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Digital Mammography and Breast Tomosynthesis Performance in Women with a Personal History of Breast Cancer, 2007–2016

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

See also the editorial by Moy and Gao in this issue.

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Background: Since 2007, digital mammography and digital breast tomosynthesis (DBT) replaced screen-film mammography. Whether these technologic advances have improved diagnostic performance has, to the knowledge of the authors, not yet been established.

Purpose: To evaluate the performance and outcomes of surveillance mammography (digital mammography and DBT) performed from 2007 to 2016 in women with a personal history of breast cancer and compare with data from 1996 to 2007 and the performance of digital mammography screening benchmarks.

Materials and Methods: In this observational cohort study, five Breast Cancer Surveillance Consortium registries provided prospectively collected mammography data linked with tumor registry and pathologic outcomes. This study identified asymptomatic women with American Joint Committee on Cancer anatomic stages 0–III primary breast cancer who underwent surveillance mammography from 2007 to 2016. The primary outcome was a second breast cancer diagnosis within 1 year of mammography. Performance measures included the recall rate, cancer detection rate, interval cancer rate, positive predictive value of biopsy recommendation, sensitivity, and specificity.

Results: Among 32 331 women who underwent 117 971 surveillance mammographic examinations (112 269 digital mammographic examinations and 5702 DBT examinations), the mean age at initial diagnosis was 59 years ± 12 (standard deviation). Of 1418 second breast cancers diagnosed, 998 were surveillance-detected cancers and 420 were interval cancers. The recall rate was 8.8% (10 365 of 117 971; 95% CI: 8.6%, 9.0%), the cancer detection rate was 8.5 per 1000 examinations (998 of 117 971; 95% CI: 8.0, 9.0), the interval cancer rate was 3.6 per 1000 examinations (420 of 117 971; 95% CI: 3.2, 3.9), the positive predictive value of biopsy recommendation was 31.0% (998 of 3220; 95% CI: 29.4%, 32.7%), the sensitivity was 70.4% (998 of 1418; 95% CI: 67.9%, 72.7%), and the specificity was 98.1% (114 331 of 116 553; 95% CI: 98.0%, 98.2%). Compared with previously published studies, interval cancer rate was comparable with rates from 1996 to 2007 in women with a personal history of breast cancer and was higher than the published digital mammography screening benchmarks.

Conclusion: In transitioning from screen-film to digital mammography and digital breast tomosynthesis, surveillance mammography performance demonstrated minimal improvement over time and remained inferior to the performance of screening mammography benchmarks.

Online supplemental material is available for this article.

Women with a personal history of breast cancer are at risk for second breast cancer events, consisting of either recurrences or new primary breast cancers (1,2). Surveillance mammography in women with treated breast cancer is conducted with the aim of detecting second breast cancers while women are asymptomatic, enabling earlier treatment to extend survival and quality of life (3–5). The Breast Cancer Surveillance Consortium (BCSC) previously reported lower sensitivity for surveillance mammography of asymptomatic women with a personal history of breast cancer (65.4%), compared with screening mammography in women without this history (76.5%) (6),

Abbreviations

BCSC = Breast Cancer Surveillance Consortium, BI-RADS = Breast Imaging Reporting and Data System, DBT = digital breast tomosynthesis, SIFU = short-interval follow-up

Summary

In transitioning from screen-film to digital mammography and digital breast tomosynthesis, surveillance mammography performance demonstrated minimal improvement over 2 decades (1996–2007 and 2007–2016) and remained inferior to digital mammography screening benchmarks.

Key Results

- In a prospective observational cohort study of 32 331 asymptomatic women with a personal history of breast cancer (stages 0–III), the diagnostic performance metrics of 117 971 surveillance mammographic examinations (112 269 digital mammographic examinations, 5702 digital breast tomosynthesis examinations) from 2007 to 2016 were comparable with those from 1996 to 2007, and interval cancer rates were higher than screening mammography benchmarks.
- Thirty percent (420 of 1418) of second breast cancers were diagnosed as interval cancers after surveillance mammography with negative results, and characteristics were associated with worse prognoses.

with primarily screen-film examinations performed from 1996 to 2007. Interval cancer rates were also higher in women with versus without a personal history of breast cancer (3.6 vs 1.4 per 1000 examinations, respectively). Since then, digital mammography and digital breast tomosynthesis (DBT) have replaced film mammography. The evidence about whether these technologic advances have improved surveillance mammography performance is sparse. In particular, DBT surveillance reports have been single-institution retrospective studies (7,8). Our purpose was to evaluate the diagnostic performance and outcomes of digital mammography and DBT for surveillance in women with a personal history of breast cancer from 2007 to 2016 in facilities across the United States representing community practice and compare these with surveillance data from 1996 to 2007 by using primarily film mammography (6) and digital mammography screening benchmarks (9).

Materials and Methods

Study Setting and Participants

Five BCSC (10) registries (Carolina Mammography Registry, Kaiser Permanente Washington, New Hampshire Mammography Network, San Francisco Mammography Registry, and Vermont Breast Cancer Surveillance System) prospectively collected data through either passive consent (three registries) or waiver of written informed consent (two registries). BCSC registries and the BCSC Statistical Coordinating Center received institutional review board approval to enroll participants and perform analyses by using 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 epidemiologic and end results programs, and local biopsy and pathologic databases. All procedures were Health Insurance Portability and Accountability Act compliant.

We included women age 18 years or older with primary breast cancer at anatomic stages 0–III, as defined by the eighth edition of the American Joint Committee on Cancer staging manual (11), who were diagnosed from 1988 onward and underwent definitive surgery (lumpectomy or mastectomy, but not bilateral mastectomy) and surveillance mammography more than 6 months after the primary breast cancer diagnosis. Additional details of data collected on characteristics of women and primary breast cancers are described in Appendix E1 (online).

Surveillance Mammography

Mammographic examinations (digital mammography or DBT) performed from 2007 to 2016 that were performed 6 months or longer after the primary breast cancer diagnosis were included for analysis. The American College of Radiology (12) specifies that screening or diagnostic examination codes may be used for mammography performed in asymptomatic surveillance of women with treated breast cancer. Therefore, we included facility-reported indication categories of screening and short-interval follow-up (SIFU) or evaluation of breast problems likely performed for asymptomatic surveillance by requiring no mammography in the prior 90 days and no self-report of symptoms other than generalized pain (13–16). Indication coding for mammographic examinations occurred at the discretion of each facility, and there were no efforts to coordinate clinical operations or policy through the BCSC. Additional details and exclusions at the examination level are described in Appendix E1 (online) and Figure 1.

