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Breast cancer characteristics associated with digital versus screen-film mammography for screen-detected and interval cancers

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Abstract

Purpose—To determine if pathologic findings of screen-detected and interval cancers differ for digital versus film mammography.

Materials and Methods—This study was institutional review board approved and HIPAA compliant. Using 2003–2011 Breast Cancer Surveillance Consortium data, we included 3,021,515 screening mammograms (40.3% digital and 59.7% film) for women ages 40 to 89 years. Cancers were considered screen-detected if diagnosed within 12 months of a positive examination and interval if diagnosed within 12 months of a negative examination. Tumor characteristics for screen-detected and interval cancers were compared for digital versus film mammography using logistic regression models to estimate the odds ratio (OR) and 95% confidence interval (95%CI),

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Conflict of interest disclosure

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adjusting for age, race/ethnicity, hormone therapy use, screening interval, examination year, and registry while accounting for correlation within facilities using generalized estimating equations.

Results—Among 15,729 breast cancers, 85.3% were screen-detected and 14.7% were interval. Digital and film mammography had similar rates of screen-detected (4.47 vs. 4.42 per 1000 examinations) and interval cancers (0.73 vs. 0.79 per 1000 examinations) for digital versus film, respectively. In adjusted analyses, interval cancers following a negative digital examination were less likely to be AJCC stage IIB or higher (OR=0.69, 95%CI:0.52–0.93), have positive nodal status (OR=0.78, 95%CI:0.64–0.95), or be estrogen receptor-negative (OR=0.71, 95%CI:0.56–0.91) compared with interval cancers following a negative film examination.

Conclusions—Screen-detected cancers following digital and film mammography had similar rates of unfavorable tumor characteristics. Interval-detected cancers after a digital examination were less likely to have unfavorable tumor features than those diagnosed after film, but absolute differences were small.

Introduction

Compared with screen-detected cancers, interval cancers are more likely to be large, poorly differentiated, estrogen-receptor (ER) negative, and have lymph node involvement.(1) Hence, interval cancers typically present with a worse prognosis than screen-detected cancers. The majority of studies examining tumor characteristics of screen-detected versus interval cancers have focused on women who were screened with film mammography.(2–6)

In the United States, digital mammography has rapidly replaced film mammography with approximately 94% of accredited mammography units being digital as of March 1, 2014.(7) The impact of this transition to digital on screen-detected versus interval cancer rates is unclear. In particular, the extent to which tumor characteristics of screen-detected versus interval cancers differ by imaging modality has not previously been studied in the United States. Using national Breast Cancer Surveillance Consortium (BCSC) data from 2000–2006, Kerlikowske et al. found no differences in distributions of cancer stage, tumor size, nodal status, tumor grade, for digital versus film, but this analysis did not stratify by screen-detected vs. interval cancer.(8) The authors did report that digital mammography had a higher sensitivity to detect ER-negative tumors than film-screen mammography.(8) A recent study from the Netherlands examined the pathologic findings of interval cancers for digital versus film and found that the tumor characteristics were comparable(9) but it is unclear if similar patterns exist in the US.

The purpose of our study was to examine and compare tumor characteristics for screen-detected and interval cancers by imaging modality (digital versus film) of the screening mammogram among women undergoing community-based mammography screening in the United States.

Materials and Methods

Data Sources

The data for this study were collected from six registries that participate in the Breast Cancer Surveillance Consortium (BCSC): Carolina Mammography Registry, Group Health Cooperative (Washington State), New Hampshire Mammography Network, New Mexico Mammography Project, San Francisco Mammography Registry, and the Vermont Breast Cancer Surveillance System.(10) Prospective data collected from participating BCSC mammography practices includes patient self-reported demographic characteristics, indication for breast imaging visit, breast cancer risk factors, mammography assessment, and management recommendations. These data are linked with tumor information from pathology databases and regional cancer registry data. Each registry site submits data to a Statistical Coordinating Center for quality control checks and pooled analyses. Each registry and the Statistical Coordinating Center received institutional review board approval for either active or passive consent or a waiver of consent to enroll participants, link study data, and perform analytic studies. All procedures are Health Insurance Portability and Accountability Act compliant and all registries have received a Federal Certificate of Confidentiality.

