10.21761/jms.v8i02.18

RESEARCH ARTICLE

Liquid Biopsy–Based Biomarkers for Early Detection of Breast and Colorectal Cancer

Nongnapat Kanthakhoo

ABSTRACT

Early detection is a very important factor of the survival rates of breast and colorectal cancer, but the traditional screening and tissue biopsy techniques are usually constrained by invasiveness, access, and decreasing sensitivity in early-stage cancer. As a potentially helpful, non-invasive intervention, liquid biopsy has become a promising intervention that can be used to identify biomarkers produced by the tumor by analyzing blood-derived substances. The main liquid biopsy elements such as circulating tumor DNA, circulating tumor cells, microRNAs, and extracellular vesicles are a better source of molecular information about tumor presence, heterogeneity, and pre-oncogenic alterations. These biomarkers have shown the potential in breast and colorectal cancer in the detection of malignancies at an early stage, the progression of the disease and as a complement to current screening modalities. Recent progress in the high-throughput sequencing and molecular profiling has further increased the accuracy of diagnosis and clinical relevancy of the liquid biopsy-based assay. Although these improvements have been made, issues to do with low levels of biomarkers, standards in technology, and clinical validation still exist. Altogether, liquid biopsy-based biomarkers are a ground-breaking method of early cancer diagnosis, and they can provide considerable prospects in increasing the accuracy of screening, facilitating personalized diagnostics, and lowering cancer-related mortality rates in the population of breast and colorectal cancer patients.

Keywords: Liquid biopsy; Breast cancer; Colorectal cancer; Circulating tumor DNA; Circulating tumor cells; MicroRNAs; Early cancer detection

How to cite this article: Kanthakhoo N. Liquid Biopsy–Based Biomarkers for Early Detection of Breast and Colorectal Cancer. SRMS J Med Sci. 2023;8(2):152-160.

Source of support: Nil

Conflict of interest: None

INTRODUCTION

Breast and colorectal cancers are still some of the most often diagnosed malignancies in the world and still one of the major causes of cancer morbidity and mortality. The stage at which the diseases are diagnosed greatly affects the clinical outcomes of the two diseases with early diagnosis of the disease enhancing the survival rate and increasing the therapeutic modalities. Although there are new methods in imaging, endoscopy, and tissue-based histopathology, the traditional methods of diagnosis can be hampered by invasiveness, sampling bias, late diagnosis, and lack of sensitivity to early-stage or minimal disease (Heitzer et al., 2017; Marrugo-Ramírez et al., 2018). Such restrictions have stimulated the quest to identify new non-invasive biomarkers that can identify malignancy at its most amenable early phases.

Liquid biopsy has emerged as a transformative approach in cancer diagnostics by enabling the detection and analysis of tumor-derived biomarkers from peripheral blood. Unlike traditional tissue biopsies, liquid biopsy offers a minimally invasive, repeatable, and dynamic means of capturing molecular information reflective of tumor heterogeneity and evolution (Hench et al., 2018; Normanno et al., 2018). Key analytes evaluated in liquid biopsy include circulating tumor DNA (ctDNA), circulating tumor cells (CTCs), microRNAs, circular RNAs, and extracellular vesicles, all of which have demonstrated diagnostic and prognostic relevance across multiple cancer types (Marrugo-Ramírez et al., 2018; Roy et al., 2022).

In breast cancer, extensive research has highlighted the potential of liquid biopsy–based biomarkers to detect early molecular alterations before clinical or radiological manifestation. Systematic reviews and clinical studies have reported promising associations between ctDNA, microRNA signatures, and early-stage breast cancer, underscoring their potential utility in screening and disease monitoring (Duque et al., 2022; Matsutani et al., 2020; D'Amico et al., 2021). Blood-based biomarkers have also been proposed as complementary tools to existing screening methods, with the potential to improve diagnostic sensitivity and reduce false-negative rates (Loke & Lee, 2018; Li et al., 2020; Freitas et al., 2022).

Similarly, liquid biopsy has gained increasing relevance in colorectal cancer, where early detection remains challenging due to asymptomatic disease progression and limited participation in invasive screening programs. Dynamic liquid biopsy components, including ctDNA mutations, epigenetic alterations, and non-coding RNAs, have shown strong potential for identifying early-stage colorectal cancer and high-risk

Submission: 15-10-2023; **Acceptance:** 28-11-2023; **Published:** 31-12-2023

University of California, Riverside United States

Corresponding Author: Nongnapat Kanthakhoo, University of California, Riverside United States, e-mail: farnongnapat20@gmail.com

individuals (Raza et al., 2022; Zhou et al., 2022). Recent advances have further demonstrated the feasibility of blood-based molecular signatures for detecting early-onset colorectal cancer, highlighting the expanding role of liquid biopsy in population-level screening strategies (Nakamura et al., 2022; Ganepola et al., 2014).

