Calcifications in Digital Mammographic Screening: Improvement of Early Detection of Invasive Breast Cancers?[1]

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Purpose: To evaluate the relevance of calcifications for invasive breast cancer detection in population-based digital mammographic screening.

Materials and Methods: This study was approved by an independent ethics committee, and no additional informed consent was required. Prospectively documented radiologic cancer features were correlated with pathologic characteristics in 241 breast malignancies diagnosed in 24067 participating women aged 50–69 years (part of the digital German Screening Program; initial screening rate, 92%; detection rate [DR], 1.0%; recall rate [RR], 7.5%). The rates of invasive cancers detected on the basis of calcifications were analyzed against pathologic tumor categories (pT categories) and histologic grades. For comparison of the study data with results of analog screening, data from the literature regarding calcification-specific RR, DR, and positive predictive value for recall (PPV_1) were calculated.

Results: The calcification-specific RR was 1.7% (416 of 24067). The calcification-specific DR for invasive cancer was 0.12% (29 of 24067), and the PPV_1 was 7.0% (29 of 416). Of all malignancies detected on the basis of calcification, 38% (29 of 77) were invasive. pT1 cancers showed an inverse association between tumor size and rate of detection on the basis of calcification; differences in rates among pT1 subcategories were statistically significant ($P < .001$). The proportion of grade 1 pT1 cancers detected on the basis of calcification (eight of 27) did not differ significantly from that of cancers detected on the basis of other radiologic features (46 of 108, $P = .24$). The calcification-specific invasive cancer DR was significantly higher for digital than for analog mammography.

Conclusion: One-third of malignancies detected on the basis of calcifications only are invasive cancers. They tend to be smaller but not less aggressive than invasive cancers detected on the basis of other features. Compared with published results of analog screening, digital screening offers the potential to increase the rate of invasive cancers detected on the basis of calcifications in population-based mammographic screening.

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The introduction of digital mammographic techniques into screening practice has been slow, despite the considerable advantages of digital mammography over conventional screen-film mammography (1,2). The most important question addressed so far is whether the accuracy of digital mammography in population-based screening is equivalent to that of analog mammography. Results of large prospective trials (1,3–10) have indicated that digital mammography is at least as accurate as screen-film mammography in current screening practice.

In contrast to the traditional belief that calcifications are best detected at screen-film mammography because of its higher spatial resolution, Del Turco et al (10) found in digital screening practice a high detection rate for cancers depicted as calcifications, most of which represented ductal carcinoma in situ (DCIS). This corresponds to the generally higher DCIS rates reported for digital screening than for screen-film screening (1,9,10). Critics of digital breast screening often conclude that the high rates of calcifications detected represent overdiagnosis, with many calcifications representing instances of DCIS that would never manifest clinically. In contrast to that idea and irrespective of the existence of evidence for a direct contribution of DCIS detection to the benefits of screening (11–13), there is a strong correlation between rates of detection of DCIS and rates of detection of small invasive cancers at screen-film mammography (14).

The objective of our study was to estimate the relevance of calcifications for invasive cancer detection in population-based digital mammographic screening.

Advances in Knowledge

- Invasive tumors detected on the basis of calcifications in population-based digital mammographic screening tend to be smaller (median, 7 mm) than those detected on the basis of masses (median, 14 mm; $P < .001$), architectural distortions (median, 15 mm; $P = .003$), or combinations of features (median, 17 mm; $P < .001$).
- Invasive tumors detected on the basis of calcifications in population-based digital mammographic screening do not show an increased rate of histologic grade 1 disease and consequently seem to be of at least no lower intrinsic aggressiveness than those generally detected with screening.
- The calcification-specific detection rate for invasive cancers in population-based screening is higher for digital than for analog mammography.

Materials and Methods

Our study correlates prospectively documented radiologic data of cancer morphology with the pathologic characteristics of 241 breast malignancies detected at one digital screening unit of the German nationwide program in 241 women who underwent mammographic screening from October 1, 2005, to August 31, 2008, and final surgical therapy by May 31, 2009.