Study Population

We included mammograms indicated to be performed for screening by the radiologist or technologist on women ages 40 to 89 years from 2003–2011.(11) We excluded mammograms performed on women with a prior breast cancer diagnosis, mastectomy, and implants. We also excluded data from eight Fuji Computed Radiography Mammography Suite machines (3.9% of the data) since the sensitivity of CR machines is lower than that of digital direct radiography and because the vast majority of digital mammography machines in use today are digital direct radiography. To avoid misclassifying diagnostic examinations as screening, we excluded examinations with a mammogram or breast ultrasound in the prior 9 months or if unilateral views were taken. The final study examinations included 3,021,515 screening mammograms of which 1,218,314 were digital examinations and 1,803,201 were film examinations.

Definitions

Women were considered to have incident breast cancer if a diagnosis of invasive carcinoma or ductal carcinoma *in situ* occurred within 12 months of the screening mammogram and prior to the next screening mammogram.(12) Invasive cancers were further categorized based on American Joint Committee on Cancer (AJCC) 6^{th} edition stage, Surveillance Epidemiology End Result (SEER) summary stage, grade, tumor size at the time of pathology, lymph node status, and hormone receptor status.

Each screening mammogram interpretation was classified as positive or negative based on the radiologists' Breast Imaging Reporting and Data System (BI-RADS) screening assessment result. We defined a positive interpretation as BI-RADS of 0 (additional imaging required), 4 (needs evaluation), or 5 (highly suggestive of malignancy), or 3 (probably benign) when the recommendation was for immediate work-up. We defined a negative

interpretation as BI-RADS of 1 (negative) or 2 (benign finding) or 3 (probably benign) with no recommendation for immediate additional imaging.(13, 14) We categorized the BI-RADS 3 assessments in this manner to account for the differences in how some practicing radiologists use BI-RADS category 3 with additional imaging recommended instead of using BI-RADS category 0.(13, 15) We defined *screen-detected cancers* as those diagnosed within 12 months of a positive screening mammogram and before the next screening mammogram. We defined *interval cancers* as those diagnosed within 12 months of a negative screening mammogram and before the next screening mammogram.

Statistical Analyses

We examined the distribution of patient characteristics and compared the tumor characteristics for those with screen-detected versus interval cancers by imaging modality. To obtain estimates of odds ratios of having favorable and unfavorable tumor characteristics for digital versus film by mode of detection, we fit two separate logistic regression models, accounting for correlation within facilities using generalized estimating equations. We separately modeled the rates of cancers with favorable and unfavorable tumor characteristics among all women, regardless of cancer status. We adjusted the models for age, race/ethnicity, current hormone therapy use, time since last mammogram (i.e., the mammogram prior to the one used in this study), examination year and registry site. We excluded examinations with unknown covariates from the logistic regression models. All analyses were performed using SAS V 9.2 (SAS Institute, Cary NC).

Results

Patient Characteristics of the Screening Mammograms

The digital (n=1,218,314) and film (n=1,803,201) examination groups had similar distributions of age, family history of breast cancer, menopausal status, history of breast biopsy, BI-RADS breast density, and BI-RADS assessment (Table 1). Asians were more likely to undergo digital mammography while Hispanics were more likely to receive film mammography. There was less hormone therapy (HT) use among women undergoing digital mammography. Women receiving digital examinations were more likely to have mammograms within the prior year versus women receiving film (69% versus 61% respectively). The uptake of digital is evident from the distribution of examination year by imaging modality during the study period. Similar proportions of digital and film examinations resulted in screen-detected (0.44% for both) and interval cancers (0.073% and 0.079%, respectively) for both modalities.

