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Research Paper

Revolutionizing Breast Cancer Screening: Integrating Artificial Intelligence With Clinical Examination for Targeted Care in South Africa

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A B S T R A C T

Introduction: Breast cancer remains a critical public health concern globally, with early detection being pivotal to improving outcomes through clinical downstaging. In low- and middle-income countries, access to traditional screening methods like mammography is limited due to high costs, infrastructure deficits, and shortages of trained professionals. This study evaluates the integration of Breast AI, an artificial intelligence (AI)-enhanced diagnostic tool, with Clinical Breast Examination (CBE) to improve breast cancer screening in resource-limited settings. Although the system demonstrated clinical utility, challenges such as cost-effectiveness, infrastructure readiness, and provider training for scaling this technology warrant further exploration.

Aim and objectives: This study aimed to assess the clinical utility of the Breast AI system in conjunction with CBE for breast cancer screening. Objectives included evaluating the system's diagnostic performance, its potential to achieve clinical downstaging, and its ability to reduce unnecessary surgical referrals. The study also aimed to identify areas for improvement, such as logistical barriers and scaling feasibility.

Methods: A prospective comparative cohort study was conducted at Daspoort PoliClinic in Gauteng Province over 6 months. A total of 1,617 women aged 25 to 85 years were screened using CBE and Breast AI. Data collection included risk stratification, Breast Imaging Reporting and Data System (BIRADS) scoring, and referral outcomes. Statistical analyses compared the diagnostic performance of CBE and Breast AI using McNemar's test, with a Chi-square value of 1.8 and a p value of 0.1797. Educational sessions on breast cancer awareness were also conducted to encourage community engagement.

Results: Of the 1,617 women, 530 presented with clinical signs or risk factors. Eight patients required short-term follow-up for BIRADS-3 findings, five of whom were identified by Breast AI, compared to two identified by CBE. No cases were classified as BIRADS-5 requiring immediate intervention. The Breast AI system demonstrated improved sensitivity, identifying four additional positive cases compared to CBE, thereby reducing false negatives. Risk stratification by Breast AI ranged between 0 and 25%, indicating a low probability of malignancy but ensuring accurate referral for symptomatic cases. The system facilitated timely surgical opinions for conditions like accessory breast tissue with lipoma that CBE had missed. Despite these findings, logistical and cost-effectiveness barriers to scaling the technology remain unaddressed.

Conclusion: The integration of Breast AI into screening programs showed promise in enhancing diagnostic accuracy, achieving clinical downstaging, and reducing unnecessary surgical referrals. The system's adjunctive use with CBE demonstrated potential for streamlining health-care delivery in resource-limited settings. However, the study highlights the need for further research on scaling this technology, addressing logistical challenges, and evaluating its cost-effectiveness. Future efforts should focus on

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expanding the sample population, integrating AI-driven tools into national screening protocols, and enhancing provider training to optimize patient outcomes and resource allocation.

Introduction

Breast cancer remains a significant public health challenge globally, particularly in low- and middle-income countries (LMICs), where limited resources often delay diagnosis and treatment, resulting in poorer outcomes (Gutnik et al., 2016; Anyigba et al., 2021; Anderson et al., 2015). Early detection is critical to improving survival rates, as it enables clinical downstaging, reducing the burden of advanced disease on health-care systems. However, traditional screening methods, such as mammography, are frequently inaccessible in LMICs due to high costs, limited infrastructure, and a shortage of trained professionals. This highlights the need for alternative approaches that are both effective and scalable within resource-constrained settings.

Artificial intelligence (AI)-enhanced diagnostic tools, such as the Breast AI system, offers a promising solution. By integrating AI with clinical breast examination (CBE) and ultrasound imaging, these tools can improve the accuracy and efficiency of early breast cancer detection, even in low-resource environments. The Breast AI system, validated in this study, has demonstrated high sensitivity in identifying breast masses and providing risk stratification, potentially reducing false negatives and streamlining referrals for further evaluation (Gutnik et al., 2016; Dan et al., 2023; Iacob et al., 2024; Shieh et al., 2017).

However, the integration of such technology into broader health-care networks poses challenges. The current study was designed as a pilot to evaluate the feasibility of using Breast AI in conjunction with CBE, focusing on its clinical utility in a single setting. Yet, critical factors such as cost-effectiveness, infrastructure requirements, and the logistical barriers to scaling this technology for widespread use remain unexplored. These include the need for health-care provider training, ensuring readiness of existing infrastructure, and addressing potential resistance to adopting AI-driven diagnostic systems. Such barriers are particularly relevant in LMICs, where resources are limited and health-care disparities are more pronounced.

