Evaluation of Breast Cancer with a Computer-Aided Detection System by Mammographic Appearance and Histopathology

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BACKGROUND. The objective of this study was to evaluate the performance of a computer-aided detection (CAD) system for the detection of breast cancer, based on mammographic appearance and histopathology.

METHODS. From 1000 consecutive screening mammograms from women with biopsy-proven breast carcinoma, 273 mammograms were selected randomly for retrospective evaluation by CAD. The sensitivity of the CAD system for breast cancer was assessed from the proportion of masses and microcalcifications detected. The corresponding tumor histopathologies also were evaluated. Normal mammograms (n = 155 patients) were used to determine the false-positive rate of the system.

RESULTS. Of the 273 breast carcinomas, 149 appeared mammographically as masses, and 88 appeared as microcalcifications, including 36 carcinomas that presented as mixed lesions. The CAD system marked 125 of 149 masses correctly (84%), marked 86 of 88 microcalcifications correctly (98%), and marked 32 of 36 of mixed lesions correctly (89%.). The system showed a high sensitivity for the detection of ductal carcinoma in situ (95%; 73 of 77 lesions), invasive lobular carcinoma (95%; 18 of 19 lesions), invasive ductal carcinoma (85%; 125 of 147 lesions), and invasive mammary carcinoma (90%; 27 of 30 lesions). The highest CAD system sensitivity was for all invasive carcinomas that presented as microcalcifications (100%). On normal mammograms, there was an average of 1.3 false-positive CAD marks per image.

CONCLUSIONS. The CAD system correctly marked a large majority of biopsy-proven breast cancers, with a greater sensitivity for lesions with microcalcifications and without significant impact of performance based on tumor histopathology. CAD was highly effective in detecting invasive lobular carcinoma (sensitivity, 95%) and ductal carcinoma in situ (sensitivity, 95%). CAD represents a useful tool for the detection of breast cancer. ***Cancer* 2005;104:931–5.**

KEYWORDS: breast neoplasms, diagnosis, cancer screening, computers, diagnostic aid.

Mammography is the gold standard for breast cancer screening, reducing mortality by as much as 30%.[1–5] This reduction in mortality is based on current screening mammography sensitivity, which ranges from 70% to 90%.[6–10] Therefore, improvements in radiologist sensitivity are needed that could reduce breast cancer mortality further. It has been shown that double reading can increase radiologist sensitivity by 5–15%.[11–14] However, even though it is effective clinically, double reading is not advocated as a standard of care.[15] The use of a computer-aided system to assist a single radiol-

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ogist is another strategy for the further improvement of mammographic sensitivity.

Computer-aided detection (CAD) has the potential to improve screening mammography significantly.[10,16] CAD can improve mammography sensitivity by marking cancerous regions.[10,16,17] It is important to assess the system's performance across variables that are correlated with the likelihood that a tumor will be missed during mammographic interpretation. In addition, evaluating the system's performance across variables that affect patient prognosis also is important to determine the clinical utility of CAD in enhancing mammography sensitivity. Mammographic appearance and histopathology can affect the possibility that a radiologist may miss a malignancy, which can affect the patient's prognosis.[18,19] Specifically, subtle masses[6,20,21] and invasive lobular carcinoma[22] are more apt to be missed. Similarly, for small invasive tumors, masses imply a better prognosis than calcifications,[23,24] ductal carcinoma in situ (DCIS) implies a better prognosis than invasive lesions,[25] and smaller tumors imply a better prognosis than larger tumors.[25]

In practice, CAD helps the radiologist detect potential areas of concern on screening mammograms after she or he performs an initial review of the films.[10,12,16,17] The CAD system processes the images and uses algorithms to detect potential areas of concern, and it highlights potentially suspicious areas (such as masses, microcalcifications, architectural distortions, and asymmetric densities). With the information provided by the CAD system, the radiologist decides whether or not true areas of concern are present at the highlighted locations, and she or he retains the ability to make the final diagnosis. CAD, therefore, may be viewed as a second reader that assists the radiologist by confirming the presence of suspicious areas or by identifying areas that otherwise would have been missed. The objective of the current study was to evaluate the performance of a CAD system in detecting breast cancer based on mammographic appearance (presentation of a mass or microcalcification) and histopathology of the detected malignancy (specifically, invasive ductal carcinoma, invasive lobular carcinoma, invasive mammary carcinoma with ductal and lobular features, and DCIS).