Patient Characteristics of Screen-Detected and Interval Cancers

A total of 15,729 breast cancers were diagnosed in the 12 months of follow-up after the screening mammogram and before the next screening mammogram, of which 85.3% (n=13,418) were screen-detected and 14.7% (n=2,311) were interval cancers. Of the screen-detected cancers, 5,441 (40.6%) were among digital examinations and 7,977 (59.4%) were among film examinations (Table 2). For interval cancers, 895 (38.7%) were in digital examinations and 1,416 (61.3%) were in film examinations. Compared with screen-detected cancers, a higher proportion of interval cancers were among younger women, pre or peri-

menopausal women, women with history of a breast biopsy, women with dense breasts, and women who had been screened in the prior 12 months, regardless of imaging modality.

Tumor Characteristics of Screen-Detected and Interval Cancers

The screen-detected cancer rate per 1000 examinations was similar for digital and film mammography (4.5 and 4.4, respectively) as was the interval cancer rate (0.73 and 0.79 per 1000 examinations, respectively) (Table 3). Compared with screen-detected cancers, interval cancers were more likely to have unfavorable tumor characteristics regardless of imaging modality. Specifically, interval cancers were more likely to be invasive, stage IIB or higher, have SEER summary regional or distant stage, be greater than 20 mm in size, have positive nodal status, be grade III, and be ER negative or progesterone receptor (PR) negative. Screen-detected cancers identified on digital were more likely to be DCIS than those detected on film (1.34 and 1.03 per 1000 examinations, respectively); yet there were little differences in invasive tumor features for digital or film screen-detected cancers. Interval cancers following digital versus film were also slightly more likely to be DCIS with few differences in invasive tumor features.

Relative Risk of Unfavorable Tumor Characteristics

The adjusted odds ratios of having unfavorable tumor characteristics are significantly different for receipt of digital versus film mammography among women with interval cancers but not among women with screen-detected cancers (Table 4). For women with interval cancers, cancers following digital mammography were slightly less likely to have unfavorable tumor features than cancers following film mammography. For example, interval cancers not seen on digital were 31% less likely to present at AJCC stage IIB or later (adjusted OR (aOR)=0.69, 95%CI:0.52–0.93 and rates 0.12 vs. 0.18 per 1000 examinations), 22% less likely to be regional or distant disease (aOR=0.78, 95%CI:0.64–0.95 and rates 0.23 vs. 0.28 per 1000 examinations), 22% less likely to have positive nodal status (aOR=0.78, 95%CI:0.64–0.95 and rates 0.22 vs. 0.27 per 1000 examinations), and 29% less likely to present with ER-negative tumors (aOR=0.71, 95%CI:0.56–0.91 and rates 0.13 vs. 0.16 per 1000 examinations) than interval cancers not seen on film. In contrast, the adjusted odds ratios of having favorable tumor characteristics (early stage, smaller tumor size, negative nodal status, lower grade, and ER-positive tumors) are not significantly different for digital versus film mammography for screen or interval detected cancers. The one exception is among screen-detected cancers, in which the adjusted odds ratios of having DCIS versus invasive disease is 1.30 (95%CI: 1.15–1.48), indicating that DCIS is more frequently detected on digital mammography compared to film.

Discussion

Our findings revealed a similar proportion of interval cancers among women screened with digital or film mammography. The proportion of interval cancers we observed is similar to the 13.8% reported in the Ontario Breast Screening Program.(1) Additionally, we found that the rates of screen-detected and interval cancers were similar across modality. Compared with a 2014 study conducted in the Netherlands by Nederend et al., which reported interval cancer rates on digital and film of 2.0 vs. 1.7 per 1000 examinations, respectively, our rates

are substantially lower.(9) Hoff et al reported similar screen-detected invasive cancer rates and interval cancer rates but higher screen-detected DCIS with digital compared to film.(16) Studies from Ireland, the Netherlands, and Norway (17–19) have reported increased cancer detection rates with digital while studies from Spain, the United Kingdom, and the U.S. show similar cancer detection rates for digital and film.(2, 8, 17–21)

As shown in prior studies based on film, we found that interval cancers were more likely to have unfavorable tumor characteristics than screen-detected cancers.(22–24) In particular interval cancers had a higher stage, larger size, positive lymph node involvement, and ER negative status. Our results also agree with a study using data from the Dutch MINDACT trial which found similar tumor characteristics for cancers screen-detected with digital versus film and more unfavorable characteristics for interval cancers following screening with film than digital.(25) We add to the existing literature in that previous work focused on screen-detected and interval cancers based on film and our study includes over 3,800 cancers diagnosed after digital.