Collectively, these developments position liquid biopsy–based biomarkers at the forefront of precision oncology for breast and colorectal cancer. While technical challenges related to biomarker sensitivity, standardization, and clinical validation remain, the growing body of evidence supports their potential to reshape early cancer detection paradigms and enhance personalized diagnostic pathways (Heitzer et al., 2017; Normanno et al., 2018).

Concept of Liquid Biopsy

Liquid biopsy refers to a minimally invasive diagnostic approach that involves the analysis of tumor-derived biomarkers released into body fluids, primarily blood, to obtain molecular information about cancer presence and behavior. Unlike conventional tissue biopsy, which requires surgical or needle-based tumor sampling, liquid biopsy enables repeated and real-time assessment of cancer dynamics, making it particularly valuable for early detection, monitoring, and prognostication (Heitzer et al., 2017; Marrugo-Ramírez et al., 2018).

The biological basis of liquid biopsy lies in the continuous shedding of tumor-related components into the circulation during tumor growth and cellular turnover. These components include circulating tumor DNA (ctDNA), circulating tumor cells (CTCs), microRNAs (miRNAs), circular RNAs (circRNAs), exosomes, and other extracellular vesicles, each reflecting distinct aspects of tumor biology (Hench et al., 2018; Freitas et al., 2022). Advances in high-sensitivity molecular techniques, such as next-generation sequencing and digital PCR, have enabled the reliable detection of these analytes even at low concentrations, which is critical for early-stage malignancies (Matsutani et al., 2020).

In breast and colorectal cancer, liquid biopsy has gained increasing attention due to its ability to capture tumor heterogeneity and molecular alterations that may not be fully represented in a single tissue specimen. ctDNA analysis allows for the identification of cancer-specific genetic and epigenetic changes, while CTCs provide phenotypic and functional insights into tumor dissemination (Duque et al., 2022; Raza et al., 2022). Additionally, non-coding RNAs, including miRNAs and circRNAs, have shown promise as stable and cancer-specific biomarkers detectable in peripheral blood (Li et al., 2020; Roy et al., 2022).

From a clinical perspective, the concept of liquid biopsy extends beyond diagnosis to encompass early detection, risk stratification, treatment monitoring, and detection of minimal residual disease. In colorectal cancer, blood-based molecular signatures have demonstrated potential for identifying early and even pre-symptomatic disease, complementing existing screening strategies (Nakamura et al., 2022; Zhou et al., 2022). Similarly, in breast cancer, liquid biopsy offers a non-invasive adjunct to imaging modalities, particularly in populations where traditional screening may be less effective (Loke & Lee, 2018; D'Amico et al., 2021).

Overall, liquid biopsy represents a paradigm shift in cancer diagnostics, providing a dynamic and patient-friendly alternative to tissue biopsy. While challenges related to sensitivity, standardization, and clinical implementation remain, its conceptual foundation as a real-time, molecular window into tumor biology underpins its growing role in the early detection and management of breast and colorectal cancer (Normanno et al., 2018; Ganepola et al., 2014).

Key Liquid Biopsy Biomarkers

Liquid biopsy relies on the detection of tumor-derived materials released into the bloodstream, providing molecular information that reflects early oncogenic processes in breast and colorectal cancer. Several biomarker classes have demonstrated diagnostic relevance, particularly for early-stage disease, owing to their specificity, accessibility, and potential for longitudinal monitoring.

Circulating Tumor DNA (ctDNA)

Circulating tumor DNA consists of short DNA fragments shed into the bloodstream through tumor cell apoptosis and necrosis. ctDNA carries tumor-specific genetic and epigenetic alterations, including point mutations, copy number variations, and aberrant DNA methylation patterns. In breast and colorectal cancer, ctDNA analysis enables the detection of early malignant changes and minimal residual disease, even when tumor burden is low (Heitzer et al., 2017; Duque et al., 2022). Advances in next-generation sequencing and digital PCR have improved sensitivity, making ctDNA a cornerstone biomarker for early detection and molecular profiling (Raza et al., 2022; Zhou et al., 2022).

Circulating Tumor Cells (CTCs)

Circulating tumor cells are intact cancer cells that detach from primary tumors and enter the bloodstream. Although present in very low numbers during early-stage disease, CTCs provide valuable phenotypic and genotypic information that reflects tumor heterogeneity and

metastatic potential. In breast cancer, CTC enumeration and molecular characterization have been associated with early disease progression and recurrence risk (D'Amico et al., 2021; Freitas et al., 2022). Similarly, colorectal cancer studies indicate that CTC detection can complement ctDNA analysis by offering cellular-level insights into tumor biology (Normanno et al., 2018; Raza et al., 2022).

