Cancer Cases from ACRIN Digital Mammographic Imaging Screening Trial: Radiologist Analysis with Use of a Logistic Regression Model[1]

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Purpose: To determine which factors contributed to the Digital Mammographic Imaging Screening Trial (DMIST) cancer detection results.

Materials and Methods: This project was HIPAA compliant and institutional review board approved. Seven radiologist readers reviewed the film hard-copy (screen-film) and digital mammograms in DMIST cancer cases and assessed the factors that contributed to lesion visibility on both types of images. Two multinomial logistic regression models were used to analyze the combined and condensed visibility ratings assigned by the readers to the paired digital and screen-film images.

Results: Readers most frequently attributed differences in DMIST cancer visibility to variations in image contrast—not differences in positioning or compression—between digital and screen-film mammography. The odds of a cancer being more visible on a digital mammogram—rather than being equally visible on digital and screen-film mammograms—were significantly greater for women with dense breasts than for women with nondense breasts, even with the data adjusted for patient age, lesion type, and mammography system (odds ratio, 2.28; $P < .0001$). The odds of a cancer being more visible at digital mammography—rather than being equally visible at digital and screen-film mammography—were significantly greater for lesions imaged with the General Electric digital mammography system than for lesions imaged with the Fischer ($P = .0070$) and Fuji ($P = .0070$) devices.

Conclusion: The significantly better diagnostic accuracy of digital mammography, as compared with screen-film mammography, in women with dense breasts demonstrated in the DMIST was most likely attributable to differences in image contrast, which were most likely due to the inherent system performance improvements that are available with digital mammography. The authors conclude that the DMIST results were attributable primarily to differences in the display and acquisition characteristics of the mammography devices rather than to reader variability.

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In the National Cancer Institute and American College of Radiology Imaging Network (ACRIN)-sponsored Digital Mammographic Imaging Screening Trial (DMIST), participants underwent both digital mammography and screen-film mammography between September 2001 and November 2003. Digital mammography was performed by using five digital systems from four manufacturers—Senoscan-Dx (Fischer, Denver, Colo), Computed Radiography (Fuji, Tokyo, Japan), Senographe (General Electric, Waukesha, Wis), Lorad CCD-OT (Hologic, Bedford, Mass), and Lorad Selenia-MG (Hologic) (1)—with each woman's mammograms interpreted independently by different radiologists. Analysis was based on the results for 42 760 women who underwent breast biopsy or follow-up more than 10 months after they entered the study and received a diagnosis of cancer within 15 months after study entry (2). The diagnostic accuracy of digital mammography was found to be significantly superior to that of screen-film mammography for women with dense breasts, women younger than 50 years, and pre- and perimenopausal women (2). A nonsignificant trend toward better diagnostic accuracy with screen-film mammography than with digital mammography was observed in women aged 65 years or older who had fatty breasts (3). Our purpose in this study was to determine which factors contributed to the DMIST cancer detection results.

Materials and Methods

Our Health Insurance Portability and Accountability Act–compliant project was approved by the institutional review boards of the University of North Carolina at Chapel Hill and ACRIN. The digital mammograms of 335 DMIST cancers were processed for use in our study by each manufacturer with use of techniques available at the time of DMIST. Although the University of North Carolina at Chapel Hill has a research agreement with General Electric, no other financial or equipment support for this study was provided by the manufacturers. Data were controlled by study personnel who were not consultants to the digital mammography manufacturers at any time. One author (R.E.H.) was recently hired as a consultant to GE Healthcare (Waukesha, Wis).

DMIST Case Mix in Current Study

Some of the 335 DMIST cancer cases were not reviewed by all readers because screen-film mammograms were not available owing to intermittent requests for them by participating sites for patient care purposes. A total of 307 cases with both digital and screen-film mammograms were available for our study. These cases included 294 cases with one cancer and 13 cases with two cancers; thus, a total of 320 cancers were available for review. The cases with two cancers were retained to provide readers with a typical clinical case mix. All soft-copy (digital mammography) cases were available in a Digital Imaging and Communications in Medicine format and varied only with respect to the machine used (Senographe, Lorad Selenia-MG, Senoscan-Dx, Computed Radiography, or Lorad CCD-OT). The images in all cases were downloaded for soft-copy review to a soft-copy review workstation (Sectra IDS5.X; Sectra North America, Shelton, Conn). Readers defined their own hanging protocols, which were set up by a research assistant (E.B.C.). Each reader rated 302–306 cases, which involved 308–319 cancers.

One radiologist (E.D.P.) with 23 years of experience in breast imaging recorded the location of each cancer on the basis of visual inspection and information provided in the radiology and pathology reports by recording the visibility of the lesion on both screen-film and digital mammograms, the size of the lesion measured on the screen-film image (or, if it was not visible on the film hard-copy image, as measured on the digital image), and the structural characteristics of the lesion (presence of mass, calcifications, architectural distortion, focal asymmetry or other finding according to Breast Imaging Reporting and Data System [BI-RADS] [4] descriptors). The radiologist also created an acetate overlay that encircled either all the lesions or the location of the known cancers on the basis of her review of the mammograms or information in the other DMIST records.