Among women with interval cancer, adjusted odds ratios of unfavorable tumor characteristics were lower for digital versus film. This finding was not observed for screen-detected cancers. A 2014 study conducted in the Netherlands compared characteristics of interval cancers among 63,182 women screened with digital and 60,770 women screened with film between 2008 and 2010.(9) This study did not find differences in breast density, tumor size, lymph node status, or hormone receptor status between digital and film interval detected cancers. It is possible that the difference in film versus digital interval cancers observed in our study compared to the Nederend study reflects the very different interval cancer rates in the two countries and/or the fact that the Nederend study defines interval cancers based on a two-year follow-up.(9)

In our study we found almost identical overall cancer detection rates of 5.20 and 5.21 per 1000 examinations for digital and film respectively. Interestingly, digital mammography found more DCIS. It is unclear what this means, but one possibility is that the types of DCIS found on digital mammography may lead to fewer interval cancers with poor prognostic characteristics. We do not believe this is the case because mammographically DCIS has a less than 10% chance of being associated with a subsequent invasive cancer in 10 years and most subsequent invasive cancers are not aggressive as the interval cancers in our study.(25) This unexplained and interesting finding deserves more study.

Strengths of our study include the ability to examine both digital and film in a national cohort of screening mammograms from community-based practices. The BCSC dataset contains a large number of screen-detected and interval cancers even after stratifying by imaging modality. However, our study also had limitations. First, in the BCSC data, we are unable to determine if the interval cancers are true interval cancers or missed cancers that were visible on the screening images. Second, we had incomplete data on HER2, another important prognostic factor. As the SEER data more comprehensively capture HER2 status, the lack of data remains a problem for many state cancer registry based studies.

Based on our study results, the transition to digital in the U.S. has not reduced the interval cancer rate. Interval cancers comprise approximately 15% of breast cancers for both digital and film. However, interval cancers detected following a negative digital examination had less unfavorable characteristics than those following a negative film examination, which may improve treatment outcomes for women. The pathologic findings of screen-detected cancers are similar for digital and film. As technologies in breast imaging change in the future, a similar study comparing the pathologic features of cancers detected on digital mammography versus tomosynthesis will be important to determine whether screen-detected and interval cancers vary in a clinically meaningful way between these two modalities.(26)

