Application of CAD in the diagnosis of breast cancer

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Abstract

Breast cancer is an extremely dangerous disease, which if diagnosed in time has a high survival rate. The incidence and mortality rate from breast malignancies are increasing, so in order to reduce these numbers, new technological solutions are being looked into, that should enable the earliest possible detection of breast carcinoma. Although the original solution was seen in traditional computer-assisted detection systems, CAD, applied to various radiological breast imaging methods, the results of various studies discussed in this paper found that they did not meet their original expectations in breast cancer diagnosis. The use of conventional CAD systems still had too many limitations such as a decrease in particularity and positive predictive value with an increase in incorrect results and an increase in revocation rates. However, the development of artificial intelligence, AI-based algorithms has improved the quality and accuracy of conventional CAD systems. Unlike conventional CAD systems based on hand-crafted features, deep learning, as a subfield of AI, is based on representational learning. In representational learning, the algorithm itself during training determines features in the image that indicate the presence of lesions. Recently, such deep learning algorithms have been applied to various radiological methods. In this paper, the analysis of various studies discusses the possibilities, but also the limitations of new AI-based applications for different modalities of breast imaging. Due to the small number of studies conducted on the topic of AI systems and the need for an extremely large set of data for training and validation of the algorithm, many scientists still doubt this new method. Despite these limitations, the AI approach has the ability to detect useful features in an image that are still invisible to the human eye. Future advances in technology will significantly improve AI systems and their implementation in health systems will be inevitable.

Key words: AI; breast cancer; CAD; digital breast tomosynthesis; mammography; radiomics.

Abbreviations and acronyms: AI (Artificial Intelligence), CADe (Computer-Aided Detection system), CADx (Computer-Aided Diagnostic system), CADT (Computer-Aided Detection triage worklist), CNN (Convolutional Neural Network), DBT (Digital Breast Tomosynthesis), DM (Digital Mammography), FFDM (Full-Field Digital Mammography), MRI (Magnetic Resonance Imaging)

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Introduction

The breast is the tissue that covers the pectoral muscle and it consists of glandular, fatty and connective tissues. The lobes of the breast are organized into 15-20 sections and situated within each lobe are smaller structures called lobules. Within the breast is a rich network of lymphatic vessels that drain lymph into the lymph nodes in the armpit. Metastases are most commonly found in these nodes [1]. Despite the fact that breast cancer is an extremely dangerous disease, if diagnosed in time, it has a high survival rate. The question arises as to how is it possible that the incidence and mortality of breast cancer are on the rise given today’s technological possibilities in medicine.

Although, digital mammography, DM, digital breast tomosynthesis, DBT and magnetic resonance imaging, MRI, are still advantageous. The rate of malignant diseases that go on undiscovered due to omission or misinterpretation of breast irregularities is still high. It was with the objective of diminishing radiological errors, occurring in identification of breast carcinoma, that a Computer-Aided Detection system, CADe was approved in 1998 [2]. CADe is a tool that analyses the image and marks the suspicious areas with potential cancer characteristics, including masses and microcalcifications. Originally CADe was made to assist experts in the examination and evaluation of medical images, replacing the extra work of another radiology expert and thus improving and speeding up the
Unlike CADe, a Computer-Aided Diagnostic system, CADx is a software that analyzes medical images based on radiographic findings while well assessing the probability that a particular feature represents a particular disease. In other words, it differentiates malignant findings from the ones that are benign [4]. With the advancement of technology, artificial intelligence, AI, techniques are also advancing. AI techniques offer promising results, in comparison to traditional CADe / CADx systems [3].

The aim of the research

The aim of this paper is to present the application of traditional CAD systems, but also new CAD systems which are based on the new AI algorithm to radiological methods of breast imaging. The analysis of various studies shows their actual clinical diagnostic effectiveness. Their advantages of use are listed, as well as their limitations.

Discussion

Traditional CAD systems

CAD algorithms can directly analyse images obtained in digital format such as images obtained by DM, DBT and MRI. Evaluation of CAD system performance is assessed in several ways: analysis of data generated in the laboratory and examination of the impact of CAD on radiologists in real clinical conditions, whose results are considered the best assessment of CAD because they assess its actual effect in clinical practice [4].