This study seeks to address these gaps by assessing the performance of Breast AI in identifying breast cancer risk and its potential to complement traditional screening methods in resource-limited environments. Although the findings provide insight into its clinical application, future research must focus on overcoming the logistical and economic challenges associated with scaling this technology. The broader adoption of AI-enhanced tools requires not only clinical validation but also strategic planning to integrate these systems into national health-care policies and workflows.

It is important to note that the terms Breast Ultrasound and Breast POCUS (Point-of-Care Ultrasound) refer to diagnostic techniques (Oto et al., 2024) utilizing ultrasound for breast imaging, but they differ in context, scope, and application, as shown in Table 1 below:

Although Breast Ultrasound is a comprehensive diagnostic tool performed by specialists, Breast POCUS is a targeted, point-of-care tool for immediate clinical decision-making. Both have distinct roles, with POCUS being particularly advantageous in resource-limited or time-sensitive settings (Dan et al., 2023; Iacob et al., 2024; Sood et al., 2019; Boyd et al., 2010).

Globally, breast cancer affects 2.1 million women annually, with 627,000 deaths reported in 2010 ((Shieh et al., 2017) (Fundytus et al., 2018), (SA, 2023)). A substantial proportion of these deaths occurred in Sub Saharan Africa (SSA). Unique challenges in the region include inaccurate assessment of disease burden, underrepresented data repositories, unvalidated biomarkers, and limited research participation, often hindered by cultural conflicts and beliefs specific to the African context.

In South Africa, 80% of breast cancer diagnoses occur at advanced stages (Stage III-IV), compared to just 15% in high-income countries. This disparity is attributed to a lack of educational awareness programs, inadequate diagnostic facilities, and limited breast cancer screening initiatives, which delay early detection. Women in SSA are also diagnosed at a younger average age of 50.25 years compared to 60.8 to 62 years in the United States. In addition, there has been a notable increase in breast cancer

Table 1
A comparative assessment of breast ultrasound vs breast POCUS and the use and scope of each in practice

Aspect	Breast ultrasound	Breast POCUS (Point-of-Care Ultrasound)
Definition	A dedicated ultrasound imaging procedure performed by specialists to evaluate breast abnormalities.	A quick, bedside ultrasound examination performed in various clinical settings to address specific questions or guide procedures.
Operator expertise	Typically performed by radiologists, sonographers, or trained specialists with advanced imaging skills.	Conducted by nonradiologist health-care providers (e.g., surgeons, general practitioners) with limited ultrasound training focused on targeted applications.
Purpose	Comprehensive imaging to detect, diagnose, and characterize breast lesions.	Rapid evaluation to answer specific clinical questions (e.g., presence of a cyst, abscess, or suspicious mass).
Equipment	High-resolution ultrasound systems designed for detailed breast imaging.	Portable, handheld ultrasound devices optimized for convenience and accessibility.
Scope of examination	Detailed evaluation of the entire breast and surrounding tissues, often including Doppler imaging.	Limited to assessing a specific area of concern or guiding interventions, like biopsies or aspirations.
Training requirements	Requires specialized training and certification in breast imaging.	Basic ultrasound training with a focus on specific clinical indications.
Clinical application	Used in diagnostic centers, hospitals, or imaging facilities as part of breast cancer screening and diagnostic workflows.	Used in emergency, outpatient, or low-resource settings to quickly assess palpable lumps, pain, or infections.
Role in resource-limited settings	Provides detailed diagnostic information, though may require skilled operators and advanced equipment.	Offers a practical, cost-effective, and portable alternative for initial assessments in underserved areas.
Examples of use	Evaluating suspicious findings from mammography, guiding biopsies, and assessing breast implants.	Quickly determining if a lump is fluid-filled or solid, evaluating localized pain, or detecting an abscess. (Dan et al., 2023; Iacob et al., 2024; Sood et al., 2019; Boyd et al., 2010)

diagnoses among women aged 35 to 49 years, often presenting with advanced-stage disease (Anyigba et al., 2021; SA, 2023; Dlamini et al., 2024; Abioye, 2024; Africa CAoS, 2024; Chaane et al., 2024).