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Table 1

Characteristics of Screening Mammography Examinations Included in the Study

Characteristic*	Digital Mammography		Film mammography	
	N	(%)	N	(%)
Number of examinations	1,218,314		1,803,201	
Number of women	528,786		860,769	
Age at examination (y)				
40–49	353,576	(29.0)	506,225	(28.1)
50–59	386,670	(31.7)	582,199	(32.3)
60–69	279,405	(22.9)	395,008	(21.9)
70–79	148,007	(12.1)	240,072	(13.3)
≥ 80	50,656	(4.2)	79,697	(4.4)
Race/Ethnicity				
White, non-Hispanic	798,587	(70.8)	1,272,476	(75.1)
Black, non-Hispanic	73,942	(6.6)	103,795	(6.1)
Asian, Native Hawaiian, PI	184,321	(16.3)	116,206	(6.9)
American Indian, Alaska Native	3,230	(0.3)	15,721	(0.9)
Hispanic	48,165	(4.3)	159,092	(9.4)
Other	19,106	(1.7)	28,204	(1.7)
Family history of breast cancer				
Yes	185,669	(15.5)	265,202	(15.4)
No	1,011,827	(84.8)	1,451,897	(84.6)
Menopausal status				
Pre/Peri-menopausal	300,255	(28.3)	397,577	(25.6)
Post-menopausal	759,995	(71.7)	1,154,689	(74.4)
Current hormone therapy use				
Yes	96,971	(9.1)	227,229	(14.3)
No	965,832	(90.9)	1,358,359	(85.7)
History of breast biopsy				
Yes	239,255	(20.6)	350,516	(20.3)
No	924,618	(79.4)	1,379,133	(79.7)
BI-RADS breast density				
Almost entirely fat	119,259	(11.6)	125,314	(9.1)
Scattered fibroglandular densities	437,719	(42.7)	633,987	(45.9)
Heterogenously dense	392,365	(38.3)	513,928	(37.2)
Extremely dense	74,597	(7.3)	106,800	(7.7)
Time since prior mammogram				
No prior	35,628	(3.1)	53,231	(3.2)
1 year (9–18 months)	803,566	(69.1)	1,032,147	(61.2)
2 years (19–30 months)	192,012	(16.5)	372,001	(22.1)
3+ years (31+ months)	130,920	(11.3)	228,519	(13.6)
Examination year				

Characteristic*	Digital Mammography		Film mammography	
	N	(%)	N	(%)
2003	33,434	(2.7)	405,357	(22.5)
2004	42,833	(3.5)	383,756	(21.3)
2005	52,876	(4.3)	340,721	(18.9)
2006	101,393	(8.3)	249,973	(13.9)
2007	175,943	(14.4)	183,751	(10.2)
2008	209,883	(17.2)	119,620	(6.6)
2009	256,168	(21.0)	70,476	(3.9)
2010	256,176	(21.0)	38,910	(2.2)
2011	89,608	(7.4)	10,637	(0.6)
BI-RADS assessment				
0: Incomplete assessment	126,018	(10.3)	165,758	(9.2)
1: Negative	791,227	(64.9)	1,142,978	(63.4)
2: Benign finding	297,560	(24.4)	482,449	(26.8)
3: Probably benign	2,513	(0.2)	9,346	(0.5)
4: Suspicious abnormality	912	(0.1)	2,274	(0.1)
5: Highly suggestive of malignancy	84	(0)	396	(0)
Outcome				
Screen-detected cancer	5,441	(0.4)	7,977	(0.4)
Interval cancer	895	(0.1)	1,416	(0.1)
No cancer	1,211,978	(99.5)	1,793,808	(99.5)

* Counts by certain characteristic do not add up to total N due to missing data.

Table 2

Characteristics of women with screen-detected and interval cancers by imaging modality, Breast Cancer Surveillance Consortium 2003–2011

Characteristic	Screen-Detected Cancer (n=13,418)				Interval Cancer (n=2,311)			
	Digital		Film		Digital		Film	
	N	(%)	N	(%)	N	(%)	N	(%)
Number of Women*	5,441	(40.6)	7,977	(59.4)	895	(38.7)	1,416	(61.3)
Age at exam (y)								
40–49	1,004	(18.5)	1,277	(16.0)	225	(25.1)	347	(24.5)
50–59	1,502	(27.6)	2,357	(29.5)	263	(29.4)	410	(29.0)
60–69	1,537	(28.2)	2,134	(26.8)	223	(24.9)	365	(25.8)
70–79	1,010	(18.6)	1,573	(19.7)	131	(14.6)	227	(16.0)
≥ 80	388	(7.1)	636	(8.0)	53	(5.9)	67	(4.7)
Race/Ethnicity								
White, non-Hispanic	3,736	(73.9)	5,914	(77.9)	642	(76.2)	1,077	(80.3)
Black, non-Hispanic	324	(6.4)	450	(5.9)	54	(6.4)	81	(6.0)
Asian, Native Hawaiian, PI	720	(14.2)	483	(6.4)	111	(13.2)	73	(5.4)
American Indian, Alaska Native	10	(0.2)	57	(0.8)	4	(0.5)	14	(1.0)
Hispanic	92	(1.8)	151	(2.0)	14	(1.7)	20	(1.5)
Other	174	(3.4)	532	(7.0)	18	(2.1)	76	(5.7)
Family history of breast cancer								
Yes	1,209	(22.6)	1,645	(21.7)	218	(24.7)	322	(23.5)
No	4,130	(77.4)	5,937	(78.3)	666	(75.3)	1,049	(76.5)
Menopausal status								
Pre/Peri-menopausal	987	(19.7)	1,243	(17.1)	229	(28.4)	322	(25.6)
Post-menopausal	4,019	(80.3)	6046	(82.9)	578	(71.6)	934	(74.4)
Current hormone therapy use								
Yes	503	(10.7)	996	(14.7)	95	(12.6)	227	(18.1)
No	4,195	(89.3)	5,764	(85.3)	659	(87.4)	1,028	(81.9)
History of breast biopsy								
Yes	1,438	(27.7)	2,166	(28.1)	288	(35.2)	464	(33.8)
No	3,762	(72.2)	5,539	(71.9)	530	(64.8)	908	(66.2)