The unit of analysis was the surveillance mammographic examination (17). A previous BCSC report of screening mammography performance in women with treated breast cancer (6) included mammographic examinations indicated for screening only from 1996 to 2007 with primarily film mammography. Our analysis focused solely on digital mammographic examinations performed with either two-dimensional digital mammography or DBT, with examinations performed from 2007 to 2016. Another BCSC study that compared the performance of mammography with the performance of MRI in women with a personal history of breast cancer (18) included only mammographic examinations with screening indication performed from 2005 to 2012 for women diagnosed with breast cancer in 2003 or later is distinct from the current analysis, which included examinations indicated for reasons other than screening that were likely performed for surveillance in women diagnosed with breast cancer as early as 1988 allowing for evaluation of performance for examinations conducted 10 years or longer after diagnosis. For each mammographic examination, women were followed for 12 months or until the next surveillance examination, whichever occurred earlier. Second breast cancers were identified as the earliest diagnosis of ductal carcinoma in situ or invasive breast cancer longer than 6 months after the primary breast cancer diagnosis date.

Statistical Analysis

Because surveillance mammography had either screening or diagnostic indications, performance metrics were based on the American College of Radiology Breast Imaging Reporting and

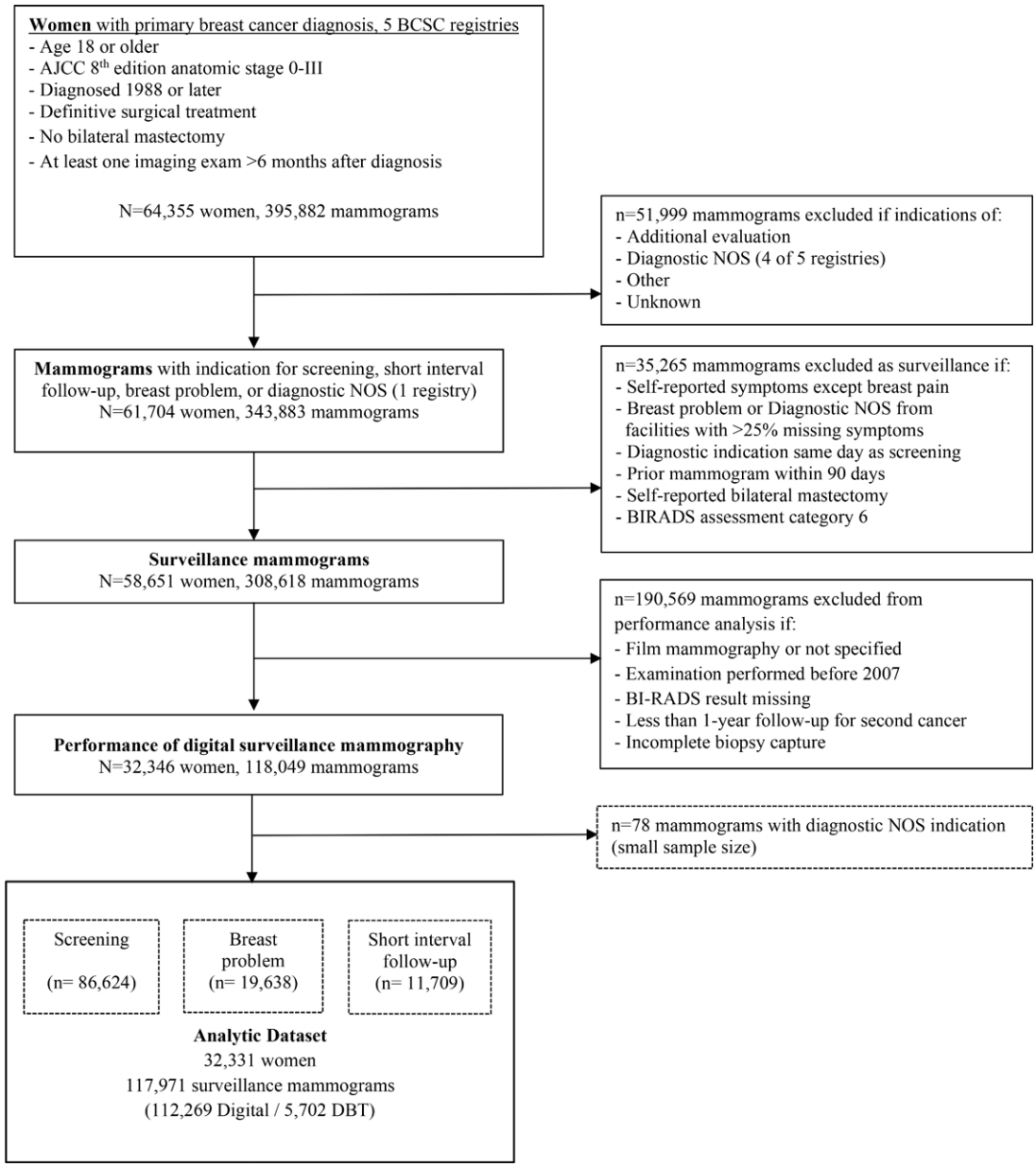

Figure 1: Diagram of study cohort. AJCC = American Joint Committee on Cancer, BCSC = Breast Cancer Surveillance Consortium, BI-RADS = Breast Imaging Reporting and Data System, DBT = digital breast tomosynthesis, NOS = not otherwise specified.

Data System (BI-RADS) (17) final-assessment categories. Final-assessment categories of 4 (suspicious) or 5 (highly suspicious) were considered to indicate positive results, and assessment categories of 1 (negative), 2 (benign), or 3 (probably benign) were considered to indicate negative results. Women with examinations resulting in a BI-RADS category 0 (needs additional evaluation) assessment result were followed up for up to 90 days to obtain the first nonzero BI-RADS assessment result. Examinations with findings that could not be resolved to a nonzero assessment result were excluded. The only performance metric using a different positivity criterion was recall rate for additional imaging. For the recall rate, a BI-RADS end-of-day assessment result of 1 or 2 was considered a negative result, and a BI-RADS end-of day assessment result of 0, 3, 4, or 5 was considered a positive result.

