Detection of Breast Cancer with Full-Field Digital Mammography and Computer-Aided Detection

Juliette S. The[1,2]
Kathy J. Schilling[1]
Jeffrey W. Hoffmeister[3]
Euvondia Friedmann[1]
Ryan McGinnis[1]
Richard G. Holcomb[1]

OBJECTIVE. The purpose of this study was to evaluate computer-aided detection (CAD) performance with full-field digital mammography (FFDM).

MATERIALS AND METHODS. CAD (Second Look, version 7.2) was used to evaluate 123 cases of breast cancer detected with FFDM (Senographe DS). Retrospectively, CAD sensitivity was assessed using breast density, mammographic presentation, histopathology results, and lesion size. To determine the case-based false-positive rate, patients with four standard views per case were included in the study group. Eighteen unilateral mammography examinations with nonstandard views were excluded, resulting in a sample of 105 bilateral cases.

RESULTS. CAD detected 115 (94%) of 123 cancer cases: six of six (100%) in fatty breasts, 63 of 66 (95%) in breasts containing scattered fibroglandular densities, 43 of 46 (93%) in heterogeneously dense breasts, and three of five (60%) in extremely dense breasts. CAD detected 93% (41/44) of cancers manifesting as calcifications, 92% (57/62) as masses, and 100% (17/17) as mixed masses and calcifications. CAD detected 94% of the invasive ductal carcinomas (n = 63), 100% of the invasive lobular carcinomas (n = 7), 91% of the other invasive carcinomas (n = 11), and 93% of the ductal carcinomas in situ (n = 42). CAD sensitivity for cancers 1–10 mm (n = 55) was 89%; 11–20 mm (n = 37), 97%; 21–30 mm (n = 16), 100%; and larger than 30 mm (n = 15), 93%. The CAD false-positive rate was 2.3 marks per four-image case.

CONCLUSION. CAD with FFDM showed a high sensitivity in identifying cancers manifesting as calcifications and masses. Sensitivity was maintained in cancers with lower mammographic sensitivity, including invasive lobular carcinomas and small neoplasms (1–20 mm). CAD with FFDM should be effective in assisting radiologists with earlier detection of breast cancer. Future studies are needed to assess CAD accuracy in larger populations.

Keywords: breast cancer, computer-aided detection, computer-aided diagnosis, digital images, full-field digital mammography, screening mammography

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[1]Center for Breast Care, Boca Raton Community Hospital, 690 Meadows Rd., Boca Raton, FL 33486. Address correspondence to J. S. The (jthe@bocaradiology.com).

[2]Boca Radiology Group, Boca Raton, FL.

[3]iCAD, Inc., Beavercreek, OH.

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Computer-aided detection (CAD) technology with full-field digital mammography (FFDM) remains an exciting technology in breast cancer detection. In the literature, FFDM has been cited as having several advantages over screen-film mammography, including higher contrast resolution, better dynamic range, and lower noise [1, 2]. Unlike screen-film mammography, which serves as image receptor and display medium, FFDM captures images with a digital detector so the images are available for immediate display on a monitor [3]. The 2005 Digital Mammographic Imaging Screening Trial (DMIST) regarding digital mammography found FFDM to be more accurate in women younger than 50 years, women with heterogeneously dense or extremely dense breasts, and premenopausal and perimenopausal women [4, 5]. Although the effectiveness of CAD with screen-film mammography systems has been established elsewhere in the literature [6–9], the clinical data show that the efficacy of CAD with FFDM is consistent with the efficacy of CAD with screen-film mammography [3, 10]. Our study contributes to the growing body of clinical evidence to evaluate the performance of CAD with FFDM according to clinically relevant metrics, including breast density, mammographic appearance, histopathology results, and mammographic lesion size.

