CAD and mammography: why use this tool?*

CAD e mamografia: por que usar esta ferramenta?

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Abstract Mammography is the best method for early detection of breast cancer. Nevertheless, approximately 10% to 30% of breast lesions are missed at screening due to limitations of human observers. Computer-aided detection (CAD) is a relatively new technology that has been implemented in some mammography services to allow a double reading of mammograms. Clinical studies have demonstrated that CAD increases the sensitivity by up to 21% in the detection of breast cancer by radiologists. A CAD system is useful in situations where there is a high interobserver variability, lack of trained observers, or impossibility to perform the double reading with two or more radiologists. The objective of the present review is based on the need to get the medical community acquainted with this tool as an auxiliary, quantitative and non-operator-dependent method, to improve the diagnosis of breast cancer.
Keywords: Breast cancer; CAD; Double reading.

Resumo A mamografia representa o melhor método de detecção precoce do câncer de mama, porém cerca de 10% a 30% das lesões mamárias são perdidas no rastreamento, devido a limitações próprias dos observadores humanos. A detecção auxiliada por computador (*computer-aided detection* – CAD) é uma tecnologia relativamente nova que tem sido implementada em alguns serviços de mamografia, com o intuito de prover uma dupla leitura. Estudos clínicos têm demonstrado que o CAD aumenta a sensibilidade de detecção do câncer da mama, por radiologistas, em até 21%. Um sistema CAD é útil em situações em que exista alta variabilidade interobservador, falta de observadores treinados, ou na impossibilidade de se realizar a dupla leitura com dois ou mais radiologistas. O objetivo desta revisão está baseado na necessidade de atualizar a comunidade médica acerca desta ferramenta, como um método auxiliar, quantitativo, não operador-dependente, e que visa a melhorar a qualidade do diagnóstico do câncer de mama.
Unitermos: Câncer de mama; CAD; Dupla leitura.

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INTRODUCTION

Mammography is the best method for early detection of breast cancer. However, mammogram interpretation constitutes a challenge for the specialist[(1)]. There are evidences that many of the cancers detected at screening mammograms would be retrospectively visible, but were not identified by the radiologist at the moment of the mammogram analysis[(2)]. Approximately 10% to 30% of breast lesions are missed during routine screenings because of limitations that are specific to human observers.

The necessity of analyzing a high number of images to detect a small number of positive cases, the complex radiographic structure of the breast, the parenchymal density that may obscure a lesion, positioning errors or inappropriate mammography technique, the location of a lesion outside the field of view, subtle characteristics of malignancy in association with radiologist fatigue or distraction contribute to false-negative interpretations of a mammogram[(1,2)]. Besides fatigue, distraction and poor experience of the radiologist, the absence of previous imaging studies for comparison and the lack of supplementary mammographic views may lead to misinterpretation[(1,2)].

In the literature, studies approaching perception and errors in radiology classify the errors into three categories, as follows: a) search errors; b) detection errors; c) interpretation errors. Search and detection errors (or perception errors) are defined as those occurring in cases where the lesion is included in the field of view and is noticeable, but is not recognized by the radiologist. Interpretation errors are those occurring in cases where the lesion is described but is not correctly classified, for example, an image with suspicious characteristics that is interpreted as being benign or probably benign. The image interpretation accuracy, although essentially dependent on the education, experience and commitment of the radiologist, is still affected by limitations of the human perception[(3)].

In mammography, double reading has shown to be highly beneficial, reducing the number of false-negative results by 5% to 15%, improving the rates of breast cancer detection[(3,4)]. In spite of its proven diagnostic benefits, double reading is not always feasible because of logistic and financial issues affecting different institutions.

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With the advances in digital image processing, imaging pattern recognition and utilization of artificial intelligence, radiologists have the opportunity to improve their diagnoses with the assistance of computer systems. Computer-aided detection (CAD) is a relatively new technology which has been implemented in some mammography centers with the purpose of providing double reading. The CAD system is useful in situations where there is high interobserver variability, absence of trained observers or impossibility of performing double reading with two or more radiologists. Clinical studies have demonstrated that CAD increases sensitivity in the detection of breast cancer by radiologists in up to 20–21%[5–12].