The recall, cancer detection rate, interval cancer rate, positive predictive value of biopsy recommendation, sensitivity, and specificity were calculated overall (Table E1 [online]) and stratified by indication (13). For each indication, we also calculated performance stratified by the primary breast cancer mode of detection and stage, the BI-RADS breast density at surveillance mammography, and the time since primary breast cancer diagnosis. The exact 95% CI was calculated for sensitivity because some strata had a small number of women who contributed at most a single observation. CIs for other performance measures were calculated from a log binomial model estimated with generalized estimation equations assuming an independent working correlation structure to account for multiple examinations per woman (19). For screening indication examinations, we also compared the performance of digital mammography and DBT subgroups

in an exploratory analysis, including only digital mammographic examinations from the same facilities and period during which DBT was performed. Sensitivity analysis excluded ipsilateral recurrences in women treated with mastectomy because the mastectomy side is not routinely included in surveillance mammographic examinations. We also compared the tumor characteristics and stages of surveillance-detected and interval second cancers.

We compared surveillance performance measures with prior BCSC studies of women with a personal history of breast cancer by using primarily film mammography (6), digital mammography screening benchmarks (9), and a sensitivity analysis with the positivity criterion of BI-RADS final assessment results of 3, 4, or 5 (any follow-up outcome besides a return to routine surveillance) (20).

Analyses were performed by using statistical software (SAS version 9.4; SAS Institute).

Results

Characteristics of Women and Surveillance Mammography

We identified 32 331 women, 21% (6794 of 32 303) of whom were of a minority race or ethnicity (Table 1). The mean age at initial diagnosis was 59 years ± 12 (standard deviation), and 20.8% (2914 of 14 041) had a first-degree family history of breast cancer. Primary breast cancers were mostly screen detected (63.4%; 12 754 of 20 129) and early stage (86.8% with stages 0–IIA; 28 079 of 32 331) with invasive ductal carcinoma histologic characteristics (66.5%; 21 485 of 32 331), positive hormone receptor status (84.3%; 23 052 of 27 359), and negative human epidermal growth factor receptor 2 receptor status (84.8%; 12 357 of 14 580). The primary surgical procedure was lumpectomy, with or without radiation therapy, in 73.1% of women (23 638 of 32 331). Most women (62.8%; 19 156 of 30 525) underwent some systemic treatment: endocrine therapy, chemotherapy, or both.

Of the 117 971 surveillance mammographic examinations that met inclusion and exclusion criteria (Fig 1), 112 269 (95.2%) were digital mammographic examinations and 5702 (4.8%) were DBT examinations. Most had screening indication (73.4%; 86 624 of 117 971), with other indications in order of prevalence including evaluation of breast problems (16.6%; 19 638 of 117 971) and SIFU (9.9%; 11 709 of 117 971) (Table 2). Most mammographic examinations were performed within 15 months of a previous examination; 39.4% (41 977 of 106 662) of examinations were classified as demonstrating dense tissue (heterogeneously or extremely dense breasts). Mammographic examinations performed for nonscreening indications were more likely to occur within 4 years of diagnosis; 78.2% (9159 of 11 709) of SIFU examinations and 43.8% (8608 of 19 638) of breast problem–related examinations occurred within this period compared with screening indication examinations (33.8%; 29 259 of 86 624).

Surveillance Mammography Overall Performance

The surveillance mammography recall rate was 8.8% (10 365 of 117 971; 95% CI: 8.6%, 9.0%; Table 3). The cancer detection rate was 8.5 per 1000 examinations (998 of 117 971; 95% CI: 8.0, 9.0). The interval cancer rate was 3.6 per 1000 examinations (420 of 117 971; 95% CI: 3.2, 3.9). The sensitivity was 70.4% (998 of 1418; 95% CI: 67.9%, 72.7%), and the specificity was 98.1% (114 331 of 116 553; 95% CI: 98.0%, 98.2%). Sensitivity was higher for ductal carcinoma in situ (83.6%; 296 of 354; 95% CI: 79.3%, 87.3%) than for invasive breast cancer (66.0%; 702 of 1064; 95% CI: 63.0%, 68.8%). The positive predictive values for biopsy recommendation and biopsy performance were 31.0%

Table 1: Characteristics of Women with Personal History of Breast Cancer

Variable	No. of Missing Women	No. of Women
Demographic information		
Age at diagnosis (y)	0 (0)	
<40		1384 (4.3)
40–49		6704 (20.7)
50–59		9449 (29.2)
60–69		8356 (25.9)
70–79		4857 (15.0)
80+		1581 (4.9)
Year of diagnosis	0 (0)	
1988–2000		7760 (24.0)
2001–2005		8249 (25.5)
2006–2010		10 496 (32.5)
2011–2015		5826 (18.0)
Race/ethnicity	28 (0.1)	
White, non-Hispanic		25 509 (79.0)
Black, non-Hispanic		2263 (7.0)
Hispanic		1005 (3.1)
Asian, Pacific Islander		3127 (9.7)
Other		399 (1.2)
First-degree family history at diagnosis*	18 290 (56.6)	
No		11 127 (79.3)
Yes		2914 (20.8)
Primary breast cancer characteristics		
Mode of detection	12 202 (37.7)	
Screen detected		12 754 (63.4)
Interval cancer†		5329 (26.5)
Clinically detected		2046 (10.2)
AJCC stage	0 (0)	
DCIS		6807 (21.1)
I		15 263 (47.2)
IIA (includes II NOS)		6009 (18.6)

Table 1 *(continues)*

Table 1 *(continued)*: Characteristics of Women with Personal History of Breast Cancer

