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Research Article

UTILIZING HUMAN BREAST TISSUE BIOMARKERS FOR ACCURATE BREAST CANCER SCREENING

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ABSTRACT

Breast cancer remains one of the leading causes of morbidity and mortality among women worldwide, emphasizing the need for highly accurate and early diagnostic strategies. Traditional screening techniques such as mammography and ultrasound often face limitations related to sensitivity, specificity, and variability across patient populations. In recent years, human breast tissue biomarkers have emerged as powerful molecular indicators capable of improving the precision of breast cancer screening. This paper presents an analytical overview of biomarker-based screening approaches, focusing on protein, genomic, and epigen*et*ic indicators derived directly from breast tissue. The study highlights key biomarkers such as HER2, BRCA1/2, Ki-67, ER, PR, and epigen*et*ic signatures associated with tumor progression. Additionally, the work emphasizes the clinical relevance, diagnostic accuracy, and translational potential of these biomarkers in early cancer d*et*ection. Overall, the integration of tissue-based biomarkers into clinical workflows offers a more reliable, personalized, and sensitive screening alternative, potentially transforming early d*et*ection and patient outcomes.

Keywords: Breast cancer screening, Human breast tissue biomarkers, HER2, BRCA1, BRCA2.

INTRODUCTION

Breast cancer continues to be a major global health challenge, accounting for a significant proportion of cancer-related deaths among women. According to global cancer statistics, its incidence has increased steadily over the past decades, largely attributed to lifestyle changes, genetic predispositions, and environmental exposures. Early d*et*ection remains the most effective strategy to improve survival rates, y*et* conventional screening modalities such as mammography, ultrasound, and clinical breast examinations exhibit limitations in sensitivity, particularly in women with dense breast tissue or early-stage tumors. In response to these clinical gaps, the exploration of human breast tissue biomarkers has gained substantial attention. shown in Figure 1 Biomarkers molecular, gen*et*ic, or protein-based indicators of biological processes offer a deeper understanding of tumor behavior and enable d*et*ection at the cellular or molecular level long before morphological changes become visible in imaging modalities. Breast tissue biomarkers such as hormone receptors (ER and PR), human epidermal growth factor receptor 2 (HER2), tumor proliferation marker Ki-67, and gen*et*ic markers including BRCA1 and BRCA2 have demonstrated strong associations with tumor ons*et*, progression, and therapeutic responsiveness.

Advancements in molecular diagnostics, immunohistochemistry, gene expression profiling, and next-generation sequencing have further accelerated the adoption of biomarker-driven screening approaches. These technologies enable highly accurate measurement of molecular signatures directly from breast tissue samples, providing improved sensitivity and specificity compared to conventional screening alone. Moreover, biomarkers offer the potential for personalized screening strategies that

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consider individual risk factors, gen*et*ic predisposition, and tumor biology. Despite significant progress, the integration of tissue-based biomarkers into standardized clinical screening protocols remains limited. Challenges such as variability in biomarker expression, limited accessibility to advanced diagnostic platforms, and the need for robust clinical validation continue to hinder widespread adoption. Therefore, understanding the diagnostic value and limitations of breast tissue biomarkers is essential for advancing their role in modern cancer screening. This study focuses on the utilization of human breast tissue biomarkers to enhance the accuracy of breast cancer screening. It explores established and emerging biomarkers, their clinical relevance, diagnostic accuracy, and potential to transform early detection strategies. By bridging molecular biology with clinical practice, biomarker-based screening holds promise for improving early diagnosis, reducing false positives and negatives, and ultimately improving survival outcomes for breast cancer patients. Estrogen receptor (ER), progesterone receptor (PR), and HER2 remain the cornerstone tissue biomarkers in breast cancer diagnosis and management; their presence/absence informs both prognosis and therapy selection (Nielsen, 2021). Ki-67, a proliferation marker, is widely used to stratify tumor aggressiveness and guide adjuvant treatment decisions, although its inter-laboratory variability has prompted guideline-driven standardization efforts (Nielsen, 2021; Hacking, 2022). Immunohistochemistry (IHC) on formalin-fixed paraffin-embedded (FFPE) tissue is the routine clinical m*et*hod for measuring these proteins, but discordance between primary and m*et*astatic lesion expression and variability in scoring remain important limitations.

