Breast Cancer Characteristics Associated With Digital Versus Film-Screen Mammography for Screen-Detected and Interval Cancers

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OBJECTIVE. The purpose of this study was to determine whether pathologic findings of screen-detected and interval cancers differ for digital versus film mammography.

MATERIALS AND METHODS. Breast Cancer Surveillance Consortium data from 2003–2011 on 3,021,515 screening mammograms (40.3% digital, 59.7% film) of women 40–89 years old were reviewed. Cancers were considered screen detected if diagnosed within 12 months of an examination with positive findings and interval if diagnosed within 12 months of an examination with negative findings. Tumor characteristics for screen-detected and interval cancers were compared for digital versus film mammography by use of logistic regression models to estimate the odds ratio and 95% CI with adjustment for age, race and ethnicity, hormone therapy use, screening interval, examination year, and registry. Generalized estimating equations were used to account for correlation within facilities.

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 (0.73 vs 0.79 per 1000 examinations) cancers for digital versus film. In adjusted analyses, interval cancers diagnosed after digital examinations with negative findings were less likely to be American Joint Committee on Cancer stage IIB or higher (odds ratio, 0.69; 95% CI, 0.52–0.93), have positive nodal status (odds ratio, 0.78; 95% CI, 0.64–0.95), or be estrogen receptor negative (odds ratio, 0.71; 95% CI, 0.56–0.91) than were interval cancers diagnosed after a film examination with negative findings.

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

Keywords: digital mammography, film mammography, interval cancer, screen-detected cancer

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Compared with screen-detected cancers, interval cancers are more likely to be large, poorly differentiated, and estrogen-receptor negative and to have lymph node involvement [1]. Hence, interval cancers typically present with a worse prognosis than do screen-detected cancers. Most studies examining tumor characteristics of screen-detected versus interval cancers have focused on women undergoing screening with film mammography [2–6].

In the United States, digital mammography has rapidly replaced film mammography; approximately 94% of accredited mammography units were digital as of March 1, 2014 [7]. How this transition to digital technology has affected 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, to our knowledge, not been studied in the United States. Using national Breast Cancer Surveillance Consortium (BCSC) data from 2000 to 2006, Kerlikowske et al. [8] found no differences in distribution of cancer stage, tumor

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size, nodal status, or tumor grade for digital versus film, but the analysis was not stratified by screen-detected versus interval cancer. The investigators did report that digital mammography had a higher sensitivity in the detection of estrogen receptor–negative tumors than did film-screen mammography. A 2014 study from The Netherlands [9] examined the pathologic findings of interval cancers for digital versus film mammography. The study showed that the tumor characteristics were comparable, but it is unclear whether similar patterns exist in the United States.

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

Materials and Methods

Data Sources

The data for this study were collected from six registries that participate in the 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]. The prospective data collected from participating BCSC mammography practices include patient self-reported demographic characteristics, indication for breast imaging visit, breast cancer risk factors, mammographic 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 were HIPAA compliant, and all registries received a federal certificate of confidentiality.

Study Population

We included mammograms of women 40–89 years old obtained from 2003 to 2011 for which the indication was screening as noted by the radiologist or technologist [11]. We excluded mammograms of women with a previous breast cancer diagnosis, mastectomy, or implants. We also excluded data from eight Fuji Computed Radiography Mammography Suite machines (3.9% of the data) because the sensitivity of computed radiography is lower than that of digital direct radiography and because almost all digital mammography machines in current use are digital direct radiography systems. To avoid misclassifying diagnostic examinations as screening, we excluded examinations of patients who had undergone mammography or breast ultrasound in the previous 9 months or in which only unilateral mages were obtained. The final study examinations included 3,021,515 screening mammograms, of which 1,218,314 (40.3%) were digital examinations and 1,803,201 (59.7%) were film examinations.

Definitions

Women were considered to have incident breast cancer if a diagnosis of invasive carcinoma or ductal carcinoma in situ (DCIS) was made within 12 months of the screening mammogram and before the next screening mammogram [12]. Invasive cancers were further categorized according to American Joint Committee on Cancer (AJCC), sixth edition, stage; Surveillance Epidemiology End Result (SEER) summary stage; grade; tumor size at the time of pathologic examination; lymph node status; and hormone receptor status.