Variable	No. of Missing Women	No. of Women
IIB-IIIC		4252 (13.2)
Histologic characteristics	0 (0)	
DCIS		6807 (21.1)
Invasive ductal		21 485 (66.5)
Invasive lobular		1953 (6.0)
Invasive mixed		2026 (6.3)
Invasive type unknown		60 (0.2)
Grade	2881 (8.9)	
Grade I		7107 (24.1)
Grade II		12 463 (42.3)
Grade III		9880 (33.6)
ER/PR status	4972 (15.4)	
ER positive or PR positive		23 052 (84.3)
ER negative and PR negative		4307 (15.7)
HER2 status	17 751 (54.9)	
Negative		12 357 (84.8)
Positive		2223 (15.3)
Primary surgery	0 (0)	
Mastectomy		8693 (26.9)
Breast-conserving with radiation		17 849 (55.2)
Breast-conserving without radiation		5371 (16.6)
Breast-conserving, radiation data missing		418 (1.3)
Systemic treatment	1806 (5.6)	
None		11 369 (37.2)
Chemotherapy only		5190 (17.0)
Endocrine therapy only		9783 (32.1)
Chemotherapy and Endocrine therapy		4183 (13.7)

Note.—Included were 32 331 women. Data are number of women and data in parentheses are percentages. AJCC = American Joint Committee on Cancer, DCIS = ductal carcinoma in situ, ER = estrogen receptor, HER2 = human epidermal growth factor receptor 2, NOS = not otherwise specified, PR = progesterone receptor.

* Information was obtained at the time of the most recent mammographic examination within 2 years before breast cancer diagnosis using the screening mammogram if available; otherwise, the diagnostic mammogram was used.

† "Interval" includes interval in screening; if no screening mammography was performed within 12 months, "interval" includes diagnostic imaging performed within 6 months prior to first breast cancer diagnosis and self-report of a prior mammographic examination within 12–27 months.

(998 of 3220; 95% CI: 29.4, 32.7) and 32.9% (773 of 2349; 95% CI: 31.0%, 34.9%), respectively.

Forty-eight local recurrences after mastectomy were identified. Sensitivity analysis excluding these local recurrences demonstrated only slight changes in performance estimates. Cancer detection and interval cancer rates remained comparable at 8.4 per 1000 (991 of 117 923) and 3.2 per 1000 (379 of 117 923) screens, respectively.

Surveillance Mammography Performance by Indication

Across indications, the recall rate varied from 7.5% (6499 of 86 624) for screening to 16.3% (1908 of 11 709) for SIFU (Table 3). The higher recall rate for SIFU examinations was related to the definition of a positive examination result to include probably benign (BI-RADS category 3) assessment results because multiple SIFU examinations were often performed before a recommendation to return to routine screening was provided. This increased the overall recall rate from 7.5% in screening indication examinations to 8.8% overall. The cancer detection rate per 1000 examinations ranged from 5.4 (63 of 11 709) for SIFU examinations to 13.0 (256 of 19 638) for breast problem–related examinations. The interval cancer rate per 1000 examinations ranged from 3.4 (292 of 86 624) for screening examinations to 4.4 (87 of 19 638) for breast problem–related examinations. The sensitivity ranged widely from 60.6% (63 of 104) for SIFU examinations and 69.9% (679 of 971) for screening examinations to 74.6% (256 of 343) for the breast problem–related examinations. The specificity varied less, spanning from 95.6% (18 447 of 19 295) for breast problem–related examinations to 98.7% (84 562 of 85 653) for screening examinations. The positive predictive values of biopsy recommendation and biopsy performance were lower for nonscreening examinations, reducing the positive predictive values of biopsy recommendation and biopsy performance percentages to 31.0% (998 of 3220) and 32.9% (773 of 2349) in the overall group, respectively, compared with 38.4% (679 of 1770) and 38.0% (529 of 1392) in the screening indication–only subgroup, respectively.

Comparison with Other Studies

Surveillance mammographic examinations were restricted to those screening indication only for comparison with other studies (Table E2 [online]). Compared with a previous BCSC study of primarily screen-film mammography during 1996–2007 in women with a personal history of breast cancer (6), the cancer detection rate per 1000 examinations was higher in the current study (7.8 [679 of 86 824] vs 6.8 [402 of 58 830]), but interval cancer rates per 1000 examinations were comparable (3.4 [292 of 86 624] in the current study vs 3.6 [213 of 58 830]). The sensitivity and specificity were also slightly higher in the current study but had overlapping 95% CIs. Sensitivity analysis by using a positivity criterion of any recommendation for nonroutine follow-up (20), including SIFU (BI-RADS category 3), indicated that the cancer detection rate per 1000 examinations increased from 7.8 (679 of 86 824) to 8.1 (699 of 86 624) and that sensitivity increased from 69.9% (679 of 971) to 72.0% (699 of 971), whereas the interval cancer rate per 1000 examinations decreased from 3.4 (292 of 86 624) to 3.1 (272 of 86 624), and the specificity decreased from 98.7% (84 562 of 85 653) to 96.0% (82 233 of 85 653).

Stratified Analyses

Separate analyses for each indication, stratified by woman and tumor characteristics, are presented in Tables E3–E5 (online). For screening indication examinations, the sensitivity increased with the time since the primary breast cancer diagnosis from 63.1% (197 of 312) within the first 5 years to 77.8% (280 of 360) beyond 10 years, but interval cancer rates remained stable (range, 3.2 [115 of 35 561] to 3.4 [80 of 23 874] per 1000 examinations). The interval cancer rate in this subgroup varied with the primary breast cancer mode of detection, being higher with interval detection (5.1 [72 of 14 109] per 1000) or clinical presentation (6.0 [25 of 4152] per 1000) than with screening detection (2.3 [86 of 36 615] per 1000) (Table E6 [online]).

Interval cancer rates across indication subgroups were also higher for advanced-stage primary breast cancers detected by using screening examinations (4.8 [52 of 10 864] per 1000) and breast problem–related examinations (4.5 [10 of 2225] per 1000). When considering breast density, interval cancer rates were lowest among women with mammographic examination results depicting almost entirely fatty breasts (0.7 [one of 1444] to 2.3 [21 of 9105] per 1000 examinations across indications), whereas interval cancer rates among women with mammographic examination results that depicted extremely dense breasts were more than twofold higher (5.4 [eight of 1478] to 9.4 [five of 532] per 1000 across indications). Within the screening indication-only subgroup, an exploratory analysis comparing DBT examinations (n = 5554) with digital mammographic examinations (n = 6125) from the same period and facilities showed no difference in crude performance on the basis of the inclusion of 0 in the 95% CIs.