Background of the study

The issue of late diagnosis in LMICs is exacerbated by limited global development assistance for noncommunicable diseases, with less than 3% of funding from WHO and UN initiatives allocated to these conditions. To address these challenges, the Breast Health Global Initiative has developed evidence-based, resource-stratified, and culturally appropriate guidelines for LMICs. These guidelines aim to integrate breast cancer detection, diagnosis, and treatment into existing health-care systems, with a strong emphasis on educational drives and screening programs. However, the implementation of screening programs remains challenging due to high costs and a lack of professional expertise in these regions (Anyigba et al., 2021; Anderson et al., 2015; Dan et al., 2023; Iacob et al., 2024; Sood et al., 2019; Dlamini et al., 2024; Friebel-Klingner et al., 2024; Jeanette et al., 2018).

The main purpose of such breast cancer screening programs would be to reduce overdiagnosis and overtreatment while promoting early detection. CBE remains a cornerstone of effective breast cancer diagnosis, particularly in resource-limited settings. When a clinically evident lump is detected, breast ultrasound is recommended as a valuable adjunct to CBE. Mammography is considered the primary imaging modality for reducing mortality rates, whereas ultrasound serves as a diagnostic tool to clarify abnormalities detected on mammograms, especially in cases of dense breast tissue. The concept of risk stratified breast programs as means of on site assessment for far to reach sites, is being suggested by the current research study (Gutnik et al., 2016; Dan et al., 2023; Iacob et al., 2024; Shieh et al., 2017; Dlamini et al., 2024).

Risk stratification in breast ultrasound as a breast cancer screening tool involves systematically categorizing patients based on their likelihood of developing or harboring breast cancer. This process integrates various factors to tailor screening and diagnostic approaches effectively (Anyigba et al., 2021; Shieh et al., 2017; Sood et al., 2019; Boyd et al., 2010; Breast Cancer Risk Assessment Tool).

Key components include assessing clinical risk factors such as age, family history, genetic predispositions, and personal health history. Imaging features are evaluated using standardized systems like the Breast Imaging-Reporting and Data System, which classifies breast lesions based on characteristics observed in ultrasound imaging. Breast tissue composition, particularly density, is also considered, as higher density can obscure lesions and is associated with an increased risk of breast cancer. Incorporating established risk prediction models, such as the Gail Model, further refines individual risk assessments (Chaane et al., 2024; Leithner et al., 2017).

In resource-limited settings, risk stratification is crucial for optimizing health-care resources. By identifying high-risk patients, health-care providers can prioritize advanced diagnostic evaluations like biopsies or magnetic resonance imaging, whereas low-risk patients may continue with routine surveillance. This targeted approach enhances early detection and efficient management of breast cancer, even when resources are constrained (Shieh et al., 2017; Boyd et al., 2010; Soceity, 2024).

Implementing risk stratification in breast ultrasound screening ensures that patients receive personalized care, aligning the intensity of screening and diagnostic interventions with their specific risk profiles. This strategy not only improves clinical outcomes but also promotes the judicious use of medical resources (Gutnik et al., 2016; Dan et al., 2023; Iacob et al., 2024; Shieh et al., 2017; Dlamini et al., 2024).

The Cancer Association of South Africa reports that 19.4 million South African women aged 15 years and older are at risk of being diagnosed with breast cancer (Africa CAoS, 2024). To address this, the South African Department of Health has developed clinical guidelines for breast cancer control and management. These guidelines recommend that women presenting with breast-related symptoms at any health-care facility should be referred directly to a dedicated breast unit. The policy states that for women under 35 years, CBE and ultrasound are the suggested diagnostic tools. For women aged 35 years and older, mammography, CBE, and ultrasound are recommended. If any abnormalities are detected, image-guided biopsy should follow to enable a comprehensive triple assessment combining clinical, radiological, and pathological evaluations. These measures are essential for improving diagnostic accuracy and treatment outcomes.

The South African Breast Cancer Policy Guideline (Health GDo, 2013) has yet to be implemented nationwide, but its adoption could significantly enhance education and awareness in underserved rural areas (Anyigba et al., 2021; Anderson et al., 2015; Dan et al., 2023; Iacob et al., 2024; Shieh et al., 2017; SA, 2023; Dlamini et al., 2024; Chaane et al., 2024; Friebel-Klingner et al., 2024; Leithner et al., 2017).

This study aimed to develop a breast cancer risk stratification program tailored to resource-limited settings, encompassing a large and diverse population in its inclusion criteria. This initiative addresses the growing incidence of breast cancer among young women in South Africa, as highlighted by the multicountry The African Breast Cancer-Disparities in Outcomes (ABC-DO) prospective cohort study (Iacob et al., 2024; Shieh et al., 2017; Abioye, 2024; Chaane et al., 2024). The study analyzed breast cancer survival rates in 2,158 women, 21.4% of whom were under 40 years old, whereas 60% fell between the ages of 40 and 64 years. Alarmingly, women under 40 exhibited the lowest 5-year survival rate at 33.5%. Contributing factors included late-stage diagnosis, comorbidities such as HIV, and geographic barriers limiting access to diagnostic and treatment infrastructure. The study underscored the urgent need for targeted strategies to improve early diagnosis and survival outcomes (Iacob et al., 2024; Shieh et al., 2017; Abioye, 2024; Chaane et al., 2024).