Each screening mammographic interpretation was classified as positive or negative on the basis of radiologists' BI-RADS screening assessments. We defined a positive interpretation as BI-RADS category 0 (additional imaging required), 4 (needs evaluation), or 5 (highly suggestive of malignancy) or as BI-RADS 3 (probably benign) when the recommendation was for immediate workup. We defined a negative interpretation as BI-RADS category 1 (negative) or 2 (benign finding) or as BI-RADS 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 screening mammographic examination with a positive finding and before the next screening examination. We defined interval cancers as those diagnosed within 12 months of a negative screening mammographic result and before the next screening examination.

Statistical Analyses

We examined the distribution of patient characteristics and compared the tumor characteristics of screen-detected versus interval cancers by imaging modality. To obtain estimates of the odds ratios (ORs) of the presence of favorable and unfavorable tumor characteristics for digital versus film by mode of detection, we fit two separate logistic regression models. We accounted for correlation within facilities by 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 and ethnicity, current hormone therapy use, time since last mammogram (i.e., the mammogram before 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 with SAS software (version 9.2, SAS Institute).

Results

Patient Characteristics for 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 category (Table 1). Asian patients were more likely to undergo digital mammography, and Hispanic patients were more likely to undergo film mammography. There was less hormone therapy use among women undergoing digital mammography. Women undergoing digital examinations were more likely to have undergone mammography within the previous year than were women undergoing film examinations (69% versus 61%). The uptake of digital mammography is evident from the distribution of examination years 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%) 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 mammographic examination and before the next one; 85.3% (n = 13,418) of these cancers were screen detected and 14.7% (n = 2311) were interval cancers. Of the screen-detected cancers, 5441 (40.6%) were in the digital and 7977 (59.4%) were in the film examination group (Table 2). For interval cancers, 895 (38.7%) were in the digital and 1416 (61.3%) were in the film examination group. Compared with screen-detected cancers and regardless of imaging modality, interval cancers were found in higher proportion among younger women, premenopausal or perimenopausal women, women with a history of breast biopsy, women with dense

breasts, and women who had undergone screening in the previous 12 months.

Tumor Characteristics of Screen-Detected and Interval Cancers

The screen-detected cancer rates per 1000 examinations were similar for digital and film mammography (4.47 and 4.42), as was the interval cancer rate (0.73 and 0.79 per 1000 examinations) (Table 3). 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; be in a SEER summary regional or distant stage; be larger than 20 mm; have positive nodal status; be grade III; and be estrogen or progesterone receptor negative. Screen-detected cancers identified with digital mammography were more likely to be DCIS than were those detected

TABLE 1: Characteristics of Patients Undergoing Screening Mammographic Examinations

Characteristic	Digital Mammography		Film Mammography	
	N	%	*N*	%
No. of examinations	1,218,314	100.0	1,803,201	100.0
No. of women	528,786	100.0	860,769	100.0
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, Pacific Islander	184,321	16.3	116,206	6.9
American Indian, Alaska Native	3230	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				
Premenopausal or perimenopausal	300,255	28.3	397,577	25.6
Postmenopausal	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
Heterogeneously dense	392,365	38.3	513,928	37.2
Extremely dense	74,597	7.3	106,800	7.7
Time since previous mammogram				
No previous	35,628	3.1	53,231	3.2
1 y (9–18 mo)	803,566	69.1	1,032,147	61.2
2 y (19–30 mo)	192,012	16.5	372,001	22.1

(Table 1 continues on next page)

TABLE 1: Characteristics of Patients Undergoing Screening Mammographic Examinations (continued)

Characteristic	Digital Mammography		Film Mammography	
	N	%	*N*	%
≥ 3 y (≥ 31 mo)	130,920	11.3	228,519	13.6
Examination year				
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 category				
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	2513	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	5441	0.4	7977	0.4
Interval cancer	895	0.1	1416	0.1
No cancer	1,211,978	99.5	1,793,808	99.5