Second Breast Cancer Characteristics

Among 1418 second breast cancers, the median number of years since the primary breast cancer diagnosis was 7.9 years (interquartile range, 3.7–12.5 years); 998 second breast cancers were surveillance-detected cancers and 420 were interval cancers (Table 4). Most second cancers were invasive, small (<20 mm), hormone receptor–positive, and early-stage (0–IIA) cancers. However, interval cancers were more likely to be larger (>20 mm) and to be associated with a hormone receptor–negative and lymph node–positive status. Consequently, more interval cancers were at stage IIB or higher compared with surveillance-detected cancers. An example of an interval second breast cancer manifesting with a palpable lump 10 months after a negative surveillance mammographic examination result is shown in Figure 2. Among the 420 interval cancers, 37 cancers (8.8%) were asymptomatically detected by using a screening breast MRI during the follow-up period after mammography. No interval cancers were detected by using screening breast US during the same follow-up period.

Discussion

We purposefully used an expanded surveillance mammography definition to capture examinations more comprehensively (13), and 27% of mammography in our data set was performed for nonscreening indications. In evaluating digital mammography surveillance performance from 2007 to 2016, we found little improvement in sensitivity and little reduction in interval cancer rates compared with the sensitivity and rates from a previous study from the preceding decade that primarily assessed film mammography (6). Overall, surveillance mammography enabled detection of the majority of second breast cancers, most with characteristics associated with a good prognosis. Although these results suggest that surveillance mammography provides a benefit in terms of earlier and potentially less morbid treatment of second breast cancers, approximately 30% (420 of 1418) of second breast cancers were diagnosed within a year after a negative surveillance mammography result, and these cancers had characteristics that were associated with a poorer prognosis. Because guidelines recommend mammography as the main breast

Table 2: Characteristics of Surveillance Mammography Examinations

Variable	No. Missing	No. of Examinations	No. of Examinations per Indication		
			Screening	Breast Problem	SIFU
Total		117 971	86 624	19 638	11 709
Demographic characteristics					
Age at mammography (y)	0 (0)				
<40		1235 (1.1)	579 (0.7)	397 (2.0)	259 (2.2)
40–49		9465 (8.0)	5751 (6.6)	2188 (11.1)	1526 (13.0)
50–59		27 918 (23.7)	19 514 (22.5)	5174 (26.4)	3230 (27.6)
60–69		38 449 (32.6)	28 838 (33.3)	6041 (30.8)	3570 (30.5)
70–79		27 282 (23.1)	21 116 (24.4)	3952 (20.1)	2214 (18.9)
≥80		13 622 (11.6)	10 826 (12.5)	1886 (9.6)	910 (7.8)
Menopausal status	3510 (3.0)				
Postmenopausal		105 612 (92.3)	78 828 (93.7)	16 824 (88.6)	9960 (87.9)
Pre- or perimenopausal		8849 (7.7)	5316 (6.3)	2164 (11.4)	1369 (12.1)
BMI group (kg/m^2)	40 951 (34.7)				
Underweight, <18.5		1600 (2.1)	1110 (2.0)	328 (2.4)	162 (2.0)
Normal, 18.5–24.9		34 733 (45.1)	23 380 (42.3)	7630 (55.3)	3723 (46.9)

Table 2 *(continues)*

Table 2 *(continued)*: Characteristics of Surveillance Mammography Examinations

Variable	No. Missing	No. of Examinations	No. of Examinations per Indication		
			Screening	Breast Problem	SIFU
Overweight, 25.0–29.9		22 443 (29.1)	16 570 (30.0)	3711 (26.9)	2162 (27.2)
Obesity I, 30.0–34.9		11 006 (14.3)	8570 (15.5)	1300 (9.4)	1136 (14.3)
Obesity II, 35–39.9		4460 (5.8)	3463 (6.3)	535 (3.9)	462 (5.8)
Obesity III, ≥40		2778 (3.6)	2185 (4.0)	294 (2.1)	299 (3.8)
Income*	8293 (7.0)				
<$60 000		24 885 (22.7)	19 910 (25.7)	2967 (15.4)	2008 (17.8)
$60 000 to <$80 000		29 004 (26.4)	22 220 (28.1)	4067 (21.2)	2717 (24.1)
$80 000 to <$100 000		24 905 (22.7)	16 735 (21.2)	5285 (27.4)	2885 (25.6)
≥$100 000		30 884 (28.2)	20 244 (25.6)	6978 (36.2)	3662 (32.5)
Education	13 019 (11.0)				
Less than high school		5916 (5.6)	4503 (6.0)	943 (5.1)	470 (4.3)
High school or GED		20 147 (19.2)	16 450 (21.8)	2196 (11.8)	1501 (13.8)
Some college, technical		26 745 (25.5)	19 640 (26.0)	4425 (23.8)	2680 (24.6)
College graduate		52 144 (49.7)	34 898 (46.2)	11 013 (59.3)	6233 (57.3)
Imaging characteristics					
BI-RADS breast density	11 309 (9.6)				
Almost entirely fatty		12 009 (11.3)	9105 (11.3)	1460 (9.3)	1444 (13.7)
Scattered fibroglandular tissue		52 676 (49.4)	41 016 (51.1)	6791 (43.1)	4869 (46.2)
Heterogeneously dense		36 508 (34.2)	26 771 (33.3)	6044 (38.3)	3693 (35.0)
Extremely dense		5469 (5.1)	3459 (4.3)	1478 (9.4)	532 (5.1)
Year of examination	0 (0)				
2007–2008		19 088 (16.2)	12 983 (15.0)	3994 (20.3)	2111 (18.0)
2009–2010		27 518 (23.3)	19 632 (22.7)	4801 (24.5)	3085 (26.4)
2011–2012		30 104 (25.5)	21 966 (25.4)	5239 (26.7)	2899 (24.8)
2013–2014		31 196 (26.4)	23 498 (27.1)	5025 (25.6)	2673 (22.8)
2015–2016		10 065 (8.5)	8545 (9.9)	579 (3.0)	941 (8.0)
Time since last mammographic examination† (mo)	0 (0)				
No prior mammographic examination		2007 (1.7)	1761 (2.0)	163 (0.8)	83 (0.7)
3 to <9		21 900 (18.6)	8372 (9.7)	3377 (17.2)	10 151 (86.7)
9 to <15		82 102 (69.6)	66 998 (77.3)	13 794 (70.2)	1310 (11.2)
15 to <27		9209 (7.8)	7232 (8.4)	1847 (9.4)	130 (1.1)
≥27		2753 (2.3)	2261 (2.6)	457 (2.3)	35 (0.3)
Time since primary breast cancer diagnosis (y)	0 (0)				
1		13 753 (11.7)	7724 (8.9)	2625 (13.4)	3404 (29.1)
2		12 357 (10.5)	7711 (8.9)	2227 (11.3)	2419 (20.7)
3–4		20 916 (17.7)	13 824 (16.0)	3756 (19.1)	3336 (28.5)
5–6		17 020 (14.4)	12 385 (14.3)	3253 (16.6)	1382 (11.8)
7–9		20 046 (17.0)	16 408 (18.9)	3132 (16.0)	506 (4.3)
≥10		33 879 (28.7)	28 572 (33.0)	4645 (23.7)	662 (5.7)