Nine additional radiologists (J.K.B., L.L.F., R.A.J., M.A.K., C.M.K., Y.L., W.P., D.P., S.C.Y.) participated in the reader study. Two readers (W.P., S.C.Y.) reported having no previous experience with digital mammography and

Advance in Knowledge

- The Digital Mammographic Imaging Screening Trial results were most likely attributable to differences in image contrast, which were most likely due to the inherent system performance improvements that are available with digital mammography rather than to differences in positioning, compression, or reader skill.

Implication for Patient Care

- These study results support the use of digital mammography in place of screen-film mammography in women with dense breasts, women younger than 50 years, and pre- and perimenopausal women.

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Abbreviations:
ACRIN = American College of Radiology Imaging Network
CI = confidence interval
DMIST = Digital Mammographic Imaging Screening Trial
OR = odds ratio

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Guarantor of integrity of entire study, E.D.P.; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; manuscript final version approval, all authors; literature research, E.D.P., M.J.Y., E.F.C., R.E.H.; clinical studies, E.F.C., R.E.H., J.K.B., R.A.J., M.A.K., C.M.K., Y.L., D.P., S.C.Y.; experimental studies, E.D.P., E.B.C., M.J.Y., J.K.B., L.L.F., C.M.K., W.P.; statistical analysis, S.A., H.S.M., M.B., C.G.; and manuscript editing, E.D.P., S.A., E.B.C., H.S.M., M.J.Y., E.F.C., R.E.H., J.K.B., L.L.F., R.A.J., M.A.K., C.M.K., D.P., W.P., C.G.

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See Materials and Methods for pertinent disclosures.

thus did not participate in our primary analysis because of the likelihood that their lack of digital mammography experience would bias their opinions in favor of screen-film mammography. The seven other readers had 4–10 years experience interpreting digital mammograms and 5–30 years experience in breast imaging.

All readers had experience using the General Electric system, and all but one had experience using more than one digital mammography system—five readers had experience using the Fischer unit; three, experience using the Fuji unit; two, experience using the Hologic machines; and one each, experience with only Siemens (Erlangen, Germany) or Hologic systems. Our study took place at a single site (University of North Carolina Biomedical Research Imaging Center), and each reader participated for at least 2 days. A multiviewer (Mammoscope MS614A; RADx, Plano, Tex) was loaded with the screen-film mammography cases. The digital mammograms were displayed on the soft-copy review workstation and processed according to algorithms that were available at the time of DMIST, including Premium View (General Electric), which was available at the DMIST sites for only the last 4 months of case accrual. The screen-film and digital mammograms were displayed simultaneously, next to each other, with minimal glare. A 2× magnifying glass and standard soft-copy image manipulations (brightness, contrast, magnification, zoom, and pan) were available.

The readers were informed that all cases included known malignancies and were provided with the annotated acetate overlay used to identify the actual cancer locations. They then rated the relative visibility of the known cancers on the screen-film mammograms versus the visibility on the digital mammograms. The visibility of each lesion with each modality was graded on a five-point scale by using a visual analogue table, on which the readers marked a point that corresponded to the relative visibility of the lesion on both types of images (digital and screen film).

If readers rated the visibility of a lesion as different between screen-film mammography and digital mammography, they recorded their opinion as to why they believed the visibility differed between the two modalities by checking all applicable reasons from the following list: positioning differences, compression differences, location of cancer in dense tissue, overlapping parenchyma obscured lesion with one modality but not with the other, location of lesion in subcutaneous fat, location of lesion in the thickest part of the breast, lesion characteristics were more evident with one modality than with the other (ie, more calcifications were seen, calcification shapes were more obvious, suspicious mass margin characteristics were more evident, or other characteristic[s]), image noise, artifacts, contrast differences, technique differences, uncertainty regarding the reason for the greater visibility, or other reason(s). The reader was asked to specify the other characteristic(s) or other reason(s) when these choices were checked.

Statistical Analyses

The seven readers provided 2211 opinions regarding the differing visibility of the 320 cancers included in our study. One reader did not report on the visibility of one lesion, so data from the remaining 2210 visibility ratings were analyzed. Descriptive tables summarizing the patient and lesion characteristics were constructed. Overall reader preferences for one modality over the other and the possible reasons for these preferences were also summarized.

Multinomial logistic regression models were used to analyze the data (5). The unit of analysis was lesion, and lesions were considered independent. Since the majority (294 [92%] of 320) of the cases involved a single cancer, additional adjustment for multiple lesions in the same patient was deemed unnecessary. However, through appropriate specification of the covariance matrix in the analysis, the correlations that resulted from several observers reading images from the same set of cases were accounted for in the analysis. The response variable for the logistic regression analysis—henceforth referred to as the combined visibility rating—was a four-level categorical variable created by condensing and combining the visibility rankings for the digital and screen-film images recorded for each cancer lesion by each reader. The four combined visibility rating levels were defined as follows: DG+, indicating the cancer was deemed to be more visible on the

