Characteristics of 117971 surveillance mammograms in 32331 women with a personal history of breast cancer

Characteristic	Values, n (%)
Age at mammography, yr	
< 40	1235 (1.1)
40–49	9465 (8.0)
50–59	27918 (23.7)
60–69	38449 (32.6)
70–79	27282 (23.1)
≥ 80	13622 (11.6)
Menopausal status*	
Post-menopausal	105612 (92.3)
Pre- or Peri-menopausal	8849 (7.7)
BI-RADS breast density†	
A: Almost entirely fatty	12009 (11.3)
B: Scattered fibroglandular tissue	52676 (49.4)
C: Heterogeneously dense	36508 (34.2)
D: Extremely dense	5469 (5.1)
Year of examination	
2007–2008	19088 (16.2)
2009–2010	27518 (23.3)
2011–2012	30104 (25.5)
2013–2014	31196 (26.4)
2015–2016	10065 (8.5)
Time since last mammogram‡, month	
No prior mammogram	2007 (1.7)
3 to < 9	21900 (18.6)
9 to < 15	82102 (69.6)
15 to < 27	9209 (7.8)
≥ 27	2753 (2.3)
Time since primary breast cancer diagnosis, yr	
1	13753 (11.7)
2	12357 (10.5)
3–4	20916 (17.7)
5–6	17020 (14.4)
7–9	20046 (17.0)
≥ 10	33879 (28.7)

*Missing: 3510/117971, 3.0%, †Missing: 11309/117971, 9.6%, ‡Either screening or diagnostic mammogram, no mammograms in prior 3 months by definition.
BI-RADS = Breast Imaging Reporting and Data System

Surveillance Mammography Follow-Up Outcomes

Overall, 23533 of the 117971 mammograms (20%) had a subsequent surveillance mammogram within one year. These surveillance mammograms with follow-up periods extending beyond the date of a subsequent surveillance mammogram occurred in all indication groups. Truncated follow-up at the next surveillance mammogram affected 68% of examinations with SIFU indications (7923/11709), 14% of screening (12136/86624), and 18% of breast problem indications (3474/19638) (Fig. 2). Most truncated follow-up periods ranged from 3 to < 9 months for SIFU (90%, 7152/7923) and breast problems (71%, 2452/3474) indications, consistent with semi-annual surveillance intervals. For screening indication mammograms, 59% (7212/12136) had a truncated follow-up of 9 to < 12 months, which is consistent with the early return of women to annual surveillance regimens.

With standard follow-up, 1597 surveillance mammograms had a second breast cancer diagnosis within one year (Table 2). With truncated follow-up, 179 of 1597 (11.2%) mammograms were reclassified. Among them, 89% (159/179) of the mammograms changed from false negatives to true negatives. The remaining 11% of the reclassified mammograms (20/179) shifted from TP to FP status. This resulted in 1418 surveillance mammograms matching the number of second breast cancers.

The reclassification of mammograms with a second breast cancer varied across the indication groups, from 7% for screening (68/1039) to 41% for SIFU mammograms (72/176). With truncated follow-up, the total number of interval cancers decreased from 579 at one-year follow-up to 420. This elimination of "overcounted" cancers represented a 27% reduction in interval cancers across all indication groups (159/579), with the reduction ranging from 15% for screening (53/355) to 62% for SIFU indications (67/108).

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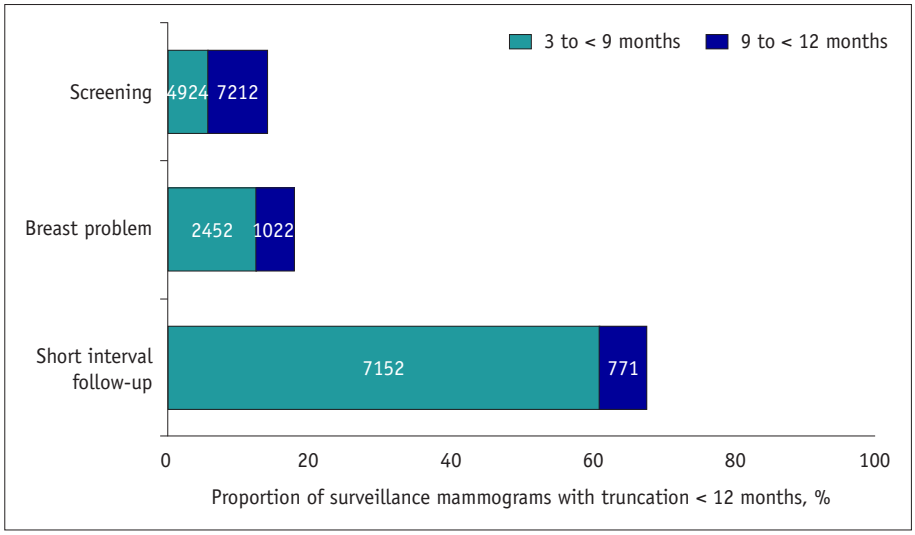

