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Breast Cancer Screening Using Artificial Intelligence Techniques: Enhancing Biochemical Insights and Diagnostic Accuracy †

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Abstract: Breast cancer, the most prevalent cancer in women worldwide, demands effective screening for early identification and improved treatment outcomes. Recent advances in artificial intelligence (AI) have resulted in dramatic developments in a variety of fields, including healthcare. In this review paper, we look at how AI approaches can be used in breast cancer screening to improve diagnostic accuracy and provide deeper molecular insights. We dig into the complex terrain of breast cancer treatment, which has transformed as a result of the discovery of prognostic and predictive biomarkers, allowing for personalised therapeutic methods based on molecular subgroups. We emphasise the importance of AI-driven approaches in optimising screening procedures and providing quick and exact findings. The potential of AI to revolutionise breast cancer screening is highlighted, including its applications in diagnostic imaging, lesion identification, and standardised imaging data interpretation. The analysis highlights AI's critical role in tackling issues associated with the integration of new technologies, providing solutions for worldwide standardisation in cancer detection.

Keywords: breast cancer screening; artificial intelligence; diagnostic accuracy; prognostic biomarkers; predictive biomarkers; AI-driven methodologies; biomarker-based diagnosis

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1. Introduction

The term "artificial intelligence (AI)" was coined by computer scientist John McCarthy in 1956, with AI aiming to create machines that replicate human intelligence [1]. Breast cancer is a significant global health challenge, particularly among women. Recent advancements in AI, especially in healthcare, offer transformative possibilities. This review explores how AI can enhance diagnostic precision, enabling early detection and providing molecular insights into breast cancer. AI has a pivotal role in optimising screening methods within the evolving landscape of breast cancer treatment. It facilitates personalised therapeutic interventions based on molecular subgroups, ensuring swift and accurate diagnoses [2].

2. Background

Breast cancer stands as a formidable challenge to global healthcare, claiming numerous lives annually and posing significant physical and psychological burdens for affected individuals [3]. The estimated new cases for breast cancer in 2023, according to the author, include 300,590 overall cases, out of which 2800 have been recognised in males and the remaining 297,790 in females. The estimated cases of death overall have been 43,700, with 530 cases being male patients and 43,170 being women [1]. Among cancers, breast cancer ranks as the most frequent malignancy diagnosed in women, demanding robust screening strategies to achieve early detection and improved treatment outcomes [4]. AI has the potential to enhance breast cancer screening by improving early diagnosis and management [2]. Traditionally, invasive procedures and histopathological assessments, often involving Hematoxylin and Eosin (H&E) staining, were relied upon for diagnosis. However, AI has introduced a transformative shift in breast cancer screening, offering advanced diagnostic tools and improving patient care [5]. AI enables multi-scale correlations between medical imaging and gene expression data, providing increased accuracy and personalised treatment recommendations, particularly in radio-genomics [6]. Challenges such as high costs and computational demands hinder widespread adoption, but deep learning models expand diagnostic capabilities [4]. This review explores the integration of AI into breast cancer screening, addressing both its potential and challenges while preserving references.

3. Biochemical Markers in Breast Cancer

Crucial biomarkers are essential in early breast cancer detection and diagnosis, playing a pivotal role in risk assessment, treatment planning, and disease recurrence monitoring, especially for screening asymptomatic individuals [7]. Ideal screening assays should be non-invasive, require minimal material, offer objective measurements, and provide observer-independent results, while maintaining an acceptable false-positive rate based on disease prevalence [3]. As per the author and adapted from [3] details are mentioned on specific biomarkers in Table 1.

Table 1. Summary of Established and Emerging Biomarkers for Breast Cancer Detection, created by the author and adapted from [3].