Figure 1

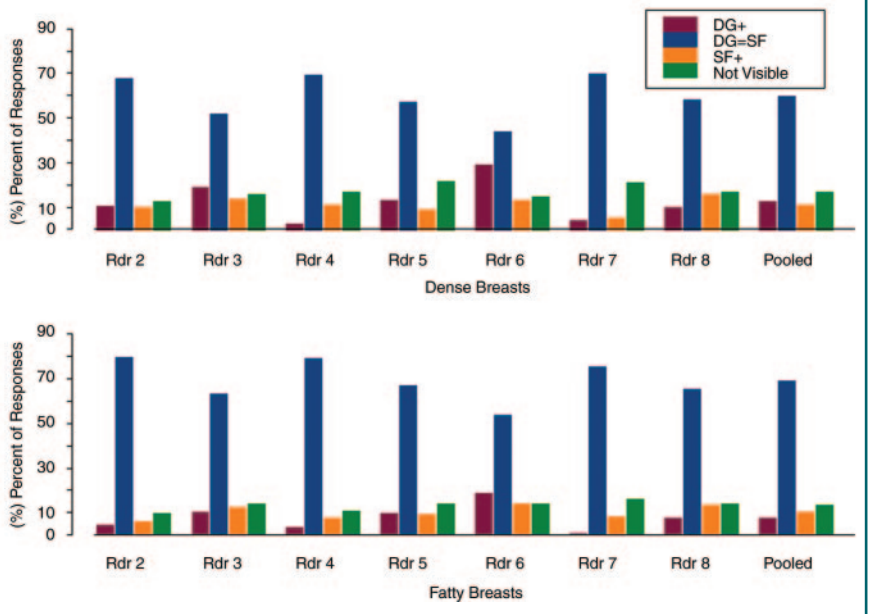

Figure 1: Graphs illustrate condensed visibility rankings assigned by each reader according to breast density. *Rdr* = reader.

Table 1

Characterization of 320 DMIST Cancers Included in Current Study

Characteristic	No. of Cancers
Mammography system	
Senoscan-Dx	78 (24.4)
Computed Radiography	59 (18.4)
Senographe	166 (51.9)
Lorad CCD-OT	3 (0.9)
Lorad Selenia-MG	14 (4.4)
Menopause status	
Data missing	4 (1.2)
Pre- or perimenopausal	94 (29.4)
Postmenopausal	222 (69.4)
Patient age (y)	
<50	65 (20.3)
50–64	160 (50.0)
≥65	95 (29.7)
Breast density*	
Nondense	164 (51.2)
Dense	156 (48.8)
Lesion number	
Multiple	13 (4.1)
One	307 (95.9)
Breast side	
Bilateral	1 (0.3)
Left	161 (50.3)
Right	158 (49.4)
Cancer location	
Not seen†	47 (14.7)
1–3 O'clock	88 (27.5)
3–6 O'clock	27 (8.4)
6–9 O'clock	34 (10.6)
9–12 O'clock	91 (28.4)
Subareolar	10 (3.1)
Axillary tail	7 (2.2)
Superior	10 (3.1)
Inferior	3 (0.9)
Lateral in right breast, medial in left breast	3 (0.9)
Medial in right breast, lateral in left breast	0
Lesion type	
No visible findings	35 (10.9)
Mass	137 (42.8)
Asymmetric density	29 (9.1)
Calcifications	104 (32.5)
Arch distortion	15 (4.7)
Cancer detection method	
455-Day follow-up‡	93 (29.1)
Digital and screen-film mammography	122 (38.1)
Digital mammography only	56 (17.5)
Screen-film mammography only	49 (15.3)
All cancers	320 (100)

Note.—Numbers in parentheses are percentages.

* Nondense refers to breasts composed almost entirely of fat and breasts with scattered fibroglandular density. Dense refers to heterogeneously dense and extremely dense breasts.

† Cancer was not visible on screen-film or digital image, so it could not be located in three dimensions.

‡ Cancer was not detected with either modality but rather during the 455-day follow-up period.

digital image than on the screen-film image; SF+, indicating the cancer was deemed to be more visible on the screen-film image than on the digital image; DG = SF, indicating the cancer was deemed to be equally visible on both images; and not visible, indicating the cancer was deemed to be not visible on either image (Fig 1). The DG = SF category had the highest frequency and was used as the reference-standard rating level when odds ratio (OR) inferences were drawn.

In addition, we fitted regular binary logistic regression models by collapsing levels of the combined visibility rating to assess the odds of the assignment of DG+ and SF+ ratings. These simplified models did not measure up to the multinomial models in terms of goodness of fit. The results of the secondary binary analysis corroborated the findings of the primary multinomial analysis in direction and statistical significance and are not reported here.

The primary model included breast density (dichotomized with the two most dense and the two least dense categories combined), patient age (three levels), lesion type (four levels), machine type (five levels), and reader (seven levels) as categorical covariates. A variant of this primary model, in which the covariate age was excluded, was also examined. The DMIST cancer characteristics included in the models are listed in Table 1. Breast density, machine type, and age were determined by using DMIST data. Lesion types were determined by a single reader (E.D.P.). Those cases in which breast cancer was not detected at digital or screen-film mammography in the primary DMIST were those in which the malignancy was detected within the 455-day follow-up period. These cases may have had some findings—albeit quite subtle ones—that were appreciable in retrospect by the reader who recorded the lesion type in our study. This would explain the difference between the number of cases in which cancers were not detected with either modality at the time of the original DMIST ($n = 93$) and the number of cases in which findings were not visible to the reader who recorded the lesion types ($n = 35$).

