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Review Article

Potential Role of Artificial Intelligence in Breast Cancer Detection- A Review

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Abstract – *Breast cancer remains a major cause of mortality in females worldwide. Detecting breast cancer at earlier stages would make a significant difference among the global population. Artificial intelligence (AI) has made its way to concern for developing technologies and approaches for detecting cancer at earlier stages, artificial intelligence (AI) has made its way. Recent research by scientific experts has concentrated on this automated process. The major advantages of enhancing the research on this particular field involving AI in detection are due to the usage of deep learning algorithms (software) and the hardware capable of using the complex and complicated algorithms of AI. The advantages also include the accessibility of larger datasets required for AI training approaches. The identification and detection of breast cancer have been performed using mammograms, ultrasound, histopathology, magnetic resonance imaging, or a conjunction of these imaging techniques in an automated manner. Combining image-specific findings and underlying genetic, pathologic, and clinical characteristics in breast cancer is becoming increasingly valuable. Radiologists now have more diagnostic tools and image collections to study and interpret because of the introduction of innovative imaging modalities. Integrating an AI-based workflow into breast imaging allows many data streams to be combined into strong multidisciplinary applications, perhaps leading to tailored patient-specific therapy. The current article analyses the role of AI in the early detection of breast cancer.*

Keywords - *Artificial intelligence, Breast cancer, Deep learning, Early detection, Medical imaging.*

1. Introduction

Cancer can be regarded as the second leading cause of mortality worldwide. In 2015, deaths from cancer and related ailments accounted for around 8.8 million. The predominant cancer type affecting females is breast cancer [1], [2]. In the United States, around 250 000 new breast cancer cases were identified in 2017, and 12 percent of all women in the country would be diagnosed with the disease at some point throughout their lives [3]. Breast cancer is diagnosed histologically using established pathologic criteria. The highly prevalent breast cancer type is invasive ductal carcinoma (50 -75 percent of patients).

In contrast, five to 15 percent were characterized by invasive lobular carcinoma and the remaining account for the combination of both ductal and lobular types [4]. In the pathogenesis of breast cancer, two major molecular targets have been found. The first target is estrogen receptor alpha (ERα), a steroid hormone receptor identified in almost 70% of invasive breast cancers. It also functions as a transcription factor. Erα, when activated by estrogen, is capable of promoting the growth pathways of oncogenes in breast cancer cells. The progesterone receptor hormone (PR) gets activated and expressed as a consequence, and it can be regarded as the indicator of ER signaling. PR is a steroid hormone closed related to Erα [5]. HR+ is a cancer cell with an expressed ER or PR, with an expression rate of 1% or higher [6], [7].

Breast cancer, if diagnosed early, can be successfully treated. Hence, finding suitable methods to diagnose breast cancer at the earliest stages is crucial [8]. The most common and important imaging tools for breast cancer screening and diagnosis include mammography, thermography, and ultrasonography [9]. One of the most significant early detection procedures for breast cancer is mammography. As it is ineffective for thick breasts, other techniques like ultrasonography and diagnostic sonography are suggested [10]. Because small malignant masses may evade radiographic radiation, thermography may be more effective than ultrasonography in detecting smaller cancerous growths [10], [11].

The application of neural networks in image and signal processing increased dramatically in the early 1980s. Because breast cancer diagnosis is challenging, statistical tools and artificial intelligence (AI) techniques can be useful [12]. In many contexts, AI is described as an artificially intelligent machine. To put it another way, these systems can respond to similar situations as an intelligent human, such as comprehending complicated matters, simulating intellectual processes, human rationalization methods, illustrating precise reactions, understanding and acquiring knowledge, and problem-solving rationality [13]. The false-positive results in breast cancer detection have to be reduced. In the current scenario, AI research has targeted the same worldwide by developing automated algorithms to screen mammograms for breast cancer [14], [15]. The effectiveness of AI in breast cancer detection has been extended to understanding pathology and imaging modalities. The images obtained from the biopsy of sentinel lymph nodes have been observed to have a better detection rate with AI in identifying metastatic breast cancer [16], [17]. In light of this, the current study sought to investigate the effect of AI on breast cancer.

