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Computed-aided diagnosis (CAD) in the detection of breast cancer

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ABSTRACT

Computer-aided detection (CAD) systems have been developed for interpretation to improve mammographic detection of breast cancer at screening by reducing the number of false-negative interpretation that can be caused by subtle findings, radiologist distraction and complex architecture. They use a digitized mammographic image that can be obtained from both screen-film mammography and full field digital mammography. Its performance in breast cancer detection is dependent on the performance of the CAD itself, the population to which it is applied and the radiologists who use it. There is a clear benefit to the use of CAD in less experienced radiologist and in detecting breast carcinomas presenting as microcalcifications. This review gives a detailed description CAD systems used in mammography and their performance in assistance of reading in screening mammography and as an alternative to double reading. Other CAD systems developed for MRI and ultrasound are also presented and discussed.

1. Introduction

Digital mammography offers new opportunities that are not provided by conventional film screen mammography for the detection of breast carcinomas. The primary benefit comes from more reliable and efficient image management. The second one comes from novel uses of X-rays for breast imaging.

Mammography has long been established as the only screening examination capable of reducing breast cancer mortality. And yet, mammography has significant limitations with a sensitivity of 85–90% for breast cancer detection. However, if missed cancer cases are analyzed retrospectively, we discover that most of them exhibit some features on mammograms. The use of the computer to assist radiologists is particularly important in mammography because the radiologist is distracted when faced with a large pile of screening mammograms to examine, because breast architecture is complex, because subtleties are present among findings and because the probability of breast cancer is low. All contribute to false-negative interpretation in about 10–15% of cases. The most frequent reasons for missed breast cancers are the misinterpretation of a perceived abnormality (a lesion with a benign appearance, or an abnormal finding on a previous mammogram seen on only one view) which is slightly more common than overlooked cases [1]. The aim of the CAD system is to offer more objective evidence and increase the radiologist's diagnostic confidence. CAD systems have been developed to improve mammographic detection of breast cancer at screening by reducing the number of false-negative interpretations.

2. Technique and interpretation

The first Food and Drug Administration approval of a CAD device was in 1998. CAD is a neural network applying calcification and mass algorithms to highlight areas of suspicious findings to assist radiologists. The CAD system helps the radiologist by defining a region of interest on the mammogram. During this process, the system analyzes each mammogram using the software of the CAD system. Most CAD devices analyze the 2 views separately and independently.

CAD systems are available for both Screen-Film and Full-Field Digital Mammography (FFDM). With Screen-Film mammography, films need to be digitalized with a dedicated unit, then digitalized images are processed with a CAD algorithm and finally prompts are printed and interpreted by the radiologist. The whole process is costly, time consuming, and it had no success in countries without any reimbursement for CAD use (Europe). With FFDM the CAD system does not require a digitizer. Due to the higher signal-to-noise ratio and a better dynamic range of FFDM, more accurate information is extracted from the image which improves the computer's ability to discriminate between true and false lesions. With FFDM, CAD devices are easily implemented, the cost much lower, and CAD marks are immediately displayed after image acquisition.

Interpretation of mammography using CAD involves several steps. Fist the radiologist performs his/her own interpretation of the original mammograms. Then he/she activates CAD marks on the workstation or views the printed prompts to see if the CAD system

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Table 1
Studies evaluating the performance of CAD-assisted reading in screening mammography.

	True-positives	False-positives
Ciatto et al. [35]	+13.7%	+35.5%
Freer et al. [2]	+19.5%	+18.7%
Birdwell et al. [3]	+11.7%	+11.7%
Helvie et al. [36]	+10%	+9.8%
Gur. et al. [5]	+1.9%	
Khoo et al. [9]	+1.3%	+5.8%
Birdwell et al. [3]	+7.4%	+8.2%
Cupples et al. [37]	+16.8%	+7.8%

marked any regions of interest. Finally, the radiologist re-inspects the original mammogram in the area marked by the CAD to determine whether an abnormal finding was overlooked on the initial assessment. Two types of marks are displayed, one for microcalcifications and one for masses. A learning curve is necessary to manage the marks. One of the challenges of the CAD system is to become comfortable with the number of false marks. With experience, the majority of false CAD marks are readily dismissed. However, the use of CAD takes more time for the interpretation of screening mammography than it does without CAD.