SAS, version 9.1.3, software (SAS, Cary, NC) was used to perform the analyses. For computational convenience, separate binary baseline-logit models—instead of a single multinomial logit model—were fitted by using the PROC GENMOD (SAS) procedure. Although separate fitting estimates tend to be less efficient compared with estimates from a simultaneous fitting, the loss in efficiency is minor when the response category with the highest prevalence is used as the baseline category, as was done in our analysis (6). The reported *P* values are not based on hypothesis testing; rather, they were used to assess whether the reported model-based ORs were significantly different from 1.

Results

The radiologist readers varied considerably in their opinions regarding the relative visibility of the cancers and the reasons for the differences in visibility between screen-film and digital mammography (Fig 1; Tables 2, 3). For both the cancers in dense breasts and those in fatty breasts, the most frequent reason for the variability in lesion visibility between the two modalities given by the readers was contrast differences between the two examinations. For the women with dense breasts, contrast differences accounted for 70 (18.5%) of the 378 reasons given by the readers that one mo-

Table 2

Radiologist Reasons for Cancer Visibility with One but Not the Other Modality

Reason	Cancers in Dense Breasts			Cancers in Fatty Breasts		
	Detected at Digital Mammography Only	Detected at Screen-Film Mammography Only	Total	Detected at Digital Mammography Only	Detected at Screen-Film Mammography Only	Total
Positioning differences	12 (4.7)	9 (7.2)	21 (5.6)	5 (3.9)	25 (11.6)	30 (8.7)
Compression differences	2 (0.8)	5 (4.0)	7 (1.9)	3 (2.3)	7 (3.2)	10 (2.9)
Lesion located in dense tissue	24 (9.5)	5 (4.0)	29 (7.7)	2 (1.6)	0	2 (0.6)
Overlapping parenchyma obscurs lesions with one but not the other modality	8 (3.2)	9 (7.2)	17 (4.5)	2 (1.6)	3 (1.4)	5 (1.5)
Lesion located in subcutaneous fat	0	0	0	0	1 (0.5)	1 (0.3)
Lesion located in thickest part of breast	1 (0.4)	0	1 (0.3)	0	2 (0.9)	2 (0.6)
Lesion characteristics more evident	22 (8.7)	10 (8.0)	32 (8.5)	6 (4.7)	19 (8.8)	25 (7.2)
More calcifications seen	17	7	24	4	4	8
Calcification shapes more obvious	5	5	10	1	3	4
Suspicious mass margin characteristics more evident	3	1	4	2	14	16
Other lesion characteristics more evident*	2	2	4	0	1	1
Image noise	5 (2.0)	3 (2.4)	8 (2.1)	1 (0.8)	4 (1.9)	5 (1.4)
Artifacts	0	0	0	0	1 (0.5)	1 (0.3)
Contrast differences	47	23	70	15	37	52
	(18.6)	(18.4)	(18.5)	(11.6)	(17.1)	(15.1)
Technique differences	5 (2.0)	4 (3.2)	9 (2.4)	4 (3.1)	12 (5.6)	16 (4.6)
Uncertain	0	0	0	0	5 (2.3)	5 (1.4)
All reasons	253	125	378	129	216	345

Note.—Data are numbers of cases of the given reason that a cancer lesion was visible with one modality but not with the other. Numbers in parentheses are percentages. Data pertain to cases in which cancers were found with only one modality and are cited according to breast density and how the cancers were detected in the primary DMIST.

* When the reason "other lesion characteristics were more evident" was cited, the reader was asked to provide details.

dality provided better visibility, with the frequency of the other opinions ranging from 0% to 8.5%. Positioning, compression, and technique differences combined accounted for only 37 (9.8%) of the 378 reasons given for improved lesion visibility.

Similar results were obtained for the women with fatty breasts, with contrast differences accounting for 52 (15.1%) of 345 opinions as to why one modality provided better visibility. However, in the subset of women in whom screen-film mammography depicted the cancers that were missed with digital mammography, the radiologists cited positioning differences as the reason for the improved lesion conspicuity in 25 (11.6%) of 216 cases. This compares with only five (3.9%) of the 129 reasons and 12 (4.7%) of the 253 reasons cited for the differences in conspicuity of cancers in the fatty and dense breasts, respectively, that were detected with digital mammography but missed with screen-film mammography.

The better visibility of all cancers judged by the readers to be more visible

Table 3

Radiologist Reasons for Better Cancer Visibility with One Modality Rather than the Other, for All Reviewed Cancers

Reason	More Visible on Digital Mammograms	More Visible on Screen-Film Mammograms
Positioning differences	37 (16.7)	69 (29.7)
Compression differences	16 (7.2)	30 (12.9)
Lesion in dense tissue	37 (16.7)	20 (8.6)
Overlapping parenchyma obscured lesions with one but not other modality	24 (10.9)	29 (12.5)
Lesion in subcutaneous fat	2 (0.9)	0
Lesion in thickest part of breast	4 (1.8)	2 (0.9)
Lesion characteristics more evident	59 (26.7)	60 (25.9)
More calcifications seen	37	30
Calcification shapes more obvious	20	17
Suspicious mass margin characteristics more evident	16	24
Other lesion characteristics more evident*	4	8
Image noise	0	28 (12.1)
Artifacts	0	1 (0.4)
Contrast differences	161 (72.8)	133 (57.3)
Technique differences	14 (6.3)	44 (19.0)
Uncertain	4 (1.8)	11 (4.7)
All reasons	221	232

Note.—Data are numbers of cases of the given reason that cancer lesion visibility was better with one modality rather than the other, as cited for all analyzed cancers according to case review visibility results. Numbers in parentheses are percentages.