Application of CAD systems in conventional mammography

The first use of CAD systems was in conventional mammography and a myriad of studies has been organized to prove their real clinical validity. The analysis studied the susceptibility of the apparatus, which demonstrated the likelihood of a positive finding in people, the precision of the apparatus, which demonstrates the likelihood of a negative finding in people who are good health, and the influence of CAD on growing patient recall rates. The research of Helvie et al. [5], Birwell et al. [6], Thurfjell et al. [7] and Ciatto et al. [8] showed a growth in sensitivity in the usage of CAD for examining medical images but in spite of that, an enlarged recall rate of patients was noted, which was not just justified as a result of the negative findings collected during the following checkups. However, the results of the work of Fenton et al. [9] are most important for the evaluation of CAD evaluation on conventional mammography. The text looks into the association among the use of CAD on conventional mammography and the explicitness, susceptibility and amount of cancer detection at the earliest possible stage. The outcomes of the study state that CAD did not achieve clinical diagnostic efficiency because its use in the analysis of conventional mammography images did not lead to a higher rate of breast carcinoma and no malignancies were detected at an earlier stage, which was the starting goal of this new technique. Furthermore, except for the fact that the system did not meet the expectations set at the first stage of the evaluation, a decrease in the specificity of the test was also observed (Figure 1) [9] and the difficulty of decreasing the distinctiveness of the search and boosting

**Figure 1.** Presentation of research results by Fenton et al. when using CAD systems on conventional mammography

Source: https://academic.oup.com/view-large/figure/42992038/jncidjr206f01_ht.jpeg
the avoidable recall rate of patients imposes the inquiry of whether there is a true profit of using a CAD system.

Application of CAD to DM

Many scientists believe that the digitalization of mammography systems and the use of CAD systems on DM will solve the current limitations of the system and improve the detection of cancer and thus help solve this major health problem. However, not all scientists agree. Scientists Murakami et al. [10] and Sadaf et al. [11] conducted retrospective studies investigating the sensitivity of CAD systems to DM, with the only difference between these two studies being that in the study by Sadaf et al. [11] sensitivity was also affected by lesion size, which is not the case in the study by Murakami et al. [10]. Both studies indicate an increase in susceptibility and better detection of cancer at an earlier stage when applying a CAD system. The works of Skaana et al. agree with their results [12] and Ko et al. [13]. These studies encourage the application of CAD to DM because they believe it will help radiologists in the earlier detection of breast cancer because of the results obtained in their research. However, the largest study conducted on this topic by Lehman et al. [14] found different results. The accuracy of DM interpretation with and without CAD system was compared on the largest sample so far and in the largest time frame. It is for these reasons that the results of this study are considered crucial in evaluating the performance of CAD systems. The study proved that the performance of CAD screening did not improve any of the measurement data, i.e. the sensitivity of the system remained approximately the same, but the specificity is significantly lower when using CAD. An increased unnecessary patient recall rate has also been observed, which in addition to increasing hospital costs also creates feelings of fear and discomfort among patients (Figure 2), [14] conducted to determine the characteristics of CAD systems on DM it is clear that traditional systems need to improve their limitations in order to be said to have real clinical efficacy.

Application of CAD to DBT

DBT transcends the current limit of 2D DM imaging and allows 3D breast imaging, shooting from multiple different angles, however due to the oversized image set requiring a lot of interpretation time, it is still not used as the primary breast imaging method [15]. Nevertheless, numerous experts argue that the evolution of the CAD apparatus should be a critical point that could make the usage of this method less challenging, perchance it may even allow DBT to become the best test for the diagnosis of breast malignancies instead of DM. Two studies conducted a preliminary assessment of the effectiveness of CAD systems on DBT examinations. Chan et al., in their study, are developing a CAD system that should help detect breast masses in DBT images, and evaluate its actual clinical effectiveness. The data set recorded by the prototype CAD system for DBT consisted of 26 patients. They established that the CAD system attained high susceptibility in the images obtained by DBT, but still with a high rate of incorrect findings [16]. Another study by Sahiner et al. took part in the evolution of a CADe apparatus for the recognition of microcalcifications in the reconstructed volume, trying to lower the high rate of false-positive labels. Their system consisted of three phases: prescreening, grouping and reduction of false positives (Figure 3), and proved the feasibility of CAD systems on DBT methods [17]. However, many authors still disagree with the stated conclusions of the study of Chan et al. [16] and Sahiner et al. [17] that conventional CAD systems have proven their clinical efficacy and feasibility on DBT methods. Despite the increased sensitivity, there is still a large number of false-positive findings, which reduces the very specificity of the search. In a study by Bernardini et al., they came to the conclusion that the commercial CADe product for

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**Figure 2.** ROC curve of interpretation of digital mammograms with and without CAD system  
Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4836172/bin/nihms771091f2.jpg

**Figure 3.** CADe diagram of the microcalcification detection system for DBT  
Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3257751/bin/MPHYA6-000039-000028_1-g002.jpg
DBT has a lesion sensitivity of 89%, with 2.7 ± 1.8 false positive rates per examination [18]. Also Chu et al. [19], Chan et al. [16], Schie et al. [20] came to the conclusion that the application of CAD systems still has higher rates of false positive findings.