Note—Counts for certain characteristics do not total to *N* owing 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* = 2311)			
	Digital		Film		Digital		Film	
	N	%	*N*	%	*N*	%	*N*	%
No. of women[a]	5441	40.6	7977	59.4	895	38.7	1416	61.3
Age at examination (y)								
40–49	1004	18.5	1277	16.0	225	25.1	347	24.5
50–59	1502	27.6	2357	29.5	263	29.4	410	29.0
60–69	1537	28.2	2134	26.8	223	24.9	365	25.8
70–79	1010	18.6	1573	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	3736	73.9	5914	77.9	642	76.2	1077	80.3
Black, non-Hispanic	324	6.4	450	5.9	54	6.4	81	6.0
Asian, Native Hawaiian, Pacific Islander	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

(Table 2 continues on next page)

TABLE 2: Characteristics of Women With Screen-Detected and Interval Cancers by Imaging Modality: Breast Cancer Surveillance Consortium 2003–2011 (continued)

Characteristic	Screen-Detected Cancer (*n* = 13,418)				Interval Cancer (*n* = 2311)			
	Digital		Film		Digital		Film	
	N	%	*N*	%	*N*	%	*N*	%
Family history of breast cancer								
Yes	1209	22.6	1645	21.7	218	24.7	322	23.5
No	4130	77.4	5937	78.3	666	75.3	1049	76.5
Menopausal status								
Premenopausal or perimenopausal	987	19.7	1243	17.1	229	28.4	322	25.6
Postmenopausal	4019	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	4195	89.3	5764	85.3	659	87.4	1028	81.9
History of breast biopsy								
Yes	1438	27.7	2166	28.1	288	35.2	464	33.8
No	3762	72.2	5539	71.9	530	64.8	908	66.2
BI-RADS breast density								
Almost entirely fat	356	8.2	325	5.7	34	4.5	37	3.4
Scattered fibroglandular densities	1918	44.2	2571	45.0	236	31.5	359	33.3
Heterogeneously dense	1800	41.5	2448	42.8	386	51.5	533	49.4
Extremely dense	264	6.1	372	6.5	93	12.4	150	13.9
Time since previous mammogram								
No previous	197	3.8	329	4.5	21	2.4	24	1.8
1 y (9–18 mo)	3021	58.9	3663	49.7	624	72.7	892	66.0
2 y (19–30 mo)	928	18.1	1804	24.5	120	14.0	280	20.7
≥ 3 y (≥ 31 mo)	982	19.1	1567	21.3	93	10.8	155	11.5

[a] Percentages are for the row by screen-detected and interval cancer groups. All other percentages are column percentages.

TABLE 3: Rates of Cancer per 1000 Mammograms by Tumor Characteristics, Mode of Detection, and Imaging Modality: Breast Cancer Surveillance Consortium 2003–2011

Cancer Characteristic	Screen-Detected Cancer (*n* = 13,418)						Interval Cancer (*n* = 2311)					
	Digital			Film			Digital			Film		
	No. of Cancers	Column %	Rate per 1000	No. of Cancers	Column %	Rate per 1000	No. of Cancers	Column %	Rate per 1000	No. of Cancers	Column %	Rate per 1000
Total[a]	5441	86	4.47	7977	85	4.42	895	14	0.73	1416	15	0.79
DCIS	1638	30	1.34	1854	23	1.03	106	12	0.09	132	9	0.07
Invasive	3803	70	3.12	6123	77	3.40	789	88	0.65	1284	91	0.71
American Joint Committee on Cancer stage												
I	2313	63	1.90	3530	61	1.96	311	41	0.26	466	39	0.26
IIA	780	21	0.64	1200	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

(Table 3 continues on next page)

TABLE 3: Rates of Cancer per 1000 Mammograms by Tumor Characteristics, Mode of Detection, and Imaging Modality: Breast Cancer Surveillance Consortium 2003–2011 (continued)