Similar findings were observed in East Africa, where poor breast cancer survival rates in LMICs were attributed to the absence of mammogram screening programs and limited access to diagnostic facilities (Anyigba et al., 2021; Dlamini et al., 2024; Abioye, 2024; Africa CAoS, 2024; Chaane et al., 2024). A study from Malawi supported this conclusion, citing a lack of mammographic infrastructure and the high cost of implementing mammography-based screening programs in LMICs. However, the study highlighted the efficacy of CBEs in clinical downstaging, reporting that 23% of new breast cancer cases were diagnosed in women aged 15 to 49 years. Given the distinct demographic profile of breast cancer patients in these regions, alternative diagnostic approaches must be considered (Gutnik et al., 2016).

A recent Johannesburg-based study involving 469 breast cancer patients at a tertiary hospital revealed a mean diagnosis age of 34.35 years, with most cases being intraductal carcinoma. The study also noted an increasing trend of younger patients being diagnosed with breast cancer since 2015. By 2040, it is projected that 69% of global cancer deaths will occur in LMICs (Dlamini et al., 2024; Chaane et al., 2024).

Evidence from clinical trials in Egypt and Malaysia supports the effectiveness of CBE in rural settings (Iacob et al., 2024). In Malaysia, rural nurses conducting CBEs achieved significant clinical downstaging of breast cancer (77% vs. 37%). These findings emphasize the cost-effectiveness of CBE in low-resource environments. In addition, the adjunct use of breast ultrasound alongside CBE has shown promise in improving diagnostic accuracy in rural areas.

Another South African study focusing on diagnostic delays during 2020 to 2021 found that the primary challenge was the prolonged time between initial consultations and referrals to diagnostic facilities. Limited access to medical oncologists further exacerbates these delays, as South African oncologists often serve over 500 patients annually, leading to significantly longer waiting times compared to HICs (Dlamini et al., 2024).

Given these challenges, the present study developed a unique breast cancer program at Daspoort Poli Clinic in Pretoria West, Gauteng. This program aims to promote education, provide CBEs, and offer initial diagnostic services using breast ultrasound enhanced by AI-driven software for risk prediction of clinically evident lumps.

The Breast AI application (Malherbe, 2021), registered with South African Pharmaceutical and Health Regulatory Authority as a Type A Medical Device for diagnostic use, has been validated on over 40,000 histologically confirmed breast cancer masses visualized through breast ultrasound. With 3 years of dataset training and validation, the app achieved an impressive accuracy rate of 97.6%. It is used in conjunction with wireless, Food and Drug Administration–approved Clarius™ point-of-care ultrasound probes deployed at Daspoort PoliClinic. The Breast AI app, an Android-based platform available on Google Play, is exclusively accessible to health-care professionals registered with the Health Professions Council of South Africa (HPCSA). User registration is verified through a secure back-end system before granting access.

This program represents a significant step forward in addressing the diagnostic and treatment gaps in breast cancer care in resource-constrained settings, offering scalable, technology-driven solutions to improve early detection and outcomes.

Aim and objectives

The aim was to develop a point-of-care risk stratified breast cancer screening program through comparison of CBE and AI breast ultrasound screening techniques and incidence rates in the Gauteng region.

The first objective was to assess breast cancer incidence rates using only CBEs at the local Daspoort PoliClinic in Gauteng. The second objective was to assess these rates using both CBEs and breast ultrasound with AI software to allow risk stratification of any clinically evident lump. The final objective was to compare patient referral pathways and diagnostic accuracy rates between CBEs and breast ultrasound using AI-assisted methods.

Methodology

This research was conducted over 6 months at an urban clinic with a patient intake, screening approximately 30 patients weekly. This resulted in a sample size of about 100 patients per month, totaling approximately 600 patients over the study period.

In addition, 1,730 patients were educated during local screening events held in rural villages, and 530 of these patients were subsequently screened using CBE and the Breast AI system at the Daspoort PoliClinic.

The study employed a prospective comparative cohort design over 6 months. Women aged 25 to 85, with or without a clinical history of breast cancer or symptoms related to breast disease, were included.