**Application of CAD to MRI**

Not long ago, MRI has become a progressively more used tool in the discovery of breast malignancies. Myriad of scientists have tried to verify the usefulness and validity of CAD to characterize breast lesions and differentiate non-cancerous from life-threatening lesions. Meeuwis et al. made a study to assess the accuracy of breast MRI interpretation with 3T using fully automated kinetic analyses and analysis by radiologists without the use of CAD. Examinations were processed retrospectively by 2 experienced radiologists and two trainees who analysed the sets using CAD and without using it. The results obtained show that CAD-based analysis improves search sensitivity and specificity for readers with different levels of experience [21]. In addition to the research of Meeuwis et al. [21], 2 studies by Lehman et al [22] and Williams et al. [23] had the same research purpose, which is to evaluate the ability of CAD system to distinguish malignant from benign lesions (Figure 4) compared to the interpretation of the radiologist himself. Furthermore, they recognized the high susceptibility and precision of the system and the reduction of incorrect uncoverings. However, traditional CAD systems have failed to take their place on MRI examinations due to the still low specificity proven in the research of Kuhl et al. [24], poorer estimates of lymph node involvement by invasive cancer demonstrated in the study of Song et al. [25] and due to the results of the largest research conducted on this topic by Dorrius et al. [26] who have proven that the specificity and sensitivity of the use of CAD are the same in experienced radiologists, as well as without its use. Despite these limitations, many scientists believe that further advances in technology will improve CAD systems and solve all its shortcomings.

**Application of AI in radiological methods**

Breast cancer is a major health problem and radiological imaging plays a key role on the way to its early diagnosis, monitoring and treatment. With the advancement of technology, imaging techniques that are more demanding and complex are also advancing, therefore it takes longer to complete their interpretation. In addition to all this, the number of requests for imaging is growing and there is a shortage of radiologists all over the world. Potential solutions are being sought that will enable radiologists to work faster and easier while improving the detection of breast cancer. Despite their higher rate of breast cancer detection, traditional CAD systems have limitations such as reduced screen specificity, a higher number of false-positive findings, and consequently a higher rate of unnecessary patient recalls. Solutions to these limitations are sought in new algorithms for classifying images based on AI. AI is a part of the computer science that focuses on the design and study of the ability of machines to produce rational behaviour from external stimuli and inputs [27]. Machine learning involves a machine or computer that can recognize patterns from examples instead of programmed rules [28]. The main feature that distinguishes this new algorithm from traditional CAD systems is that deep learning as an AI subfield is based on representational learning in which the algorithm itself determines image features that indicate the presence of a lesion during its training, rather than hand-crafted features like traditional CAD [2]. The application of AI can be divided into two categories. The first category is called “broad artificial intelligence"
which is used as a substitute for routine tasks such as checking image quality, adjusting the contrast in the image and booking appointments. This system also speeds up the process of breast imaging and facilitates the work of radiologists. The second category is called “narrow AI” which includes CADe, CADx and triage worksheets (CADt) as well as lesion segmentation and predicts treatment response. These AI systems can be used in two ways to support, i.e. help radiologists, or independently, both have the same goals, which is to improve patient outcomes, reduce the burden on the health system and improve its efficiency [29]. The question is whether AI, driven by machine learning advances, using deep multilayer convolutional neural networks CNN (Figure 5), can make traditional CAD mammography systems more valuable in clinical practice.

Application of AI system to DM

The majority of current CAD systems show their conclusions in the shape of instructions on a mammogram that behove the specialist to make the decision for himself whether a certain label displays a potential malignant lesion. Several different studies have concluded that CAD systems could have clinical benefit only with significant improvement. This encourages the development of new testing and research of new AI systems. Two studies evaluated the success of discovering breast carcinoma with and in the absence of the help from AI. In a study by Rodriguez-Riz et al. 14 radiologists who interpreted mammograms with and without AI support participated. They spotted a boost in susceptibility and precision of screening when using the help of AI [30]. In their study, Watanabe et al. tried to determine the usefulness of cmAssist ™, a computer-assisted detection algorithm based on artificial intelligence (AI-CAD), in improving the sensitivity of radiologists to earlier detection of breast cancer. Seven radiologists took part and they all enhanced their skill in breast carcinoma identification using cmAssist ™ (Tables 1 and 2) [31]. Both studies conclude that radiologists benefited from the usage of an AI support system.