Cancer Characteristic	Screen-Detected Cancer (*n* = 13,418)						Interval Cancer (*n* = 2311)					
	Digital			Film			Digital			Film		
	No. of Cancers	Column %	Rate per 1000	No. of Cancers	Column %	Rate per 1000	No. of Cancers	Column %	Rate per 1000	No. of Cancers	Column %	Rate per 1000
Surveillance, Epidemiology, and End Results summary stage												
Local	2868	78	2.35	4433	76	2.46	492	64	0.40	723	59	0.40
Regional	776	21	0.64	1362	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 (mm)												
≤ 10	1184	34	0.97	1778	32	0.99	124	17	0.10	193	16	0.11
11–20	1410	40	1.16	2266	41	1.26	269	36	0.22	431	37	0.24
> 20	903	26	0.74	1536	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	2917	78	2.39	4534	76	2.51	504	65	0.41	757	61	0.42
Positive	812	22	0.67	1425	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
Grade												
1	1142	32	0.94	1635	29	0.91	153	21	0.13	235	21	0.13
2	1597	45	1.31	2436	44	1.35	313	43	0.26	455	40	0.25
3	838	23	0.69	1512	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	4630	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	1373	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
ERBB2[b]												
Positive	316	12	0.26	549	15	0.30	76	14	0.06	125	18	0.07
Negative	2243	88	1.84	2995	85	1.66	478	86	0.39	574	82	0.32
Unknown	1244	33	1.02	2579	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	1260	33	1.03	2688	44	1.03	238	30	0.20	603	47	0.33

[a]Percentages are for the row. All other percentages are column percentages.
[b]Also known as known as HER2 or HER2/neu.

with film mammography (1.34 vs 1.03 per 1000 examinations). Yet there was little difference in invasive tumor features for digital or film screen-detected cancers. Interval cancers diagnosed after digital mammography were also slightly more likely to be DCIS but with few differences in invasive tumor features.

Relative Risk of Unfavorable Tumor Characteristics

The adjusted ORs of having unfavorable tumor characteristics were significantly dif-

ferent for 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 diagnosed after digital mammography were slightly less likely to have unfavorable tumor features than were cancers diagnosed after film mammography. For example, interval cancers not seen on digital mammograms were 31% less likely than interval cancers not seen on film mammograms to present at AJCC stage IIB or higher (adjusted OR, 0.69; 95% CI, 0.52–0.93; rate, 0.12 vs 0.18 per 1000 examinations), 22% less likely to be regional or distant disease (adjusted OR, 0.78; 95% CI, 0.64–0.95; rate 0.23 vs 0.28 per 1000 examinations), 22% less likely to have positive nodal status (adjusted OR, 0.78; 95% CI, 0.64–0.95; rate, 0.22 vs 0.27 per 1000 examinations), and 29% less likely to present with estrogen receptor–negative tumors (adjusted OR, 0.71; 95% CI, 0.56–0.91; rate, 0.13 vs 0.16 per 1000 examinations).

In contrast, the adjusted ORs of having favorable tumor characteristics (early stage, smaller tumor size, negative nodal status, lower grade, and estrogen receptor–positive tumors) were not significantly different for digital versus film mammography for screen-detected or interval cancers. The one exception was among screen-detected cancers, in which the adjusted OR of having DCIS versus invasive disease was 1.30 (95% CI, 1.15–1.48), indicating that DCIS is more frequently detected on digital than on film mammograms.

Discussion

Our findings revealed a similar proportion of interval cancers among women screened with digital mammography and those screened with film mammography. This proportion is similar to the 13.8% reported in the Ontario Breast Screening Program [1]. We also found that the rates of screen-detected and interval cancers were similar across modalities. Our rates are substantially lower than those found in a 2014 study conducted in The Netherlands by Nederend et al. [9], who reported an interval cancer rate for digital mammography of 2.0 per 1000 examinations versus 1.7 per 100 for film mammograms. Hoff et al. [16] reported similar rates of screen-detected invasive cancer and interval cancer but higher rates of screen-detected DCIS on digital than on film mammograms. Studies from Ireland, The Netherlands, and Norway [17–19] showed increased cancer detection rates with digital mammography, whereas studies from Spain, the United Kingdom, and the United States showed similar cancer detection rates for digital and film mammography [2, 8, 17–21].