MATERIALS AND METHODS

Patient Selection: Breast Carcinoma

One thousand consecutive, screen-detected, biopsy-proven breast carcinomas that were identified between 1992 and 1995 from 3 institutions were collected. Every third tumor was selected as the consecutive carcinomas were identified, until 275 tumors were chosen randomly for system testing. Tumors from two patients had incomplete data and were excluded from the data set. This study constitutes the 273 carcinomas that were selected randomly for system testing.

The pathology report was obtained for each biopsy-proven tumor to document the histopathology. All patients had a two-view mammogram of each breast for a total of four images per patient.

Patient Selection: Normal Mammograms

One hundred fifty-five normal screening mammograms were selected from a series of 494 women who underwent consecutive, normal screening. Of the consecutive normal mammograms, every third mammogram was included in this study. Normal mammograms were interpreted as BI-RADS 1 or 2, and all had a 3-year follow-up that demonstrated no mammographic or clinical abnormality. All mammograms were evaluated retrospectively by the CAD system to determine the number of false-positive marks per image. All CAD marks on the normal mammograms were counted as false positives.

For the 256 patients with cancer who had age data available, the mean age was 60.6 years (range, 31–87 yrs). For 154 women who had normal mammograms and had age data available, the mean age was 58.9 years (range, 38–80 yrs).

Analysis of Mammograms with the CAD System

The Second Look CAD system (version 3.4; i-CAD, Inc., Beavercreek, OH) was used in this study. CAD sensitivity in the detection of cancer was evaluated by the number of masses and microcalcifications identified and by tumor histopathology. The CAD system consists of a film digitizer that uses a 43-μm resolution with 12 bits of gray scale, a processing unit, and a CAD print-out. The processing unit utilizes proprietary signal-processing software. The results of the analysis are presented on a paper print-out. The CAD print-out consists of the digitized images with ellipses and rectangles highlighting potential areas of concern. The ellipses mark potential masses (nonspiculated masses, spiculated masses, architectural distortions, or asymmetric densities), and the rectangles mark potential microcalcifications.

The precise mammographic location of each biopsy-proven carcinoma was correlated with the location of the CAD mark by a mammographer. The type of lesion marker (i.e., mass or calcification) had to correlate with the mammographic characteristic of the lesion. If the CAD system marked the correct type of lesion at the precise mammographic location of the tumor in at least one view, then the result was con-

TABLE 1
Sensitivity of the Computer-Aided Detection System Based on the Mammographic Appearance of the Lesions

Histopathology	Masses	Microcalcifications	Mixed	All patients
Total (% of all 273 patients)	149 (68)	88 (45)	36 (13)	273
CAD detected (no.)	125	86	32	243
CAD sensitivity (%)	84	98	89	89

CAD: computer-aided detection.

sidered a true positive. If both mass and microcalcification features were noted for the lesion, then either marker type was considered correct. The sensitivity of the CAD algorithm was calculated as the number of lesions correctly marked divided by the total number of lesions.

Tumor histopathology was based on pathologic findings. Tumors were classified as invasive ductal carcinoma, invasive lobular carcinoma, invasive mammary carcinoma (i.e., with ductal and lobular features), and DCIS. CAD performance correlated by tumor histopathology was evaluated for all tumors and for tumors that manifested mammographically as masses, as microcalcifications, and as masses with microcalcifications. Evaluation of statistically significant performance of the CAD system for detection of cancer was performed utilizing a chi-square analysis.

Normal studies were used to determine the number of false-positive marks on the mammograms. False-positive marks were assessed individually for masses and microcalcifications.