Materials and Methods

Technology and Sample Criteria

One-hundred twenty-three consecutive biopsy-proven breast cancers identified from March 1, 2005, through February 28, 2006, originating from Boca Raton Community Hospital were evaluated retrospectively under institutional review board (IRB) approval using CAD (Second Look, version 7.2, iCAD, Inc.) with FFDM

(Senographe DS, GE Healthcare). Screening and diagnostic mammograms were included. Each case included a craniocaudal (CC) and mediolateral oblique (MLO) view of the breast with cancer at the time of cancer diagnosis; comparable projections including exaggerated craniocaudal lateral (XCCL), medial lateral, and lateral medial views were acceptable alternatives to CC or MLO views. However, excluded were nondisplaced implant views; magnification and compression views; and images taken for biopsy with needles, wires, or other equipment. Unilateral cases were accepted. In all cases, a malignant lesion was visible mammographically in at least one view.

Sensitivity and Scoring

Each CAD mark was scored as either a true-positive or a false-positive mark, where true-positive marks correctly indicated a malignant lesion and all other CAD marks were false. For cancers that were masses, true-positive was determined if the center of the CAD mark fell within a "truth box" that was sized to the extent of the mass. The same marking principle held true for focal architectural distortions and asymmetries. For calcifications, true-positive was determined when the CAD mark overlapped with any portion of the truth box sized to the extent of the calcifications. As case-based sensitivity was calculated, a true-positive determination required at least one true-positive marking per case. CAD sensitivity was evaluated based on breast density, mammographic presentation, histopathology results, and mammographic lesion size.

For false-positive determinations, only cases with all four standard views (i.e., right CC, left CC, right MLO, left MLO) were used. As a result, the 17 unilateral cases were excluded from the false-positive calculations, as was one case with right XCCL and right lateral medial views of a cancer and left CC, left MLO, and left lateral medial views of the other breast. Thus, 105 cases were evaluated for false-positive rating. Samples included in the calculation of the false-positive rate were any mark not scored as true-positive. A case-based average false-positive rate was calculated from all 105 cases with four standard images available. Postsurgical mammograms of these patients were then examined to determine whether false-positive marks were truly false-positive. In other words, were there any CAD marks on the original mammograms that were wrongly considered to be false-positive because future mammograms or surgery showed an existing cancer in retrospect at the location of the CAD mark? The classifications of CAD marks as true-positives or false-positives at this postsurgical review were used to assess CAD sensitivity and false-positive rate.

Results

Breast Density

CAD correctly marked 94% (115/123) of biopsy-proven cancers with a rate of 2.3 false-positives per case. Based on breast density, CAD correctly marked 100% of cancers in fatty breasts, 95% of cancers in breasts containing scattered fibroglandular densities, 93% of cancers in heterogeneously dense breasts, and 60% of cancers in extremely dense breasts. These results are summarized in Table 1. Statistical analysis of CAD sensitivity based on breast density with an exact two-sided Jonckheere-Terpstra test for a doubly-ordered contingency table and exact Kruskal-Wallis test for a singly-ordered contingency table both resulted in a nonsignificant p value of 0.0985; however, the evidence suggests a trend for a reduction in CAD sensitivity with increased breast density.

Combining fatty and scattered fibroglandular cases as "nondense" showed a CAD sensitivity of 96% (69/72), and combining heterogeneously dense and extremely dense cases as "dense" showed a CAD sensitivity of 90% (46/51). The nondense and dense groups showed no statistically significant difference in CAD sensitivity, with a p value of 0.274 based on a two-sided Fisher's exact test.

Mammographic Presentation

CAD detected 93% (41/44) of cancers manifesting as calcifications, 92% (57/62) as masses, and 100% (17/17) as mixed masses and calcifications. Based on the mammographic presentation of the lesion marked by CAD as a "mass," CAD sensitivity was similarly high, with 94% for both nonspiculated and spiculated masses and 100% for architectural distortion. The sensitivity for asymmetries was 75%. These results are shown in Table 2.

Histopathology

As shown in Table 3, CAD detected 94% of the invasive ductal carcinomas, 100% of the invasive lobular carcinomas, 91% of other invasive carcinomas, and 93% of DCIS (39/42). CAD sensitivity was consistent across all histopathology. Statistical analysis of CAD sensitivity based on the histopathology results showed no statistically significant difference in CAD sensitivity due to histopathology, with an exact two-sided Fisher-Freeman-Halton test resulting in a p value of 0.922.

