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The Role of Liquid Biopsies in Early Cancer Detection and Monitoring

Kirolos Eskandar*

Diakonie Klinik Mosbach – Germany

Abstract

Liquid biopsies have emerged as a transformative tool in oncology, offering a minimally invasive method for early cancer detection and real-time monitoring of disease progression. This literature review explores the technological advancements and clinical applications of liquid biopsies, focusing on their role in detecting circulating tumor cells (CTCs), cell-free DNA (cfDNA), and other biomarkers. We examine the efficacy of liquid biopsies in early cancer screening, their potential for monitoring treatment response, and their ability to detect recurrence and metastasis. Despite the promising applications, challenges such as technical limitations, biological variability, and cost-effectiveness must be addressed to fully integrate liquid biopsies into routine clinical practice. The future of liquid biopsies looks promising, with emerging trends in multi-omic approaches and artificial intelligence paving the way for more personalized and effective cancer care. This review included 34 peer-reviewed studies identified through a systematic PRISMA-guided search across four databases.

Keywords: *circulating tumor cells (CTCs), cell-free DNA (cfDNA), cancer monitoring, multi-omics, artificial intelligence in cancer diagnostics.*

INTRODUCTION

Liquid biopsies represent a transformative approach in oncology, offering a non-invasive method to detect and monitor cancer by analyzing circulating biomarkers in body fluids, primarily blood. Unlike traditional tissue biopsies, which require invasive procedures to obtain solid tumor samples, liquid biopsies utilize circulating tumor cells (CTCs), cell-free DNA (cfDNA), and circulating tumor DNA (ctDNA), and other cancer-related molecules that are shed into the bloodstream from primary and metastatic tumor sites (Lone, *et al*., 2022). cfDNA refers to all DNA fragments circulating in the bloodstream, whereas ctDNA is the fraction of cfDNA that originates specifically from tumor cells.

One of the most significant advantages of liquid biopsies is their minimally invasive nature. Traditional tissue biopsies often involve surgical procedures that can be painful, carry risks of complications, and may not be feasible in all patients, especially those with tumors located in hard-to-reach areas or those in poor health. In contrast, liquid biopsies can be performed through a simple blood draw, making the process more patient-friendly and repeatable over time. This allows for real-time monitoring of tumor dynamics and treatment response, providing a more

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*Corresponding author: kiroloss.eskandar@gmail.com

comprehensive picture of the disease's progression (Ogt, *n.d*.).

Additionally, liquid biopsies offer a broader snapshot of tumor heterogeneity. Tumors often consist of multiple subclones with distinct genetic profiles, which might not be fully captured in a single tissue biopsy due to sampling bias. Liquid biopsies can potentially detect genetic alterations from different tumor subclones circulating in the blood, providing a more complete understanding of the genetic landscape and evolution of the cancer (Staff, 2021).

Delays in tissue biopsy due to procedural complexity can lead to late-stage diagnosis, contributing to poor survival rates in cancers such as pancreatic and lung cancer. However, liquid biopsies are not without limitations. One of the primary challenges is the sensitivity of detecting ctDNA or CTCs, especially in early-stage cancers where the concentration of these biomarkers in the bloodstream may be very low. This can lead to false-negative results, where significant genetic mutations go undetected. Moreover, the interpretation of liquid biopsy results can be complicated by the presence of genetic alterations from non-cancerous cells, such as those resulting from clonal hematopoiesis, which can confound the analysis (Ogt, *n.d*.).

Despite these challenges, the advantages of liquid biopsies in providing a less invasive, more comprehensive, and dynamic method for cancer detection and monitoring make them a promising complement to traditional tissue biopsies. As the technology and methodologies continue to evolve, the integration of liquid biopsies into clinical practice holds the potential to significantly enhance personalized cancer care and improve patient outcomes (Staff, 2021).

MATERIALS AND METHODS

A systematic approach was utilized for this literature review, adhering to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to gather relevant articles and studies in oncology. A thorough search was conducted in reputable databases, including PubMed, Google Scholar, Scopus, and Web of Science, using specific keywords such as "Liquid Biopsies," "Early Cancer Detection," "Circulating Tumor Cells (CTCs)," "Cell-Free DNA (cfDNA)," "Cancer Monitoring" to ensure comprehensive coverage of pertinent literature.