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Characteristic	Screen-Detected Cancer (n=13,418)				Interval Cancer (n=2,311)			
	Digital		Film		Digital		Film	
	N	(%)	N	(%)	N	(%)	N	(%)
BIRADS breast density								
Almost entirely fat	356	(8.2)	325	(5.7)	34	(4.5)	37	(3.4)
Scattered fibroglandular densities	1,918	(44.2)	2,571	(45.0)	236	(31.5)	359	(33.3)
Heterogenously dense	1,800	(41.5)	2,448	(42.8)	386	(51.5)	533	(49.4)
Extremely dense	264	(6.1)	372	(6.5)	93	(12.4)	150	(13.9)
Time since prior mammogram								
No prior	197	(3.8)	329	(4.5)	21	(2.4)	24	(1.8)
1 year (9–18 months)	3,021	(58.9)	3,663	(49.7)	624	(72.7)	892	(66.0)
2 years (19–30 months)	928	(18.1)	1,804	(24.5)	120	(14.0)	280	(20.7)
3+ years (31+ months)	982	(19.1)	1,567	(21.3)	93	(10.8)	155	(11.5)

* row percent is given in parentheses for the number of mammograms row

Table 3

Rates of cancer per 1000 mammograms by tumor characteristics, mode of detection, and imaging modality, Breast Cancer Surveillance Consortium 2003–2011