THE OBJECTIVE OF CAD

The medical community should be aware of the role played by the CAD system as an ancillary, quantitative and non-operator dependent tool in the improvement of breast cancer diagnosis.

Investigations on CAD started in 1960, when the first articles on computed analysis of radiographic images were published. Various CAD systems are available and have the approval of the American Food and Drug Administration (FDA). In 1998, the R2® technology pioneered the utilization of CAD in mammography in the USA, with the approval of the ImageChecker® CAD system by the FDA for screening mammography, and was also the first to be approved for utilization with digital mammography. The SecondLook® system (iCAD Systems, Canada) obtained FDA approval for digital mammography in 2001. Most recently, other systems have been marketed, while other companies still have pending FDA approvals for their systems[11–21].

The reproducibility of CAD systems may vary according to image acquisition, i.e., it may reach 85% in cases where the analysis is done on digitized films[22]. Such variability is probably caused by incoherences in digitization and by the electronic noise produced during the digitization process. However the CAD reproducibility is complete in cases of digital acquisition. The quality of such systems essentially depends on the tumor detection rate or the sensitivity and number of marked false positive regions per image. The principle of any CAD system is the implemented algorithm. That is why the mathematical details of such algorithms are strictly confidential[11–21].

The CAD analysis is materialized through markers superimposed on the suspicious areas. Different types of markers can be utilized: asterisk or ovoid markers for masses, triangular or rectangular markers for microcalcifications. The shape of a marker may influence the effect of CAD on the reader performance, and have been extensively analyzed by means of studies on observers' perception[11–19].

The objective of CAD is not diagnosing, but rather to bring the radiologist attention to specific areas whose analysis will determine the need for further studies. Destounis et al. have evaluated the role of CAD in the reduction of the rate of false-negative results in screening mammograms considered as normal (BI-RADS® 1) at double reading. The CAD system has correctly identified 71% of 52 findings diagnosed as negative in the year of screening. This shows the potential of CAD to reduce the rate of false-negative results in double reading cases[13].

In cases where CAD correctly identifies a proven cancer, it is said that such marking is a true positive CAD, even if the identification is not present on both mammographic views. If no marking is observed on both views, it is considered a CAD false-negative. On the other hand, the false-positive rate is evaluated by the number of markings per image. Ikeda et al. have calculated the number of cancers detected by CAD in relation to the number of indicated false-positives. They have found two false-positives marked by CAD per image[17]. The study developed by Destounis et al. has demonstrated the average of one false-positive marking per case, with 37% of the markings recognized as false-positives on the mediolateral oblique views and 63% on the craniocaudal views[19]. Such prevalence of false-positive markings is in agreement with other findings reported in literature, which range from 1 to 2.2 markings[20,21].

The CAD systems can be utilized either for detection or for classification. Firstly, in a detection task, the computer finds a lesion that is not perceptible to the radiologist. On the other hand, in a classification task, the radiologist and the computer will both analyze the same lesion in order to evaluate its malignancy probability. In case of disagreement, the computer analysis will be a challenge for the radiologist. In a detection task, the computer assistance is represented as a binary result, for example, an arrow-shaped marker may be used to indicate the detection of an abnormality, or no arrow at all to indicate a normal mammogram. The comparable form of representing the computer analysis in a classification task would be to show a binary result of malignant or benign[11–21].

Currently, the CAD system marks two types of changes: microcalcifications and nodules, with the later including nodules, architectural distortions, and asymmetries. It does not differentiate between nodules and architectural distortion, which is a less frequent form of cancer presentation that is more difficult to be detected. As regards the type of detected image, the CAD sensitivity is higher for detecting calcifications (sensitivity: 80–100%) than for detecting nodules (sensitivity: 88– 92%)[11–21].

STUDIES WITH CAD

Lesion size

CAD systems have been developed to detect small lesions (smaller than 3 cm), possibly missing more noticeable lesions. As a result, CAD system cannot be utilized on a stand-alone basis, without a radiologist. In most systems, the best CAD performances occur for lesions measuring between 1 and 3 cm[22,23].

