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Detection of Breast Cancer with a Computer-Aided Detection Applied to Full-Field Digital Mammography

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Abstract A study was conducted to evaluate the sensitivity of computer-aided detection (CAD) with full-field digital mammography in detection of breast cancer, based on mammographic appearance and histopathology. Retrospectively, CAD sensitivity was assessed in total group of 152 cases for subgroups based on breast density, mammographic presentation, lesion size, and results of histopathological examination. The overall sensitivity of CAD was 91 % (139 of 152 cases). CAD detected 100 % (47/47) of cancers manifested as microcalcifications; 98 % (62/63) of those manifested as non-calcified masses; 100 % (15/15) of those manifested as mixed masses and microcalcifications; 75 % (12/16) of those manifested as architectural distortions, and 69 % (18/26) of those manifested as focal asymmetry. CAD sensitivity was 83 % (10/12) for cancers measuring 1–10 mm, 92 % (37/40) for those measuring 11–20 mm, and 92 % (92/100) for those measuring >20 mm. There was no significant difference in CAD detection efficiency between cancers in dense breasts (88 %; 69/78) and those in non-dense breasts (95 %; 70/74). CAD showed a high sensitivity of 91 % (139/152) for the mammographic appearance of cancer and 100 % sensitivity for identifying cancers manifested as microcalcifications. Sensitivity was not influenced by breast density or lesion size. CAD should be effective for helping radiologists detect breast cancer at an earlier stage.

Keywords Breast neoplasm · Cancer detection · Computer-aided diagnosis (CAD) · Digital mammography

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Background

Computer-aided detection (CAD) technology with full-field digital mammography (FFDM) is a promising and innovative technique for detection of breast cancer. In the literature, FFDM has been cited as having several advantages over screen-film mammography (SFM), including higher contrast resolution, better dynamic range, and lower noise [1, 2]. Unlike SFM, which serves as an image receptor and display medium, FFDM captures images with a digital detector so that the images are available for immediate display on a monitor [3]. CAD in FFDM does not require a digitizer and allows rapid display of marks from the CAD system after image acquisition. Thus, CAD provides an optimized workflow and may allow faster interpretation of FFDM images.

The CAD system has been shown to be a helpful tool for early detection of breast cancer, using algorithms to identify potential areas of concern in images, and highlighting potentially suspicious areas (such as masses, microcalcifications, architectural distortions, and asymmetric densities). With the information provided by the CAD system, radiologists can decide whether true areas of concern are present in the highlighted locations, and further steps can then be taken to arrive at a final diagnosis. Retrospective studies have evaluated the performance of CAD when used in parallel with FFDM [4–9]. The reported sensitivity of

CAD with FFDM varies from 78 % to 96 % [8, 10]. However, it is not necessarily shown that the efficacy of CAD with FFDM for clinical evidence and the optimal conditions and parameters remain to be determined.

This retrospective study was performed to evaluate the sensitivity of CAD with FFDM for detection of breast cancers under clinically relevant conditions, in terms of parameters such as breast density, mammographic features, histopathological findings, and mode of presentation in images.

Materials and Methods

Patients

Institutional review board approval was obtained for this retrospective study, and informed consent was not required. One hundred fifty-two consecutive primary breast cancers (three with bilateral cancers) treated surgically at our institution were identified between April 1, 2010 and March 31, 2011. The 152 patients (ranged in age from 25 to 87 years with mean age of 62.2 years) included in this study. Standard mammographic views were obtained for all of them using FFDM (Senographe 2000D and Senographe DS Laverite, GE Healthcare) at the time of diagnosis. Both screening and diagnostic mammograms were included. For each case, both craniocaudal (CC) and mediolateral oblique (MLO) views of the breast containing the cancer were taken at the time of diagnosis. Unilateral cases were included. Magnification and compression views were excluded. In all cases, a malignant lesion was visible mammographically in at least one view.

Mammograms

The mammographic characteristics of all visible cancers were recorded. Mammographic lesion types were classified as one of the following: mass, mass with microcalcification, microcalcification, architectural distortion, or focal asymmetry. The lesions were divided into three subgroups according to size (1–10 mm, 11–20 mm, and >20 mm) based on the results of pathologic examinations.

Mammographic breast density was determined on the basis of the ACR (American College of Radiology) criteria [11]. For the purpose of CAD sensitivity assessment, we defined fatty and scattered fibroglandular breast densities as non-dense, and heterogeneously dense and extremely dense mammographic densities as dense breast tissue.