The implementation of the population-based mammographic screening program started in October 2005. The program adheres to the European guidelines (15,16). Accordingly, the target population includes all women between the ages of 50 and 69 years who are invited within the specified screening interval of 2 years. Before a participant undergoes mammography, she has to give written informed consent to have her personal data handled according to the national program rules (16,17). These rules allow the use of personal data for the internal quality assurance of the screening unit. For this scientific study, the data were used anonymously. Our study was approved by the independent Ethics Committee of Westphalia-Lippe and the Medical Faculty of the University of Muenster. Additional informed consent was not required.

Implication for Patient Care

- Implementation of digital mammography increases the calcification-specific invasive cancer detection rate in population-based screening.

Performance Parameters

During the study period, 92.0% (22 142 of 24 067) of participants underwent initial mammography within the organized screening program, and 8.0% (1925 of 24 067) had previously undergone screening examinations with an interval of 2 years. The performance of the screening unit during the study period was characterized by a cancer detection rate of 1.0% (247 of 24 067 [the number of women with screening-detected invasive breast cancer or DCIS among the total number of screened women]); the detection rate at initial screening was 1.0% (225 of 22 185), and the detection rate at subsequent screening was 1.2% (22 of 1882). The recall rate was 7.5% (1809 of 24 067); the recall rate at initial screening was 7.7% (1707 of 22 185), and the recall rate at subsequent screening was 5.4% (102 of 1882). The positive predictive value for recall (PPV_1) was 13.7% (247 of 1809); the PPV_1 at initial screening was 13.2% (225 of 1707), and the PPV_1 at subsequent screening was 21.6% (22/102). The biopsy rate (number of invasive assessments per number of screened women) was 2.6% (626 of 24 067).

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Abbreviations:
BI-RADS = Breast Imaging Reporting and Data System
DCIS = ductal carcinoma in situ
PPV_1 = positive predictive value for recall

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Equipment and Routine Screening Process

The screening unit obtained all screening mammograms by using exclusively digital techniques. One full-field scanning system (MicroDosis Mammography, MDM/L30; Sectra Medical Systems, Linköping, Sweden) (pixel size, 50 μm) and one computed radiography system (Mammomat 3000 Nova, Siemens, Erlangen, Germany; with DirectView CR 975 EHR-M2, Carestream Health, Rochester, NY) (pixel size, 50 μm) were used. All devices fulfilled national requirements (18), as well as the requirements for contrast resolution of the European Protocol for the Quality Control of the Physical and Technical Aspects of Mammography Screening Addendum on Digital Mammography (15). Two-view mammograms were obtained at each screening examination.

The screening unit had been certified according to the regulations of the screening program, which included dedicated training and qualification of radiographers and radiologists (15,16). Readings were performed by two of five specialized radiologists (eg, S.W., W.H.), each of whom had at least 4 years of experience in breast imaging prior to the start of screening. Each interpreted a volume of 3000 mammograms in the 1st year of the program, followed by 5000–6000 mammograms in each subsequent year.

In the screening setting, soft-copy double reading was performed independently by using a monochrome liquid crystal display panel (ME 511; Totoku Electric, Tokyo, Japan) with a resolution of 2560 × 2048 pixels and high luminance and contrast (maximum luminance, 750 candelas per square meter; contrast: 800:1); the hanging protocol included full resolution with a 1:1 pixel ratio.

No computer-assisted detection system was used. Results of prior screening examinations were provided for reading; no magnification views existed.