Note.—Data in parentheses are percentages. Percentages may not sum to 100% due to rounding. BI-RADS = Breast Imaging Reporting and Data System, BMI = Body mass index, GED = General Education Development, SIFU = short-interval follow-up.

* Annual median income in a woman's zip code on the date of mammography based on 2007–2011 American Community Survey data.

† Either screening or diagnostic mammography, no mammography in prior 3 months by definition.

surveillance imaging modality for women with treated breast cancer (21), our findings are relevant to current clinical practice, highlighting that technical advances over the last decade may not have improved surveillance outcomes.

In comparing our results for the subgroup of women with a personal history of breast cancer who underwent screening indication–only surveillance mammography with screening digital mammography benchmarks from 2007 to 2013 (9), for which 95% of examinations were performed in women without a personal history of breast cancer, we found that the surveillance mammography sensitivity of 69.9% (679 of 971) was substantially lower than the screening benchmark sensitivity

Table 3: Performance Measures and Outcomes

Parameter	Overall	Screening	Breast Problem	SIFU
No. of surveillance mammographic examinations	117 971	86 624	19 638	11 709
Recall rate* (%)	8.8 (10 365/117 971 [8.6, 9.0]	7.5 (6499/86 624) [7.3, 7.7]	10.0 (1958/19 638) [9.5, 1054]	16.3 (1908/11 709) [15.5, 17.0]
Cancer detection rate per 1000	8.5 (998/117 971) [8.0, 9.0]	7.8 (679/86 624) [7.3, 8.4]	13.0 (256/19 638) [11.5, 14.7]	5.4 (63/11 709) [4.2, 6.9]
Interval cancer rate per 1000	3.6 (420/117 971 [3.2, 3.9]	3.4 (292/86 624) [3.0, 3.8]	4.4 (87/19 638) [3.6, 5.5]	3.5 (41/11 709) [2.6, 4.8]
Interval invasive cancer rate per 1000	3.1 (362/117 971) [2.8, 3.4]	3.0 (260/86 624) [2.7, 3.4]	3.5 (68/19 638) [2.7, 4.4]	2.9 (34/11 709) [2.1, 4.1]
Overall cancer rate per 1000	12.0 (1418/117 971) [11.4, 12.7]	11.2 (971/86 624) [10.5, 11.9]	17.5 (343/19 639) [15.7, 19.4]	8.9 (104/11 709) [7.3, 10.8]
Sensitivity (%)				
Overall	70.4 (998/1418) [67.9, 72.7]	69.9 (679/971) [66.9, 72.8]	74.6 (256/343) [69.7, 79.2]	60.6 (63/104) [50.5, 70.0]
Invasive second cancer	66.0 (702/1064) [63.0, 68.8]	65.3 (490/750) [61.8, 68.7]	72.2 (177/245) [66.2, 77.8]	50.7 (35/69) [38.4, 63.0]
DCIS second cancer	83.6 (296/354) [79.3, 87.3]	85.5 (189/221) [80.2, 89.9]	80.6 (79/98) [71.4, 87.9]	80.0 (28/35) [63.1, 91.6]
Specificity (%)	98.1 (114 331/116 553) [98.0, 98.2]	98.7 (84 562/85 653) [98.6, 98.8]	95.6 (18 447/19 295) [95.2, 96.0]	97.6 (11 322/11 605) [97.3, 97.9]
PPV2 (%)	31.0 (998/3220) [29.4, 32.7]	38.4 (679/1770) [36.2, 40.7]	23.2 (256/1104) [20.7, 26.0]	18.2 (63/346) [14.5, 22.8]
PPV3 (%)	32.9 (773/2349) [31.0, 34.9]	38.0 (529/1392) [35.5, 40.6]	26.7 (189/708) [23.6, 30.2]	22.1 (55/249) [17.5, 27.0]

Note.—Data in parentheses are numerator/denominator; data in brackets are 95% CIs. DCIS = ductal carcinoma in situ, PPV2 = positive predictive value of biopsy recommendation, PPV3 =positive predictive value of biopsy performance, SIFU = short-interval follow-up.

* American College of Radiology Breast Imaging Reporting and Data System end-of-day assessment result of 0, 3, 4, or 5.

of 86.9% (8529 of 9812). Although the use of surveillance mammography enabled higher cancer detection rates, resulting in detection of almost three additional cancers per 1000 examinations (7.8 [679 of 86 624] vs 5.1 [8529 of 1 682 504] per 1000 screening examinations), interval cancer detection rates were also substantially higher with the use of surveillance mammography compared with the use of screening mammography (3.4 [292 of 86 624] vs 0.8 [1283 of 1 682 504] per 1000 examinations). When an alternative positivity criterion similar to that of screening mammography (20) was used, the sensitivity increased and the interval cancer rate decreased. However, the 95% CIs for surveillance performance did not overlap with those of digital mammography screening benchmarks (9), suggesting that substantially poorer performance remained. Our results were also comparable with an additional analysis of women with a personal history of breast cancer in the BCSC who underwent mammography between 2005 and 2012 (18), 80% of which were digital examinations.