Sensitivity and Scoring of Mammograms Using the CAD System

Routine screening mammograms (CC and MLO) from each patient were analyzed using the commercially available CAD system Second Look, version 7.2 (iCAD Inc.). To create a digital image of each mammographic view, we used the standard digitizer included with the CAD system. The digital images were then analyzed using proprietary software (included with the CAD system) designed to identify breast cancers presenting as microcalcifications or mass lesions.

The CAD marks are ellipses and rectangles highlighting potential areas of concern overlaid on the digital images. An ellipse indicates a pattern suggestive of mass (irregular, spiculated, or circumscribed density and an area of architectural distortion which is a radiating line without a central density), whereas a rectangle indicates an area of clustered bright spots that are suggestive of microcalcifications. Images with CAD marks were saved in the review workstation and then forwarded to a picture archiving. The output of the CAD system can be displayed on a five-megapixel display system workstation.

Each CAD mark was scored as either true-positive or false-positive, a true-positive mark correctly indicating a malignant lesion and all other CAD marks being false. For cancers that were manifested as masses, a decision of true-positivity was made if the center of the CAD mark fell within a “truth box” whose size was ascertained according to the extent of the mass. The same marking principle was applied for architectural distortions and focal asymmetries. For calcifications, a decision of true-positivity was made if the CAD mark overlapped any portion of the truth box sized to the extent of the calcifications.

All cases were diagnosed using a core or vacuum-assisted biopsy procedure under ultrasound or stereotactic imaging guidance. Final surgical histologic diagnosis of breast cancers included invasive ductal carcinoma (n=111, 73.0 %), invasive lobular carcinoma (n=9, 5.9 %), other invasive carcinoma (n=16, 10.5 %), and DCIS (n=16, 10. 5 %).

CAD marks that did not mark the known malignancy were considered as false-positive marks. False-positive marks were counted per image and assessed separately for masses and microcalcifications

The sensitivity of the CAD system was calculated as the number of lesions that had been correctly marked divided by the total number of lesions; a true-positive determination required at least one true-positive mark per lesion. Sensitivity was also calculated based on mammographic lesion type, breast density, histopathological subtype, lesion size, and mode of presentation of breast cancer. The statistical significance of differences in the sensitivity of the CAD system between the above-mentioned subgroups was assessed using chi-squared analysis. Two-tailed p values<0.05 were considered statistically significant.

Results

CAD correctly marked 100 % (47/47) of cancers manifested mammographically as microcalcifications (punctate 12,

Table 1 Sensitivity of computer-aided detection (CAD) based on lesion type

Lesion	CAD sensitivity (%)	No. of true-positive cases/total cases
Total	91	139/152
Calcification	100	47/47
Mass	99	77/78
Without microcalcification	98	62/63
Associated with microcalcification	100	15/15
Architectural distortion	75	12/16
Focal asymmetry	69	18/26

amorphous 18, pleomorphic 10, linear 7; grouped 21 segmental 26), 98 % (62/63) of cancers manifested as masses without associated microcalcifications, 100 % (15/15) of cancers manifested as masses with associated microcalcifications, 75 % (12/16) of cancers manifested as architectural distortion, and 69 % (18/26) of cancers manifested as focal asymmetry (Table 1). Therefore, the overall sensitivity of the CAD system was 91 % (139/152) of breast cancers.

The mean box size was 28.8±14.6 mm of microcalcifications, 20.2±12.1 mm of mass, 13.0±4.1 mm of architectural distortion, and 13.9±6.4 mm of focal asymmetry. Image sensitivity was found to be 93 % (n=139) for the MLO view and 75 % (n=114) for the CC view. There was an average of 1.8 false-positive marks per case and 0.45 per image, with 0.25 false-positive marks for masses and 0.2 false-positive marks for microcalcifications.

On the basis of breast density, CAD correctly marked 95 % (70/74) of cancers in non-dense breasts and 88 % (69/78) of cancers in dense breasts (Table 2). Statistical analysis based on breast density revealed no significant difference in CAD sensitivity between the non-dense and dense groups (p=0.274).

CAD detected 92 % (101/110) of invasive ductal carcinomas, 89 % (8/9) of invasive lobular carcinomas, 88 % (14/16) of other invasive carcinomas, and 94 % (16/17) of DCIS (Table 3). CAD sensitivity was consistent across all types of histopathology; statistical analysis demonstrated no significant differences in CAD sensitivity among histopathologic types (p=0.904).