If at least one reader classified abnormalities as Breast Imaging Reporting and Data System (BI-RADS) category 4a, BI-RADS category 4b, or BI-RADS category 5 (19) abnormalities, the case was presented at a consensus meeting. Both of the primary readers and one additional third reader decided at the consensus meeting whether patient recall for further assessment was recommended. The recalled cases were finally classified during the consensus meeting as BI-RADS category 4a, 4b, or 5. Each lesion was described according to the following terminology: *(a)* calcifications only, *(b)* calcifications in combination with a mass lesion, *(c)* calcifications in combination with an architectural distortion, *(d)* mass only, and *(e)* architectural distortion only. Both the final BI-RADS category and the morphology assigned at the consensus meeting were directly recorded into a central database. Once documented in the file, the data were no longer alterable and were used for the present study. No cancer was detected at clinical presentation only.

Study Design and Patients

The centrally prospectively documented data from the consensus meetings as part of the routine screening process were used for the analysis of BI-RADS category (19) and cancer morphology in digital screening mammography. There was no further review of images for this study. Results of further assessment procedures after the primary mammographic examination were not taken into account for this study.

The included breast cancers comprised 97.2% (241 of 248) of all malignancies detected in 24067 participants screened during the same period. The remaining seven patients were not included because surgery was not performed by May 2009. Of the 241 included screening-detected malignancies, 22 (9.1%) were diagnosed in the subsequent round of screening. Because of this small proportion of second round–detected cancers resulting from the small number of women undergoing a subsequent screening examination in our cohort (8% [1925 of 24067]), we decided not to analyze the data from both screening rounds separately.

Pathologic investigation of all surgical specimens was performed according to the European guidelines (20). All three pathologists (T.D., D.H., and W.B., each of whom had 5–25 years of experience in breast pathology) involved in our study went through the dedicated training courses of the national mammographic screening program. For invasive cancers, the pathologic size and Nottingham histologic grade (21,22) were documented. Pathologic staging was documented according to the International Union Against Cancer classification system (23), which is congruent to the system described in the American Joint Committee on Cancer cancer staging manual (24) (Table 1).

The median age of the 241 patients with cancer was 63 years. Of the malignancies, 73.9% (178 of 241) were invasive, and 26.1% (63 of 241) were DCIS only. The median size of the invasive cancers at pathologic examination was 12 mm (range, <1 to 130 mm; mean, 17 mm). Fifty-seven percent (102 of 178) of the invasive cancers measured less than 15 mm and 38.8% (69 of 178) measured 10 mm or less in the pathology specimen.

The distribution of the pathologic tumor (pT) categories is shown in Table 1. To avoid hampering of the downstream analysis by the extremely low number of pTmic cancers, they were combined with the pT1a cancers into one group (pT1a/pTmic) for further analysis. This combination was also justified by a lack of evidence of different prognoses for these subcategories in patients with negative lymph nodes.

Finally, so that we could compare our results with those from screen-film mammographic screening, we used data published by Del Turco et al (10). They examined the diagnostic accuracy of digital and screen-film mammography within a population-based screening program that adhered to the European guidelines in a setting similar to that of our study. We rendered their detailed data and calculated the recall rate, detection rate, and PPV_1 of calcifications regarding invasive cancer separately for the digital and analog cohorts of their series.

Statistical Analysis

For the finding of isolated calcifications, recall rate, detection rate, and PPV_1 were

calculated separately. The calcification-specific rate of invasive cancers was analyzed for the individual pT categories and for different histologic grades. The calculations were performed (E.K.) with statistical software (S-Plus, version 6.2; Insightful [now TIBO] Palo Alto, Calif) and with R, version 2.8 *(http://www.r-project.org/)*. To compare sample proportions, the Fisher exact test was applied in its two-sided variant for 2×2 up to 2×4 tables. The P (observed $\geq$ expected|observed $\leq$ expected) value was used. In cases where use of the Fisher test was not advisable, the χ^2 test was used. The Mann-Whitney U test was used to compare the size of invasive cancers detected on the basis of calcifications with those detected on the basis of other features of the following categories: mass, distortion, and a combination of calcifications with mass and/or distortion (no overlap between the categories).

$P \leq .05$ was considered to indicate a statistically significant difference.