	Screen-Detected Cancer (n=13,418)						Interval Cancer (n=2,311)					
	Digital			Film			Digital			Film		
Cancer Characteristic	***N* cancers**	**Column %**	**Rate per 1000**	***N* cancers**	**Column %**	**Rate per 1000**	***N* cancers**	**Column %**	**Rate per 1000**	***N* cancers**	**Column %**	**Rate per 1000**
Total	5,441	(86%)	4.47	7,977	(85%)	4.42	895	(14%)	0.73	1416	(15%)	0.79
DCIS	1,638	(30%)	1.34	1,854	(23%)	1.03	106	(12%)	0.09	132	(9%)	0.07
Invasive	3,803	(70%)	3.12	6,123	(77%)	3.40	789	(88%)	0.65	1,284	(91%)	0.71
For invasive cancers:												
AJCC Stage												
I	2,313	(63%)	1.90	3,530	(61%)	1.96	311	(41%)	0.26	466	(39%)	0.26
IIA	780	(21%)	0.64	1,200	(21%)	0.67	229	(30%)	0.19	338	(28%)	0.19
IIB	334	(9%)	0.27	552	(10%)	0.31	103	(14%)	0.08	162	(13%)	0.09
III	211	(6%)	0.17	393	(7%)	0.22	97	(13%)	0.08	187	(16%)	0.10
IV	34	(1%)	0.03	67	(1%)	0.04	21	(3%)	0.02	48	(4%)	0.03
Unknown	131	*(3%)*	0.11	381	*(6%)*	0.21	28	*(4%)*	0.02	83	*(6%)*	0.05
SEER summary stage												
Local	2,868	(78%)	2.35	4,433	(76%)	2.46	492	(64%)	0.40	723	(59%)	0.40
Regional	776	(21%)	0.64	1,362	(23%)	0.76	252	(33%)	0.21	459	(37%)	0.25
Distant	36	(1%)	0.03	68	(1%)	0.04	23	(3%)	0.02	49	(4%)	0.03
Unknown	123	*(3%)*	0.10	260	*(4%)*	0.14	22	*(3%)*	0.02	53	*(4%)*	0.03
Tumor size												
<=10 mm	1,184	(34%)	0.97	1,778	(32%)	0.99	124	(17%)	0.10	193	(16%)	0.11
11–20 mm	1,410	(40%)	1.16	2,266	(41%)	1.26	269	(36%)	0.22	431	(37%)	0.24
>20 mm	903	(26%)	0.74	1,536	(28%)	0.85	346	(47%)	0.28	548	(47%)	0.30
Unknown	306	*(8%)*	0.25	543	*(9%)*	0.30	50	*(6%)*	0.04	112	*(9%)*	0.06
Nodal status												
Negative	2,917	(78%)	2.39	4,534	(76%)	2.51	504	(65%)	0.41	757	(61%)	0.42
Positive	812	(22%)	0.67	1,425	(24%)	0.79	270	(35%)	0.22	493	(39%)	0.27
Unknown	74	*(2%)*	0.06	164	*(3%)*	0.09	15	*(2%)*	0.01	34	*(3%)*	0.02

	Screen-Detected Cancer (n=13,418)						Interval Cancer (n=2,311)					
	Digital			Film			Digital			Film		
Cancer Characteristic	***N* cancers**	**Column %**	**Rate per 1000**	***N* cancers**	**Column %**	**Rate per 1000**	***N* cancers**	**Column %**	**Rate per 1000**	***N* cancers**	**Column %**	**Rate per 1000**
Grade												
I	1142	(32%)	0.94	1,635	(29%)	0.91	153	(21%)	0.13	235	(21%)	0.13
II	1597	(45%)	1.31	2,436	(44%)	1.35	313	(43%)	0.26	455	(40%)	0.25
III	838	(23%)	0.69	1,512	(27%)	0.84	269	(37%)	0.22	447	(39%)	0.25
Unknown	226	*(6%)*	0.19	540	*(9%)*	0.30	54	*(7%)*	0.04	147	*(11%)*	0.08
Estrogen receptor status												
Positive	3137	(87%)	2.57	4,630	(85%)	2.57	589	(79%)	0.48	836	(74%)	0.46
Negative	468	(13%)	0.38	807	(15%)	0.45	161	(21%)	0.13	294	(26%)	0.16
Unknown	198	*(5%)*	0.16	686	*(11%)*	0.38	39	*(5%)*	0.03	154	*(12%)*	0.09
Progesterone receptor status												
Positive	2798	(78%)	2.30	4022	(75%)	2.23	521	(70%)	0.43	733	(65%)	0.41
Negative	804	(22%)	0.66	1,373	(25%)	0.76	227	(30%)	0.19	393	(35%)	0.22
Unknown	201	*(5%)*	0.16	728	*(12%)*	0.40	41	*(5%)*	0.03	158	*(12%)*	0.09
HER2												
Positive	316	(12%)	0.26	549	(15%)	0.30	76	(14%)	0.06	125	(18%)	0.07
Negative	2243	(88%)	1.84	2,995	(85%)	1.66	478	(86%)	0.39	574	(82%)	0.32
Unknown	1,244	*(33%)*	1.02	2,579	*(42%)*	1.43	235	*(30%)*	0.19	585	*(46%)*	0.32
Triple Negative												
Yes	210	(8%)	0.17	287	(8%)	0.17	78	(14%)	0.06	103	(15%)	0.06
No	2333	(92%)	1.91	3148	(92%)	1.91	473	(86%)	0.39	578	(85%)	0.32
Unknown	1,260	*(33%)*	1.03	2,688	*(44%)*	1.03	238	*(30%)*	0.20	603	*(47%)*	0.33