The search covered studies published between 2010 and 2024. Search terms included 'liquid biopsy', 'ctDNA', 'cancer detection', and 'real-time cancer monitoring.'

The inclusion criteria for the studies were as follows: (1) publications in English, (2) studies focusing on liquid biopsy applications in oncology, and (3) articles reporting on early detection or monitoring of cancer. Initially, 131 articles were retrieved from the databases. After a meticulous examination to eliminate duplicate references, 34 unique articles met the inclusion criteria (Table 1). These articles underwent rigorous evaluation through a comprehensive assessment of their titles, abstracts, and full texts, confirming their alignment with the established inclusion criteria and warranting their inclusion in the review.

To provide a clear overview of the study selection process, the PRISMA flow diagram (Figure 1) is included below, illustrating the number of records identified, screened, and included in the review, along with reasons for exclusion at each stage.

TECHNOLOGICAL ADVANCES IN LIQUID BIOPSIES

The field of liquid biopsies has seen significant technological advancements, enabling more precise and comprehensive cancer diagnostics and monitoring. Liquid biopsies primarily employ technologies such as next-generation sequencing (NGS) and PCR-based methods to analyze ctDNA, CTCs, and other biomarkers in blood samples.

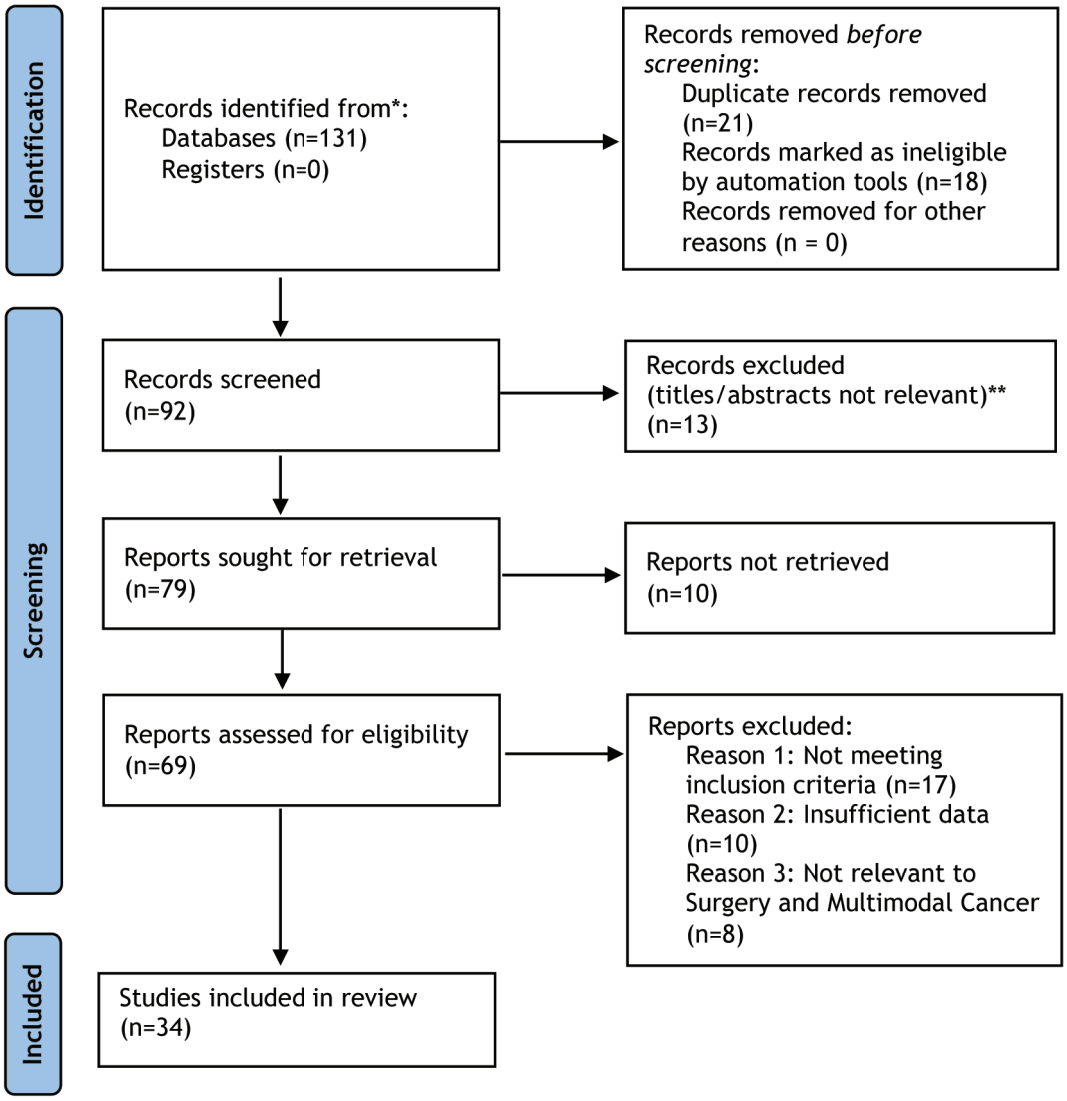

Figure 1. PRISMA flow diagram.

Table 1. Summary table of included studies.

Author	Year	Cancer Type	Biomarker	Platform	Key Findings	Study Type
Lone, *et al.*	2022	Various	ctDNA, CTCs, exosomes	NGS, PCR	Comprehensive review of liquid biopsy applications in diagnosis and treatment	Review
OGT (blog)	n.d.	Various	ctDNA, CTCs	Various	Discusses practical advantages, limitations, and future outlook	Commentary
Staff (AACR)	2021	Various	ctDNA, CTCs	NGS	Highlights complementary role of liquid biopsies alongside tissue biopsy	Commentary
Robertson & Baxter	2011	Various	NA	Needle Biopsy	Raises concerns about tumor seeding post-biopsy	Review
Milbury, *et al.*	2009	Various	Mutant alleles	PCR	Methodological study on allele enrichment for mutation detection	Experimental