Fig. 2. Truncated follow-up by surveillance mammography indication. Among 117971 surveillance mammograms evaluated, 23533 (20%) had a subsequent surveillance mammogram within one year. For screening indication mammograms, truncated follow-up at the next mammogram occurred within 9 to < 12 months. For breast problems and short-interval follow-up mammograms, truncated follow-up at the next mammogram occurred within 3 to < 9 months.

Table 2. Surveillance mammograms and breast cancer status with standard or truncated follow-up, overall and by mammography indication

	Surveillance mammograms and cancer status			
	Overall	Screening	Breast problem	Short interval follow-up
Total surveillance mammograms	117971	86624	19638	11709
Surveillance mammograms with second breast cancer				
Standard one year follow-up	1597	1039	382	176
Truncated follow-up	1418	971	343	104
Decrease from standard to truncated follow-up	179	68	39	72
Surveillance detected second breast cancers				
Standard one year follow-up	1018	684	266	68
Truncated follow-up	998	679	256	63
Decrease from standard to truncated follow-up	20	5	10	5
Interval second breast cancers				
Standard one year follow-up	579	355	116	108
Truncated follow-up	420	292	87	41
Decrease from standard to truncated follow-up	159	53	29	67

The total number of cancers classified as surveillance-detected declined from 1018 with standard follow-up to 998 with truncated follow-up, representing a 2% overall decrease (20/1018), with the reduction range from 0.7% for screening (5/684) to 7% for SIFU indication (5/68). The remaining mammograms had unchanged breast cancer status with either standard or truncated follow-up.

Performance Measures with Standard One-Year versus Truncated Follow-Up Periods

With standard follow-up, the overall cancer detection rate was 8.6 per 1000 examinations, the interval cancer rate was 4.9 per 1000 examinations, the sensitivity was 63.7% (1018/1597), and the specificity was 98.1% (114172/116374) (Table 3). With truncated follow-up, the overall cancer detection rate declined slightly to 8.5 per 1000 examinations (difference of -0.2 per 1000 after rounding [95% CI -0.3, -0.1]) and the interval cancer rate declined from 4.9 to 3.6 per 1000 examinations (difference of -1.3 per 1000 [95% CI -1.6, -1.1]). Across the indication groups, the greatest decline in the interval cancer rate (per 1000) was observed for SIFU mammograms, decreasing from 9.2

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Table 3. Performance measures with standard versus truncated follow-up, overall and by recorded indication

	Overall	Screen	Breast problem	SIFU
Cancer detection rate per 1000 examinations				
Standard	8.6 (1018/117971)	7.9 (684/86624)	13.5 (266/19638)	5.8 (68/11709)
Truncated	8.5 (998/117971)	7.8 (679/86624)	13.0 (256/19638)	5.4 (63/11709)
Difference (95% CI)	-0.2 (-0.3, -0.1)	-0.06 (-0.1, -0.01)	-0.5 (-0.9, -0.1)	-0.4 (-0.8, -0.1)
Interval cancer rate per 1000 examinations				
Standard	4.9 (579/117971)	4.1 (355/86624)	5.9 (116/19638)	9.2 (108/11709)
Truncated	3.6 (420/117971)	3.4 (292/86624)	4.4 (87/19638)	3.5 (41/11709)
Difference (95% CI)	-1.3 (-1.6, -1.1)	-0.7 (-0.9, -0.5)	-1.5 (-2.0, -0.9)	-5.7 (-7.1, -4.4)
Sensitivity, %				
Standard	63.7 (1018/1597)	65.8 (684/1039)	69.6 (266/382)	38.6 (68/176)
Truncated	70.4 (998/1418)	69.9 (679/971)	74.6 (256/343)	60.6 (63/104)
Difference (95% CI)	6.6 (5.6, 7.7)	4.1 (3.1, 5.1)	5.0 (2.9, 7.1)	21.9 (16.3, 27.6)
Specificity, %				
Standard	98.1 (114172/116374)	98.7 (84499/85585)	95.6 (18418/19256)	97.6 (11255/11533)
Truncated	98.1 (114331/116553)	98.7 (84562/85653)	95.6 (18447/19295)	97.6 (11322/11605)
Difference (95% CI)	-0.1 (-0.2, -0.06)	-0.05 (-0.1, 0.002)	-0.04 (-0.08, -0.01)	-0.03 (-0.07, 0.01)