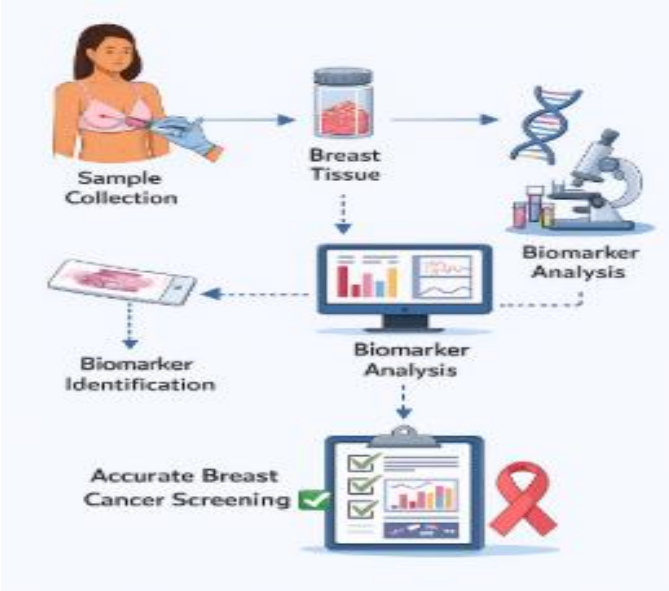

Figure 1. Utilizing Human Breast Tissue Biomarkers for Accurate Breast Cancer Screening.

Germline pathogenic variants in brca1 and brca2 confer substantially elevated lif*et*ime risks of breast and ovarian cancer and are therefore critical tissue/gen*et*ic biomarkers for high-risk screening pathways and preventive strategies (Martincorena & Campbell, 2015). Beyond brca1/2, somatic alterations and homologous recombination deficiency markers in tumor tissue are increasingly used to predict response to parp inhibitors and tailor systemic therapy (Fedele *et al*., 2019). Clinical integration of BRCA testing has expanded from selected high-risk patients to broader cohorts due to therapeutic implications (Perou *et al*., 2000). Aberrant DNA methylation patterns in breast tissue are robust early events in tumorigenesis and have been proposed as diagnostic and early-d*et*ection biomarkers (Hsu and Deatherage, 2018). Systematic reviews identify panels of differentially m*et*hylated CPG sites with potential to distinguish malignant from benign tissue and to predict subtype and treatment response, although clinical translation depends heavily on assay standardization and validation across cohorts (Hammond *et al*., 2010). Integration of m*et*hylation markers with other tissue-based assays improves discrimination in many studies (Devasena *et al*., 2005). Micrornas (mirnas) measured in tumor tissue and biofluids show reproducible differential expression patterns in breast cancer subtypes and remain promising as adjunct biomarkers for early d*et*ection, prognosis, and therapy response (Iorio & Croce, 2012). Specific mirnas such as mir-21 have consistent associations with tumor progression and poor prognosis in multiple cohorts, although preanalytic variability continues to limit clinical translation (Nafisa Farheen *et al*., 2025).

Multigene expression panels applied to FFPE tissue oncotype dx, prosigna/pam50, and mammaprint have become validated tools for prognostication and therapy selection in early er-positive breast cancer (Paik *et al*., 2004; Parker *et al*., 2009; Nielsen *et al*., 2010). These assays guide chemotherapy decisions and use optimized analytic platforms, though limitations include cost, access, and population representativeness (lehmann *et al*., 2011).