Siravegna, *et al.*	2017	Various	ctDNA	NGS	Integrates liquid biopsy in clinical management	Review
Nair, *et al.*	2016	Endometrial	cfDNA	NGS	Detected early-stage mutations via uterine lavage	Cross-sectional study
Bettegowda, *et al.*	2014	Multiple	ctDNA	PCR	Detection of ctDNA in early and late malignancies	Experimental
El Achi, *et al.*	2019	Hematologic	ctDNA	NGS	Utility of NGS for multimodal testing	Review
Jensen, *et al.*	2019	Various	cfDNA	NGS	Detected CNAs in cfDNA to monitor immunotherapy	Experimental
Ju, *et al.*	2022	Various	CTCs	Imaging	Describes challenges and advances in CTC detection	Review
Vidlarova, *et al.*	2023	Various	CTCs	Microfluidics	Describes novel methods for CTC detection	Review
Heitzer, *et al.*	2019	Various	ctDNA	NGS	Discusses current and future genomic perspectives	Review
Dao, *et al.*	2023	Various	cfDNA, ctDNA	NGS	Path toward clinical validation of cfDNA and ctDNA	Review
Mitchell, *et al.*	2008	Various	miRNA	qPCR	Demonstrates miRNAs as stable cancer biomarkers	Experimental
Théry, *et al.*	2018	Various	Exosomes	EV Isolation	MISEV2018 guidelines for exosome studies	Guidelines
Kalluri & LeBleu	2020	Various	Exosomes	EV Isolation	Biological function and diagnostic utility of exosomes	Review
Wishart	2019	Various	Metabolites	Metabolomics	Highlights metabolite profiling in cancer	Review
Tao, *et al.*	2024	Colorectal	ctDNA	NGS	ctDNA in detection and monitoring of CRC	Clinical study
Shen, *et al.*	2022	Lung	ctDNA, CTCs	NGS	Early NSCLC detection via liquid biopsy	Clinical study
Zhu, *et al.*	2023	Lung	ctDNA	NGS	Screening and early detection via liquid biopsy	Review
Bankó, *et al.*	2019	Various	CTCs	Separation Tech	Describes CTC isolation technologies	Review
Ignatiadis & Reinholz	2011	Breast	CTCs	Imaging	CTCs and MRD in breast cancer	Review
Souza, *et al.*	2023	Lung	ctDNA	NGS	Liquid biopsy in recurrence/metastasis	Clinical study
Trapp, *et al.*	2019	Breast	CTCs	Imaging	CTC presence predicts prognosis in high-risk breast cancer	Clinical study
Pierga, *et al.*	2015	Breast	CTCs	Imaging	HER2+ IBC patients and CTC count correlations	Clinical trial

Table 1. Summary table of included studies (continuous).