3. CAD performance

3.1. CAD-assisted reading in screening mammography

CAD-assisted reading is associated with a moderate increase in sensitivity and with a drop in specificity (Table 1). Freer et al. studied prospectively the effect of CAD on recall rate [2]. Among 12,860 mammograms, there were 986 recalls and 49 cancers. Eight of the cancers were detected with CAD alone which increases the detection rate by 19.5%. Birdwell et al. studied prospectively 8682 patients [3]. Ten percent of patients were recalled and CAD contributed 8% of total recalled findings and 7% of the cancers detected (2 of the 29 cancers found). Ko et al. prospectively interpreted 5016 mammograms without and with CAD in a working clinical environment [4]. The recall rate increased from 12% to 14% with the use of CAD. Of the 107 patients who underwent biopsies, 6% were prompted by CAD. The radiologist detected 43 of the 48 cancers without CAD and 45 of the 48 cancers with CAD (+4%). CAD missed 8 cancers that were detected by the radiologist. Gur et al. reported that no statistically significant increase in cancer detection between radiologists who used CAD and those who did not [5]. A more recent study of Fenton et al. published in the New England Journal of Medicine in 2007 [6], questioned the diagnostic contribution of CAD by concluding that the use of CAD is associated with reduced accuracy of screening mammogram interpretation, an increased rate of biopsies and is not clearly associated with enhanced detection of invasive breast cancer. They analyzed screen-film mammograms of 222.135 women, before and after the implementation of CAD. CAD increased sensitivity from 80.4% to 84%, decreased specificity from 90.2% to 87.2%, and increased the rate of biopsies by 19.7%, and the rate of detection of invasive cancer decreased by 12%. However, the rate of detection of ductal carcinomas in situ was increased by 34%. These differences observed in the rate of detection of breast cancer with the use of CAD has been reported to be due to the practice setting, the volume of cases interpreted by the radiologist, the number of radiologists dedicated to interpreting the mammograms and the experience of the radiologists with the CAD system [3].

3.2. CAD should be addressed as an alternative to double reading

Indeed it is well established that prospective double reading of screening mammograms increases the detection of cancer from 4 to 15% [7] (Fig. 1). Like double reading, CAD could increase the cancer detection rate and could be easier to implement and cheaper than double reading. Gilbert et al. showed that single reading with CAD yielded the same performance as double reading. The proportion of cancers detected was 199 of 227 (87.7%) for double reading and 198 of 227 (87.2%) for single reading with computer-aided detection ($P = 0.89$) [8]. However, the specificity of CAD is low with about 1 false positive mark per view (Fig. 2). These false positive marks may cause the radiologist to underestimate and disregard CAD findings. Khoo et al. studied the use of CAD as a second reader in 6111 women [9]. CAD increased sensitivity by 1.3%. However, of 12 cancers missed on single reading, 9 were correctly prompted by CAD, but 7 of these prompts were overruled by the reader. On the other hand, double reading increased sensitivity by 8.2%. This study highlights the need to learn to manage the marks and the need for preliminary training of the radiologist in the use of the CAD.

3.3. Factors influencing CAD performance

The performance of CAD in breast cancer detection is dependent on the performance of the CAD itself, the population to which it is applied and on the radiologists who use it. Most studies suggest that there is a clear benefit in using CAD in less experienced or low volume reviewers. Balleyguier et al. showed that the use of CAD is more useful for the junior radiologist with an improvement in sensitivity from 61.9% to 84.6% compared to a slight improvement from 76.9% to 84.6% for the experienced radiologist [10]. Feig et al. showed that the use of CAD by low-volume readers allowed an increased rate of both recall and cancer detection rates of approximately 19% [11]. CAD devices are particularly helpful in detecting breast carcinomas presenting as microcalcifications, with a reported sensitivity for microcalcification detection ranging from 86% to 99% [12–14]. CAD clearly increases the efficiency and confidence level of radiologists when searching for subtle microcalcifications. Moreover, the rate of false positive marks is about 0.6 marks/image and is lower than for mass detection. Yang et al retrospectively evaluated the sensitivity of CAD applied to FFDM in 103 cases of asymptomatic non-palpable breast cancers detected with screening and 100 cases of normal mammograms [15]. The overall sensitivity was 96.1%. The CAD system marked all 44 breast cancers that manifested exclusively as microcalcifications, all 23 breast cancers that manifested as masses with microcalcifications and 32 of the 36 lesions that appeared exclusively as a mass. On normal mammograms, the mean number of false positive marks per patient was 1.8 leading to a rate of 360 false positive marks for 1 cancer. Hall et al. showed that CAD clearly increases the efficiency and confidence level of radiologists when searching for subtle microcalcification clusters [16]. The main limitation of CAD is amorphous calcifications for which the CAD system has a limited value. Soo et al. in 85 cases of amorphous calcifications evaluated by CAD reported a sensitivity of 57% for the detection of malignant calcifications [17].

For mass detection, the sensitivity is lower ranging from 83% to 90% and is adjustable according to the specificity desired. There is also a higher rate of false positives for the detection of masses than for microcalcifications [from 0.72 to 1.82 marks/image] [18] (Fig. 2). Moreover, this sensitivity has been shown to be greater for masses with spiculation than for architectural distortions (sens 50%) [19]. Radiologists must consider that CAD was optimized for detecting small-sized opacities < 3 cm but should be aware of the possibility of false negatives for obvious and voluminous cancers (Fig. 3). Improving the performance of CAD in detecting masses is necessary and could probably be obtained by multiview-based analyses.