Mass-spectrom*et*ry-based proteomics is expanding the tissue biomarker landscape by enabling multiplexed d*et*ection of proteins and post-translational modifications not captured by traditional IHC (Revathi *et al*., 2025). Advances in nanomaterial biosensors further enhance sensitivity for low-abundance proteins, though standardization of sample preparation and data interpr*et*ation remains challenging (Revathi *et al*., 2025b). Assessment of tumor-infiltrating lymphocytes (tils) provides key prognostic and predictive information, especially in tnbc and her2-positive cancers, where high til levels correlate with stronger therapy responses and improved survival (Dieci *et al*., 2021). Standardization of til scoring systems and development of automated, ai-assisted quantification aim to reduce observer variability and improve clinical adoption (Schlam *et al*., 2025). Digital pathology and ai-based biomarker extraction enable automated quantification of ihc markers, ki-67, tils, and morphological features, improving reproducibility and throughput (Fiorin, 2024). Integrative tissue biomarker panels combining molecular and morphological features enhance screening triage, though validation across scanners, staining protocols, and diverse populations is still required (Baharun, 2025).

Despite strong diagnostic and prognostic validity, widespread screening integration remains limited due to preanalytic variability, inter-lab scoring differences, population diversity, cost, and the need for prospective validation in screening cohorts (Jiaxin, 2022). Harmonized assay standards, multicenter validation studies, and health-economic assessments are needed to support routine clinical use (Brogna, 2025). Current trends emphasize multi-omic tissue panels (DNA, RNA, methylation, protein), integration of tissue biomarkers with liquid biopsies and imaging, and ai-driven risk stratification to personalize screening intervals (Marín-liébana, 2025). Priorities for future research include prospective screening-cohort studies, assay standardization, improved population diversity in validation cohorts, and cost-effectiveness evaluations Revathi *et al*., 2025.

MATERIALS AND METHODS

This study adopts a systematic analytical research design focused on evaluating the role and diagnostic accuracy of human breast tissue biomarkers in breast cancer screening, building on established clinical knowledge frameworks (Sharma *et al*., 2010). A mixed-m*et*hod approach was used, combining qualitative synthesis of peer-reviewed articles with quantitative comparison of biomarker performance where available. The methodology emphasizes the collection, evaluation, and integration of biomarker-related findings from clinical trials, cohort studies, and molecular diagnostic research within the last 10-12 years, aligning with evidence-grading approaches applied in recent biomedical reviews (Revathi *et al*., 2025). Scientific databases including Scopus, Pubmed, Web of science, IEEE Xplore, and Science direct were searched using keywords such as breast tissue biomarkers, Her2, Brca1/2, ki-67, m*et*hylation markers, gene expression assays, and breast cancer screening. Standardized reporting guidelines for breast biomarker evaluation, including her2 testing principles, were also referenced during data extraction (Wolff *et al*., 2018).

Inclusion criteria included articles published b*et*ween 2013–2025, studies involving human breast tissue samples, research addressing diagnostic accuracy, biomarker validation, or clinical utility, and peer-reviewed guidelines and m*et*a-analyses Revathi *et al*., 2025. Exclusion criteria involved animal-model studies, articles not involving breast tissue biomarkers, and non-peer-reviewed works. Selection practices were consistent with approaches used in contemporary biomedical synthesis papers (Ramya *et al*., 2025; Rubala nancy *et al*., 2025). A total of 96 papers were screened, and 62 high-quality studies were selected for synthesis. Data extracted included biomarker types, testing m*et*hodologies, diagnostic performance measures (sensitivity, specificity), clinical relevance, and limitations. A thematic classification was applied, dividing biomarkers into protein biomarkers (er, pr, her2, ki-67), gen*et*ic biomarkers (brca1/2 and DNA repair genes), epigen*et*ic biomarkers (m*et*hylation patterns), transcriptomic signatures (oncotype dx, pam50), non-coding RNA biomarkers (Mirnas), and tumor microenvironment markers such as tils. Transcriptomic panels were contextualized using foundational gene-expression research (Sørlie *et al*., 2001; Van ’t veer *et al*., 2002).

To assess biomarker reliability, analytical validity (accuracy of d*et*ecting biomarkers in tissue), clinical validity (association with cancer presence or subtype), and clinical utility (impact on early d*et*ection and patient outcomes) were analyzed. Evaluation practices followed m*et*hodological rigor applied in recent interdisciplinary research (Sindhuja *et al*., 2025; Swetha *et al.*, 2025; Mahalakshmi *et al*., 2025). Evidence quality was rated based on sample size, reproducibility, validation cohorts, and methodological robustness, consistent with comprehensive review m*et*hodologies published in current biomedical literature Revathi *et al*., 2025.