In South Africa's health-care referral system, primary care providers, such as doctors and nurses, refer patients with breast conditions either to academic tertiary hospitals for advanced care or to secondary hospitals for basic diagnostic services. The Daspoort PoliClinic, which serves approximately 30 patients daily, provides CBE to all women aged 25 to 85 who visit the clinic.

As part of their general clinic visits, all women referred to the Daspoort PoliClinic were informed about the breast screening services. They were invited to participate in the study through a process of informed consent, which included written approval. Educational sessions on breast cancer awareness were provided to encourage breast self-examination within the community. The study integrated AI into the existing CBE protocol to enhance diagnostic accuracy and optimize referrals for suspected breast disease.

Women who consented to participate provided their information for statistical purposes. CBEs were performed by a registered clinical nurse accredited by the Nursing Council of South Africa, whereas breast ultrasounds with the AI system were conducted by a qualified general practitioner registered with the HPCSA Medical and Dental Council and experienced in sonographic imaging.

Inclusion Criteria

- Women aged 25 to 85 years, with or without a clinical history of breast cancer or breast disease symptoms.
- Patients of any race or socio-cultural background, selected based on homogenous convenience sampling.
- Biologically female patients attending the Daspoort PoliClinic for health-care services and educated about breast cancer screening as part of their clinic visits.
- Patients from Tshwane West and neighboring regions who sought care at the Daspoort PoliClinic.

Exclusion Criteria

- Patients younger than 25 years or older than 85 years.
- Patients unwilling to provide informed consent. Standard care for these patients was not affected by their exclusion from the study.

The decision to exclude women younger than 25 years was based on a lack of local statistics supporting their inclusion and limited research regarding prophylactic treatment for Breast Cancer Tumor Suppressor Gene gene mutation carriers in South Africa. A study by Johnson et al. noted a high incidence of locally advanced breast cancer among adolescents aged 25 to 39 years in LMICs. However, as this study was conducted in the United States with a different population and ethnic profile, its findings may not directly apply to South Africa. The absence of local policies and data on breast cancer in women under 25 years further justified their exclusion from this study.

Results of the study

For objectives, the Pearson chi-squared and Fisher's exact tests were used to examine the differences between CBE and the use of POCUS and AI for early discernment of any clinical palpable masses as benign or malignant (refer to Table 2 and Table 3). Means and medians were computed for differences between the groups. To examine the association with advanced stage, a multivariate logistic regression model will be used. p values of $< .1$ was prompted in bivariate analysis. Analysis was performed using STATA software (version 14; StataCorp Ltd., Texas, USA).

The study analyzed a total of 203 patients, of whom 99.5% were females, and 0.5% were males (Table 2). Age demographics were distributed broadly across the 25 to 85 years age range, with clustering in the 30 to 63 years age groups, reflecting the typical age profile of breast cancer risk (Figure 1).

Table 2
Overall descriptive statistics including number of female to male patients, positive and negative clinical breast examination findings, and breast AI findings

Gender				
Gender	Frequency	Percent	Cumulative frequency	Cumulative percent
Female	202	99.51	202	99.51
Male	1	0.49	203	100.00

Clinical breast examination				
Clinical_breast_examination	Frequency	Percent	Cumulative frequency	Cumulative percent
Negative	201	99.01	201	99.01
Positive	2	0.99	203	100.00

Breast AI exam				
Breast_AI_exam	Frequency	Percent	Cumulative frequency	Cumulative percent
BIRADS 2	1	0.49	1	0.49
Negative	197	97.04	198	97.54
Positive	5	2.46	203	100.00

Table of clinical_breast_examination by breast_AI_exam				
Clinical_breast_examination (clinical breast examination)	Breast_AI_exam (breast AI exam)			
Frequency Percent Row Pct Col Pct	BIRADS 2	Negative	Positive	Total
Negative	0	197	4	201
	0.00	97.04	1.97	99.01
	0.00	98.01	1.99	
	0.00	100.00	80.00	
Positive	1	0	1	2
	0.49	0.00	0.49	0.99
	50.00	0.00	50.00	
	100.00	0.00	20.00	
Total	1	197	5	203
	0.49	97.04	2.46	100.00

CBE revealed that 99.01% of participants were categorized as negative for suspicious findings, whereas 0.99% was positive (Table 2). When Breast AI was incorporated, it identified a broader range of risk stratifications: 97.04% were negative, 2.46% were positive, and a single patient was classified with a BIRADS 2 score (See Figure 2). These findings suggest that the Breast AI system detected slightly more positive cases compared to CBE, potentially reflecting its enhanced sensitivity (Table 2) (Table 3).