Author	Year	Cancer Type	Biomarker	Platform	Key Findings	Study Type
Goodman, *et al.*	2018	Breast	CTCs	Imaging	CTCs linked to radiotherapy outcomes	Clinical study
Tsui, *et al.*	2020	Various	ctDNA	NGS	Development and regulatory issues of ctDNA tests	Review
Deveson, *et al.*	2021	Various	ctDNA	NGS	Analytical validation for ctDNA assays	Experimental
Cristiano, *et al.*	2019	Various	cfDNA	Whole genome	cfDNA fragmentation as cancer biomarker	Experimental
Hasin, *et al.*	2017	Various	Multi-omics	Various	Advocates multi-omics for disease profiling	Review
Kumar, *et al.*	2022	Various	Multi-omics	Various	Application of omics in diagnostics	Book chapter
Graves & Haystead	2002	Various	Proteins	Proteomics	Intro to proteomics in cancer	Review
Horgan & Kenny	2011	Various	Multi-omics	Various	Overview of omics in medicine	Review

NGS and PCR-based methods are primarily utilized for detecting cfDNA and its tumor-specific component, ctDNA, due to their sensitivity in identifying genetic mutations. In contrast, CTCs are typically isolated and analyzed using microfluidic enrichment technologies, immuno-magnetic separation, or imaging-based platforms. Exosomes and other extracellular vesicles require ultracentrifugation, size-exclusion chromatography, or microfluidic capture for downstream molecular characterization.

NGS has revolutionized the detection of ctDNA due to its high throughput and ability to identify unknown variants. NGS-based methods, like Tagged-Amplicon deep sequencing (TAm-Seq) and CAncer Personalized Profiling by deep sequencing (CAPP-Seq), allow for the detection of mutations with high sensitivity and specificity. TAm-Seq can detect mutations with a mutant allele fraction (MAF) as low as 0.1%, and CAPP-Seq can identify MAFs as low as 0.02%, making these methods highly effective for early-stage cancer detection (Robertson & Baxter, 2011; Milbury, *et al*., 2009). Innovations like unique molecular identifiers and molecular barcoding further enhance the accuracy of NGS by reducing sequencing error rates (Nair, *et al*., 2016).

PCR-based methods, including quantitative PCR (qPCR) and digital PCR (dPCR), are also extensively used due to their high sensitivity and cost-effectiveness. dPCR, for example, partitions the sample into thousands of parallel PCR reactions, significantly reducing background noise and enabling the detection of very low MAFs, sometimes below 0.1% (Bettegowda, *et al*., 2014). These methods are particularly beneficial for monitoring known mutations over time, providing a reliable means to assess treatment response and disease progression (Siravegna, *et al*., 2017).

Recent advancements in liquid biopsy technologies have also focused on improving the sensitivity and specificity of these platforms. Techniques like Safe-Sequencing System (Safe-SeqS) reduce sequencing errors by assigning unique identifiers to each DNA template, thus distinguishing true mutations from sequencing artifacts (Achi, *et al*., 2019). Similarly, the Ion Torrent NGS platform offers robust detection capabilities for a wide range of mutations with minimal DNA input, demonstrating high concordance with traditional tissue biopsies in identifying actionable mutations (Jensen, *et al*., 2019).

TYPES OF BIOMARKERS IN LIQUID BIOPSIES

Liquid biopsies leverage various types of biomarkers, each offering distinct advantages for cancer detection and monitoring. Among these biomarkers are CTCs, cfDNA, and ctDNA, circulating RNA, exosomes and extracellular vesicles, and proteins and metabolites.