Biomarker	Role	Prognostic Value	Predictive Value	Method of Measurement
Estrogen Receptor (ER)	Sensitivity to endocrine treatment	Predicts benefit from endocrine therapy	Predicts response to chemotherapy in neoadjuvant setting	Immunohistochemistry, Gene expression
Progesterone Receptor (PgR)	Dependent on ER expression, prognosis on endocrine therapy	Strong prognostic value, little predictive significance	Response to anti-estrogen treatment	Immunohistochemistry
HER2	Indicates prognosis, predicts response to anti-HER2 therapy	Amplification status predictive	Response to anthracycline-based chemotherapy	Immunohistochemistry, FISH, CISH
Ki67	Marker of proliferation, potential prognostic and predictive value	Discriminates between luminal A and B subtypes	Predicts response to chemotherapy	Immunohistochemistry
Cyclin D1	Overexpression, correlates with ER and PgR expression	Prognostic factor for a better outcome	Predicts poor response to anti-estrogen treatments	Immunohistochemistry
Cyclin E	Regulator of cell cycle, associated with prognosis	Discriminant of overall and disease-free survival	Altered levels affect chemotherapy and endocrine therapy response	Immunohistochemistry
ERß	Expression varies in ERa-negative breast cancer	Associated with good prognosis, response to tamoxifen	Correlates with Ki67 and HER2 overexpression	Immunohistochemistry

4. Traditional Screening Techniques

4.1. Mammography

Mammography, crucial for breast cancer screening, involves X-ray imaging of breast tissue [8]. Digital mammography (DM) has replaced conventional film-screen mammography due to its advantages, including computer-aided detection and centralised film reading, which enhance screening efficiency and accuracy. While mammography offers benefits, its frequent use requires a careful assessment of potential radiation risks and long-term effects due to repeated screenings. Mammography may lead to false-positive results, necessitating additional tests, including breast biopsies [9]. Independent reviews confirm mammography's effectiveness in reducing (from 20% to 35%) breast cancer mortality, particularly among women aged from 50 to 69, although its impact is somewhat less for women in their 40s due to factors such as lower disease incidence, dense breast tissue, and faster-growing cancers. Incorporating digital mammography into breast cancer screening requires a comprehensive understanding of its benefits, drawbacks, and potential radiation risks. Careful consideration and ongoing research are essential for optimising mammography's role in breast cancer detection and diagnosis. It is worth noting that a significant number of screenings may be needed to prevent a single breast cancer death, such as from 500 to 1800 screenings for women at age 40 over 14–20 years [10–12].

4.2. Magnetic Resonance Imaging

Magnetic Resonance Imaging (MRI) provides high-resolution, radiation-free breast imaging, leveraging proton density principles akin to nuclear magnetic resonance. While not commonly used for routine diagnosis, MRI supplements mammography in select cases, particularly for high-risk individuals like those with BRCA1 or BRCA2 mutations. MRI's high sensitivity aids in early breast cancer detection and staging, notably for invasive ductal carcinoma (IDC), utilising contrast agents to enhance lesion visibility. Various paramagnetic metal ion complexes, including manganese (Mn), iron (Fe), and gadolinium (Gd), serve as MRI contrast agents, but concerns over toxicity, especially with gadolinium, exist. Ongoing research explores innovative carrier systems and advanced targeting techniques to improve contrast agent effectiveness while reducing toxicity. Limited studies on high-risk women show higher sensitivity with MRI compared to mammography and ultrasound. MRI offers radiation-free imaging with high sensitivity, paving the way for early breast cancer detection and precise staging, despite challenges associated with contrast agents [13–15].

4.3. Molecular Breast Imaging

Molecular Breast Imaging (MBI) is an innovative breast cancer screening approach that uses a radioactive tracer to highlight cancerous breast tissue, visualised with a nuclear medicine scanner. It is known by various names, including the Miraluma test, the sestamibi test, scintimammography, or specific gamma imaging [11]. MBI employs Tc-99m sestamibi, an approved tracer, with comparable sensitivity to MRI but higher specificity for detecting small breast lesions [16]. Breast biopsy is the cornerstone of breast cancer diagnosis, often using a "triple test" combining clinical examination, imaging, and biopsy procedures [11]. Needle biopsy includes fine needle aspiration cytology (FNAC) and core needle biopsy (CNB). FNAC is less invasive and quick, involving the extraction of cells from suspicious breast lesions for laboratory analysis. CNB, more invasive, extracts small tissue cores, enhancing diagnostic accuracy [17]. The choice of biopsy depends on imaging findings, with FNAC being cost-effective and suitable for palpable lesions, while CNB is preferred for non-palpable lesions. Excisional biopsy is an option for larger samples, following CNB diagnosis of indeterminate lesions. Needle or wire localisation guides an excisional biopsy for non-palpable findings. In certain cases, observation may replace an excisional biopsy [17]. MBI is a promising breast cancer screening technique using radioactive tracers and nuclear medicine scanners, while advanced needle biopsy methods, like FNAC and CNB, enhance diagnostic accuracy and minimise invasiveness [11].