Values are presented with raw numbers in parentheses for the standard and truncated rows and 95% confidence interval (CI) for the difference rows.
SIFU = short-interval follow-up

with standard follow-up to 3.5 with truncated follow-up (difference of -5.7 per 1000 [95% CI -7.1, -4.4]). The overall sensitivity increased from 63.7% to 70.4% (difference of 6.6% [95% CI 5.6%, 7.7%]). When sensitivity across indication groups was examined, the SIFU indication showed the greatest increase in sensitivity from 38.6% to 60.6% with standard versus truncated follow-up (difference of 21.9% [95% CI 16.3%, 27.6%]). Specificity remained stable at 98.1%.

DISCUSSION

For surveillance mammography in United States community practice, we found that 20% of the surveillance mammograms had shared follow-up periods when the American College of Radiology recommendations for determining breast cancer outcomes were applied. Ending follow-up at the next surveillance mammogram if within one year, eliminated these shared follow-up periods and reduced the overestimation of interval cancer rates. Importantly, eliminating the shared follow-up time ensured that second breast cancers were associated with a single preceding mammogram, leading to a revised cancer status for some surveillance examinations, and the vast majority of mammograms with revised cancer status (89%) were reclassified from FN exams to TN exams. Sensitivity concomitantly increased without meaningful changes to the cancer detection rate or specificity.

It should be noted that the focus of our study was to improve the evaluation of surveillance diagnostic performance, accounting for variability in observed imaging use, whether related to the early return of patients at annual surveillance intervals or surveillance at intervals more frequent than one year. While 20% of mammograms were followed by another surveillance mammogram within one year, the overall observed pattern of care reflected guideline-concordant annual surveillance for the majority of patients in our dataset. In some clinical practices, reducing interval cancers after surveillance mammography included more frequent surveillance, either mammography at semiannual intervals [5] or mammography and MRI, alternating at six month intervals [19,20]. Current guidelines recommend surveillance mammography at annual intervals, and the results of this study do not imply that different recommendations are needed. Further research is needed to clarify which modalities and imaging intervals, tailored to patient characteristics and treatment regimens, improve surveillance imaging use and outcomes.

Our results suggest that non-screening indication use for mammography performed for asymptomatic surveillance and at more frequent than annual intervals contributed to the overestimation of interval cancer rates and underestimation of sensitivity when a standard one-year follow-up was applied for auditing outcomes and performance. In

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particular, SIFU indication mammograms showed the greatest decrease in the interval cancer rate (-5.7 per 1000) and increase in sensitivity (21.9%) when truncated follow-up was applied. The observed use of non-screening indications for surveillance mammography reflects clinical practice in the United States, where persistently increased interval cancer rates with surveillance mammography alone have motivated strategies aimed at reducing interval cancers. In a national survey of breast imaging facilities [6], 73% of the facilities offered diagnostic mammography every six months for women with breast cancer treated for 1–5 years before recommending a return to screening mammography.

Diagnostic indication coding for surveillance mammography also likely reflects insurance policies that may not cover screening mammograms performed more frequently than at annual intervals. A strength of this analysis is the inclusion of mammograms with diagnostic indications to more comprehensively reflect clinical practice, as well as the large, diverse sample of breast imaging facilities in the BCSC, linked to pathology databases, as well as state and regional tumor registries, to provide comprehensive capture of cancer outcomes for accurate assessment of performance. This analysis, in which 28% of surveillance mammograms performed in United States community practice had non-screening indications, corroborates the results of the national survey.