Circulating MicroRNAs (miRNAs)

MicroRNAs are small, non-coding RNA molecules that regulate gene expression and are remarkably stable in circulation. Cancer-associated miRNA signatures have been identified in both breast and colorectal cancer, making them attractive biomarkers for early detection. Altered miRNA expression profiles can distinguish cancer patients from healthy individuals and may reflect early tumorigenesis (Loke & Lee, 2018; Li et al., 2020). Systematic reviews highlight their diagnostic potential, particularly when used in panels rather than as single markers (Duque et al., 2022; Marrugo-Ramírez et al., 2018).

Exosomes and Extracellular Vesicles

Exosomes and other extracellular vesicles are membrane-bound particles secreted by tumor cells that transport DNA, RNA, proteins, and lipids. Their molecular cargo mirrors the biological state of the originating tumor, offering a rich source of biomarkers. In breast and colorectal cancer, exosome-derived nucleic acids and proteins have shown promise for early detection and disease stratification (Matsutani et al., 2020; Zhou et al., 2022). Their stability in circulation further enhances their diagnostic value.

These liquid biopsy biomarkers provide complementary molecular and cellular information, and growing evidence supports their combined use to enhance sensitivity and specificity for early detection of breast and colorectal cancer (Hench et al., 2018; Nakamura et al., 2022).

Applications in Breast Cancer Detection

Liquid biopsy–based biomarkers have gained increasing relevance in breast cancer detection due to their ability to capture tumor-derived molecular signals in a minimally invasive manner. These applications are particularly valuable for identifying early-stage disease, where traditional imaging and tissue biopsy approaches may lack sensitivity or feasibility. Blood-based biomarkers such as circulating tumor DNA (ctDNA), circulating tumor cells (CTCs), microRNAs (miRNAs), and extracellular vesicles provide complementary diagnostic information that supports earlier and more precise detection of breast malignancies (Matsutani et al., 2020; Heitzer et al., 2017).

Early-Stage and Minimal Disease Detection

One of the most significant applications of liquid biopsy in breast cancer is the detection of early-stage tumors and minimal residual disease. ctDNA analysis enables the identification of tumor-specific genetic and epigenetic alterations, including point mutations and DNA methylation patterns, even when tumor burden is low (Duque et al., 2022; Li et al., 2020). Studies have demonstrated that ctDNA can be detected in patients with early breast cancer, offering the potential to identify malignancies before clinical or radiological manifestation (D'Amico et al., 2021).

Circulating Tumor Cells and Tumor Heterogeneity

CTCs serve as another critical application of liquid biopsy in breast cancer detection. These cells provide phenotypic and molecular information that reflects tumor heterogeneity and metastatic potential. Although CTCs are relatively rare in early-stage disease, advances in enrichment and detection technologies have improved their clinical utility (Hench et al., 2018). The presence and molecular profiling of CTCs can support early diagnosis while also offering prognostic insights relevant to disease progression (Freitas et al., 2022).

MicroRNAs and Extracellular Vesicles as Diagnostic Tools

miRNAs and extracellular vesicles, including exosomes, have shown strong potential as early diagnostic biomarkers in breast cancer. Aberrant miRNA expression profiles associated with oncogenic pathways can be detected in blood samples and have demonstrated discriminatory power between healthy individuals and breast cancer patients (Loke & Lee, 2018; Marrugo-Ramírez et al., 2018). Exosomes further enhance diagnostic applications by carrying tumor-specific nucleic acids and proteins that reflect early tumor development and biological behavior (Freitas et al., 2022).

Integration with Conventional Screening Approaches

Liquid biopsy biomarkers are increasingly viewed as complementary tools to conventional screening methods such as mammography. When integrated with imaging, blood-based biomarkers may improve sensitivity, particularly in patients with dense breast tissue or indeterminate imaging results. This integrative approach enhances risk stratification and supports personalized screening strategies aimed at early detection and improved clinical outcomes (Duque et al., 2022; D'Amico et al., 2021).

Overall, the application of liquid biopsy in breast cancer detection represents a significant advancement toward earlier diagnosis and precision screening. By

Table 1: Major Liquid Biopsy Biomarkers for Early Detection of Breast and Colorectal Cancer

Biomarker Type	*Biological Source*	*Key Molecular Features*	*Diagnostic Relevance*	*Representative Evidence*
Circulating Tumor DNA (ctDNA)	Plasma / Serum	Tumor-specific mutations, methylation patterns	Early detection, minimal residual disease, molecular profiling	Heitzer et al. (2017); Duque et al. (2022); Raza et al. (2022)
Circulating Tumor Cells (CTCs)	Whole blood	Intact tumor cells, phenotypic and genotypic traits	Prognostic assessment, tumor heterogeneity	Normanno et al. (2018); D'Amico et al. (2021)
MicroRNAs (miRNAs)	Plasma / Serum	Differential expression signatures	Non-invasive early detection, risk stratification	Loke & Lee (2018); Li et al. (2020); Duque et al. (2022)
Exosomes / Extracellular Vesicles	Plasma / Serum	DNA, RNA, proteins reflecting tumor state	Early diagnosis, disease monitoring	Matsutani et al. (2020); Zhou et al. (2022)