* When the reason "other lesion characteristics were more evident" was cited, the reader was asked to provide details.

at digital mammography was attributed most frequently to differences in image contrast (161 [72.8%] of 221 opinions) (Table 3). Other leading reasons that the readers rated cancers to be more visible on the digital images were more evident lesion characteristics (59 [26.7%] of 221 opinions), location of lesion in dense tissue (37 [16.7%] of 221 opinions), positioning differences (37 [16.7%] of 221 opinions), and overlapping parenchyma obscuring the lesion on the screen-film images (24 [10.9%] of 221 opinions).

Similar results were obtained for all cancers judged to be more visible on the screen-film images. Specifically, the most common explanation for the greater visibility was contrast differences, which accounted for 133 (57.3%) of 232 opinions. Other commonly mentioned reasons for the greater visibility on the screen-film images were positioning differences (69 [29.7%] of 232 opinions), more evident lesion characteristics (60 [25.9%] of 232 opinions), overlapping parenchyma obscuring the lesion on the digital images (29 [12.5%] of 232 opinions), technique differences (44 [19.0%] of 232 opinions), and image noise (28 [12.1%] of 232 opinions).

Table 4

Logistic Regression Analyses Results

Variables and Covariates	DG+ vs SF = DG		SF+ vs SF = DG	
	Model A	Model B	Model A	Model B
Mammography system				
Senographe*				
Senoscan-Dx	0.52 (0.33, 0.84)	0.52 (0.33, 0.84)	1.88 (1.35, 2.62)	1.89 (1.35, 2.64)
	.0068†	.0070†	.0002†	.0002†
Computed Radiography	0.55 (0.36, 0.84)	0.55 (0.35, 0.85)	0.39 (0.24, 0.66)	0.40 (0.24, 0.67)
	.0064†	.0070†	.0004†	.0005†
Lorad CCD-OT	0.94 (0.19, 4.70)	1.02 (0.20, 5.23)	0.58 (0.07, 4.60)	0.46 (0.06, 3.72)
	.9396	.9800	.6052	.4698
Lorad Selenia-MG	1.30 (0.64, 2.63)	1.34 (0.66, 2.74)	0.92 (0.39, 2.15)	0.85 (0.36, 2.00)
	.4719	.4230	.8407	.7107
Lesion type				
Mass*				
Arch distortion	1.26 (0.63, 2.54)	1.20 (0.59, 2.43)	1.08 (0.54, 2.14)	1.11 (0.56, 2.20)
	.5159	.6118	.8331	.7680
Asymmetric densities	1.40 (0.75, 2.62)	1.41 (0.75, 2.65)	1.27 (0.66, 2.44)	1.24 (0.64, 2.39)
	.2928	.2813	.4801	.5251
Calcification	1.35 (0.95, 1.92)	1.36 (0.96, 1.95)	1.13 (0.82, 1.57)	1.14 (0.82, 1.59)
	.0898	.0862	.4585	.4257
Breast density				
Fatty*				
Dense	2.25 (1.61, 3.15)	2.28 (1.61, 3.23)	1.11 (0.82, 1.52)	1.17 (0.85, 1.61)
	<.0001†	<.0001†	.4906	.3414
Age (y)				
≥65*				
<50	. . .	0.86 (0.52, 1.43)		0.87 (0.57, 1.34)
		.5621		.5317
50–64	. . .	1.24 (0.83, 1.86)		0.64 (0.45, 0.92)
		.2858		.0142†

Note.—For each data set, the first set of numbers are ORs, with 95% confidence intervals (CIs) in parentheses. The second numbers are *P* values, which reflect the statistical difference in the OR from 1. DG+ vs SF = DG refers to comparison of case in which cancer is more visible on the digital image than on the screen-film image versus case in which cancer is equally visible on both images. SF+ vs SF = DG refers to comparison of case in which cancer is more visible on the screen-film image than on the digital image versus case in which cancer is equally visible on both images.

* Reference-standard variable with which covariate or covariates were compared.

† Significant difference in OR from 1.

The results of the two models are presented in Table 4. Both models included machine type and lesion type as covariates. In addition, model A included the dichotomized breast density variable. Model B included age. Our analyses revealed that when the breasts were dense, the readers were twice as likely to rate a cancer as more visible on the digital images than to rate a cancer as equally visible on the digital and screen-film images (OR, 2.28; 95% CI: 1.61, 3.23; $P < .0001$). There was a nonsignificant tendency of the readers to rate lesion visibility as superior on the screen-film mammograms for fatty breasts.