The observed surveillance mammography use patterns after breast cancer treatment are more heterogeneous than those in the overall screening population, and our results may be less applicable to population screening mammography, which is more consistently performed at annual or biennial intervals [21]. However, our findings have implications for other settings where screening is performed at more frequent intervals than one year, such as for multimodality strategies using MRI or ultrasound to supplement mammography screening for women at increased risk of breast cancer [22,23]. Similar issues of shared follow-up periods and breast cancer ascertainment can arise in these settings, with a single cancer potentially counted as a TP for one modality and a FN for another. Current auditing guidelines suggest that interval cancers detected with supplemental screening modalities or semiannual mammography are harms associated with the routine mammography examinations that do not detect asymptomatic cancers. Yet, these same interval cancers are concurrently counted as "screen-detected cancers" and considered to be a benefit ascribed to the supplemental imaging modality. This double-edged sword of interval cancers in multimodality screening and whether these cancers truly represent benefits versus harms of screening warrant further investigation and discussion among stakeholders in the breast imaging community.

A potential limitation of our evaluation was the possibility of misclassified examination indications. It is unclear whether the variability in performance measured across the indication groups of screening, breast problems, and SIFU reflects the different underlying prevalences of breast cancers across groups, the relatively small sample sizes of second cancers with correspondingly wide confidence intervals, differential mammography indication coding across facilities, or (most likely) a combination of these factors. Our extensive process of excluding mammograms associated with symptomatic presentation and the observation that truncated follow-up periods corresponded with semi-annual and annual surveillance intervals support the premise that the mammograms in our dataset were obtained for periodic surveillance of asymptomatic women.

In conclusion, when more than one mammogram is performed within an annual interval, shared follow-up periods that extend beyond the date of the next mammogram pose a challenge for breast cancer status ascertainment. Truncated follow-up at the next surveillance mammogram improved performance assessment and improved alignment with diagnostic outcomes by associating unique breast cancers with a single preceding examination. Our results have clinical practice implications beyond auditing surveillance mammography performance, to include multi-modality screening performance assessment and benchmarking to evaluate screening and surveillance effectiveness. It may also be relevant to international screening contexts, where some groups (including but not limited to women with a personal history of breast cancer) may undergo repeat screening within an annual interval.

Availability of Data and Material

The data underlying this article are available on reasonable request to the corresponding author and with approval from the Breast Cancer Surveillance Consortium, subject to appropriate regulatory approvals.

Conflicts of Interest

The authors have no potential conflicts of interest related to this study to disclose. Potential conflicts of interest unrelated to this study: Janie M. Lee grant from GE Healthcare; Jennifer M. Specht payment to author for

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Author Contributions

Conceptualization: Janie M. Lee, Diana S. M. Buist. Data curation: Diana S. M. Buist, Karla Kerlikowske, Erin J. A. Bowles, Tracy Onega, Laura E. Ichikawa. Formal analysis: Laura E. Ichikawa, Janie M. Lee, Diana S. M. Buist, Karen J. Wernli. Funding acquisition: Diana L. Miglioretti, Karla Kerlikowske, Anna N. A. Tosteson, Janie M. Lee, Diana S. M. Buist, Erin J. A. Bowles, Natasha K. Stout, Tracy Onega. Investigation: all authors. Methodology: Janie M. Lee, Diana S. M. Buist, Laura E. Ichikawa, Diana L. Miglioretti, Karla Kerlikowske, Karen J. Wernli. Project administration: Janie M. Lee, Diana S. M. Buist, Laura E. Ichikawa. Resources: Diana L. Miglioretti, Karla Kerlikowske. Software: Laura E. Ichikawa. Visualization: Laura E. Ichikawa. Writing—original draft: Janie M. Lee, Laura E. Ichikawa. Writing—review & editing: all authors.

ORCID iDs

Janie M. Lee
https://orcid.org/0000-0002-6452-8168
Laura E. Ichikawa
https://orcid.org/0000-0002-0882-6662
Karen J. Wernli
https://orcid.org/0000-0001-7945-0327
Erin J. A. Bowles
https://orcid.org/0000-0001-6287-7391
Jennifer M. Specht
https://orcid.org/0000-0003-1484-2113
Karla Kerlikowske
https://orcid.org/0000-0001-8793-8779
Diana L. Miglioretti
https://orcid.org/0000-0002-5547-1833
Kathryn P. Lowry
https://orcid.org/0000-0002-0840-7855
Anna N. A. Tosteson
https://orcid.org/0000-0001-7718-8943
Natasha K. Stout
https://orcid.org/0000-0002-7946-5649
Nehmat Houssami
https://orcid.org/0000-0002-3641-952X
Tracy Onega
https://orcid.org/0000-0002-1633-3040
Diana S. M. Buist
https://orcid.org/0000-0001-5408-2804

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