Results

Of 24067 participants, 416 were recalled because of calcifications, resulting in a calcification-specific recall rate of 1.7%. Of all invasive and noninvasive cancers, 32.0% (77 of 241) showed calcifications as the only mammographically suspicious feature. The calcification-specific detection rate was 0.32% (77 of 24067). Of the malignancies detected on the basis of calcifications, 38% (29 of 77) were invasive cancers and 62% (48 of 77) were DCIS (Table 1). The calcification-specific detection rates for invasive cancers and DCIS were 0.12% (29 of 24067) and 0.20% (48 of 24067), respectively.

Whereas the overall PPV_1 was 13.7% (247 of 1809), the PPV_1 for calcifications was 18.5% (77 of 416), consisting of 7.0% (29 of 416) invasive cancers and 11.5% (48 of 416) instances of DCIS.

Of all invasive cancers, 16.3% (29 of 178) were detected at screening on the basis of calcifications alone. Of these 29 cancers, 27 (93%) were categorized as pT1 tumors (≤20 mm), and the remaining two were pT2 tumors. Calcification-specific tumor detection rates differed significantly between the individual pT1 subgroups, being highest in the pT1a/pTmic subgroup at 55% and decreasing to 5% in the pT1c subgroup ($P < .001$, Table 2). The calcification-specific DCIS detection rate was not significantly higher than the detection rate for pT1a/pTmic invasive cancers (76% [48 of 63] vs 55% [11 of 20], $P = .53$).

The median tumor diameter of invasive cancers detected on the basis of calcifications was smaller (median, 7 mm; range, microinvasion to 37 mm) than that of cancers detected on the basis of masses (median, 14 mm; range, 3–130 mm; $P < .001$) or architectural distortions (median, 15 mm; range, 8–40 mm; $P = .003$) only or on the basis of calcifications associated with masses or architectural distortions (median, 17 mm; range, 2–127 mm; $P < .001$).

Invasive cancers showed rates of histologic grade 1, 2, and 3 disease of 33.7% (60 of 178), 51.7% (92 of 178), and 14.6% (26 of 178), respectively. Of the 27 invasive cancers 20 mm or smaller (pT1) detected on the basis of calcification alone, 30% (eight of 27) were grade 1. Within the pT1 category, calcification-detected cases split up by histologic grade 1 versus 2 plus 3 showed no significant difference in proportions compared with the remaining pT1 cases detected on the basis of other features ($P = .24$). In comparison to invasive cancers detected on the basis of other features, the grade 1 rate of those detected on the basis of calcifications only was not statistically different ($P = .53$, 30% [eight of 27] vs 42.6% [46 of 108] (Table 3).

Table 1

Distribution of Pathologic Tumor Categories for All Included Breast Cancers and for Cancers Detected on the Basis of Calcifications

pT Category	Description	All Cancers	Cancers Detected on Basis of Calcifications
pTis	DCIS	63 (26.1)	48 (62)
pTmic	Invasive tumor ≤ 0.1 cm	1 (0.4)	1 (1)
pT1a	Invasive tumor > 0.1 to 0.5 cm	19 (7.9)	10 (13)
pT1b	Invasive tumor > 0.5 to 1.0 cm	49 (20.3)	13 (17)
pT1c	Invasive tumor > 1.0 to 2.0 cm	66 (27.4)	3 (4)
pT2	Invasive tumor > 2.0 to 5.0 cm	36 (14.9)	2 (3)
pT3	Invasive tumor > 5.0 cm	5 (2.1)	0
pT4	Invasive tumor with infiltration of chest wall or skin	2 (0.8)	0
Total		241 (100)	77 (100)

Note.—Data in parentheses are percentages.