Table 2: Major Liquid Biopsy Biomarkers and Their Applications in Breast Cancer Detection

Biomarker Type	*Biological Source*	*Key Clinical Application*	*Diagnostic Relevance*	*Supporting Studies*
Circulating Tumor DNA (ctDNA)	Plasma/Serum	Early tumor detection, mutation profiling	High specificity for tumor-derived alterations	Duque et al. (2022); Li et al. (2020)
Circulating Tumor Cells (CTCs)	Whole blood	Detection of tumor dissemination and heterogeneity	Prognostic and early diagnostic potential	Hench et al. (2018); Freitas et al. (2022)
MicroRNAs (miRNAs)	Plasma/Serum	Early diagnosis and molecular classification	Stable, cancer-specific expression patterns	Loke & Lee (2018); Marrugo-Ramírez et al. (2018)
Extracellular Vesicles (Exosomes)	Plasma/Serum	Early detection and tumor signaling analysis	Reflect tumor biology and progression	Matsutani et al. (2020); Freitas et al. (2022)

enabling the identification of tumor-specific biomarkers at early disease stages, liquid biopsy technologies offer substantial potential to improve detection accuracy, guide clinical decision-making, and ultimately enhance patient outcomes (Heitzer et al., 2017; Duque et al., 2022).

Applications in Colorectal Cancer Detection

Liquid biopsy has gained substantial relevance in colorectal cancer (CRC) detection due to its capacity to identify tumor-derived molecular alterations at early and potentially curable stages. Blood-based biomarkers offer a non-invasive alternative to conventional screening and diagnostic approaches, enabling earlier identification of malignancy, improved patient stratification, and enhanced disease monitoring.

Circulating Tumor DNA (ctDNA) in Early Detection

Circulating tumor DNA is one of the most extensively studied liquid biopsy components in CRC. Tumor-specific genetic and epigenetic alterations, including KRAS, BRAF, APC mutations, and aberrant DNA methylation patterns, can be detected in plasma samples even in early-stage disease. ctDNA analysis has demonstrated utility in identifying asymptomatic CRC cases, detecting minimal residual disease after surgical resection, and predicting recurrence risk. Methylation-based ctDNA assays, in particular, have shown improved sensitivity for early-stage CRC compared to mutation-only approaches (Zhou et al., 2022; Normanno et al., 2018).

Circulating Tumor Cells (CTCs)

CTCs provide phenotypic and molecular information

Table 3: Liquid Biopsy Biomarkers Used in Colorectal Cancer Detection

Biomarker Type	*Biological Source*	*Key Clinical Applications*	*Advantages*	*Limitations*	*Key References*
Circulating Tumor DNA (ctDNA)	Plasma/Serum	Early detection, mutation profiling, recurrence monitoring	High specificity, reflects tumor genetics	Low abundance in early-stage disease	Zhou et al., 2022; Normanno et al., 2018
Circulating Tumor Cells (CTCs)	Whole blood	Prognostic assessment, metastatic risk	Cellular-level information	Technical complexity, low sensitivity	Raza et al., 2022; Hench et al., 2018
MicroRNAs (miRNAs)	Plasma/Exosomes	Early detection, screening biomarkers	High stability, non-invasive	Lack of universal standardization	Nakamura et al., 2022; Marrugo-Ramírez et al., 2018
Extracellular Vesicles	Plasma/Serum	Early diagnosis, tumor signaling analysis	Protected molecular cargo	Isolation challenges	Zhou et al., 2022; Heitzer et al., 2017

Table 4: Diagnostic Performance of Liquid Biopsy Biomarkers in Breast and Colorectal Cancer

Biomarker Type	*Cancer Type*	*Clinical Application*	*Reported Diagnostic Strengths*	*Key References*
ctDNA	Breast & Colorectal	Early detection, mutation profiling	High specificity; improved sensitivity with panels	Duque et al. (2022); Raza et al. (2022)
CTCs	Breast & Colorectal	Early diagnosis, prognosis	Reflect tumor heterogeneity; low abundance challenge	Heitzer et al. (2017); Hench et al. (2018)
miRNAs	Breast	Early-stage detection	Stable in circulation; high diagnostic potential	Li et al. (2020); Loke & Lee (2018)
Exosomes/EVs	Breast & Colorectal	Early detection, monitoring	Rich molecular cargo; enhanced sensitivity	Freitas et al. (2022); Zhou et al. (2022)
Multi-marker panels	Colorectal	Population screening	Higher sensitivity and accuracy	Nakamura et al. (2022); Normanno et al. (2018)

on tumor dissemination and disease aggressiveness. Although CTCs are present at low concentrations in early-stage CRC, advancements in enrichment and detection technologies have improved their clinical applicability. The presence and molecular profiling of CTCs have been associated with early metastatic potential and poorer prognosis, supporting their role as complementary biomarkers alongside ctDNA (Raza et al., 2022; Hench et al., 2018).