The odds of a cancer being more visible on the screen-film image rather than being equally visible on both the screen-film and digital images were significantly lower for women between ages 50 and 64 years than for women aged 65 years or older, regardless of breast density. The model also revealed that the odds of the radiologists rating lesions as more visible on the digital image rather than rating lesions as equally visible on both images were significantly lower when the Fischer (OR, 0.52; 95% CI: 0.33, 0.84; $P = .0070$) and Fuji (OR, 0.55; 95% CI: 0.35, 0.85; $P = .0070$) systems were used than when the General Electric machine was used, regardless of patient age and breast density. The odds of screen-film mammography receiving a better visibility rating rather than digital and screen-film mammography having equal visibility ratings were higher when the Fischer digital system was used (OR, 1.89; 95% CI: 1.35, 2.64; $P = .0002$) than when the General Electric system was used. These odds were lower when the Fuji digital system was used (OR 0.40; 95% CI: 0.24, 0.67; $P = .0005$) compared with when the General Electric machine was used, regardless of patient age. The nonsignificant tendency toward better lesion visibility with screen-film mammography in older women with fatty breasts was higher with use of the Fischer system than with use of the Fuji and General Electric systems (Table 5).

Reader identity also significantly affected the likelihood of digital mammography having a higher visibility rating than screen-film mammography. Four readers

Table 5

Condensed Visibility Ratings for Cases of Fatty Breasts and DMIST Subjects Aged 65 Years or Older

Cancer Visibility	Fischer Senoscan-Dx	Fuji Computed Radiography	GE Senographe	Hologic Lorad-CCD-OT	Hologic Lorad-Selenia-MG	All Systems
Cancer not seen*	2/43 (5)	9/43 (21)	27/43 (63)	0	5/43 (12)	43/43 (100)
	2/75 (3)	9/77 (12)	27/270 (10)	0	5/12 (42)	43/441 (10)
Cancer seen						
Equally on both images	52/318 (16)	62/318 (20)	192/318 (60)	6/318 (2)	6/318 (2)	318/318 (100)
	52/75 (69)	62/77 (81)	192/270 (71)	6/7 (86)	6/12 (50)	318/441 (72)
Better on digital images	1/29 (3)	2/29 (7)	26/29 (90)	0	0	29/29 (100)
	1/75 (1)	2/77 (3)	26/270 (10)	0	0	29/441 (7)
Better on screen-film images	20/51 (39)	4/51 (8)	25/51 (49)	1/51 (2)	1/51 (2)	51/51 (100)
	20/75 (27)	4/77 (5)	25/270 (9)	1/7 (14)	1/12 (8)	51/441 (12)
All cancers	75/441 (17)	77/441 (18)	270/441 (61)	7/441 (2)	12/441 (3)	
	75/75 (100)	77/77 (100)	270/270 (100)	7/7 (100)	12/12 (100)	441/441 (100)

Note.—Data are numbers of cases ranked for cancer visibility according to the digital mammography system used to assess the cases for cancer. For each data set, the top set of numbers is the number of cases and percentage based on the total number of cancers seen and not seen, and the bottom set is the number of cases and percentage based on the total number of cases assessed with the different mammography systems.

* Cancer was not visible with either screen-film or digital mammography.

were more likely to rate screen-film imaging higher than digital imaging, and three were more likely to rate digital imaging higher. Lesion type did not significantly affect the visibility ratings of the two modalities.

Figure 2 shows an example of a DMIST case in which a cancer was detected at digital mammography but missed at screen-film mammography. Figure 3 shows an example of a DMIST case in which a cancer was detected on the screen-film images but missed on the digital images and in which a different image processing algorithm (Premium View) has been applied. We include this case here to demonstrate the effect of image contrast on cancer visibility.

Discussion

Our analysis suggests that image contrast was the most important factor in the improved performance of digital mammography, as compared with screen-film mammography, in DMIST. Similarly, where DMIST suggested a trend toward better accuracy with screen-film mammography than with digital mammography, image contrast again seemed to be a strong contributing factor. The decrement in lesion visibility in the fatty breasts with digital mammography that was attributed to image contrast was most marked for those cases acquired by using the Fischer system. In addition, positioning differences more frequently contributed to the nonsignificant trend in improved cancer visibility for screen-film mammography relative to digital mammography in the women with fatty breasts.

How might digital mammography yield contrast that is superior to that of screen-film mammography in women with dense breasts while exhibiting inferior contrast in women with fatty breasts? The factors that affect image contrast in digital mammography include the choice of the x-ray spectrum, the efficiency of the x-ray scatter rejection, and display image processing. In DMIST, these factors varied somewhat by machine type (7–9).

In addition, the nature and quality of the image data processing varied considerably. The visibility of lesion features is influenced substantially by the image processing algorithm and whether the lesion lies within a dense or fatty background (10). We believe that this is the most likely explanation for the conflicting results for dense and fatty breasts. The linear relationship between x-ray exposure and image signal that is achievable with digital detectors should allow inherently better image contrast (11).

We hypothesize that the manufacturers of the digital mammography systems focused their efforts on designing image processing algorithms that improve the gray scale in dense breasts while relatively deemphasizing the optimization of image processing in fatty breasts. This might seem justified since screen-film mammography misses more cancers in patients with dense breasts while having high sensitivity in fatty breasts (12,13). In addition, radiologists may behave differently when they interpret mammograms of fatty breasts compared with when they interpret mammograms of dense breasts because they know that lesions can hide in dense breasts. Readers may just spend more time evaluating dense breasts.