Table 2 Sensitivity of computer-aided detection (CAD) based on breast density

BI-RADS breast density	CAD sensitivity (%)	No. of true-positive cases/total no. of cases
Dense	88	69/78
Non-dense	95	70/74

Table 3 Sensitivity of computer-aided detection (CAD) based on histopathology results

Histopathology results	CAD sensitivity (%)	No. of true-positive cases/ total no. of cases
Invasive ductal carcinoma	92	101/110
Invasive lobular carcinoma	89	8/9
Other invasive carcinoma	88	14/16
Ductal carcinoma in situ	94	16/17

The sensitivity of CAD according to the histologically determined lesion size is shown in Table 4. CAD sensitivity for 1–10-mm cancers was 83 % (10/12), that for 11–20-mm cancers was 92 % (37/40), and that for cancers larger than 20 mm was 92 % (92/100). Although the sensitivity of CAD varied depending on the histologically determined lesion size, statistical analysis revealed that none of the differences in CAD sensitivity were significant (p=0.575).

Among the 13 cancers not revealed by CAD, one was a mass without associated microcalcifications, four were manifested mammographically as architectural distortion, and eight were manifested as focal asymmetry. Histopathologically, 12 of the lesions were invasive cancers (nine ductal, one lobular, and two other invasive carcinomas) and one was DCIS. Details of the lesion characteristics are summarized in Table 5.

Discussion

The use of CAD in clinical practice has evolved, and now it is utilized more as a second reading modality than simply an image checker. If a questionable area is seen on a mammogram and is also highlighted by CAD, then the radiologist is more likely to perform a work-up of the lesion. In our study, a commercially available CAD system in combination with FFDM was retrospectively applied to postoperative cases of breast cancer, and 91 % (139/152) of the malignancies were detected by CAD. Although derived from a small sample size, this result shows an improvement of accuracy in

Table 4 Sensitivity of computer-aided detection (CAD) based on lesion size

Histopathologically determined lesion size	CAD sensitivity (%)	No. of true-positive cases/total cases
1–10	83	10/12
11–20	92	37/40
>20	92	92/100

Table 5 Characteristics of cancers unidentified by CAD

	Breast density	Type of lesion	BI-LADS	Histopathology	Size (mm)
1	Dense	Mass	4	Invasive ductal carcinoma	45
2	Dense	Architectural distortion	4	Invasive ductal carcinoma	26
3	Dense	Architectural distortion	4	Invasive ductal carcinoma	25
4	Dense	Focal asymmetry	3	Invasive ductal carcinoma	17
5	Dense	Focal asymmetry	3	Invasive ductal carcinoma	8
6	Dense	Focal asymmetry	3	Neuroendocrine carcinoma	35
7	Dense	Focal asymmetry	3	Invasive ductal carcinoma	45
8	Dense	Focal asymmetry	3	Invasive ductal carcinoma	25
9	Dense	Focal asymmetry	3	Mucinous carcinoma	8
10	Non-dense	Architectural distortion	4	Invasive ductal carcinoma	18
11	Non-dense	Architectural distortion	4	DCIS	50
12	Non-dense	Focal asymmetry	3	Invasive ductal carcinoma	55
13	Non-dense	Focal asymmetry	3	Invasive ductal carcinoma	35

comparison with other versions of the CAD system with SFM, for example, 84 % (906/1,083) reported by Burhenne [12] and 89 % (809/906) reported by Brem et al. [13]. Our findings are roughly comparable to those of similar retrospective studies of CAD with FFDM reported recently, which showed sensitivities of 96 % (99/103) [3], 94 % (115/123) [4], 93 % (141/151) [14], and 91 % (115/127) [15]. In addition, the CAD system in FFDM has been shown to have greater sensitivity for calcifications than for mass lesions [3–6, 8, 15]. Previous studies have shown that CAD in SFM has a markedly lower sensitivity for malignant amorphous calcifications than for malignant calcifications overall [16]. In our present study, however, CAD detected 100 % (47/47) of cancers that were manifested as microcalcifications and 100 % (15/15) of cancers that were mass associated with microcalcifications. This may have been related to the improved CAD algorithms employed. Therefore, it may be possible to improve the workflow of mammogram reading by avoiding an exhaustive search for microcalcifications and instead concentrate on areas with microcalcifications detected by CAD.

Previous studies have shown that the performance of CAD for the detection of cancer in non-dense breast tissue is similar to that for dense breast tissue in combination with either SFM (90 % versus 88 %, respectively; $p=0.38$) [13] or FFDM (95 % versus 98 %; $p=0.537$ and 96 % versus 90 %; $p=0.274$) [3, 4]. Our study of CAD performance for each category of breast density indicated that the sensitivity with FFDM was similar in 69 of 78 (88 %) dense breasts, which included both heterogeneously dense and extremely dense breasts, and in 70 of 74 (95 %) non-dense breasts, which included scattered fibroglandular densities and fatty breasts. Thus, breast density did not significantly impact on CAD performance for detection of breast cancer.