A comparative analysis between CBE and Breast AI demonstrated high agreement in negative cases, with 197 patients classified as negative by both methods. However, discrepancies were observed in the positive cases: four patients identified as positive by Breast AI were classified as negative by CBE, whereas one patient was identified as positive by both methods. McNemar's test for agreement yielded a Chi-square value of 1.8 with a p value of 0.1797, indicating no statistically significant difference between the methods (Table 3).

Table 3
Cross-evaluation between positive and negative cases using CBE and breast AI including chi-square evaluation (McNemar's test)

Table of clinical_breast_examination by breast_AI_exam			
Clinical_breast_examination (clinical breast examination)	Breast_AI_exam (breast AI exam)		
Frequency Percent Row Pct Col Pct	Negative	Positive	Total
Negative	197	4	201
	97.04	1.97	99.01
	98.01	1.99	
	99.49	80.00	
Positive	1	1	2
	0.49	0.49	0.99
	50.00	50.00	
	0.51	20.00	
Total	198	5	203
	97.54	2.46	100.00

McNemar's test		
Chi-square	DF	Pr > ChiSq
1.8000	1	0.1797

Chi-square divided by the degrees of freedom ($\chi 2/df$) as a measure of model fit, with values of 5 or less being a common benchmark.

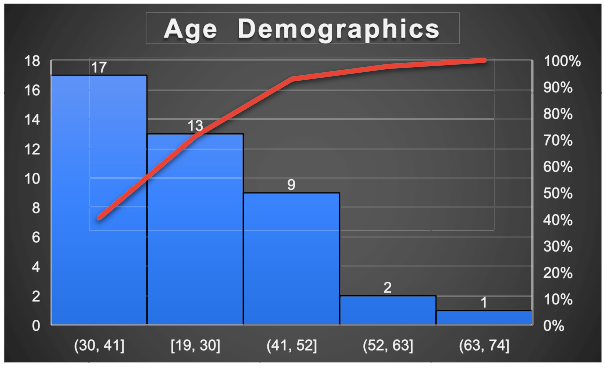

Figure 1. Age Demographics.

The integration of Breast AI provided notable advancements in diagnostic accuracy, particularly in identifying early-stage or low-risk cases that may have been missed during CBE alone. This aligns with global findings where adjunctive methods, such as AI-enhanced imaging, improve the sensitivity of traditional examination techniques, especially in low-resource settings (Table 2) (Table 3).

The inclusion of breast ultrasound with AI-driven risk stratification offers a promising solution to improve early detection in high-risk populations. This approach is particularly valuable in settings like the Daspoort PoliClinic, where resources are limited, and diagnostic delays are common. The findings also highlight the importance of tailoring breast cancer screening protocols to incorporate advanced technologies alongside traditional methods to address diagnostic gaps (Table 2) (Table 3).

Although Breast AI showed potential for greater sensitivity in detecting positive cases, further studies with larger sample sizes and diverse populations are necessary to validate these findings and explore the broader applicability of this technology in resource-constrained environments.

Discussion

Out of the 1,617 women screened, 530 presented with clinical signs such as palpable lumps, mastalgia, or significant risk factors like a strong family history of breast cancer. Within this subset, only 8 patients required short-term follow-up due to BIRADS-3 findings. The Breast AI system identified 5 of these cases, whereas CBE flagged only 2, highlighting the AI system's potential for increased sensitivity. Importantly, the Breast AI system also identified one case of bilateral accessory breast tissue with underlying lipoma formation that CBE had classified as inconclusive, facilitating timely referral for surgical consultation. This finding underscores the AI system's ability to detect subtle or atypical presentations that might otherwise go unnoticed during standard clinical examination.

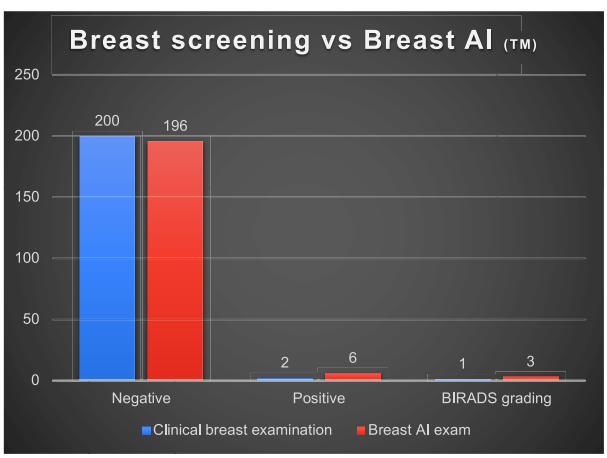

Figure 2. Breast Screening versus Breast AI™.