2. A brief overview of AI

A branch of AI involved in algorithm development that helps the computer acclimate to a problem that was not programmed earlier without re-programming is called machine learning (ML) [18]. In other words, it can be defined that the system "learns" and solves the problem by itself using the provided information. Statistical methods can be used without manual intervention to identify patterns among sets. Almost all the algorithms in ML use mathematical algorithms for transferring the data from one set to another. The “features” or “predictors” are the related variables, whereas “labels” or “targets” are the terms referring to outcome variables [19], [20]. More complicated algorithms have become accessible as computing power has grown. For learning a complicated interlink between the image pixel values and semantic segments without using the features engineered manually, a million units similar to neurons were employed by deep learning techniques. These features are, instead, learned automatically from the data provided [21], [22]. The categorization of algorithms in deep learning is generally based on network designs. Conventional neural networks (CNN) were used for image recognition issues. The hierarchical network of pattern detectors in CNN has been reported to be promising. For the identification and quantification of cells, strategies based on CNN are utilised, which involve the detection and segmentation of cells based on images [23]–[25] and features of histology [26], [27]. Finally, the sequence is processed using the self-connecting pattern through recurrent neural networks (RNN).

3. AI and breast cancer

Since the period of "old AI," breast cancer has piqued attention, with applications involving differential diagnosis [28], grading [29], and prognosis and therapeutic approaches [30]. Breast cancer is another common application of 'new AI,' particularly for diagnosis and treatment [14], [31]. The visual perception and training of radiologists, as well as their field experience and attention, are crucial in image reading; the best possible image reading by humans is not always perfect, and it is sometimes unclear how it can be refined [32], [33], making way for some interest by solutions using AI. The risk prediction and detection, as well as in the case of clinical decision-support of breast cancer, involve the use of "New AI" [34]–[36], development of a management plan [37], and translation of genomics into precision medicine [38], [39]. In a fiercely competitive private industry, AI-based products are being developed, particularly for image processing, such as for reading mammography and diagnosing the pathological features of tissue [31], [40]. AI systems for detecting breast cancer are already accessible for clinical use, with increased effectiveness, reliability, and profitability marketing claims. However, the available evidence does not always support the market's enthusiasm. According to a recent scoping literature, the reliability of AI models for screening breast cancer ranged between 69.2% and 97.8% (median AUC 88.2%) [31]. Furthermore, most research findings were limited and retrospective, with algorithms evolved from data sources with a high proportion of mammograms with malignancies (higher than 25%, but among the females subjected to mammography, only 0.5–0.8% were identified with breast cancer), significant data bias, restricted validation accuracy, and limited evidence for comparing the AI's performance to that of radiologists [31].

Outside of traditional healthcare facilities, there is also a growing market for screening and diagnosis of breast cancer using AI. Since 2008, start-ups researching artificial intelligence for breast screening have debuted at least once a year, with angel and seed capital funding, in developed and developing nations, particularly India. In August 2019, we looked for such start-ups [41]. The most striking trend we discovered across the start-ups was a link between the technology delivered, and the market intended. Certain start-up firms are creating AI to optimize mammography procedures and market them to healthcare systems; they may collaborate with or be acquired by larger technological corporations. The other set of companies is delivering services based on; novel and undetected, unidentified AI test technology; the major target of these companies is the general public, with women younger than the acceptable age to perform mammography. The AI in the healthcare system has a commercial form that is crucial when addressing the ethical, legal, and societal consequences, which we will now discuss.