4.4. HER-2/neu Detection Assay

The assessment of HER-2/neu expression is crucial in breast cancer diagnosis and treatment planning [18]. It identifies patients who can benefit from targeted therapies using two primary techniques: Immunohistochemistry (IHC) and Fluorescence In Situ Hybridisation (FISH) [11]. IHC uses antibodies to detect protein expression, making it widely adopted for diagnostic purposes in identifying tissue markers associated with specific cancers, including breast cancer [11]. FISH, on the other hand, identifies specific chromosomes or chromosomal regions within a cell by hybridising fluorescently labelled DNA probes to denatured chromosomal DNA, allowing for the assessment of HER-2/neu gene amplification in breast cancer samples [11]. Combining IHC and FISH enhances breast cancer diagnosis precision and aids in personalised treatment strategies [11,18].

4.5. Blood-Based Assay

Blood-based assays are being explored for non-invasive breast cancer screening due to their ease of sample collection and potential for early-stage cancer detection. Multiple biomarkers, encompassing serum tumour biomarkers, proteins, cancer cells, DNA, RNA, autoantibodies, and genomic/proteomic markers, are under investigation for their usefulness in breast cancer detection [11]. Serum tumour biomarkers like CA 15-3, carcinoembryonic antigen (CEA), and CA 27-29 have been studied for breast cancer screening. However, their low sensitivity and specificity make them unsuitable for early detection, and they are primarily recommended for metastatic settings [11].

4.6. Markers under Research

In blood-based breast cancer screening, promising markers include proteins like Mammaglobin (detectable through ELISA) and S100A11, known for early-stage breast cancer detection. Additionally, circulating cells like CECs and EPCs play roles in tumour growth and neovascularisation, while CSCs are explored as potential markers. Elevated free DNA/RNA in the blood, due to cancer tissue changes, offer insights into breast cancer. Abnormal DNA methylation analysis provides a promising detection approach, and circulating miRNAs in serum show potential for breast cancer detection. Autoantibodies against TAAs are emerging as tumour markers, and combining them with serologic biomarkers may enhance diagnostic accuracy. Specific autoantibodies, such as those targeting p90/CIP2A, hold promise for early-stage breast cancer screening. Genomic studies offer gene signatures for prognosis prediction (e.g., Oncotype DX and Mammaprint), and blood-based proteomics identifies markers like HSP27 and 14-3-3 σ, aiding personalised therapies and prognosis [11].

5. Integration of AI with Screening Techniques

5.1. AI-Enhanced Mammography

The authors of [13] emphasise mammography's role in breast cancer screening but note limitations like missed cases and high false positives. AI, especially convolutional neural networks (CNNs), is used to enhance accuracy (AUC~0.9) and reduce recall rates [9]. Combining AI with radiologist assessment is effective, as shown in multi-reader studies. AI also helps distinguish normal mammograms and predict breast cancer risk, offering potential workflow improvements and personalised screening. AI-driven breast density assessment outperforms human evaluation, with hybrid models integrating AI-driven density analysis and traditional risk factors expected to enhance risk prediction [13].

5.2. AI-Enhanced Ultrasound

In [13], AI's significant role in enhancing breast cancer detection using ultrasound is highlighted. Ultrasound is more sensitive than mammography but lacks specificity, especially for older women. AI focuses on distinguishing benign and malignant breast masses based on BI-RADS criteria, using features like shape, orientation, margin, and echo pattern. Deep learning, particularly CNNs, achieves accurate results [9]. AI models perform comparably or better than radiologists, aiding decision-making. AI is integrated into ultrasound devices for real-time decision support. AI also benefits ultrasound elastography by automatically extracting features and achieving high accuracy in lesion differentiation. However, clinical integration awaits specific guidelines and standardisation [13].