Table 2

Distribution of Mammographic Features of DCIS and Invasive Cancers 2 cm or Smaller (pT1) in Digital Screening

Feature	pTis Cancer	pTmic/pT1a Cancer	pT1b Cancer	pT1c Cancer
Calcifications	48 (76)	11 (55)	13 (27)	3 (5)
Calcifications plus mass and/or distortion	10 (16)	1 (5)	4 (8)	9 (14)
Mass	5 (8)	8 (40)	30 (61)	51 (77)
Distortion	0	0	2 (4)	3 (5)
Total	63 (100)	20 (100)	49 (100)	66 (100)

Note.—Data are numbers of cancers, with percentages in parentheses. $P < .001$ for calcifications versus calcifications plus mass and/or distortion and for calcifications versus mass; $P = .003$ for calcifications versus distortion.

A majority (70 of 77) of malignancies detected on the basis of calcifications were labeled as BI-RADS category 4. Of the seven remaining cases classified as BI-RADS category 5, six were DICS and one was invasive cancer. Moreover, 48% (14 of 29) of all invasive cancers detected on the basis of calcifications were categorized as BI-RADS category 4a, indicating low suspicion for malignancy (Table 4, Figure).

Compared with the calcification-specific invasive cancer detection rate of 0.04% (overall detection rate, 0.58%) in the analog screening cohort of Del Turco et al (10), the respective rates were significantly higher in both the digital screening cohort of Del Turco et al (0.11%; $P = .032$; overall detection rate, 0.72%) and in our study group (0.12%; $P = .013$; overall detection rate, 1.0%). Although the PPV_1 (30%) of isolated calcifications in all malignancies in the analog cohort was significantly higher than the PPV_1 in both digital studies—the digital cohort of Del Turco et al (25%, $P < .001$) and our study group (19%, $P < .001$)—the respective difference for invasive cancers detected on the basis of calcifications was smaller (Table 5).

Table 3

Distribution of Histologic Grade in Invasive Cancers 2 cm or Smaller (pT1) according to Detection Mode at Screening Mammography: Calcifications versus Other Features

Histologic Grade	Isolated Calcifications	Masses, Distortions, or Combinations*	*P* Value
1	8 (30)	46 (42.6)	.53
2	18 (67)	49 (45.4)	.28
3	1 (4)	13 (12.0)	.47
Total	27 (100)	108 (100)	

Note.—Data are numbers of cancers, with percentages in parentheses.

* Including associated calcifications.

Table 4

Distribution of BI-RADS Categories for 77 Malignancies Detected on the Basis of Calcifications Only

Malignancy Type	BI-RADS Category 4a	BI-RADS Category 4b	BI-RADS Category 5
Invasive carcinoma	14 (18)	14 (18)	1 (1)
DCIS	16 (21)	26 (34)	6 (8)
Total	30 (39)	40 (52)	7 (9)

Note.—Data are numbers of malignancies, with percentages based on the total of 77 malignancies in parentheses. Categories were defined at screening mammography during the consensus meeting.

Discussion

More than 20 years ago, Sickles (25) demonstrated that calcifications are relevant for the detection of invasive cancers, which was further confirmed by more recent studies of screen-film

Table 5

Results of Present Study Compared with Those of a Cohort Study of Digital versus Screen-Film Mammography in Population-based Screening of Women 50–69 Years of Age