It has been reported that histopathology has little influence on CAD performance. Brem et al. found that CAD sensitivity for detection of invasive ductal carcinoma, invasive lobular carcinoma, other invasive carcinomas, and DCIS varied from 85 % to 95 % [16]. Malich et al. reported a CAD sensitivity range of 90–97 % for invasive ductal carcinoma, invasive lobular carcinoma, invasive tubular carcinoma, and DCIS, whereas that for the less common histopathologic types, mucinoid, and other invasive cancers (comprising five or fewer cases) was 75 % and 80 %, respectively [17]. Similarly, we found a consistent 88–94 % sensitivity rate across all histopathologic types including invasive ductal carcinoma ($n=110$), invasive lobular carcinoma ($n=9$), other invasive carcinomas ($n=16$), and DCIS ($n=17$). Invasive lobular carcinomas are more difficult to detect mammographically than other breast carcinomas [18]. In addition, the sensitivity of conventional imaging and CAD for DCIS lesions (93 %; 39/43) is also an improvement that can allow earlier detection of breast cancer. These findings are consistent with previously reported data for invasive lobular carcinoma and DCIS [16–18].

Earlier detection of breast cancer may be dependent on detection of small lesions at initial screening examinations. Our present study showed that CAD with FFDM enhances earlier detection, identifying 83 % (10/12) of 1–10-mm tumors and showing 92 % (129/140) sensitivity for lesions larger than 10 mm. These results are similar to those reported recently for CAD in combination with FFDM [15]. Thus, CAD may exert an important impact by reducing the occurrence of missed cancers and thus improving the prognosis of breast cancer.

Our study revealed 13 cancers that were not detected by CAD. One was a mass without associated microcalcifications, and 12 were manifested mammographically as architectural distortion/focal asymmetry. Architectural distortion has been reported to be the third most frequent mammographic manifestation of breast cancer [19, 20] and described as "distortion of the normal architecture with no definite mass visible" [11]. This category includes spiculations radiating from a point and

focal retraction or distortion of the edge of the parenchyma. The differential diagnosis of architectural distortion includes malignant lesions such as invasive ductal carcinoma, invasive lobular carcinoma, DCIS, and benign lesions such as surgical scars, radial scars, complex sclerosing lesions, fat necrosis, and intralobular fibrosis [20]. Despite the subtlety of architectural distortion and its potential for malignancy, few studies have investigated the efficacy of CAD algorithms for specific detection of distortion. Evans et al. [18] investigated the sensitivity of CAD for detection of lobular carcinoma and found that 17 (85 %) of 20 cases presenting as architectural distortion were successfully identified by CAD. Likewise, Baker et al. [21] evaluated the sensitivity of two commercially available CAD systems for identifying architectural distortion in 45 such cases. One of these systems detected 22 of 45 cases (49 %) and the other 15 of 45 cases (33 %). Our results also indicated that CAD correctly marked 75 % of cancers (12/16) manifested mammographically as architectural distortion. The difference between a cancerous mass and architectural distortion/focal asymmetry is that the latter does not have a precise area that can be measured because its edges are indistinct, and the difference from background density is subtle. Therefore, it is difficult to analyze architectural distortion/focal asymmetry by CAD in comparison with microcalcifications or a mass.

There were several limitations to our study. CAD systems for use with mammography have been employed over the past 10 years [5]. Although some previous studies have assessed the utility of different CAD systems, there few retrospective studies have focused on the use of CAD in digital mammography. In the present study, we showed that commercially available FFDM with a CAD system is able to maintain high sensitivity in a relatively large heterogeneous cohort of diagnostic cases. Therefore, our results support the routine use of CAD with FFDM as an adjunct for early detection of breast cancer.

Other limitations of our study include inability to assess specificity of CAD system and lack assessment of CAD effect on workflow. Importantly, our study did not evaluate the performance of radiologists, and it remains to be clarified whether a CAD system with FFDM can improve a radiologist's performance in the detection of breast cancer.

In conclusion, the results of the present study show that the use of a CAD system with FFDM images can identify 91 % of breast cancers. Sensitivity was high for cancers manifesting as calcifications (100 %) or masses (98 %). Of particular interest is the finding that sensitivity was maintained for cancers with a histopathology for which the sensitivity of mammography is known to be lower (i.e., invasive lobular carcinomas and small neoplasms). Thus, CAD with FFDM continues to be an effective tool for assisting the diagnosis of early breast cancer. Future studies are needed to assess the impact of CAD on efficacy and workflow in relation to the interpretation and the optimal integration of CAD for FFDM reading.

Declaration of interest The authors report no conflicts of interest and are alone responsible for the content and writing of this paper.

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