The McNemar's test, with a chi-square value of 1.8 and a p value of 0.1797, revealed no statistically significant difference between the performance of CBE and Breast AI. However, the AI system demonstrated an ability to detect additional positive findings, effectively reducing false negatives. This aligns with the observed discrepancy between the two methods, where Breast AI identified four additional cases that CBE classified as negative. Although these differences were not statistically significant, they are clinically relevant in terms of ensuring accurate diagnosis and timely intervention.

The Breast AI system's risk prediction ranged between 0 and 25%, indicating a low probability of malignancy among the cases reviewed. However, its integration into the diagnostic workflow proved valuable for triaging patients requiring symptomatic relief, such as those with accessory breast tissue, abscesses, or fibrocystic breast disease. These conditions, although not malignant, often necessitate surgical or pharmacological intervention, and their identification through AI-driven screening reduced the likelihood of misclassification or delayed care. Notably, none of the patients were classified as BIRADS-5, requiring immediate surgical intervention or biopsy, further validating the program's ability to efficiently prioritize care and reduce the burden on surgical services.

The comparison between Breast AI and CBE also highlighted key age-related trends. Patients referred for further evaluation ranged from 25 to 74 years, with the majority in the 30 to 41 years age group. This reflects the demographic profile of patients at higher risk of breast-related conditions in this setting, emphasizing the importance of targeted screening in this age bracket. The Breast AI system's ability to provide accurate BIRADS grading and identify a broader spectrum of positive cases enhances the diagnostic process, ensuring that patients requiring further evaluation or intervention are promptly identified.

These findings reinforce the study's assertion that most referrals generated through AI-supported screening do not require immediate surgical intervention. By alleviating surgical workloads and reducing waitlists, the Breast AI system contributes to more efficient use of health-care resources. Its performance as an adjunct to clinical examination enhances diagnostic accuracy while supporting patient stratification and referral pathways in resource-limited settings.

Limitations of Current Study

Although the study demonstrates promising outcomes in integrating Breast AI into routine screening practices, several limitations must be acknowledged to contextualize its findings.

Firstly, the study's population and sampling were geographically and demographically constrained. Conducted primarily at the Daspoort PoliClinic in Gauteng Province, the population was predominantly urban, which limits the generalizability of the results to rural communities or other provinces with differing health-care access and patient demographics. This limitation mirrors issues seen in prior studies, where sampling was confined to specific racial groups or urban settings, reducing the applicability of findings to broader, more diverse populations. Despite efforts to include patients from varying socio-cultural backgrounds, the study could not adequately capture the unique challenges faced by rural or

underserved populations, such as limited access to diagnostic facilities and specialized care.

In addition, the study was conducted in conjunction with the existing standard of care, which may have inadvertently influenced the outcomes. Although this approach ensured that patients received appropriate medical attention without deviation from established protocols, it also limited the study's ability to evaluate the standalone efficacy of Breast AI. The adjunctive use of AI alongside CBE may have confounded the results, as health-care providers potentially leveraged both methods in decision-making, blurring the distinct impact of each approach.

Another limitation pertains to the study's reliance on short-term follow-up for BIRADS-3 cases without assessing long-term patient outcomes. Although Breast AI identified additional cases requiring follow-up, the absence of longitudinal data limits the ability to evaluate its true impact on early detection, treatment initiation, and survival rates. Furthermore, no BIRADS-5 cases requiring immediate intervention were identified, which may reflect either the study's limited sample size or the low prevalence of advanced malignancy in the screened population. A larger cohort may be necessary to assess the system's ability to detect more severe cases accurately.

The study's use of McNemar's test revealed no statistically significant difference between Breast AI and CBE, with a chi-square value of 1.8 and a p value of 0.1797. Although this finding supports the comparability of the two methods, it also underscores the need for larger sample sizes to better assess statistical differences and validate the system's sensitivity and specificity in diverse clinical scenarios.

Moreover, the study did not explore cost-effectiveness or logistical barriers to scaling the Breast AI system for widespread use. Although the technology demonstrated utility in this pilot setting, its integration into larger health-care networks, particularly in resource-limited environments, may face challenges such as training health-care providers, ensuring infrastructure readiness, and addressing potential resistance to new technology adoption.

Lastly, although the study incorporated ongoing education and advisory support for primary and secondary-tier doctors, these efforts were not rigorously evaluated for their effectiveness in improving breast cancer detection and referral pathways. Future studies should consider structured assessments of educational initiatives to measure their impact on diagnostic accuracy and patient outcomes.