Parameter	DM in Present Study	DM in Reference 10	SFM in Reference 10	*P* Value for DM in Current Study vs DM in Reference 10	*P* Value for DM vs SFM in Reference 10	*P* Value for DM in both Studies vs SFM
No. of participants	24 067	14 385	14 385			
Recall rate (%)	7.5 (1809/24 067)	4.6 (657/14 385)	4.0 (570/14 385)	<.001	.035	<.001
Recall rate for calcifications (%)	1.7 (416/24 067)	1.1 (151/14 385)	0.4 (60/14 385)	<.001	<.0001	<.001
Detection rate (%)	1.00 (247/24 067)	0.72 (104/14 385)	0.58 (84/14 385)	<.001	.12	<.001
Detection rate for calcifications (%)	0.32 (77/24 067)	0.26 (38/14 385)	0.13 (18/14 385)	.001	.006	<.001
Detection rate of DCIS for calcifications (%)	0.20 (48/24 067)	0.15 (22/14 385)	0.08 (12/14 385)	.002	.055	.005
Detection rate of invasive cancer for calcifications (%)	0.12 (29/24 067)	0.11 (16/14 385)	0.04 (6/14 385)	.013	.032	.013
PPV_1 for calcifications (%)	19 (77/416)	25 (38/151)	30 (18/60)	<.001	<.0001	<.001
PPV_1 for calcifications and DCIS (%)	12 (48/416)	15 (22/151)	20 (12/60)	<.001	<.0001	<.001
PPV_1 for calcifications and invasive cancer (%)	7 (29/416)	11 (16/151)	10 (6/60)	<.001	.005	<.001

Note.—DM = digital mammography, SFM = screen-film mammography. Unless otherwise specified, data are percentages, with raw data in parentheses.

mammography (26–29). However, to our knowledge, the studies on digital mammography have not specifically analyzed the rate of invasive cancers detected on the basis of calcifications as the sole finding (1,3,4,8–10,30). To date, because of widespread national implementation of digital mammography in practice, it is not feasible to generate data comparing digital and screen-film techniques in prospective randomized studies.

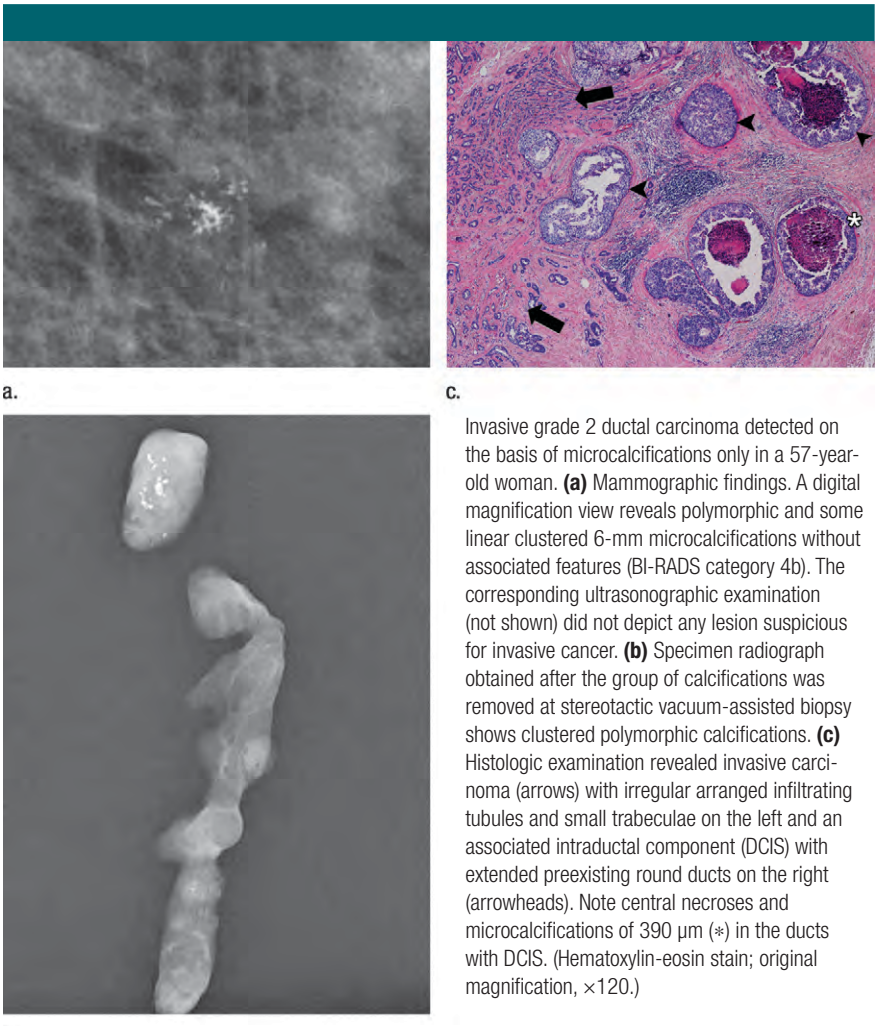
Looking at detailed data, the percentages of malignancies detected on the basis of calcifications at digital screening reported by Skaane and Skjennald (6) and Del Turco et al (10) were, at 32% and 37%, respectively, similar to our rate of 32%.