In a study analyzing lesions size *versus* CAD performance (SecondLook system), the lowest sensitivity values were those obtained for lesions = 4 cm (detection rate = 52.9%), while small lesions (< 10 mm) and larger lesions (> 30 mm) were detected with intermediate sensitivity (detection rate = 83%; 25/30 and 31/40 cases, respectively). All of the lesions with sizes between 10 and 30 mm were detected (100%; 45/45 and 46/46 cases, respectively)[23].

Breast density

Brem et al. have evaluated the effect of breast density on the CAD performance and found no statistically significant difference between rates of cancer detection in dense and non-dense breasts. As regards nodule detection, the rate of false-positive results was lower for non-dense than for dense breasts. The authors have suggested that CAD may be particularly advantageous in cases of patients with dense breasts, whose mammograms are more challenging[24]. On the other hand, the studies developed by Yang et al. and Baum et al. suggest that the prevalence of false-positive markings increase with breast density[20,21]. Obenauer et al. have demonstrated a possible tendency of breast density to affect the CAD performance in the detection of cancer[25]. Ho & Lam have demonstrated a decrease in the statistical sensitivity of CAD with the increase of breast density. The CAD sensitivity was 93.3%, with specificity of 1.3 false-positives per image in cases of fatty breasts, but the sensitivity decreased to 64.3% (specificity of 1.2) for very dense breasts[26].

Histological tumor type

Brem et al. suggest that CAD performance in the detection of cancer depends neither on the size nor on the histopathology of the tumor[27]. Studies comparing CAD performance in 208 different histopathological results in malignant lesions have demonstrated a global detection rate of 93.8%. The lowest rate was observed with mucinous carcinomas (75%), as well as in other rare tumors (80%, including metastases, metaplastic carcinomas and neuroendocrine tumors)[24–27].

Sensitivity was lower for detection of tubular carcinoma as compared with invasive ductal carcinoma. Normally, tubular carcinomas are less common and are many times occult at mammography, and are characterized by density with spicules larger than the lesion itself. This may explain the fact that it is not detected by CAD. The histologically benign lesion with the lowest rate of detection by CAD is adenosis (37.9%), which is explained by its own morphology. Therefore, differentiation of neoplasms is many times impossible. Further versions of the software should approach such differences[25,27,28].

Lesion characterization

The CAD systems were first developed for detecting nodules, but the characterization of a breast lesion is also a relevant topic in the investigation with such systems[28–34]. Paquerault et al. have observed an increase in sensitivity from 62% to 73%, with one false-positive result per image in the performance of their CAD system for analysis of suspicious nodules[2]. Studies have designed a likelihood classifier for categorizing nodules as malignant or benign, and try out its performance in an independent data set[28–34]. The area under the ROC curve, *Az*, ranged from 0.87 to 0.90[29,30]. Hadjiiski et al. have evaluated the CAD effects on the characterization of nodules by eight radiologists, utilizing 253 images (138 malignant and 115 benign nodules). For estimates of malignancy risk, the *Az* was 0.79 without CAD and 0.84 with CAD. The improvement was statistically significant ($p = 0.005$). Based on the BI-RADS system, it was estimated that with CAD each radiologist reduced by an average of 0.7% the number of unnecessary biopsies, and 5.7% correctly recommended additional biopsies[31].

Calcifications

In different studies, the best CAD performances are obtained in the detection of microcalcifications, with sensitivity ranging between 80% and 100%[35–38]. The size of the microcalcifications does not affect the rate of detection by CAD. In the study developed by Soo et al., 85 mammograms with findings of histologically confirmed calcifications (21 malignant, 14 high-risk and 50 benign calcifications). The CAD system detected amorphous calcifications in 43 of the 85 cases (case sensitivity = 51%) and in 59 of 146 mammographic images (image sensitivity = 40%). The sensitivity of each group as compared with the histological results was 57% for malignant calcifications, 29% for high-risk calcifications, and 54% for benign calcifications[35]. Kallergi[36], Leichter et al.[37], Wei et al.[38] and Papadopoulos et al.[39] have presented different methods for classifying microcalcifications into benign or malignant. Linear discriminant analysis, artificial neural networks, support vector machines and Bayesian networks were utilized as classification methods. The classification accuracy ranged from an *Az* value of 0.80 to 0.98. Duarte et al. have published an automatic microcalcification segmentation method based on the Otsu method and morphological filters. The analysis of the proposed method covered 236 regions of interest, captured from 54 images. Based on the joint opinion of two experienced radiologists, the algorithm has appropriately demonstrated 88.6% of the segmented cases[40].