As in previous studies based on film mammography [22–24], we found that interval cancers were more likely than screen-detected cancers to have unfavorable tumor characteristics. In particular, interval cancers had a higher stage, larger size, and greater frequencies of positive lymph node involvement and estrogen receptor–negative status. Our results also agree with those of a study

TABLE 4: Odds Ratios of Having Tumor Characteristics With Worse Prognosis (Relative to Better Prognosis or No Cancer) and Better Prognosis (Relative to Worse Prognosis or No Cancer) for Digital Versus Film Mammography: Breast Cancer Surveillance Consortium 2003–2011

Cancer Characteristic	Screen-Detected Cancers		Interval Cancers	
	Unadjusted Odds Ratio	Adjusted Odds Ratio[a]	Unadjusted Odds Ratio	Adjusted Odds Ratio[a]
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 cancers	**0.92 (0.85–0.90)**	0.98 (0.89–1.07)	0.91 (0.79–1.04)	0.90 (0.77–1.06)
AJCC stage IIB or higher	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[b]	**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 3	**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)[c]
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[c]	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)

Note—Values in parentheses are 95% CI. **Bold** type indicates statistically significant value. AJCC = American Joint Committee on Cancer, SEER = Surveillance, Epidemiology, and End Results, DCIS = ductal carcinoma in situ.

[a]Adjusted for current hormone therapy use, age, race and ethnicity, screening interval, examination year, and Breast Cancer Surveillance Consortium registry.

[b]SEER summary stages are local, regional, and distant.

[c]Models adjusted for screening interval or race did not converge.

conducted with data from the Dutch Microarray in Node-Negative Disease May Avoid Chemotherapy trial. That study [25] showed that tumor characteristics of cancers screen detected with digital mammography were similar to those of cancers detected with film mammography and that interval cancers diagnosed after screening with film mammography had more unfavorable characteristics than cancers diagnosed after digital mammography. We add to the existing literature in that previous work focused on screen-detected and interval cancers based on film mammographic findings and our study includes more than 3800 cancers diagnosed after digital mammography.

Among women with interval cancer, adjusted ORs of unfavorable tumor characteristics were lower for digital than for film mammography. This finding was not observed for screen-detected cancers. A 2014 study conducted in The Netherlands [9] compared characteristics of interval cancers among 63,182 women screened with digital mammography and 60,770 women screened with film mammography between 2008 and 2010. That study did not show differences in breast density, tumor size, lymph node status, or hormone receptor status between digital- and film-detected interval cancers. It is possible that the difference between the film versus digital interval cancers we observed and the findings of Nederend et al. [9] reflects the different interval cancer rates in The Netherlands and the United States or that Nederend et al. defined interval cancers on the basis of 2 years of follow-up.

In our study we found almost identical overall cancer detection rates of 5.20 and 5.21 per 1000 examinations for digital and film mammography. Interestingly, digital mammography showed more instances of DCIS. The meaning of this finding is unclear, but one possibility is that the types of DCIS found at digital mammography may lead to fewer interval cancers with poor prognostic characteristics. We do not believe this is the case because mammographically detected 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 as aggressive as the interval cancers in our study [25]. This unexplained and interesting finding deserves more study.

The strengths of our study include the ability to examine both digital and film mammograms 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 stratification by imaging modality. Our study also had limitations, however. First, in the BCSC data, we were unable to determine whether the interval cancers were true interval cancers or missed cancers that were visible on the screening images. Second, we had incomplete data on ERBB2 status (also known as HER2 or HER2/neu), another important prognostic factor. Because the SEER data more comprehensively capture ERBB2 status, the lack of data remains a problem for many studies conducted with state cancer registries.

Our study results suggest that the transition to digital mammography in the United States has not reduced the interval cancer rate. Interval cancers constitute approximately 15% of breast cancers for both digital and film mammography. However, interval cancers detected after negative results of a digital examination had a lower rate of unfavorable characteristics than those detected after negative results of a film examination, which may improve treatment outcomes. The pathologic findings are similar for screen-detected cancers whether the modality is digital or film. As technologies in breast imaging change in the future, a study similar to this one that compares the pathologic features of cancers detected with digital mammography with those of cancers detected with tomosynthesis will be important to determine whether screen-detected and interval cancers vary in a clinically meaningful way between these two modalities.

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