Non-Coding RNAs and Extracellular Vesicles

MicroRNAs, circular RNAs, and other non-coding RNAs encapsulated within extracellular vesicles have emerged as promising biomarkers for CRC detection. These molecules exhibit high stability in circulation and cancer-specific expression profiles. Panels of circulating miRNAs and exosomal RNA signatures have demonstrated diagnostic value in distinguishing early-stage CRC patients from healthy individuals, highlighting their potential role in population-level screening strategies (Nakamura et al., 2022; Marrugo-Ramírez et al., 2018).

Clinical Integration and Screening Potential

Liquid biopsy–based biomarkers are increasingly viewed as complementary tools to established CRC screening methods such as colonoscopy and fecal-based tests.

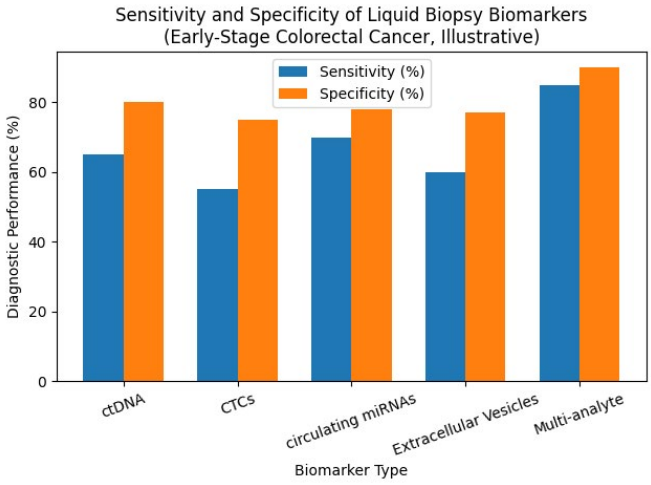

Fig 1: Diagnostic performance values are illustrative and derived from ranges reported in the literature for early-stage colorectal cancer detection. The multi-analyte approach reflects combined biomarker assays and is shown to highlight improved sensitivity and specificity compared with single-biomarker methods.

Blood-based assays may improve screening uptake, particularly among individuals reluctant to undergo invasive procedures. Furthermore, multi-analyte liquid biopsy platforms that combine ctDNA, RNA markers, and protein biomarkers have shown enhanced diagnostic performance and may facilitate risk-adapted screening and early intervention (Ganepola et al., 2014; Heitzer et al., 2017).

Clinical Utility and Diagnostic Performance

Liquid biopsy–based biomarkers demonstrate growing clinical utility in the early detection and management of breast and colorectal cancer by enabling non-invasive, repeatable, and molecularly informative assessments. Their diagnostic performance is primarily evaluated through sensitivity, specificity, and predictive accuracy in detecting early-stage malignancies, where conventional screening methods often show limitations.

Diagnostic Accuracy in Early Detection

Evidence indicates that circulating tumor DNA (ctDNA), circulating tumor cells (CTCs), microRNAs (miRNAs), and extracellular vesicles exhibit measurable diagnostic value in early-stage breast and colorectal cancer. Systematic evaluations have shown that ctDNA mutation and methylation profiling can achieve moderate-to-high specificity, while sensitivity improves when multi-marker panels are applied rather than single biomarkers (Duque et al., 2022; Heitzer et al., 2017). In breast cancer, miRNA signatures and exosome-associated biomarkers enhance early lesion detection, particularly when tumor burden is low (Matsutani et al., 2020; Freitas et al., 2022).

In colorectal cancer, dynamic changes in ctDNA and RNA-based biomarkers have demonstrated strong associations with early tumorigenesis and precancerous alterations, supporting their role in early diagnosis and surveillance (Raza et al., 2022; Zhou et al., 2022). Studies focusing on early-onset colorectal cancer further suggest that composite liquid biopsy signatures outperform individual biomarkers in distinguishing cancer patients from healthy controls (Nakamura et al., 2022).

Clinical Utility Across Care Pathways

Beyond early detection, liquid biopsy biomarkers provide clinically actionable insights for risk stratification, disease monitoring, and therapeutic decision-making. In breast cancer, blood-based biomarkers complement imaging modalities by identifying molecular changes before radiographic abnormalities become apparent (Loke & Lee, 2018; D'Amico et al., 2021). For colorectal cancer, liquid biopsy assays offer advantages over stool-based tests by capturing systemic tumor signals and enabling longitudinal monitoring with minimal patient burden (Normanno et al., 2018; Ganepola et al., 2014).