4. AI application for breast density

The evaluation of the density of the breast in an automated manner with various software is approved by the FDA as the higher the density of the breast, the higher the risk for breast cancer [42], with high interobserver inconsistency in assessing the breast density estimation [43]. The highly dense breast may be masked, which delays the identification of risk for breast cancer and diagnosis, leading to delayed treatment [44]. The necessity for ultrasound-assisted supplemental imaging, mammography with contrast enhancement, or magnetic resonance imaging (MRI) could be guided by an assessment of breast density in an automated manner, with an authentic quantitative classification. Breast Imaging Reporting and Data System (BI-RADS) classification has been provided by radiologists accordingly [45]. When tested on 8,677 undiscovered mammograms, a therapeutic adaptation study found 77.7% concordance between a classification of BI-RADS by a single radiologist and an algorithm of deep CNN, and additionally gross acceptance into everyday work routine [46]. The scattered tissues of the fibro gland (BIRADS B) varied significantly from the heterogeneously dense category (BIRADS C). An authentic identification of breast density between two classes (B and C) has been achieved by using the CNN assessment on 1,850 pictures of healthy individuals that contain processed and perfectly labelled data. To confirm the accuracy of data, instances were chosen numerically. An algorithm without pre-training had an AUC of 0.9882, while one with pre-training had an AUC of 0.9857 [47]. Volpara Density (Volpara Solutions) calculates the volumetric breast density by calculating fibroglandular tissue density and fat density from regions of intensity in mammography images [48]. FDA approved 510(k) of Hologic for their Quantra 2.2 Breast Density Assessment software in December 2017 [49]. The authorized software is employed in analyzing the distribution and texture of mammographic breast tissue by using ML. The output of this software is produced in the alignment categories ranging from one to four based on the US breast density rating system: BI-RADS 5th edition [50]. In February 2018, FDA approved Densitas 510(k); ML is used in breast density software that is automated [49]. This software calculated the breast density in percentage, producing an output with the details of grade and categories of breast and BI-RADS density, respectively, in a computerized manner.

5. Digital breast tomosynthesis and AI

Three-dimensional (3D) technology of imaging, known as digital breast tomosynthesis (DBT), has been reported to produce higher detection rates of breast cancer [51] and lower rates of false positives [52] when compared to two-dimensional (2D) digital mammography results [53]. The 2D results of digital mammography have been observed to be interfered with by the tissue superimposition, whereas the shadow overlapping is reduced in DBT and 3D imaging. It also increases the conspicuousness of the lesions and lowers the recall rates. Mass detection, as well as higher breast density women or heterogeneously dense breasts, were detected efficiently by DBT, according to recent studies [54], [55]. The reading period of DBT is relatively higher than that of 2D imaging techniques as it has a larger number of images. The variation in reading time ranges from 50 to 200% more than the other techniques [56]. To decrease the time taken for assessment by a radiologist and to increase effectiveness, DBT has to be provided with optimised CAD and diagnostic systems. The first FDA clearance was obtained by iCAD's PowerLook Tomo Detection [57] in 2017 in this field. To reduce DBT time for education, the software employs DL technology. To improve the exploration of tomosynthesis data, the proposed approach comprises identifying the targeted areas from 3D images and applying those areas of interest in the 2D images, which have already been developed. With the growing popularity of DBT, AICAD system designers have taken this developing imaging method into account. ScreenPoint Medical, a Netherland-based company, developed the DL software package Transpara for various modes and purposes [58].

For automatic detection of soft tissues and identification of calcification lesions, Transpara involves various views in 2D mammography. Finally, the score for cancer suspiciousness is calculated (on a point scale of 10: a low score indicates no possible anomalies) [59]. Compared to standard CAD prompts, the software's interactive decision support feature is unique, as CAD indications remain undetected unless explored by the viewer [60]. Two mammography vendors have provided around 240 mammograms. A review of Transpara version 1.3.0 has been assessed and examined by 14 radiology experts from US health care institutions and found that the device enhanced breast early diagnosis without increasing time for reading [61]. However, more research is needed to explore the implementation of this method to eradicate the "laboratory effect" on the results of a screening group with blinded readers. The data is used in 3D format by Transpara for DBT dimensions to analyse lesions and calcification of the soft-tissue, highlighting the important parts in the hopes of reducing DBT reading durations [62]. Because mammograms may be classified as to the risk of detecting breast cancer, the Transpara Score has the capability to be used for triaging. Figure 1 shows the AI recognised breast cancer digital mammograph.