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Table 4

Odds ratios (95% confidence intervals) of having tumor characteristics with worse prognosis (relative to better prognosis or no cancer) and for of having tumor characteristics with better prognosis (relative to worse prognosis or no cancer) for digital vs. film mammography, Breast Cancer Surveillance Consortium 2003–2011

	Screen-detected Cancers		Interval Cancers	
Cancer Characteristic	**Unadjusted OR (95% CI)**	**Adjusted OR* (95% CI)**	**Unadjusted OR (95% CI)**	**Adjusted OR* (95% CI)**
All				
Cancer diagnosis	1.01 (0.94, 1.09)	1.06 (0.97, 1.16)	0.94 (0.81, 1.08)	0.93 (0.78, 1.10)
Unfavorable prognosis:				
Invasive cancer	**0.92 (0.85, 0.90)**	0.98 (0.89, 1.07)	0.91 (0.79, 1.04)	0.90 (0.77, 1.06)
For invasive cancers:				
AJCC Stage IIB or later	0.85 (0.70, 1.02)	1.02 (0.85, 1.23)	0.82 (0.68, 1.01)	**0.69 (0.52, 0.93)**
Regional or distant SEER summary stage***	**0.84 (0.74, 0.95)**	1.07 (0.93, 1.24)	**0.80 (0.68, 0.94)**	**0.78 (0.64, 0.95)**
Tumor size >20 mm	0.87 (0.76, 1.00)	0.96 (0.81, 1.14)	0.94 (0.78, 1.13)	0.83 (0.66, 1.04)
Positive nodal status	0.84 (0.75, 0.95)	1.07 (0.93, 1.24)	0.81 (0.69, 0.95)	**0.78 (0.64, 0.95)**
Grade III	**0.82 (0.73, 0.92)**	0.99 (0.85, 1.15)	0.89 (0.72, 1.09)	0.84 (0.67, 1.06)
Estrogen receptor negative	0.86 (0.73, 1.00)	0.96 (0.78, 1.18)	0.81 (0.64, 1.03)	**0.71 (0.56, 0.91)**
Favorable prognosis:				
DCIS	**1.31 (1.17, 1.46)**	**1.30 (1.15, 1.48)**	1.19 (0.88, 1.60)	1.19 (0.71, 1.98)**
For invasive cancers:				
AJCC Stage IIA or earlier	0.97 (0.88, 1.06)	0.99 (0.90, 1.09)	0.99 (0.86, 1.15)	1.03 (0.85, 1.24)
Local SEER summary stage***	0.96 (0.88, 1.04)	0.95 (0.87, 1.05)	1.01 (0.86, 1.18)	0.99 (0.80, 1.24)
Tumor size <=20 mm	0.95 (0.86, 1.05)	1.00 (0.90, 1.11)	0.93 (0.79, 1.09)	0.97 (0.80, 1.19)
Negative nodal status	0.95 (0.88, 1.03)	0.96 (0.87, 1.05)	0.99 (0.84, 1.16)	0.97 (0.78, 1.21)
Grade I or II	1.00 (0.91, 1.09)	1.01 (0.90, 1.12)	1.00 (0.84, 1.19)	1.01 (0.83, 1.24)
Estrogen receptor positive	1.00 (0.91, 1.10)	0.97 (0.88, 1.07)	1.04 (0.90, 1.21)	0.98 (0.81, 1.18)

* Odds ratios are adjusted for current hormone therapy use, age, race/ethnicity, screening interval, exam year, and BCSC registry. Bolded ORs indicate those that are significant.

** Models adjusting for screening interval or race did not converge.

*** The SEER summary stages are local, regional, and distant