In our study, in accordance with other studies of population-based digital mammography programs (1,9,10), most malignancies detected on the basis of calcifications were DCIS; however, 38% proved to be invasive cancers. A similar proportion was reported by Stomper et al (29); they found that of all breast malignancies detected on the basis of calcifications on mammograms, 36% were invasive cancers. However, their results are not necessarily comparable to ours, which come from a population-based program with a different target population. On the basis of the detailed data presented by Del Turco et al (10), we calculated that even in their digital study cohort, about 42% of malignancies detected on the basis of calcifications were invasive cancers. This suggests that calcifications, which are a typical feature of DCIS, represent invasive cancers in more than a third of all malignancies detected on the basis of calcifications.

The sensitivity indicators in our study are in keeping with the European standards for screening and with recent reports (9,30). Therefore, we assume that our study population is representative of patients with cancers detected at population-based digital mammographic screening.

To our knowledge, there are no previous reports about the tumor sizes and grades of invasive cancers diagnosed after recall of patients with calcifications in population-based digital screening. We detected an inverse relationship between invasive tumor size and the rate of cancers detected on the basis of calcifications. The smaller the tumors, the more likely they were to be detected on the basis of calcifications alone (Figure). Within the group of small invasive cancers that were 10 mm or smaller (pT1b, pT1a/pTmic), the rate of tumors detected on the basis of calcifications was 35%, representing 83% of all invasive cancers detected on the basis of this feature.

Histologic grade according to the Nottingham system is generally accepted as a strong prognostic factor, even for tumors 10 mm or smaller (31). Moreover, data suggest that grade 1 cancers less than 20 mm in size (pT1) and grade 2 and 3 cancers less than 10 mm in size detected at screening show a lower likelihood of developing metastases (32). Therefore, to answer the question of whether invasive pT1 cancers detected on the basis of calcifications tend to be of higher or lower malignant potential, we analyzed their histologic grade distribution. According to the grade distribution of carcinomas detected on the basis of calcifications, grade 1 cancers were at least not overrepresented, and we interpret this result as an indication of a similar rate of aggressive cancers in this group. This suggests that detection of invasive tumors on the basis of calcifications alone does not mean detection of predominantly less aggressive cancers but rather contributes to the



Invasive grade 2 ductal carcinoma detected on the basis of microcalcifications only in a 57-year-old woman. **(a)** Mammographic findings. A digital magnification view reveals polymorphic and some linear clustered 6-mm microcalcifications without associated features (BI-RADS category 4b). The corresponding ultrasonographic examination (not shown) did not depict any lesion suspicious for invasive cancer. **(b)** Specimen radiograph obtained after the group of calcifications was removed at stereotactic vacuum-assisted biopsy shows clustered polymorphic calcifications. **(c)** Histologic examination revealed invasive carcinoma (arrows) with irregular arranged infiltrating tubules and small trabeculae on the left and an associated intraductal component (DCIS) with extended preexisting round ducts on the right (arrowheads). Note central necroses and microcalcifications of 390 μm (*) in the ducts with DCIS. (Hematoxylin-eosin stain; original magnification, ×120.)

screening benefit. To verify this, studies with larger sample sizes and longer follow-up are needed. This result is in line with the study of Del Turco et al (10), but the value of that study concerning grade is limited, because five of 16 invasive tumors detected on the basis of calcifications could not be included.