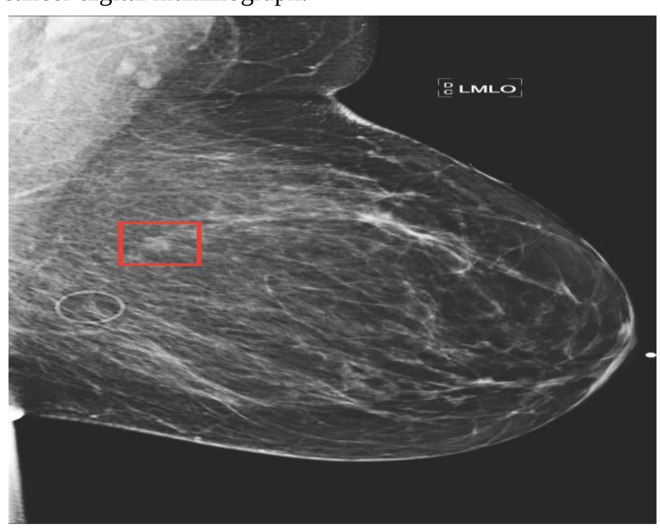

Fig. 1 A mediolateral oblique digital mammography with a region of interest (denoted by a bounding box) that the AI algorithm recognised as suggestive of breast cancer

Source: Marinovich et al. [63]

6. Prognostic applications

Numerous morphological characteristics of malignant cells have been linked to prognosis. Veta et al. [64] demonstrated that the detection of breast cancer prognosis in a male patient using tissue microarray (TMA) is obtained using variables like nuclear form or structure. Whitney et al. [65] have reported that quantitatively aspects of structure and embodiment of the nucleus and topology can be used to identify the risk of recurrence in ER-positive breast cancer patients (based on Oncotype DX, a diagnostic analysis grounded on 21-gene expression). The prognosis predictors of tumor-infiltrating lymphocytes (TILs) are based on their structural morphology and distribution. TIL structure was indicative of prognosis for 13 cancer subgroups in research that employed a CNN to identify and quantify it in pictures from The Cancer Genome Atlas [66]. On triple-negative breast cancer WSIs, Yuan suggested an approach to characterize and evaluate the spatial pattern of lymphocytes among tumour cells [67]. Using this methodology, they classified lymphocytes into three categories based on their spatial closeness to cancer cells.

Gene expression profiling by TMA revealed that the proportion of intra-tumoral lymphocytes to cancerous cells was independently predictive of longevity and linked with the expression ranges of cytotoxic T lymphocyte protein 4 (CTLA-4). This strategy was further developed by these researchers, who discovered that the spatial pattern of the immune system cells was likewise linked to the delayed occurrence of ER-positive breast cancer [68]. *Ali* et al. used traditional machine learning algorithms to count characteristics on breast cancer samples and could depict the responses of neoadjuvant [69]. The density of lymphocytes in the neighboring tissues was regarded as the most significant predictor.

The risk of repeated occurrence is one of the most important characteristics of prognosis. Klimov et al. (2019) have recently developed a novel undiscovered ML pipeline, which can depict the ipsilateral recurrence risk in DCIS. The pipeline incorporates digital WSI, data collected from DCIS patients for a longer period, and clinical and pathological information from a retrospective cohort (n = 344) treated with lumpectomy [70]. The primary malignant cells were stained with H & E stain, and the stained cells were digitalized for analysis by pipeline. A classifier was used to label the regions of stroma, normal and benign ducts, malignant glands, concentrated lymphocyte zone, and blood vessels in the first stage. In the next phase, architectural and spatial patterns (n = 8) were utilized for training the classifier involved in classifying recurrence risk. The architectural and spatial patterns of tissue are obtained from the labelled areas for estimating the recurrence risk. In an independent validation study, the recurrence predictor calculated the 10-year recurrence risk (85%). In identifying recurrences, this approach outperformed evaluated clinical and pathological factors in terms of precision, selectivity, steadiness, risk ratios ($p<0.0001$), and prediction ranges (positive). Furthermore, the patients who need additional treatments were perfectly identified by this (validation cohort p = 0.0006) [70].