McKinney et al. in their work, represented that an AI system which has the competence to excel radiologists in foreseeing breast cancer, should also conquer the biggest limitation to date of screening mammography that has high values of incorrect positive and negative results. The study showed a reduction in false-positive and negative results. Also, their AI system managed to surpass the performance of 6 radiologists who participated in the study. In the double reading procedure, AI proved the same performance as the radiologist, thus pointing out the possibility of reducing the load on the second reader by 88%, which greatly facilitates and speeds up the work of radiologists and reduces the burden on the health system. This appraisal of the AI apparatus clears the way for new systems of use that can be used in interventional studies to boost correctness and capability in the screening of breast malignancies [32]. Although many studies have proven the effectiveness of applying new AI systems to mammography, fear and unreliability of the new still prevails among people. It is Ongena et al. who conducted the research on the general population’s view of the use of AI systems for the diagnostic interpretation of screening mammograms. Women in the Netherlands aged 16 to 75 were surveyed. They determined that the vast majority still does not condone the autonomous use of AI systems for the analysis of screening mammograms. The system has the support of the population only if it is used in combination with an experienced radiologist as the first reader and that the AI system is used as the second reader [33]. Apart from the opinion of the general population, the question also arises as to how radiologists view the AI system, whether they see it as a threat or as a useful aid in screening mammography. The solution to this inquiry was provided by January Lopez, MD, who is a specialist in the field of breast imaging, also an officially recognized diagnostic radiologist and director of the breast imaging department at Hoag Breast Centres. He states that the

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AI system is not being viewed as a competition. On the contrary, it should be seen as a prospective co-partner. His belief is that AI holds the capability to be of service to radiologists in improving their performance as well as success in discovering the carcinoma of the breast [34].

Application of AI system to DBT

Given that conventional CAD systems have not experienced the expected revolution, further research into new AI systems is underway. This should finally solve the problem of long image interpretation time, reduce the number of false positives leading to increased patient recalls and higher health costs, also it should increase the specificity of the examination itself. Two studies, Benedict et al. [35] and Conant et al. [36] examined the performance of a commercial AI system for DBT. In the study of Benedict et al [35] the system could only detect soft tissue lesions while in the study of Conant et al. [36] used a more advanced algorithm that was able to detect calcifications as well. Both studies observed that reading with the AI system increases specificity and sensitivity while significantly reducing reading time (Figure 6).

Application of AI system to MRI

The biggest limitation of traditional CAD systems so far, when used on MRI recordings is a reduction in specificity and it is being addressed by introducing new-based systems on AI. It is Dermis et al [37] and Jiang et al. [38]...
who compared the new CAD systems that are based on AI with traditional CAD systems. The results of their research indicate how new AI systems increase sensitivity, significantly improve the performance of radiologists in distinguishing benign and malignant breast lesions on MRI examination, also the average specificity remained the same among the different stages of cancer. For MRI examination in patients who have a proven tumour, it takes a lot of time for the radiologist to review a large set of data in looking for the cross-section on which the cancer is marked. Eskreis-Winkler et al. explore feasibility using deep learning to recognize tumours on axial sections of MRI images of breasts. Their retrospective study involved patients diagnosed with invasive breast cancer. The study consisted of 2 radiologists who analysed the images using an algorithm based on deep learning and thus estimated time saving. Axial tumour sections from the first stage were collected after contrast application on MRI examination. The principle of operation was based on the classification of axial images into two sub-images, one sub-image contained cancer and the other contained only a healthy breast. Different cases were randomly assigned to system training, assessment, and testing kits. The new algorithm was developed for the purpose of classifying subimages into two categories, the first category being the subtypes with cancer and the second category the subtypes without cancer, so pathology was the reference standard, on the basis of which sensitivity, precision and the specificity of this classification system were determined. The results of the study proved the accuracy of the new tumour detection algorithm which adds up to 92.8%, sensitivity equals 89.5%, and specificity was 94.3%. The conclusion of the study is that deep learning in MRI examinations is easily used for spotting the cross-section containing the tumour and thus allowing significant time savings [39]. Sheet et al. in their study prove that the application of new CAD e systems based on AI systems allows the detection of suspicious lesions, predicts subtypes and recurrence of tumours based on computer-derived MRI features. They believe that by introducing AI systems in recording breasts could allow the creation of special imaging biomarkers that would include patient’s characteristics and specific characteristics for different types of tumours. They consider that by using this approach a systematization can be made, which would allow patients to have personalized filming guidelines [40]. Many scientists believe that AI-based systems will continue to develop, though will not completely replace the radiologist but will greatly facilitate him making the correct diagnosis, workflow and enable easier interpretation of medical images.