Detection and recall

James et al. have evaluated 31,057 women, with 227 detected cancers. A total of 170 cases were recalled with both reading systems. The lesion types were the following: 66% of nodules, 25% of microcalcifications, 6% of architectural distortion of parenchyma and 3% of cases of focal asymmetry. The recall rate varied significantly according to lesion type ($p < 0.001$): the recall rate was higher in cases of architectural distortion originated from double readings, and focal asymmetry, by single reading and CAD. There was no statistically significant difference in the recall rate regarding type of reading in the cases of nodule and calcification. The CAD system correctly marked 100% of the microcalcifications, 87% of the nodules, 80% of the focal asymmetries and 50% of the parenchymal distortions. Carcinomas detected at double readings, but not perceptible at single reading and CAD, were most frequently observed in women with dense breasts. The lesions size is not related to the type of reading[41]. Freer et al. have prospectively evaluated 12,860 screening mammograms. As the radiologist performance without CAD and with CAD was compared, the authors observed: a) an increase in the recall rate from 6.5% to 7.7%; b) no change in the positive predictive value of biopsies, in 38% of cases; c) an increase of 19.5% in the number of detected cases; d) an increase in the proportion of stages 0 and I among malignant neoplasms, from 73% to 78% of cases. The utilization of CAD resulted in an increase of 19.5% in the detection of early stage cancers, without undue effects on the recall rate or on positive predictive value of biopsies[10].

In a prospective study of 21,349 mammograms, Morton et al. have observed a relative increase in the breast cancer detection rate of 7.62%[11]. Retrospective studies developed by Brem et al. and Romero et al. reported an increase of approximately 20% in the detection of breast cancer[5,6]. In a prospective study, Freer & Ulissey reported an increase of 19.5%[10]. Cupples et al. reported an increase of 16.1% in the rate of cancer detection, with increase in the rate of detection of invasive carcinomas < 1 cm, as well as an increase of 8.1% in the recall rate with the utilization of CAD[42]. Gur et al. have not observed any significant change in the detection of breast cancer in 59,139 screening mammograms analyzed with the support of CAD, as compared with 56,432 mammograms analyzed before the introduction of CAD[43]. In the study developed by Ciatto et al., ten radiologists performed conventional reading of screening mammograms, and subsequently repeated the process with the assistance of CAD. The double reading was simulated by combining conventional readings by four specialist radiologists and comparison with the CAD reading. Considering all the readings (ten radiologists), the cancer was identified in 146 or 153 of 170 cases (85.8% *versus* 90.0%; $p = 0.31$) and the recall rate was 106 or 152 out of 1,330 cases (7.9% *versus* 11.4%; $p = 0.003$) in the conventional reading or with CAD, respectively. The CAD reading produced essentially the same results, as compared with the double reading (sensitivity of 97.0% *versus* 96.0%, $p = 0.93$); recall rate of 10.7% *versus* 10.6%, $p = 0.96$. A mean absolute increase of sensitivity of 4.2% could be observed, without statistical significance. The recall rate increased for all the observers, with a mean absolute increase of 3.5%, and increase in sensitivity, but with less impact on specificity[44]. Burhenne et al. have retrospectively analyzed 1,083 mammograms with biopsy-proven results; 427 out of these cases with availability of previous mammogram from 13 different institutions. In the retrospective analysis, 67% (286 out of 427 cases) carcinomas were visible at the previous mammograms; 27% (115 of 427) were interpreted as requiring further investigation (i.e., recall), and the CAD system correctly detected 77% (89 of 115) of the cases. The radiologists' sensitivity was 79%. No significant increase was observed in the recall rate, as compared with values before (8.3%) and after (7.6%) implementation of the CAD system. The rate of false-negative results the radiologists evaluation was 21%. The CAD system may have potentially contributed to the rate of false-negative results (77%; 89 out of 115), without increase in the recall rate[29]. Ciatto et al. have presented divergent findings[44]. Helvie et al. have performed a pilot prospective clinical trial with a non-commercialized CAD system, where a total of 2,389 screening cases were reviewed by 13 radiologists in two different academic institutions. Among the 11 cases of cancer detected at the screening of such patients, the CAD system detected 10 cases, while the radiologists also detected 10 cases. One of the carcinomas detected by the CAD system was not initially seen by the radiologist (increase of 10% in the detection rate). An increase of 10% was observed in the rate of recall for study of cases involving CAD[45]. Birdwell et al. have evaluated 8,682 cases with and without CAD. They performed 165 interventions and found 29 cases of cancer. Twenty-one cancers were detected both by CAD and radiologists, six were detected only by the radiologists and two were detected only by CAD. In the cases where the radiologist utilized the CAD system, there was an increase of 7.4% in the number of detected cancers. The increase in the rate of recall resulting from the utilization of CAD was 7.6%. A modest increase in such a rate was observed for cases evaluated without CAD, as compared with a similar previous period where the radiologists analyzed the mammograms without the CAD system[46].