Of particular interest, given the results of our recently published DMIST cost-effectiveness analysis (14), which showed that digital mammography performed in patients older than 65 years is not cost-effective, is the excess number of cases of mammography performed with the Fischer system, which is no longer commercially available, among the cancers that were seen better on screen-film than digital images. Several factors related to the design of this system may have been responsible for the reduced performance in fatty breasts: The detector comprised a charge-coupled device with an x-ray absorbing phosphor. The

digitization was limited to 12 bits or 4096 gray levels, whereas the other systems typically provide the equivalent of 14 bits or 16 384 gray levels. With the 12-bit digitization of the Fischer system, to avoid overdriving the digital detector past its maximal value, the user operated the detector in the lower part of its range, possibly resulting in increased image noise.

In addition, the Fischer system did not have an automatic exposure control, so technologists had to guess the breast density to set the exposure level. The limited dynamic range of the detector probably made it more difficult to optimize image display, possibly resulting in poor contrast. Finally, the tungsten-aluminum x-ray spectrum provided excellent penetration of the dense breast and allowed low radiation doses to be used. For the fatty breasts, however, the more penetrating x-ray spectrum of the Fischer system may have been a detriment.

Figure 2

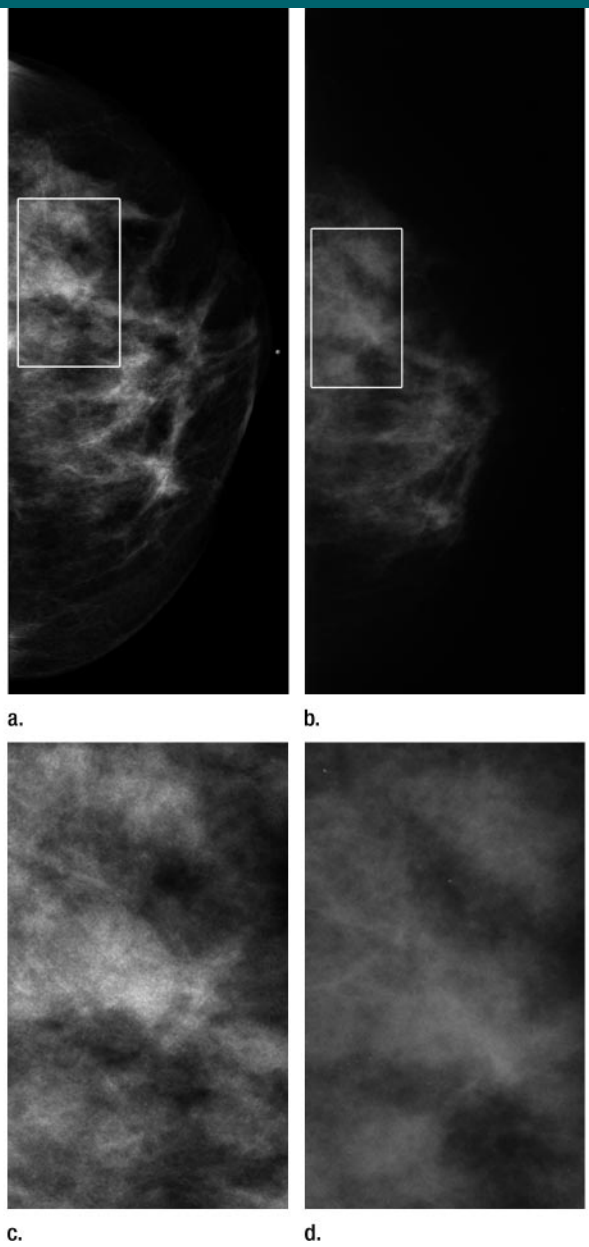

Figure 2: Craniocaudal mammographic views of dense left breast in 52-year-old-woman. **(a)** Full digital mammogram obtained by using Senographe system and **(c)** close-up view of area outlined (in rectangle) in **a**, as compared with **(b)** full screen-film mammogram of same breast and **(d)** close-up view of area outlined (in rectangle) in **b**, reveal how improved contrast in dense part of the breast depicted on the digital mammogram enables visualization of the cancer, an invasive ductal carcinoma, on the digital image but not on the screen-film image. The lesion was not visible on either the mediolateral oblique screen-film or digital mammograms.

Our study demonstrates that the results obtained in DMIST were not due primarily to accidents in positioning or interpretation (15,16). That is, digital mammography performed significantly better in particular subsets of women because of the better conspicuity of lesions in those subgroups. Screen-film mammography tended nonsignificantly to perform better in the subset of women aged 65 years or older with fatty breasts because of the improved conspicuity of lesions on film hard-copy images in this subgroup. This suggests that digital system manufacturers should improve the quality of their image processing algorithms, especially for fatty breasts—perhaps by applying different algorithms, for different breast densities, ideally based on reader performance data and not simply aesthetic factors (10).

A limitation of our analysis was the inclusion of very few cancers that were detected by using the Hologic systems, which reduced the power of our analysis for these units. In addition, our study reports on the opinions of radiologist readers. The basis for differences in opinion among readers is unclear and may include personal preferences, the amount of experience the readers had with both modalities and/or with specific machine types, and the availability of newer image processing algorithms for viewing some cases. Newer image processing algorithms perhaps explain the performance of the General Electronic system relative to the performance of the Fuji and Fischer units, since all readers had experience with that system and the Premium View algorithm was available for all General Electronic cases evaluated in this study but only for a 4-month period in DMIST itself.