**Radiomics**

All cancers have strong phenotypic differences that can be shown non-invasively by medical methods. Radiomics actually encompasses the spread of CAD and refers to the conversion of medical images into quantitative features of the images being analysed [41]. This procedure can be used with the help of the AI approach, and aims to provide data on the phenotype of breast cancer with the purpose of better classification of tumours [42]. The purpose of radiogenomics is to establish a link between clinical data, imaging data, molecular data, genomic data and outcome data [43]. Data for radiomics studies are mostly taken from MRI examination of the breast, however it has...
been shown that DM data can also be used for insight into the breast cancer phenotype. Yang et al. in their study, developed radiographic-based mammography-based nomogram for preoperative prediction of lymph node metastases in breast cancer patients (Figure 8). They attained an accuracy of 84% certainty in prognosticating lymph node participation based on the mammographic attributes of the initial tumour. Correspondingly, they demonstrated that the nomogram which they developed is a well-founded and non-invasive apparatus which can be used for seeking the ideal strategy of treatment for people with breast malignancies and therefore immensely aid the labour of specialists [44]. In addition to the use of radiomics features on DM and MRI scans, their use has also been proven on DBT scans. In their study, Tagliafico et al. compared DBT for cancers and normal findings in women with dense breasts with a radiomics approach. The results showed that radiomics characteristics in patients with dense breasts and negative mammography differentiate between carcinogenic and normal breast tissue with evidence of correlation with tumour size [45].

Conclusion

With the development of medicine and technology in the world, radiological breast imaging techniques are also advancing. Following a long period of using traditional CAD systems, retrospective analysis of various studies found that they failed to live up to expectations regarding the discovery of breast carcinoma. Research indicates that the usage of conventional CAD systems still has many limitations, such as reduction of meticulousness and positive predictive value without an appreciable increase in sensitivity. The biggest limitation of conventional CAD is the rate of false-positive findings, which unnecessarily increases the patient recall rate, health care costs, and creates a sense of discomfort and concern in patients. However, new research conducted using new CAD systems based on AI algorithms gives new hope. The main difference between deep learning systems, compared to conventional CAD systems based on hand-made features, is that they are based on representational learning. In representational learning, the algorithm itself determines image features during training that indicate the presence of a lesion. This system has better performance than the conventional ones, and many studies have proven that their capabilities are closer to those of experienced radiologists. Fast improvements in deep learning are considered to represent a key function in radiological methods of breast image analysis in FFDM, DBT, and MRI. In addition to cancer detection, AI will play a role in predicting cancer risk, selecting therapy, and ultimately predicting outcome. However, there are also shortcomings of new AI solutions, such as the need for very large data sets for training and validation of algorithms, and there is still a small number of studies conducted on this topic. Nevertheless, regarding the additional improvements in the field of technology and medical science, AI is anticipated to have a place among other imaging methods used in early distinguishment of breast carcinoma. AI may not be of great use on its own, but it will certainly assist experts in finding cancer.
**Sažetak**

Karcinom dojke iznimno je opasna bolest, koja ako se dijagnosticira na vrijeme ima visok stopu preživljenja. Incidencija i stopa smrtnosti od karcinoma dojke sve više su u porastu, stoga se u svrhu smanjenja ovih brojki traže nova tehnološka rješenja koja će omogućiti što raniju detekciju karcinoma dojke. Iako se prvobitno rješenje vidjelo u tradicionalnim računalno potpomognutim sustavima detekcije, CAD, koji su se primjenjivali na različitim radiološkim metodama snimanja dojke, rezultatima različitih studija koji su obrađeni u ovom radu, utvrđeno je da nisu ispunili svoja prvobitna očekivanja u dijagnostici karcinoma dojke. Uporaba konvencionalnih CAD sustava još uvijek je imala prevelika ograničenja poput smanjenja specifičnosti i pozitivne prediktivne vrijednosti uz povećanje lažno pozitivnih nalaza te povećanje stope opoziva. Međutim, razvojem algoritama temeljenih na umjetnoj inteligenciji, AI, poboljšana je kvaliteta i točnost konvencionalnih CAD sustava. Za razliku od konvencionalnih CAD sustava koji se temelje na ručno izrađenim značajkama, dubinsko učenje, kao potoploj AI-a temelji se na reprezentacijama koje su nezvane na slici koje su još uvijek neprimjetne. Budućim napredcima tehnologije značajno će se unaprijediti AI sustavi i njihova implementacija u zdravstvenim sustavima bit će neizbježna.

**Ključne riječi:** AI; CAD; digitalna tomosinteza dojki; karcinom dojke; mamografija; radiomika.

**Literature**