In conclusion, although this study highlights the potential of Breast AI as an adjunct to traditional screening methods, its limitations underscore the need for larger, more diverse samples, long-term outcome tracking, and comprehensive cost-effectiveness analyses. Addressing these gaps in future research will be essential to validate the findings and ensure equitable and scalable integration of this technology into broader health-care systems.

Conclusion

This study highlights the potential of integrating Breast AI into breast cancer screening programs as an adjunct to CBE, with the ultimate goal of achieving clinical downstaging. Clinical downstaging, defined as diagnosing diseases at earlier, more treatable stages, is a key outcome of effective screening programs. By detecting conditions such as breast cancer before they progress, clinical downstaging has been shown to improve prognosis, reduce treatment burdens, and lower mortality rates.

The importance of early detection through risk stratification tools cannot be overstated. Numerous studies have demonstrated that screening programs like regular mammography lead to earlier detection and improved survival rates (Gutnik et al., 2016; Dan et al., 2023; Iacob et al., 2024; Shieh et al., 2017; Dlamini et al., 2024). For example, widespread mammography adoption in high-resource settings has been associated with a significant reduction in late-stage breast cancer diagnoses and mortality rates. However, mammography is often inaccessible in low-resource settings due to cost, infrastructure limitations, and trained personnel shortages. In such environments, alternative methods such as CBE combined with AI-powered ultrasound systems offer promising solutions (Anderson et al., 2015; Dan et al., 2023; Iacob et al., 2024; Shieh et al., 2017; Sood et al., 2019).

In this study, of the 1,617 women screened, 530 presented with clinical signs or significant risk factors. Eight patients required short-term follow-up for BIRADS-3 findings, and only one patient required a surgical opinion following an inconclusive CBE. Typically in the South African context, referral to main hospital centers would range between 6 months to a year for surgical intervention. Through use of the current breast program at Daspoort PoliClinic, the referral period was reduced to 1 week. Importantly, the Breast AI system identified additional positive cases beyond those detected by CBE, suggesting its potential to reduce false negatives and improve the accuracy of initial breast examinations. These results align with existing literature emphasizing the role of risk stratification tools in resource-limited settings to optimize the referral process and improve clinical outcomes.

Risk stratification tools such as Breast AI not only enhance the precision of diagnosis but also streamline health-care delivery by ensuring that resources are directed toward patients with the highest need. For example, this study found that most patients did not require surgical intervention, reducing the volume of referrals for nonsymptomatic patients and alleviating pressure on surgical waitlists. Such efficiency gains are critical in low-resource environments, where health-care systems are often overburdened and underresourced.

The ability of Breast AI to accurately stratify risk and identify subtle findings, such as accessory breast tissue with underlying lipomas, demonstrates its potential to facilitate clinical downstaging. By integrating AI-based systems into existing screening protocols, health-care providers can ensure earlier diagnosis and timely referral for high-risk patients, aligning with the overarching goal of screening programs.

To maximize the benefits of both methods, a hybrid approach combining CBE and Breast AI should be implemented for breast screening, particularly in rural and low-resource settings. This integration can enhance diagnostic accuracy, reduce false negatives, and improve early detection rates. Future studies should involve larger and more diverse populations, including rural and underserved communities, to validate the findings and improve generalizability. Expanding the study scope to include longitudinal follow-up will help evaluate the long-term impact of Breast AI on clinical downstaging, treatment initiation, and survival outcomes. Emphasizing the role of Breast AI as a risk stratification tool can improve patient triage and resource allocation, ensuring that high-risk patients receive timely diagnostic and therapeutic interventions while minimizing unnecessary referrals. Governments and health-care stakeholders should prioritize investments in infrastructure and policies that support the integration of AI-based technologies into national screening programs. Such efforts can help address gaps in early detection and reduce disparities in breast cancer outcomes.

By advancing the adoption of Breast AI and integrating it into hybrid screening protocols, this study contributes to the broader

goal of clinical downstaging. Early detection and accurate risk stratification are essential for improving breast cancer outcomes, particularly in low-resource settings where traditional methods face significant limitations.

Ethical approval and consent to participate

Ethical approval is obtained from the Research Ethics Committee of the University of Pretoria, as proposal reference nr 384/2023. Informed consent was obtained from all the participants and/or their legal guardians. All experiments were performed in accordance with relevant guidelines and regulations (such as the Declaration of Helsinki).

Availability of data and materials

Data is available for a period of 15 years from corresponding author upon request.

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CRediT authorship contribution statement

Kathryn Malherbe: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

Conflict of interest statement

The author has no relevant disclosures.

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