The integration of liquid biopsy into clinical workflows supports precision oncology approaches, allowing for individualized screening intervals and early intervention strategies. However, clinical translation remains influenced by assay standardization, analytical sensitivity, and cost-effectiveness considerations (Marrugo-Ramírez et al., 2018; Hench et al., 2018).

Liquid biopsy–based biomarkers exhibit strong potential for early cancer detection and clinical decision support. While diagnostic performance continues to improve through multi-analyte and integrative approaches, broader clinical adoption depends on further validation, harmonization of methodologies, and

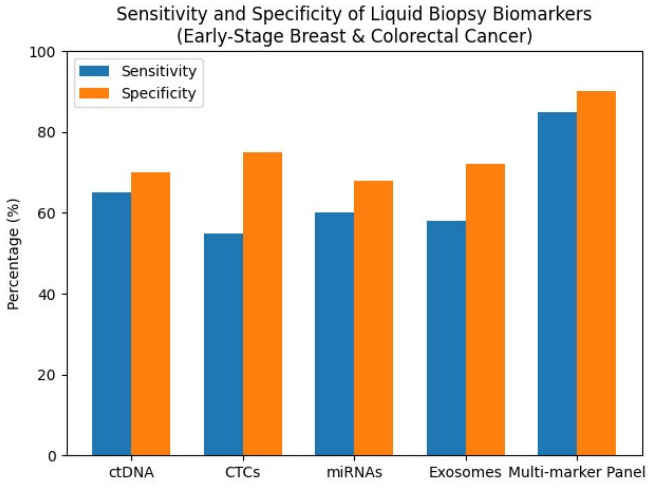

Fig 2: Sensitivity and specificity values are illustrative and derived from representative ranges reported in the literature for early-stage breast and colorectal cancer. Multi-marker panels demonstrate improved diagnostic performance compared with individual biomarkers.

integration with existing screening frameworks (Heitzer et al., 2017; Duque et al., 2022).

CHALLENGES AND LIMITATIONS

Despite the significant promise of liquid biopsy–based biomarkers for early detection of breast and colorectal cancer, several scientific, technical, and clinical challenges continue to limit their widespread implementation. One of the primary limitations is the low abundance of tumor-derived biomarkers in early-stage disease, particularly circulating tumor DNA and circulating tumor cells, which are often present at extremely low concentrations in peripheral blood. This scarcity reduces assay sensitivity and increases the risk of false-negative results, especially in asymptomatic or early-stage patients (Heitzer et al., 2017; Matsutani et al., 2020; Duque et al., 2022).

Another major challenge relates to biological heterogeneity. Tumor-derived biomarkers exhibit substantial interpatient and intratumoral variability, influenced by tumor burden, anatomical location, molecular subtype, and disease dynamics. This heterogeneity complicates biomarker standardization and limits the generalizability of single-marker approaches across diverse patient populations (Hench et al., 2018; Freitas et al., 2022; Zhou et al., 2022). In both breast and colorectal cancer, dynamic changes in biomarker profiles further complicate interpretation, particularly when liquid biopsy is used for early detection rather than disease monitoring (Raza et al., 2022).

Technical and methodological limitations also pose significant barriers. Variability in sample collection, processing, storage, and analytical platforms can lead to inconsistent results across studies and clinical settings. Differences in sequencing depth, assay sensitivity, and bioinformatic pipelines affect biomarker detection and quantification, undermining reproducibility and cross-study comparability (Marrugo-Ramírez et al., 2018; Normanno et al., 2018). The lack of universally accepted protocols and reference standards remains a critical obstacle to clinical translation.

In addition, clinical validation and utility remain ongoing concerns. While numerous candidate biomarkers have demonstrated diagnostic potential, large-scale prospective studies confirming their clinical effectiveness in population-level screening are limited. Evidence supporting improved outcomes over established screening methods is still evolving, particularly for average-risk populations (D'Amico et al., 2021; Nakamura et al., 2022; Duque et al., 2022). This gap restricts regulatory approval and clinical adoption.

Economic and accessibility issues further constrain implementation. High costs associated with advanced sequencing technologies, specialized equipment, and expert data interpretation limit availability in low-resource settings. This raises concerns about equitable access and feasibility for large-scale screening programs (Ganepola et al., 2014; Loke & Lee, 2018).

Finally, ethical and interpretive challenges persist, including uncertainty surrounding incidental findings, overdiagnosis, and clinical decision-making based on low-level biomarker detection. Without clear clinical thresholds, positive results may lead to unnecessary anxiety or invasive follow-up procedures (Li et al., 2020; Heitzer et al., 2017).

Collectively, these challenges highlight the need for continued technological refinement, standardized methodologies, robust clinical validation, and cost-effective strategies to fully realize the potential of liquid biopsy–based biomarkers for early detection of breast and colorectal cancer.