An interesting observation from the studies developed by Helvie et al. and Birdwell et al. is that the rate of recall in cases analyzed by radiologists increased even before the utilization of CAD, indicating that radiologists may become more alert when they know that their readings can be compared with a second analysis[45,46].

In a prospective study, Gur et al. have found no statistically significant changes in the rates of recall and detection among 56,432 cases analyzed by 24 radiologists before the introduction of CAD and among the 59,139 cases analyzed after its introduction[43]. Such findings, therefore, seem to be different from the one observed in the above mentioned studies[45,46], probably because of differences between the casuistries.

The retrospective study developed by Destounis et al. evaluated 45 biopsy-proven cases on digital mammograms with the utilization of CAD. Forty-four cases of screening classified as BI-RADS category 1 constituted the control group. The collected data were the following: patients' age (mean = 53 years, ranging from 29 to 84 years); breast density (predominance of heterogeneously dense breasts); BI-RADS category; lesion type, lesion size (mean = 1.8 cm, ranging from 0.5 to 5.9 cm); number, type and location of the CAD markings per image (on average, four markings per case, ranging from 0 to 13); CAD system capacity of marking lesions (the system was effective in all the cases of nodules, calcifications and architectural distortion); histopathological results (the CAD system correctly marked 21 of the 26 cases of infiltrating ductal carcinoma, and all the 19 cases of ductal carcinoma in situ). The CAD system sensitivity for detecting positive lesions was of 87%, with a sensitivity of 69% ($n = 31$) for marking a lesion on oblique mediolateral views, and 78% ($n = 35$), on craniocaudal views. The mean rate of false-positive results (type and location of CAD markings) among the 44 normal mammograms was 2.0 (ranging between 1 and 8)[19].

Butler et al. have studied the effect of CAD on the detection of clinically unsuspected breast cancers. Breast carcinomas were observed in sites different from those described at the moment the tumor was clinically detected in 15% (30/197) of the patients with detected cancer. The CAD system identified 87% of those incidentally detected carcinomas, being useful as a support for the radiologists[47].

Biopsy recommendation

In 15% to 30% of cases, biopsy of non-palpable breast lesions demonstrate malignant disease. The excess of benign results represent a limitation of screening mammography. Therefore, the improvement of the mammography specificity will increase the quality in the early diagnosis of breast cancer[5,7,10–13,16,20,27,28,32,42,48,49].

Jiang et al. have concluded that the radiologists' performance in the differentiation between benign and malignant lesions can be improved by means of computer-aided systems. Those investigators could find a higher number of carcinomas while reducing the number of biopsy procedures performed on benign lesions, maintaining or improving the sensitivity in the diagnosis of breast cancer[48,50].