5.3. AI-Enhanced MRI

Breast MRI is a focus of AI research for lesion detection and classification [13]. AI aids in diagnostic interpretation and locating tumour-containing slices. AI distinguishes between benign and malignant lesions, with CNNs outperforming radiomics/ML (AUC 0.88 vs. AUC 0.81), though radiologists remain superior [9]. Combining MRI information enhances accuracy. AI, using DWI and T2-weighted imaging, improves specificity and reduces unnecessary biopsies. It assists in diagnosing challenging lesions like sub-centimetre or high-risk ones. AI predicts breast cancer molecular subtypes based on DCE-MR images, useful for monitoring treatment-related changes. AI-derived signatures offer insights into tumour biology [13].

A summarised overview of AI-Enhanced Breast screening techniques as per the authors and adapted from [9,13] is shown in Table 2.

Table 2. Summarised overview of artificial intelligence (AI)-enhanced breast cancer screening in the context of mammography, ultrasound, and MRI, including their roles, AI techniques employed, performance, applications, and the status of clinical integration adapted from [9,13].

AI-Enhanced Breast Screening	Mammography	Ultrasound	MRI
Role and Objective	Enhancing cancer detection and reducing recall rates. Optimising screening efficiency and risk prediction.	Distinguishing between benign and malignant breast masses. Improving specificity and aiding radiologists.	Detecting breast cancer, lesion classification, enhancing specificity, predicting molecular subtypes.
AI Techniques	Predominantly convolutional neural networks (CNNs). Hybrid approaches with radiologist assessment. Multitask learning.	Deep learning methods, especially CNNs. Integration into ultrasound devices.	Machine learning, CNNs, radiomics signatures on DCE-MR images.
Performance	AUC around 0.9, improved accuracy when combined with radiologist assessment.	Comparable or superior performance to radiologists. High accuracy in lesion differentiation.	CNNs outperform radiomics/ML (AUC 0.88). Enhanced accuracy with combined MRI information.
Applications	Alleviating the burden of reading normal exams, improving workflow. Predicting breast cancer risk.	Distinguishing between benign and malignant lesions, aiding radiologists' decision-making.	Lesion detection, classification as benign or malignant, predicting molecular subtypes, enhancing specificity.
Clinical Integration	Potential for improved workflow without compromising diagnostic precision. Awaiting specific guidelines and standardisation.	Awaiting specific guidelines and standardisation.	AI-derived signatures offer insights into tumour biology, relevant for monitoring changes during treatment.

6. Conclusions

The landscape of breast cancer screening is undergoing a transformative shift with the integration of cutting-edge technology, particularly artificial intelligence (AI). AI's synergy with medical imaging shows great potential in improving early cancer detection, subtype diagnosis, and treatment strategies. This review explores AI's multifaceted role in breast cancer screening, spanning various techniques, biomarkers, and its integration into medical practice. In mammography, AI aims to enhance cancer detection accuracy and reduce recall rates. Convolutional neural networks (CNNs) excel at characterising mammographic abnormalities, working alongside radiologists to improve diagnostic precision. AI also streamlines screening efficiency through multitask learning and personalised risk prediction, potentially revolutionising mammographic interpretation. In ultrasound imaging, AI effectively distinguishes between benign and malignant breast masses, often outperforming radiologists. In breast MRI, AI enhances lesion detection, classification, and molecular subtype prediction. AI-driven breast cancer detection on MRI supports systematic interpretation and interdisciplinary discussions, reducing unnecessary biopsies in challenging cases. Successful AI integration into clinical practice requires standardised protocols, rigorous validation, and ongoing collaboration among medical professionals, AI researchers, and regulatory bodies. Ethical considerations, transparent decision-making, and synergy with human expertise are pivotal in AI's journey to revolutionise breast cancer screening, ultimately improving patient care, enabling early intervention, and enhancing treatment outcomes.

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