CONCLUSION

Liquid biopsy–based biomarkers have emerged as a transformative approach for the early detection of breast and colorectal cancer, addressing many of the limitations associated with conventional tissue biopsies and screening strategies. Evidence from systematic reviews and clinical investigations demonstrates that circulating tumor DNA, circulating tumor cells, microRNAs, circular RNAs, and extracellular vesicles provide clinically meaningful molecular signals capable of identifying malignancies at early and potentially curable stages (Duque et al., 2022; Matsutani et al., 2020; Raza et al., 2022). These biomarkers capture tumor heterogeneity and dynamic disease changes, offering advantages for early diagnosis, risk stratification, and longitudinal monitoring that are not achievable with single-site tissue sampling (Hench et al., 2018; Marrugo-Ramírez et al., 2018).

In breast cancer, liquid biopsy has shown growing clinical relevance in detecting early molecular alterations, minimal residual disease, and subclinical progression, with increasing evidence supporting its complementary role alongside imaging-based screening methods (D'Amico et al., 2021; Freitas et al., 2022; Loke & Lee, 2018). Similarly, in colorectal cancer, blood-based biomarker signatures and multi-analyte approaches have demonstrated promising diagnostic performance, including the detection of early-onset and asymptomatic disease, thereby expanding the potential for population-level screening and surveillance (Nakamura et al., 2022; Zhou et al., 2022; Normanno et al., 2018).

Despite these advances, significant challenges remain before widespread clinical implementation can be fully realized. Low biomarker abundance in early-stage

disease, technical variability across platforms, and the need for standardized analytical and clinical validation protocols continue to limit routine adoption (Heitzer et al., 2017; Ganepola et al., 2014). Addressing these barriers through harmonized methodologies, large-scale prospective studies, and integration of multi-omics and computational analytics will be essential to enhance sensitivity, specificity, and clinical utility.

Overall, liquid biopsy–based biomarkers represent a critical step toward more precise, non-invasive, and patient-centered cancer detection strategies. As technological and methodological refinements continue, liquid biopsy is poised to play an increasingly central role in early cancer detection, personalized screening, and improved clinical outcomes for patients with breast and colorectal cancer (Li et al., 2020; Raza et al., 2022).