Marx et al. have evaluated the rate of unnecessary supplementary procedures recommended by the radiologists utilizing the CAD system. One hundred and eighty-five mammograms were evaluated (group 1, with 36 cases of malignant histology; group 2, with 49 cases of benign histology, and group 3 with 100 screening cases with four-year follow-up), by five radiologists, without and with CAD. The CAD system detected 32/36 (88.9%) carcinomas (rate of false-positive results: 1.04 markings on nodules and 0.27 marking on calcifications per image). The following mean values were obtained by all observers without/with CAD: sensitivity of 80.6%/80%, specificity of 83.2%/86.4%, positive predictive value of 53.1%/58.1%, and negative predictive value of 94.6%/97%. The observers described similar number of additional lesions without/with the use of CAD (325/326). In spite of the number of short-term follow-up procedures having increased in all the sub-groups with the utilization of CAD (40.8%/42.9% for group 1, 35.6%/38.1% for group 2, and 44.7%/46.8% for group 3, respectively). The number of recommended biopsies decreased in all the sub-groups, as follows: group 1, 34.7%/27.1%; group 2, 47.4%/41.5%; group 3, 33.3%/22%. The decrease in the number of recommended biopsies resulting from the utilization of CAD in the screening group suggests a potential benefit of CAD, with an increase of approximately 2% in accuracy[51].

Observers' experience

The prospective study developed by Khoo et al. correlating the performance of single reading and CAD with double reading has demonstrated that, among the 12 cases of cancer that were not identified by the radiologist, nine were marked by CAD, but only two of them were retained by the first radiologist after analyzing the markings. Seven cases of cancer were identified by the double reading[52].

One of the largest studies on the effect of CAD on diagnoses by radiologists with different levels of experience was published by Thurfjell et al., who have found an increase in sensitivity with the use of CAD for both experienced and inexperienced radiologists as follows: from 80% to 84% in the case of experienced radiologists, and from 67% to 75% for radiologists who were not specialists in breast radiology. Such values are suggestive of an increase in accuracy (approximately 4%) in spite of a subtle decrease in specificity, from 83% to 80% for a non-specialist radiologist[28].

Balleyguier et al. have analyzed the performance of a senior radiologist and a junior radiologist in the evaluation of 100 cases of proven carcinomas and 100 normal mammograms, with and without CAD. With similar and unaltered specificity, the sensitivity increased for both, the senior radiologist from 76.9% to 84.6%, and at a statistically significant rate for the junior radiologist, from 61.5 to 84.6%. Such study indicates that the CAD system may be more useful for the junior radiologist than for the senior one. Thus, the CAD system may play the role of an educational tool in mammography training courses[53].

Sohns et al. have evaluated the clinical usefulness of CAD in the interpretation of screening mammography and mammograms with benign and malignant findings, depending on the observers' experience level. The CAD system was utilized in the evaluation of digital mammograms of 303 patients, divided into three groups as follows: screening group (n = 103), benign lesions group (n = 102) and malignant lesions group (n = 98). The mammograms were analyzed by three radiologists: one medicine student, one general radiologist and one radiologist with experience in mammography. All the groups benefited from the utilization of CAD. The highest benefit level was observed with the medicine student (10% increase in accuracy), followed by the general radiologist (4%) and, finally, by the mammography specialist (3%). No significant difference was observed in accuracy with respect to the analyzed patients group and the utilization of CAD. All three observers presented almost the same rate of increase in accuracy in the evaluation of the studies of the group with malignant disease and in the screening group. Finally, the increase in accuracy depends on the observers' experience. For all patient groups evaluated with CAD, the utilization of the system causes a sharp increase of the ROC curve and, consequently, a gain in sensitivity[4].

Karssemeijer et al. have compared CAD with double reading of nodules on 500 screening mammograms with 125 cases of screening-detected carcinomas screenings and 125 cases of interval carcinomas. All mammograms were analyzed by ten experienced radiologists and by a CAD system, which detected mass regions, assigning a suspicion level to each nodule. The CAD markings on areas not reported by the radiologist were not utilized. The independent double reading was performed utilizing rules to combine the suspicion levels assigned to the findings by two radiologists. In a total of 141 cases, there was visible change in the cancer location on the previous mammography, and 115 of them were classified as mass cases. For the previous mammograms where masses were detected, the mean sensitivity of the radiologists, as well as the mean false-positive rate, was 39.4%, corresponding to a 7.0% increase with the utilization of CAD, and 10.5% with double reading. The differences between single readings, double readings and CAD were statistically significant ($p < 0.001$). Although the independent double reading has produced the best performance in cancer detection, the presence and the probability of CAD system mass markers can improve mammograms interpretation[3].