Stratified analyses indicated that cancer detection varied substantially by factors known at the time of primary breast cancer diagnosis, highlighting identifiable factors that may be used to select supplemental surveillance strategies for subgroups of women who experienced poor surveillance performance. For example, interval second breast cancer rates were higher in women whose first cancers had an interval or clinical mode of detection. These results suggest that aggressive biological characteristics in a woman's first breast cancer, which influences detection at screening mammography (22–25), likely continue to mediate her subsequent outcomes (26). Previous reports identified interval presentation of first breast cancers as an independent predictor of interval invasive second breast cancer risk in multivariable analysis, including adjustment for age and breast density (27,28). Sensitivity was also higher for mammographic examinations of women with a second cancer diagnosis of ductal carcinoma in situ.

Breast density at surveillance was another important mediator of mammography performance. Across indications, lower sensitivity and higher interval second cancer rates were observed for women with extremely dense breasts. The highest density category was identified in approximately 5% of surveillance examinations. These results in the surveillance setting are analogous to results from screening women without a history of breast cancer. A recent report of screening mammography with both digital mammography and DBT (29) found that in women with extremely dense breasts of any age, no increase in cancer detection rate was obtained by using DBT. Another study of screening DBT (30) found that the cancer detection rate was increased for women with dense versus nondense breasts but did not report stratified analyses between heterogeneously dense and extremely dense subgroups. Our results suggested a potential role

Table 4: Characteristics of Second Breast Cancers

Variable	No. Missing	Overall	Surveillance-detected Cancers by Indication			Interval Cancers
			Screening	Breast Problem	SIFU	
Total		1,418	679	256	63	420
DCIS or invasive	0 (0)					
DCIS		354 (25.0)	189 (27.8)	79 (30.9)	28 (44.4)	58 (13.8)
Invasive		1064 (75.0)	490 (72.2)	177 (69.1)	35 (55.6)	362 (86.2)
AJCC stage	238 (17)					
0		354 (30.0)	189 (31.3)	79 (37.3)	28 (50.9)	58 (18.7)
I		584 (49.5)	326 (54.1)	95 (44.8)	22 (40.0)	141 (45.5)
IIA		126 (10.7)	50 (8.3)	20 (9.4)	3 (5.5)	53 (17.1)
IIB–IV		116 (9.8)	38 (6.3)	18 (8.5)	2 (3.6)	58 (18.7)
Tumor size of invasive cancer (mm)	538 (38)					
0–10		369 (41.9)	212 (47.6)	60 (43.8)	15 (51.7)	82 (30.5)
11–15		192 (21.8)	103 (23.1)	27 (19.7)	7 (24.1)	55 (20.5)
16–20		112 (12.7)	58 (13.0)	17 (12.4)	2 (6.9)	35 (13.0)
>20		207 (23.5)	72 (16.2)	33 (24.1)	5 (17.2)	97 (36.1)
Grade*	322 (23)					
Grade I		244 (22.3)	135 (23.7)	44 (23.7)	12 (25.5)	53 (18.0)
Grade II		487 (44.4)	254 (44.6)	84 (45.2)	17 (36.2)	132 (44.9)
Grade III		365 (33.3)	180 (31.6)	58 (31.2)	18 (38.3)	109 (37.1)
Hormone receptor status*	305 (22)					
ER positive or PR positive		918 (82.5)	495 (86.4)	155 (81.2)	39 (92.9)	229 (74.6)
ER negative and PR negative		195 (17.5)	78 (13.6)	36 (18.9)	3 (7.1)	78 (25.4)
Nodal status of invasive cancer	545 (38)					
Negative		720 (82.5)	376 (86.4)	115 (83.9)	25 (89.3)	204 (74.7)
Positive		153 (17.5)	59 (13.6)	22 (16.1)	3 (10.7)	69 (25.3)

Note.—Data in parentheses are percentages. Percentages may not sum to 100% due to rounding. AJCC = American Joint Committee on Cancer, DCIS = ductal carcinoma in situ, ER = estrogen receptor, PR = progesterone receptor, SIFU = short-interval follow-up.

* Includes both invasive and noninvasive cancers.

for supplemental surveillance in women with a personal history of breast cancer and extremely dense breasts, perhaps with breast MRI (31) or with breast US (32,33).

Beyond the more traditional detection measures (cancer detection rates and positive predictive values), an increased focus on the risk of interval cancers (34) or advanced-stage cancers at diagnosis (35) with screening offers an opportunity to improve screening outcomes and suggests a path forward for surveillance. A multicenter, randomized controlled trial conducted in the Dutch screening program focused on breast MRI for supplemental screening of women at average risk with extremely dense breasts and normal results at mammography (36), with incidence of interval cancers as the primary outcome. Supplemental MRI significantly reduced the interval cancer rate by 2.5 per 1000 examinations (95% CI: 1.0, 3.7; $P < .001$). Although these results are promising, data from subsequent screening rounds and longer-term follow-up are needed to definitively assess the impact on outcomes. Identification of women who may benefit from supplemental imaging is another important consideration guiding the use of MRI in the surveillance setting. In the United States, a study of 2506 screening MRI examinations in 1521 women with a personal history of breast cancer referred at the discretion of their providers in community practice (18) reported no significant difference between the interval cancer rate determined by using screening MRI and the interval cancer rate determined by using screening mammography alone (adjusted odds ratio, 1.1; 95% CI: 0.6, 2.2). However, the study did not present findings to suggest whether subgroups of women might benefit from breast MRI in the surveillance setting. We are unaware of any studies that have demonstrated improved longer-term outcomes such as survival or breast cancer mortality reduction with the use of supplemental surveillance in women with a personal history of breast cancer.

Our study had limitations. First, there was a possibility of misclassified examination indications, with the number and effect of misclassifications unknown. We observed variability in performance measures across indication subgroups of screening, SIFU, and breast problems. It was unclear whether this reflected a different underlying prevalence of second breast cancers across indication subgroups, relatively small sample sizes of second cancers with correspondingly wide CIs, differential mammographic indication coding across facilities, or a combination of these factors. We included asymptomatic surveillance examinations with nonscreening indications to provide a more comprehensive, accurate, and less biased assessment of surveillance mammography performance and outcomes.