Analyzing the distribution of the BI-RADS categories, BI-RADS 4 was the dominant category for malignancies detected on the basis of calcifications for DCIS and invasive cancer. About half of these invasive cancers were categorized as BI-RADS 4a.

In European trials, there is evidence of a significantly higher detection rate for malignancies detected on the basis of calcifications in digital versus analog screening against the background of significantly higher recall and overall cancer detection rates (5,9,10,33). In accordance with this, when we compared the digital and analog techniques, we found in both digital studies—the digital cohort of Del Turco et al (10) and our digital study group—higher calcification-specific recall rates (1.1% and 1.7%, respectively) associated with higher calcification-specific detection rates (0.26% and 0.32%, respectively) than in the analog screen-film cohort in the study of Del Turco et al (calcification-specific recall rate, 0.4%; calcification-specific detection rate, 0.12%). Analyzing the calcification-specific detection rate for invasive cancers, we found a similar trend (the calcification-specific detection rate for invasive cancers was 0.11% for the digital cohort in the Del Turco et al study and 0.12% in our study, vs 0.04% for the analog cohort in the former study). Consequently, our observations suggest that digital screening may increase the detection rate of invasive carcinomas—in our study, predominantly those 2 cm or smaller.

Accordingly, in the Dutch study by Karssemeijer et al (34), the comparison of full-field digital mammography (FFDM) performed with computer-aided diagnosis (CAD) and screen-film mammography resulted in a finding of improved detection of microcalcifications with FFDM. The fraction of invasive cancers with microcalcifications alone increased significantly with FFDM, from 8.1% to 15.8%. In the Irish study by Hambly et al (35), the calcification-specific detection rate was significantly higher for FFDM than for screen-film mammography for all cancers (0.19% vs 0.13%, $P = .01$) and DCIS (0.12% vs 0.07%, $P = .009$) but not for invasive cancers (0.07% for FFDM vs 0.06% for screen-film mammography); this may have been related to a small number of cases.

Whereas European guidelines recommend a target recall rate of less than 7% for first screenings (15), the American College of Radiology and the U.S. Agency for Health Care Policy and Research both recommend an overall recall rate of less than 10% (36,37). Our first-round recall rate is slightly higher than the acceptable target given in the European guidelines, lower that recommended in the United States, and in agreement with the evidence-based results of Schell et al (38). Our relatively high recall rate of 7.5% was not due to the calcification-specific recall rate (1.7%), while the calcification-specific PPV_1 (19%) was higher than the overall PPV_1 of 14%.

Our study had further limitations. First, we used the 3rd edition of the BI-RADS manual and therefore did not have a category 4c (39). Thus, our results cannot be directly compared with those obtained by using current BI-RADS descriptors. Second, we combined our prevalent and incident screens, and our data are thus not directly comparable to either prevalent or incident screens. Third, our data are from a single screening program with double reading, with techniques that may not necessarily be applicable to other programs that use a different protocol. Fourth, we did not assess breast density, which could have obscured masses associated with calcifications. Finally, the comparison of our results from 2005 to 2008 to those in the report of Del Turco et al (10) is hampered by the different timing of the analog examinations, which were obtained from 2004 and 2005 and were from a different location. However, recently published data of population-based mammographic screening from Ireland and the Netherlands are in line with their and our results (34,35).

Overall, for population-based mammographic screening, our results suggest that in comparison to screen-film mammography, digital mammography has the potential to increase the rate of invasive cancers detected on the basis of isolated calcifications—cancers that tend to be smaller than those depicted by other radiologic features. Regarding histologic grade as criterion of intrinsic aggressiveness, small invasive tumors detected on the basis of calcifications are not less aggressive and are therefore not less relevant for screening benefit than those detected on the basis of other features. Invasive cancers detected on the basis of calcifications are not categorized with a higher probability of malignancy than DCIS detected on the basis of calcifications at screening mammography.

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