RESULTS

CAD Performance: Breast Carcinoma

Among the 273 women with confirmed breast cancer who were included in the current study, there were 149 masses, 88 microcalcifications, and 36 mixed mass/microcalcifications lesions (Table 1). The CAD system detected 84% of the masses (125 of 149 patients), 98% of the microcalcifications (86 of 88 patients), and 89% of the mixed mass/microcalcification lesions (32 of 36 patients). Therefore, the overall sensitivity of the CAD system was 89% (243 of 273 patients) (Table 1).

Histopathologic analysis of the tumors revealed the presence of 147 invasive ductal carcinomas, 19 invasive lobular carcinomas, 30 invasive mammary carcinomas, and 77 DCIS (Table 2). CAD correctly identified 125 of 147 patients (85%) with invasive ductal carcinoma, 18 of 19 patients (95%) with invasive lobular carcinomas, 27 of 30 patients (90%) with invasive mammary carcinomas, and 73 of 77 patients (95%) with DCIS (Tables 2, 3).

Invasive ductal carcinomas were evaluated by lesion type as well as by CAD sensitivity of detection. In total, there were 147 patients with invasive ductal carcinomas. Of these, 101 tumors (69%) manifested mammographically as masses, with a CAD sensitivity of 81% (82 of 101 tumors). Of the 147 tumors, 19 tumors (13%) manifested mammographically as microcalcifications, with a CAD sensitivity of 100% (19 of 19 tumors). The mixed masses/microcalcifications constituted 27 of 147 (18%) invasive ductal carcinomas. The CAD sensitivity for the mixed lesions was 89% (24 of 27 tumors).

TABLE 2
Sensitivity of the Computer-Aided Detection System Based on the Histopathology of the Lesions

	Invasive carcinomas			
Histopathology	Ductal	Lobular	Mixed/ various	DCIS
Total no. (% of all 273 patients)	147 (68)	19 (7)	30 (11)	77 (28)
CAD detected (no.)	125	18	27	73
CAD sensitivity (%)	85	95	90	95

DCIS: ductal carcinoma in situ; CAD: computer-aided detection.

TABLE 3
Sensitivity of the Computer-Aided Detection System Based on the Histopathology and Mammographic Appearance of the Lesions

Histopathology	Masses	Microcalcifications	Mixed	All patients
Invasive lobular carcinomas				
Total no. (% of all 147 patients)	101 (69)	19 (13)	27 (18)	147
CAD detected (no.)	82	19	24	125
CAD sensitivity (%)	81	100	89	85
Invasive lobular carcinomas				
Total no. (% of all 19 patients)	16 (84)	3 (16)	0 (0)	19
CAD detected (no.)	15	3	—	18
CAD sensitivity (%)	94	100	—	95
Invasive mammary carcinomas				
Total no. (% of all 30 patients)	25 (83)	2 (7)	3 (10)	30
CAD detected (no.)	22	2	3	27
CAD sensitivity (%)	88	100	100	90
DCIS				
Total (% of all 77 patients)	7 (9)	64 (83)	6 (8)	77
CAD detected (no.)	6	62	5	73
CAD sensitivity (%)	86	97	83	95

CAD: computer-aided detection; DCIS: ductal carcinoma in situ.

The lesions that were identified as pure invasive lobular carcinomas were evaluated by lesion type as well as by CAD sensitivity of detection. In total, there were 19 pure invasive lobular carcinomas. Of these, 16 tumors (84%) manifested mammographically as masses, with a CAD sensitivity of 94% (15 of 16 tumors). Of the 19 tumors, 3 tumors (16%) manifested mammographically as microcalcifications, with a CAD sensitivity for invasive lobular carcinoma of 100% (3 of 3 tumors). There were no invasive lobular carcinomas that manifested mammographically as mixed lesions.

The lesions that were identified as invasive mammary carcinomas, i.e., those with ductal and lobular features, were evaluated by lesion type as well as by CAD sensitivity of detection. In total, there were 30 invasive mammary carcinomas. Of these, 25 tumors (83%) manifested mammographically as masses, with a CAD sensitivity of 88% (22 of 25 tumors). Of the 30 tumors, 2 tumors (7%) manifested mammographically as microcalcifications, with a CAD sensitivity of 100% (2 of 2 tumors). The mixed masses/microcalcifications constituted 3 of 30 (10%) invasive mammary carcinomas. The CAD sensitivity for the mixed lesions was 100% (3 of 3 tumors).