Tumor Size

Sensitivity was not dependent on tumor size: CAD performed consistently with small lesions as well as large lesions. As summarized in Table 4, CAD sensitivity for cancers 1–10 mm was 89%; 11–20 mm, 97%; 21–30 mm, 100%; and larger than 30 mm, 93%. Statistical analysis of CAD sensitivity based on mammographic lesion size using an exact two-sided Jonckheere-Terpstra test for doubly-ordered contingency table and an exact Kruskal-Wallis test for singly-ordered contingency table both resulted in a p value of 0.138, which shows no statistically significant difference in CAD sensitivity due to tumor size.

TABLE 1: Computer-Aided Detection (CAD) Sensitivity Based on Breast Density

BI-RADS Breast Density	CAD Sensitivity (%)	No. of True-Positive Cases/ Total No. of Cases
Fatty	100	6/6
Scattered fibroglandular	95	63/66
Heterogeneously dense	93	43/46
Extremely dense	60	3/5

TABLE 2: Computer-Aided Detection (CAD) Sensitivity Based on Lesion Type

Mass Type	CAD Sensitivity (%)	No. of True-Positive Cases/ Total No. of Cases
Nonspiculated mass	94	30/32
Spiculated mass	94	15/16
Focal asymmetry	75	6/8
Architectural distortion	100	6/6

TABLE 3: Computer-Aided Detection (CAD) Sensitivity Based on Histopathology Results

Histopathology Result	CAD Sensitivity (%)	No. of True-Positive Cases/ Total No. of Cases
Invasive ductal carcinoma	94	59/63
Invasive lobular carcinoma	100	7/7
Other invasive carcinoma	91	10/11
Ductal carcinoma in situ	93	39/42

TABLE 4: Computer-Aided Detection (CAD) Sensitivity Based on Mammographic Lesion Size

BI-RADS Breast Density	CAD Sensitivity (%)	No. of True-Positive Cases/ Total No. of Cases
1–10 mm	89	49/55
11–20 mm	97	36/37
21–30 mm	100	16/16
> 30 mm	93	14/15

False-Positive Rate

Postsurgical review of subsequent follow-up mammograms after cancer treatment showed that 16 of the 105 patients included in the study for false-positive analysis were lost to follow-up after surgery. Eighty-five of the remaining 89 patients had no additional cancers, as determined by negative findings on 1- to 3-year follow-up mammograms or by surgical pathology results from bilateral mastectomies showing no unsuspected neoplasms. Three of the 105 patients developed an interval cancer that was not visible mammographically even in retrospect and was not detected by CAD on the initial screening mammograms after treatment for the original cancer between March 1, 2005, through February 28, 2006.

Only one patient had a synchronous cancer in the contralateral breast that was originally reported as benign calcifications by the radiologist. CAD marked these contralateral calcifications on the original mammogram. Biopsy of these contralateral calcifications on request of the surgeon yielded atypical intraductal clear cell proliferation, and infiltrating lobular carcinoma was found on the surgical excision. Although these contralateral calcifications were detected by CAD, they were misinterpreted by the radiologist as benign. Therefore, CAD marks on the contralateral cancer (marked in the CC and MLO views) that were originally considered false-positives were actually true-positives. These CAD marks were counted as true-positives rather than false-positives in the CAD false-positive rate, which was 2.3 marks per four-image case. These CAD marks were also considered as true-positives in the CAD sensitivity calculations.

Discussion

In our study, a commercially available CAD system with FFDM was retrospectively applied after IRB approval to biopsy-proven breast cancer cases from a community hospital in Florida; 94% (115/123) of malignancies were detected with CAD with 2.3 false-positive marks per case. Although derived from a small sample size, this result shows improved accuracy over findings from older versions of CAD systems with screen-film mammography, including 84% (906/1,083) and 89% (809/906) as reported by Warren Burhenne and colleagues [6] and Brem and colleagues [11], respectively. Our findings are nearly comparable to a more recently reported sensitivity of 96% (99/103) [3] for CAD with FFDM in a similar retrospective study. In addition, in our study, CAD detected 93% (41/44) of cancers manifesting as calcifications, 92% (57/62) as masses, and 100% (17/17) as mixed masses and calcifications.