While most of the research focused on epithelial cells inside cancer, several publications also investigated the tumour microenvironment for its importance to prognosis. Beck et al. reported that the morphology, spatial interactions, and image characteristics of epithelial and stromal parts could be retrieved from digitized WSIs from breast cancer patient tissues. The overall survival (OS) rate in two breast cancer populations from two different institutions was closely interlinked with the prototype of prognosis attributes. The stromal chamber characteristics showed a highly significant variation (p = 0.004) when compared to epithelial chamber characteristics (p = 0.02) [71].

7. Role of AI in breast cancer detection

In Computer-Aided Detection (CADe), detection denotes the location of items of interest in photographs [72]. The presence of structural noise (e.g., dense breast parenchyma concealing an intrinsic cancerous lesion), imperfect image search patterns, erroneous evaluation of subtle or complex disease states, enormous quantities of image files, suboptimal physical picture quality, fatigue, and distractions all limit radiologists' ability to detect cancer. Connectivity with AI-based detection technologies can be employed as a localization activity and as a helper for radiologists looking for worrisome lesions in pictures. To assist radiologists in reading breast MRI, particularly DCEMRI, techniques were developed to enhance the computer images. Because these methods can emphasize lesions of concern, even those that may be misconstrued or overlooked by radiologists during the screening of breast MRI, and because these systems can reduce the reading time and diagnostic errors [73]. Most MRI image analysis techniques depend on the full-breast MRI procedure, which includes both temporal and morphological data from the images of late and early phases. Researchers have observed CADe systems using morphology and kinetics to identify probable dangerous lesions on DCEMRIs. MRI has been considered to have the greatest sensitivity for breast cancer diagnosis of all the various modalities for breast examination, regardless of breast density [74]. Breast MRI is recommended to complement mammography for people with a relative lifetime risk of higher than 20% based on evidence from nonrandomized clinical trials and observational research [75]. However, screening MRI for females at intermediate risks, such as those with thick breast tissue, is still rising in the United States. Shortening the procedures of MRI breast screening, decreasing image capture time, and shortening image processing and analysis time are all ways to attain the effectiveness and speedy throughput seen with mammography screening. Using shortened and ultrafast MRI procedures could result in cheaper costs and faster throughput, expanding access to breast MRI for women with thick breasts or at-risk populations (lifetime risk, 15–20%) [76]. However, these significant improvements in MRI acquisition technology come at the expense of lagged phase kinetic data. The first computerized detection algorithms for breast anomalies were based on computerized mammograms, which were eventually replaced by FFDM (full-field digital mammography), both of which have been thoroughly evaluated over the years [77].

Computers analyzed mammograms to improve the indications of the lesions, proceeded by computerized segmentation (feature extraction) of lesions and false-positive detections, which were originally exploited in the identification of masses and aggregated micro-calcifications. Intriguingly, deep networks for detecting lesions in imaging of breasts were also tested on mammography for use in detection methods, with the first occurrence being in 1994 when a shift-invariant (aka CNN) was employed in the detection of micro-calcifications [78], [79]. Assessments of multi-institutional instances later led to the translation of such computer-aided detection systems. Recent AI advancements in detecting breast density images have focused on the breast imaging methods used in monitoring, such as FFDM and tomosynthesis, in recent years [62]. Further AI screening approaches for breast MRI are now being evolved as the purpose and protocol variants of MRI for usage as an adjuvant to mammographic screening grow. Dalmis et al. work on a deep learning-based CADe system that uses initial spatial rather than late-phase temporal features. Their CADe technology outperformed their prior CADe system, indicating that it might be used in shorter MRI protocols [80]. Radiologists will increasingly value upcoming CADe devices that can obtain data from initial scan images. It's worth noting that, based on the complexity of the radiological exam, the radiologist may gain from computer-aided identification through efficacy and effectiveness. Considering the image-integration needed by the human visual system during the identification process, multiparametric MRI offers itself to computer analysis.

8. Enhancement of Breast Cancer Diagnosis by AI

CADx has provided various machine learning strategies to identify normal and cancerous breast tissue samples and lesions since the 1980s [81]. The automated identification of a tumour, originally identified by either a radiologist or a machine, is the focus of these AI approaches for CADx. The computer identifies and calculates the likelihood of disease in the concerned region or lesion, leaving patient treatment to the clinician. Few AI techniques used in breast cancer detections are shown in Table 1.