DCIS was evaluated by lesion type and by CAD sensitivity of detection. In total, there were 77 invasive ductal carcinomas. Of these, 7 tumors (9%) manifested mammographically as masses, with a CAD sensitivity of 86% (6 of 7 tumors). Of the 77 tumors, 64 (83%) manifested mammographically as microcalcifications, with a CAD sensitivity of 97% (62 of 64 tumors). The mixed masses/microcalcifications constituted 6 of 77 (8%) DCIS tumors, with a CAD sensitivity of 83% (5 of 6 tumors). The sensitivity of the CAD system for all invasive carcinomas was 87% (170 of 196 tumors), and the CAD sensitivity for DCIS was 95% (73 of 77 tumors).

CAD Performance: Normal Mammograms

Of the 155 normal mammograms that were evaluated with the CAD system, there was an average of 1.3 false-positive marks per image, with 1.1 marks for masses and 0.2 marks for calcifications. More recent software (iCAD Medical Systems, version 5.0) demonstrated 0.6 false-positive marks per image. with 0.2 false-positive marks for microcalcifications and 0.4 false-positive marks for masses.

DISCUSSION

The limitations of mammography for the detection of breast cancer have resulted in the development of novel approaches for the improved diagnosis of breast cancer. Over the past decade, CAD has been developed and has demonstrated an improvement in breast cancer detection by > 20%.[10,16,26] However, the impact of CAD for the detection of breast cancer may be most significant for those tumors that are most challenging to detect. Prior studies demonstrated that subtle masses[6,20,21] and invasive lobular tumors[22] are more likely to be missed. It is for this reason that we undertook an evaluation of the performance of the CAD system for the detection of breast cancer based on histopathology.

The CAD system showed a high sensitivity for the detection of mass and microcalcification lesions, a sensitivity that was greater for microcalcifications. On the basis of lesion histopathology, CAD showed a higher detection rate for DCIS and invasive lobular carcinomas. This indicates that CAD has an important role in reducing the occurrence of missed cancers, even with difficult to detect lesions, such as invasive lobular carcinoma.

The performance of the CAD system was better for microcalcifications than for masses, as reported previously. This confirms multiple prior studies that demonstrated these findings.[10,16,26,27]

It is not understood fully why some malignancies are more difficult to detect mammographically. Various causes have been suggested, including scirous reaction to the tumor, as well as pathologic characteristics of various histopathologies, which may differ from the characteristics that are detected during screening.[8,18] In particular, subtle masses[6,20,21] and invasive lobular carcinomas[22] are more likely to be missed. The current results suggest that mammographic appearance and histopathology do not appear to affect the performance of the Second Look CAD system. CAD may have an important impact not only on the reduction of the occurrence of missed tumors but also on the prognosis for women with breast cancer.

Invasive lobular carcinomas are recognized as more challenging lesions to detect mammographically, because they often present with subtle signs clinically, mammographically, and sonographically. The high sensitivity of CAD for this difficult to diagnose lesion has been reported previously[28] and was confirmed in the current study.

The intrinsic limitations of mammography result in failure to detect 10–15% of breast cancers,[6–10] and mammographic sensitivity is reduced particularly in women with dense breast tissue.[6,27] A recent study demonstrated that CAD is not significantly impacted by breast density.[29] It has been shown that interpretation of the mammogram by a second reader increases sensitivity by up to 15%.[11–14] However, double reading is not advocated as a standard of care, because it is extremely resource-intensive.[15] Thus, improved methods are needed to assist radiologists in their interpretation of mammography. This has led to the development of CAD over the past decade.[10,12] Using CAD as a prompt for the radiologist to identify potential areas of abnormality on the mammogram, with the final decision rendered by the radiologist, is a useful tool for the improved detection of breast cancer, regardless of the histopathologic type of the tumor.

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