Previous studies have shown that CAD performance is similar for the detection of cancer in fatty breasts and dense breasts with screen-film mammography (90% vs 88%, respectively; $p = 0.38$) [11] and with FFDM (95% vs 98%; $p = 0.537$) [3], grouping fatty breasts and breasts containing scattered fibroglandular tissue into "fatty breasts" and heterogeneously dense breasts and extremely dense breasts into "dense breasts." Our study provides CAD performance for each category of breast density and indicates that the CAD sensitivity with FFDM was similar in six of six (100%) fatty breasts, in 63 of 66 (95%) breasts containing scattered fibroglandular densities, and in 43 of 46 (93%) heterogeneously dense breasts. Sensitivity in extremely dense breasts was only 60% (3/5) in our study, although the small sample size may result in some uncertainty associated with this estimate.

Other studies have indicated that histopathology has little influence on CAD performance. Brem and colleagues [12] found that CAD sensitivity for invasive ductal carcinoma, invasive lobular carcinoma, and mixed and various invasive carcinomas and DCIS varied from 85% to 95%. Malich et al. [13] reported a sensitivity range of 90–97% for invasive ductal carcinoma, invasive lobular carcinoma, invasive tubular carcinoma, and DCIS, whereas less common histopathologies with five or fewer cases in that study such as mucinoid and other invasive cancers showed CAD sensitivities of 75% and 80%, respectively. Similarly, we found a consistent 91–100% sensitivity rate across all histopathology results including invasive ductal carcinomas ($n = 63$), invasive lobular carcinomas ($n = 7$), other invasive carcinomas ($n = 11$), and DCIS ($n = 42$). Notable was the finding that CAD with FFDM in the present study positively marked all seven cases of invasive lobular carcinomas, which traditionally are more difficult than other breast carcinomas to detect mammographically [14]. In addition, the 93% (39/42) sensitivity for DCIS lesions with conventional imaging and CAD also improves earlier detection of breast cancer. These findings are consistent with previously reported data regarding DCIS and invasive lobular carcinoma [12–14].

Detection of small lesions may lead to earlier breast cancer detection. Our study shows that CAD with FFDM enhances earlier detection by showing 89% of tumors that are 1–10 mm. Moreover, detection was fairly consistent among moderate to large tumors despite the fact that CAD systems are generally not designed to identify them, because large tumors are more readily identifiable by the radiologist without CAD. In our study, 93% (14/15) of tumors > 30 mm were detected by CAD.

The measurement of false-positive rates is important to the usefulness of CAD in FFDM

because false-positives potentially can distract radiologist interpretation. In our study, 2.3 false-positive marks were observed in examinations with four standard views. This is lower than the 2.8–5.2 marks per case achieved using CAD and analog mammograms [6, 11, 12, 15]. In another recent retrospective study of CAD with FFDM, Yang and colleagues [3] recently found a similar false-positive rate of 1.8 per patient case.

A limitation of our study is that we did not have postsurgical follow-up for 16 of the 105 patients included in the false-positive analysis. Therefore, the marks considered as false-positives in those 16 patients could not be confirmed, and a few may have actually been true-positive marks. The follow-up data we had for 89 patients resulted in only a 0.02 per case change in the false-positive rate, from 2.30 to 2.28, and no change in the 94% overall CAD sensitivity, so additional follow-up data for 16 more patients is unlikely to have a significant impact on the reported CAD performance.

The strengths of our study include assessment of CAD sensitivity based on clinically relevant metrics including breast density, mammographic presentation, histopathology results, and lesion size to provide expectations for CAD performance with FFDM.

In conclusion, the results of the present study show that the use of a CAD system with FFDM images can mark a high percentage (94%) of breast cancers with an acceptable false-positive rate of 2.3 marks per case. Of particular interest is the finding that sensitivity was maintained in cancers with histopathology traditionally known to lower the sensitivity of mammography (i.e., invasive lobular carcinomas and small neoplasms). Thus, CAD with FFDM continues to be an effective tool for assisting radiologists with the early detection of breast cancer. Future studies are needed to assess the accuracy of CAD in a larger population, including prospective studies in a clinical setting to assess the potential for CAD to reduce radiologist false-negatives—that is, for CAD to help radiologists find more cancers.

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