Figure 3

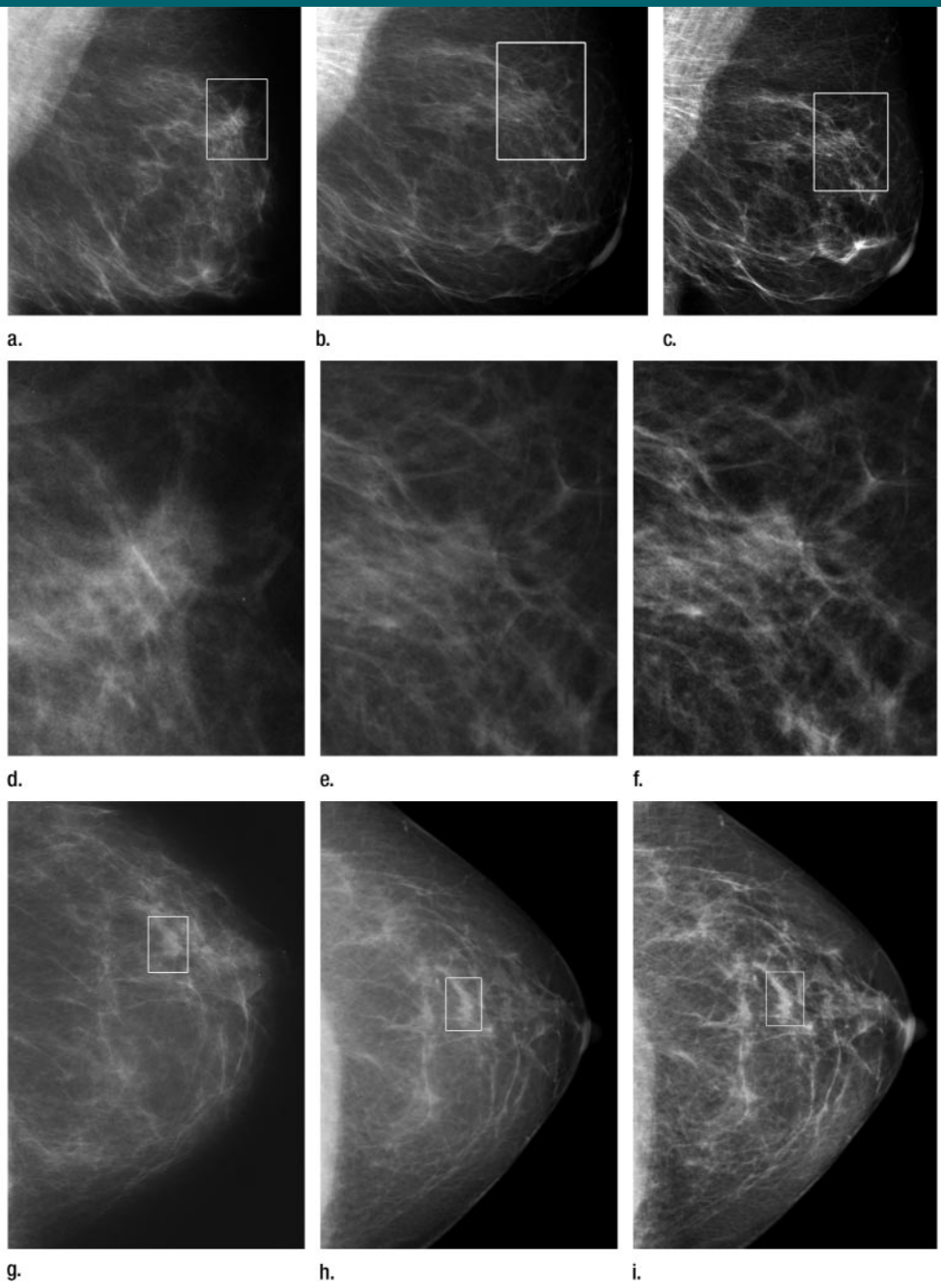

Figure 3: Fatty breast depicted on **(a, d, g)** screen-film and **(b, c, e, f, h, i)** digital left mammograms obtained in 53-year-old woman. Cancerous areas are outlined in rectangles. **(a–f)** Mediolateral oblique and **(g–i)** craniocaudal views are shown. The cancer, a mass that proved to be an invasive ductal carcinoma, is much more apparent on the screen-film images than on the digital images, with visibility being greatest on the screen-film mediolateral oblique views. The difference in lesion visibility between the screen-film and digital mammograms is accentuated when the screen-film overview image (**a**) is compared with the digital overview image obtained by using the default image processing algorithm (**b**). Close-up views of cancerous areas outlined in **a** (**d**) and **b** (**e**) are shown. There is a slight improvement in the visibility of the lesion depicted at digital mammography performed by using the Premium View image processing software, as seen on digital mediolateral oblique overview (**c**), screen-film mediolateral oblique close-up view (**d**), and digital craniocaudal (**i**) images.

Three of the four manufacturers contributed nearly equally to the significant findings in favor of digital mammography in the women with dense breasts and the women younger than 50 years, while we suspect that the relatively weaker performance of digital imaging in the women with fatty breasts was attributable primarily to the use of the Fischer machine. How the machines performed relative to each other cannot be determined with certainty from these data because different women were examined with each machine. In conclusion, the DMIST results are most likely attributable to differences in image contrast between the two modalities—not to positioning or reader variability factors.

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