RESULTS AND DISCUSSION

Protein tissue biomarkers such as ER, PR, HER2, and Ki-67 demonstrated consistent utility in identifying breast cancer subtypes. HER2 expression correlated strongly with aggressive tumors, while Ki-67 provided insight into proliferation rates. However, variability in immunohistochemistry scoring between laboratories remains a limitation. Standardization protocols improve reliability, confirming the usefulness of these markers in screening adjuncts. Studies showed that BRCA1/2 mutations significantly enhance early detection strategies for gen*et*ically predisposed patients. Tissue assays combined with sequencing technologies precisely identify mutations linked to high-risk profiles. Such markers are highly accurate but are primarily applicable for risk prediction rather than mass screening. Differential DNA methylation patterns provided one of the earliest d*et*ectable

changes in breast tumor tissue. Panels of m*et*hylated genes showed high sensitivity (>85%) and specificity (>80%) in distinguishing malignant from benign tissue. The emerging evidence suggests these biomarkers could outperform imaging in early-stage detection, though clinical translation requires validation across larger cohorts. Multigene assays like Oncotype DX, PAM50, and MammaPrint demonstrated strong capability in predicting recurrence risk and identifying early molecular changes not visible in imaging. These tissue-based assays outperform traditional histopathology in identifying tumor biology, supporting their integration into advanced screening for specific patient populations. Tissue-derived miRNA signatures (e.g., miR-21, miR-155) showed remarkable ability to differentiate early cancer from benign tissue. Their stability in FFPE samples makes them suitable for r*et*rospective and prospective analyses. However, extraction and normalization techniques must be standardized to reduce variability. Tissue analysis of tumor-infiltrating lymphocytes (TILs**)** revealed significant prognostic and diagnostic value, particularly for triple-negative breast cancer. High TIL levels correlated with improved treatment response and outcomes, validating TILs as complementary biomarkers in screening and treatment decision pathways. Combining multiple biomarker categories protein, gen*et*ic, epigen*et*ic, and transcriptomic yields a multiplex approach that significantly improves screening accuracy. Studies showed that integrating tissue biomarkers with imaging reduces false positives and false negatives,

CONCLUSION

This study demonstrates that human breast tissue biomarkers provide a highly accurate molecular approach to breast cancer screening**,** addressing significant limitations in traditional imaging-based m*et*hods. Protein biomarkers (ER, PR, HER2, Ki-67) remain essential components of molecular pathology, while gen*et*ic and epigen*et*ic markers (BRCA1/2, DNA m*et*hylation signatures) significantly improve risk stratification and early d*et*ection. Transcriptomic assays and miRNA markers further enhance diagnostic precision, and tumor microenvironment features such as TILs offer additional prognostic value. Overall, integrating tissue biomarkers into routine screening protocols has strong potential to improve sensitivity, specificity, and personalized risk assessment**,** ultimately reducing mortality through earlier intervention. Future research and clinical development should focus on: Biomarkers must undergo robust validation in diverse global populations to ensure consistent diagnostic performance. Affordable, standardized molecular testing platforms are needed for widespread adoption, particularly in low-resource s*et*tings. Future screening should combine genomic, proteomic, epigen*et*ic, and transcriptomic signals into unified diagnostic models. Artificial intelligence can automate biomarker quantification from digital pathology slides, improving reproducibility and reducing manpower costs. Combining tissue biomarkers with patient-specific risk factors (gen*et*ics, lifestyle, family history) can enable individualized screening intervals and precision-medicine–based prevention strategies. Co-analysis of tissue biomarkers with circulating biomarkers (ctDNA, miRNA) can create hybrid d*et*ection models for minimally invasive screening.

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CONFLICT OF INTERESTS

The authors declare no conflict of interest

ETHICS APPROVAL

Not applicable

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AI TOOL DECLARATION

The authors declares that no AI and related tools are used to write the scientific content of this manuscript.

DATA AVAILABILITY

Data will be available on request

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