Jiang et al. have investigated whether CAD can reduce interobserver variability in mammograms interpretation. Ten radiologists interpreted mammograms showing clustered microcalcifications in 104 patients. With the CAD system, the variation in the radiologists' accuracy was reduced by 46%. The CAD system increased the interobserver agreement from 13% to 32% of the total of cases ($p < 0.001$), while the k value increased from 0.19 to 0.41 ($p <$ 0.05). The CAD system eliminated two thirds of the significant disagreements in cases where two radiologists recommended biopsy and routine screening for a same patient ($p < 0.05$). This system can reduce the interobserver variability in mammograms interpretation[50].

Analysis time with and without CAD

In a prospective study with five radiologists, Tchou et al. have determined the time required for interpretation of 267 digital mammograms, with and without CAD, besides analyzing whether any changes would occur in the radiologists' decision (level of confidence). On average, the time required for mammograms interpretation without CAD was 118 seconds ± 4.2 (standard deviation). The mean time required to review the CAD marked images was 23 seconds ± 1.5, with additional 3.2 seconds for each calcification cluster and 7.3 seconds for each mass, representing a change in approach by the radiologists in 2% of the cases. The utilization of the CAD system in the evaluation of digital mammography has led to changes in the radiologists' confidence level in 22% of cases, with increase in confidence in 14% of the cases and decrease in confidence in 8% of the cases. The additional time required to review the CAD marked images represented an increase of 19% in the time of interpretation without CAD, as well as a 11% increase in the rate of recall[54].

Negative CAD results

Fenton et al. have studied 429,000 mammograms and 2,351 cases of cancer detected in 43 institutions during a four-year observation period. Seven (16%) of the 43 institutions implemented the utilization of CAD, allowing the comparison of the performance of such institutions and their radiologists on an individual basis, before and after the utilization of CAD. The institutions where the CAD system had not been implemented constituted the control group. The diagnosis specificity decreased from 90.2% before CAD implementation to 87.2% after implementation ($p < 0.001$). The positive predictive value decreased from 4.1% to 3.2% ($p = 0.01$) and the rate of biopsies increased 19.7% ($p < 0.001$). The increase in sensitivity from 80.4% before CAD implementation to 84.0% after implementation was not statistically significant ($p = 0.32$). The change in the rate of cancer detection (including invasive breast cancer and ductal carcinoma in situ) was not significant (4.15 cases for every 1,000 mammograms before the implementation, and 4.2 cases after implementation; $p = 0.90$). The analysis of data regarding all 43 institutions demonstrated that the utilization of CAD was significantly associated with a lower overall accuracy than the accuracy observed before CAD implementation (area under the ROC curve: 0.871 *versus* 0.919; $p = 0.005$). One has also observed that the utilization of CAD did not significantly increase the rate of cancer detection, and also caused a negative impact, considering the increase in the number of false-positive mammograms resulting in a higher number of recalls and biopsies[30].

CONCLUSION

The CAD systems can improve the diagnostic performance and, at the same time, reduce the radiologists' interpretation variability. The CAD system can play the role of a reference reader completely immune to human variability, i.e., it can reduce the variability which is dependent on the radiologists' interpretation that is subject to variations inherent to the human perception and to the decision making process.

In the current circumstances, the CAD system can only be utilized together with the observers. Neither the first observer can be replaced, nor the second, as well as the double reading is superior to the association of one observer with CAD.

The rate of detection of architectural distortion by CAD is low, increasing for masses, and achieving almost 100% for microcalcifications, helping radiologists in reducing errors in the detection of carcinomas, potentially avoiding unnecessary biopsies.

The CAD system constitutes an active area of investigation and development in radiodiagnosis. Its technological features and software versions have undergone swift changes. The performance of CAD and, specially, the false-positive rate critically depend on the selection criteria in the studies, the software version, the included malignancy rate and experience of the radiologists involved in the utilization of CAD.

Recently, there has been an increase in the number of CAD system applications. Currently the utilization of this system has been extended to ultrasonography and breast magnetic resonance imaging studies interpretation.

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