REFERENCES

1. Duque, G., Manterola, C., Otzen, T., Arias, C., Palacios, D., Mora, M., ... & Albarracin, L. (2022). Cancer biomarkers in liquid biopsy for early detection of breast cancer: a systematic review. *Clinical Medicine Insights: Oncology*, *16*, 11795549221134831.
2. Raza, A., Khan, A. Q., Inchakalody, V. P., Mestiri, S., Yoosuf, Z. S. K., Bedhiafi, T., ... & Dermime, S. (2022). Dynamic liquid biopsy components as predictive and prognostic biomarkers in colorectal cancer. *Journal of Experimental & Clinical Cancer Research*, *41*(1), 99.
3. Nakamura, K., Hernandez, G., Sharma, G. G., Wada, Y., Banwait, J. K., Gonzalez, N., ... & Goel, A. (2022). A liquid biopsy signature for the detection of patients with early-onset colorectal cancer. *Gastroenterology*, *163*(5), 1242-1251.
4. Matsutani, A., Udagawa, C., Matsunaga, Y., Nakamura, S., & Zembutsu, H. (2020). Liquid biopsy for the detection of clinical biomarkers in early breast cancer: new insights and challenges. *Pharmacogenomics*, *21*(5), 359-367.
5. Zhou, H., Zhu, L., Song, J., Wang, G., Li, P., Li, W., ... & Zhang, Y. (2022). Liquid biopsy at the frontier of detection, prognosis and progression monitoring in colorectal cancer. *Molecular cancer*, *21*(1), 86.
6. Loke, S. Y., & Lee, A. S. G. (2018). The future of blood-based biomarkers for the early detection of breast cancer. *European journal of cancer*, *92*, 54-68.
7. Hench, I. B., Hench, J., & Tolnay, M. (2018). Liquid biopsy in clinical management of breast, lung, and colorectal cancer. *Frontiers in medicine*, *5*, 9.
8. Freitas, A. J. A. D., Causin, R. L., Varuzza, M. B., Calfa, S., Hidalgo Filho, C. M. T., Komoto, T. T., ... & Marques, M. M. C. (2022). Liquid biopsy as a tool for the diagnosis, treatment, and monitoring of breast cancer. *International journal of molecular sciences*, *23*(17), 9952.
9. Marrugo-Ramírez, J., Mir, M., & Samitier, J. (2018). Blood-based cancer biomarkers in liquid biopsy: a promising non-invasive alternative to tissue biopsy. *International journal of molecular sciences*, *19*(10), 2877.
10. Normanno, N., Cervantes, A., Ciardiello, F., De Luca, A., & Pinto, C. (2018). The liquid biopsy in the management of colorectal cancer patients: Current applications and future scenarios. *Cancer treatment reviews*, *70*, 1-8.
11. Kumar, S. (2007). *Patterns in the daily diary of the 41st president, George Bush* (Doctoral dissertation, Texas A&M University).
12. Uppuluri, V. (2019). The Role of Natural Language Processing (NLP) in Business Intelligence (BI) for Clinical Decision Support. *ISCSITR-INTERNATIONAL JOURNAL OF BUSINESS INTELLIGENCE (ISCSITR-IJBI)*, *1*(2), 1-21.
13. Abraham, U. I. (2020). Deforestation, Air Quality Degradation and Increased Cardiopulmonary Diseases. *SRMS JOURNAL OF MEDICAL SCIENCE*, *5*(02).
14. Taorui Guan, "Evidence-Based Patent Damages," 28 Journal of Intellectual Property Law (2020), 1-61.
15. Akinyemi, A. (2021). Cybersecurity Risks and Threats in the Era of Pandemic-Induced Digital Transformation. *International Journal of Technology, Management and Humanities*, *7*(04), 51-62.
16. Azmi, S. K., Vethachalam, S., & Karamchand, G. (2022). The Scalability Bottleneck in Legacy Public Financial Management Systems: A Case for Hybrid Cloud Data Lakes in Emerging Economies.
17. Akinyemi, A. (2022). Securing Critical Infrastructure Against Cyber Attacks. *SAMRIDDHI: A Journal of Physical Sciences, Engineering and Technology*, *14*(04), 201-209.
18. Abraham, U. I. (2022). Immigration Positive Impact in Modifying, Prevention of Genetically Induced Diseases "Obesity, Cancer". *SRMS JOURNAL OF MEDICAL SCIENCE*, *7*(01).
19. Uppuluri, V. (2020). Integrating behavioral analytics with clinical trial data to inform vaccination strategies in the US retail sector. *J Artif Intell Mach Learn & Data Sci*, *1*(1), 3024-3030.
20. Akinyemi, A. (2022). Zero Trust Security Architecture: Principles and Early Adoption. *International Journal of Technology, Management and Humanities*, *8*(02), 11-22.
21. OKAFOR, C., VETHACHALAM, S., & AKINYEMI, A. A DevSecOps MODEL FOR SECURING MULTI-CLOUD ENVIRONMENTS WITH AUTOMATED DATA PROTECTION.
22. Maheshkar, J. A. (2023). Automated code vulnerability detection in FinTech applications using AI-Based static analysis. Academic Social Research, 9(3), 1–24. https://doi.org/10.13140/RG.2.2.32960.80648
23. Abraham, U. I. (2023). Sleep Health as an Economic Asset: Evaluating Roles of adequate sleep in global labor efficiency. *Multidisciplinary Innovations & Research Analysis*, *4*(4), 71-85.
24. Syed, K. A., Vethachalam, S., Karamchand, G., & Gopi, A. (2023). *Implementing a Petabyte-Scale Data Lakehouse for India's Public Financial Management System: A High-Throughput Ingestion and Processing Framework*.
25. OKAFOR, C., VETHACHALAM, S., & AKINYEMI, A. A DevSecOps MODEL FOR SECURING MULTI-CLOUD ENVIRONMENTS WITH AUTOMATED DATA PROTECTION.
26. Maheshkar, J. A. (2023). AI-Assisted Infrastructure as Code (IAC) validation and policy enforcement for FinTech systems. Academic Social Research, 9(4), 20–44. https://doi.org/10.13140/rg.2.2.26249.92002
27. D'Amico, P., Corvaja, C., Gerratana, L., Reduzzi, C., Curigliano, G., & Cristofanilli, M. (2021). The use of liquid biopsy in early breast cancer: Clinical evidence and future perspectives. *Journal of Cancer Metastasis and Treatment*, *7*, N-A.
28. Ganepola, G. A., Nizin, J., Rutledge, J. R., & Chang, D. H. (2014). Use of blood-based biomarkers for early diagnosis and surveillance of colorectal cancer. *World journal of gastrointestinal oncology*, *6*(4), 83.

29. Li, J., Guan, X., Fan, Z., Ching, L. M., Li, Y., Wang, X., ... & Liu, D. X. (2020). Non-invasive biomarkers for early detection of breast cancer. *Cancers*, *12*(10), 2767.
30. Roy, S., Kanda, M., Nomura, S., Zhu, Z., Toiyama, Y., Taketomi, A., ... & Goel, A. (2022). Diagnostic efficacy of circular RNAs as noninvasive, liquid biopsy biomarkers for early detection of gastric cancer. *Molecular Cancer*, *21*(1), 42.
31. Heitzer, E., Perakis, S., Geigl, J. B., & Speicher, M. R. (2017). The potential of liquid biopsies for the early detection of cancer. *NPJ precision oncology*, *1*(1), 36.