Table 1. Various AI techniques in image processing

Images	Accuracy (%)	Sensitivity (%)	Specificity (%)	Advantages	Reference
Medical infrared thermal imaging – Support vector machine	90.91	81.82	100	Use of curve let before feature extraction	[82]
Ultrasound - Support vector machine	95.85	96.00	91.46	Combined textural and morphological Features	[83]
Mammography – Cascade forward backpropagation artificial neural network	67.8	Not reported	Not reported	Features extracted from the known mammogram images are stored in the knowledge base	[84]
Mammography - Feed-forward backpropagation artificial neural network	92.8	Not reported	Not reported	Using image registration techniques	[85]
Mammography – Support vector machine	93.06	97.82	89.09	1. Intensity- and shape-driven features have the greatest role in the later classification stage 2. Normal-abnormal classification stage before benign-malignant classification can be effective and reduce false positives	[86]

The size, structure, and organisation of tumors can be quantified using artificial intelligence approaches applied to breast imaging data. For example, the assessment of MRI by dynamic contrast uptake helps the experts evaluate cancers on a heterogeneous basis. The spatial patterns and dynamic features can be identified. [87]. For instance, entropy, for instance, is a mathematical predictor of randomization that describes the varied pattern of contrast uptake by the circulatory system inside cancer tissues detected on breast MRI scans enhanced with contrast. These assessments could represent the varied nature of angiogenesis and therapeutic vulnerability, according to The Cancer Genome Atlas (TCGA) Breast Cancer Phenotype Group [88].

Both the preset and deep-learned software programs have been tested with CADx. It's worth noting that researchers have demonstrated that digital mammograms are well categorised and differentiated between normal and malignant tissues by human-engineered features and machine-learning digital algorithms. Hence, the conjunction of these two strategies can result in a statistically significant enhanced performance [89], [90]. The "fusion" classifier showed the best performance across all three modes of breast screening with DCE-MRI (n = 690), FFDM (n = 245), and ultrasound cases (n = 1125), suggesting the possibility for complimentary usage of engineered feature in combination with deep learning tumour features for detecting the breast cancer [90]. Other researchers employed learning algorithms with CNNs and FFDMs on automated films (n = 2282) and 324 breast tomosynthesis data to characterize tumors, demonstrating the capacity to transfer information about observed patterns between imaging modalities [91].

9. Future perspective

With the significant degree of activity in the treatment of breast cancer, AI development has brought with it both benefits and liabilities. Vanguard technologies can establish guidelines for an excellent practice, but they can also become notorious for failure and unexpected effects instances. What would it require for breast cancer AI to be recognised as a best practice model? The following is our main conclusion: *Administrators, clinicians, and engineers in the healthcare industry must recognise that AI-assisted breast treatment is not only a technological solution but also a responsibility comprising ethics, legality, and social concern. When taken into serious consideration, AI treatment may enhance and pave the way for a stronger collaboration of stakeholders in the health care system, clinical experts, and patients from the conception of AI to its deployment and evaluation.* Value-sensitive design is a considered heritage in data and information that might inform such involvement [92], [93]. Below are some particular suggestions.

The current healthcare system is already filled with responsibilities of informing the details and ethical, medical, and legal concerns. In this case, AI usage, which is practically unexplainable, is not recommended. Moreover, AI needs exposure and accessibility to larger and more sensitive data, making it vulnerable to breaching sensitive information and dangerous and improper delivery of public goods. A privatized market exacerbates these dangers. According to research, the public has expressed their willingness to provide the use of sensitive information on their medical history for the advancement of technology. But their only concern is proper control, maintaining confidentiality, and governing with the appropriate use for the public good, which the data operators and software developers have to consider [94].

10. Conclusion

The available scientific literature required for the clinical deployment of AI on a quality and quantity basis is lagging far behind. Commercially accessible AI systems should be evaluated with radiologists on larger populations involving different cohorts, comparative analysis test accuracy, and randomised control studies. Such research will help researchers understand how an integrated AI system might affect the performance of breast screening programs.

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