A second limitation was the relatively small sample size of DBT surveillance examinations. An exploratory analysis that compared

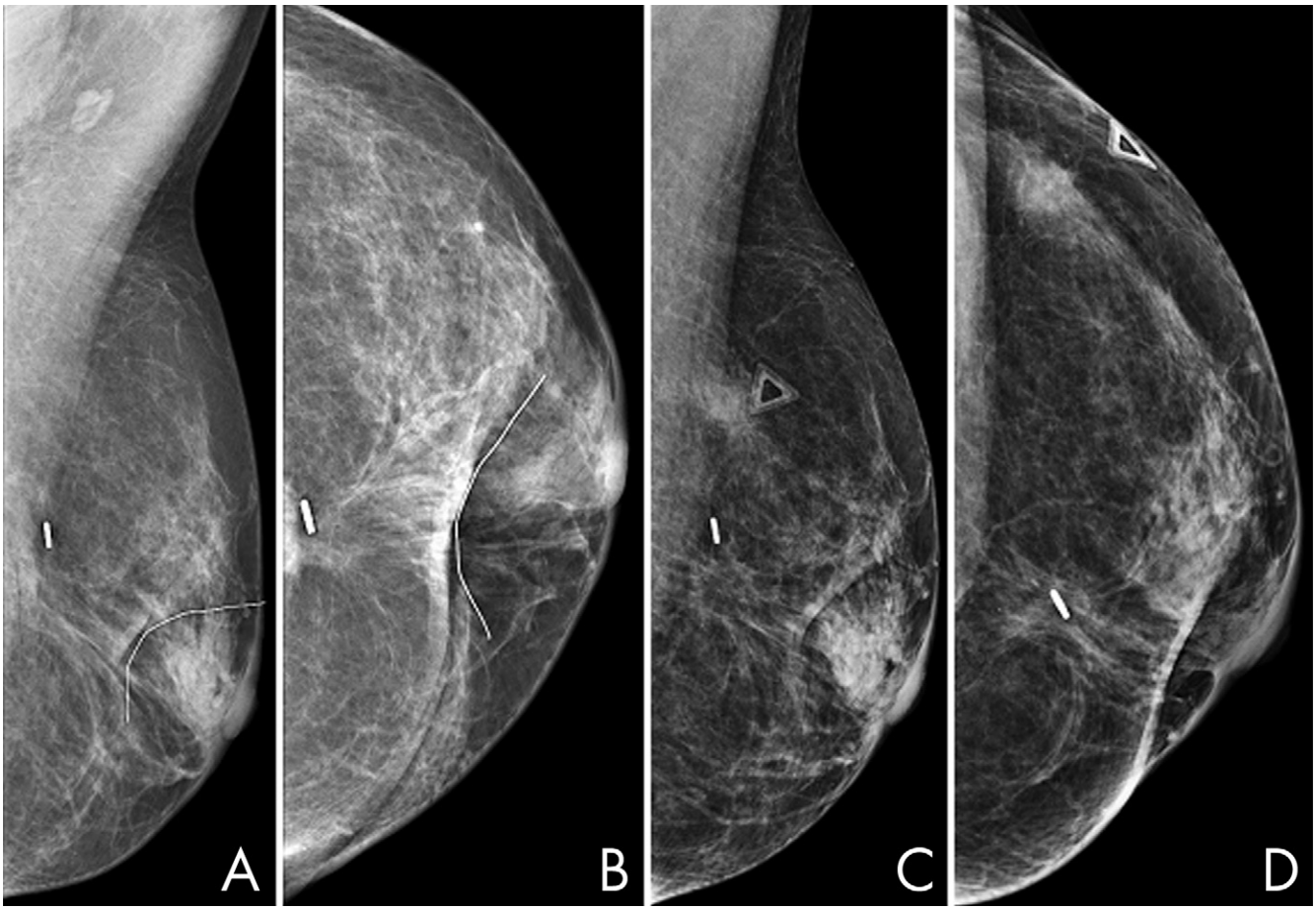

Figure 2: Interval second breast cancer. Surveillance mammograms in a 43-year-old woman obtained 10 years after treatment of primary breast cancer show negative results. *A*, Mediolateral oblique and, *B*, craniocaudal views show postlumpectomy changes in the upper inner quadrant. *C*, Mediolateral oblique and, *D*, craniocaudal views from diagnostic mammography performed 10 months later show a round mass with indistinct margins in the upper outer quadrant, deep to a triangular skin marker indicating a new palpable lump. A high-grade invasive ductal carcinoma with triple-negative receptor status was subsequently diagnosed in this location.

DBT performance with digital mammography performance for screening indication examinations from the same facilities and period demonstrated overlapping 95% CIs for the difference in crude performance measures, which suggested comparable performance for digital mammography and DBT. Our results added to a report of diagnostic performance from a single academic medical center. Bahl et al (7) reported 22 887 DBT examinations in 7154 women and 9019 digital mammography examinations in 4085 women with treated breast cancer at a single academic medical center. That study and ours from multiple community and academic facilities found that cancer detection rates and interval cancer rates were higher in women with a personal history of breast cancer, regardless of modality. Specifically, Bahl et al (7) reported interval cancer rates of 3.5 and 2.4 per 1000 examinations for digital mammography and DBT, respectively (P = .94), which was similar to our results of 2.1 and 3.6 per 1000 examinations for digital mammography and DBT, respectively (P values were not reported for this exploratory analysis). These results contrasted with those in another analysis from a single academic institution of 5706 screening DBT examinations in women with a personal history of breast cancer (8), which reported a significantly reduced interval cancer rate with the use of DBT (0.2 per 1000) versus the use of digital mammography (3.0 per 1000; P = .002). It is unclear why interval cancer rates in the DBT period were lower than those in the preceding digital mammography period, given stable cancer detection rates across the evaluation periods. To our knowledge, these studies represent the largest samples of DBT for surveillance to date but may have been underpowered for detection of statistically significant differences in important performance metrics such as the interval cancer rate.

In conclusion, technical advances in mammography have not markedly improved performance and outcomes of mammographic surveillance in women with a personal history of breast cancer. Interval cancer rates, in particular, have not declined following the transition to digital mammography and remained substantially higher than those in the screening population overall. Additional studies are needed to better determine the performance level of digital breast tomosynthesis for surveillance and to identify women with a personal history of breast cancer who may benefit from adding supplemental imaging to their surveillance regimens.

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