CTCs are cells that have shed from the primary tumor into the bloodstream. CTCs provide comprehensive biological information, including RNA, proteins, and DNA, making them valuable for monitoring tumor progression and response to therapy (Ju, *et al*., 2022). They are utilized in various malignancies such as breast, prostate, and colorectal cancers. Despite their potential, the rarity of CTCs in the bloodstream poses a significant challenge, requiring advanced enrichment and detection technologies (Vidlarova, *et al*., 2023).

cfDNA and its subset, ctDNA, represent fragments of DNA released into the bloodstream. While cfDNA includes DNA from both healthy and cancerous cells, ctDNA specifically reflects tumor-derived genetic material. These DNA fragments can provide insights into tumor genetic alterations, such as mutations and copy number variations. ctDNA analysis allows for non-invasive tumor genotyping and real-time monitoring of treatment responses. The high sensitivity and specificity of NGS have significantly enhanced the detection capabilities of ctDNA (Heitzer, *et al*., 2019). However, cfDNA also includes DNA from normal cells, necessitating precise methods to distinguish ctDNA from the total cfDNA pool (Dao, *et al*., 2023).

Circulating RNA, including microRNA (miRNA) and long non-coding RNA (lncRNA), are RNA molecules found in the blood, either free-floating or within extracellular vesicles. These RNA molecules can regulate gene expression and are often deregulated in cancer. miRNAs are small, stable, and can be easily detected, making them attractive biomarkers for early cancer detection and prognosis (Mitchell, *et al*., 2008). Similarly, lncRNAs offer another layer of regulatory complexity, although their clinical application is still under investigation.

Exosomes and extracellular vesicles (EVs) are lipid bilayer-enclosed particles released by cells into the extracellular environment. They carry proteins, lipids, and nucleic acids, reflecting the molecular composition of their cell of origin. Exosomes are involved in intercellular communication and play roles in cancer progression and metastasis (Théry, *et al*., 2018). Their ability to protect their cargo from degradation makes them robust carriers of biomolecular information, useful for non-invasive cancer diagnostics (Kalluri & LeBleu, 2020). Common exosomal markers include ALIX, TSG101, and CD63. Exosomal miRNAs such as miR-21 and miR-1246 are under investigation for their role in tumor progression and have shown promise as biomarkers for early cancer detection and prognosis.

Proteins and metabolites in the bloodstream can also serve as biomarkers. Protein biomarkers, such as carcinoembryonic antigen (CEA) and prostate-specific antigen (PSA), are well-established in clinical practice for cancer detection and monitoring. Metabolites, small molecules involved in metabolic processes, can reflect changes in tumor metabolism and provide additional diagnostic information (Wishart, 2019). The integration of proteomic and metabolomic data enhances the understanding of tumor biology and improves the accuracy of liquid biopsy tests.

CLINICAL APPLICATIONS IN EARLY CANCER DETECTION

Liquid biopsies have emerged as a promising tool for the early detection of various cancers, offering a non-invasive alternative to traditional tissue biopsies. This approach has

shown significant potential in screening and early detection for cancers such as lung, colorectal, breast, and prostate.

In lung cancer, particularly non-small cell lung cancer (NSCLC), liquid biopsies have demonstrated significant utility. Studies have shown that biomarkers like ctDNA and CTCs can be detected in the blood of patients with early-stage NSCLC. The diagnostic accuracy of these biomarkers is notable, with high sensitivity and specificity, making them valuable for early detection and monitoring of lung cancer (Zhu, *et al*., 2023; Shen, *et al*., 2022).

However, the extent of detection varies by methodology—while Shen, *et al*. (2022) demonstrate early detection via ctDNA with strong predictive power, Zhu, *et al*. (2023) highlight limitations in using liquid biopsies as a stand-alone screening tool due to variability in shedding rates across tumor types.

Colorectal cancer (CRC) is another area where liquid biopsies have shown promise. Early detection of CRC is crucial for improving patient outcomes, as survival rates are significantly higher when the disease is identified at an early stage. Liquid biopsy markers such as CTCs have been shown to effectively identify early-stage CRC, with studies indicating high sensitivity and specificity. This non-invasive method could potentially increase patient compliance compared to traditional, invasive methods like colonoscopy (Adler, *et al*., 2021; Shen, *et al*., 2022).

While Tao, *et al*. (2024) report high sensitivity for ctDNA in early CRC detection, Adler, *et al*. (2021) found limitations in specificity, suggesting that assay performance may vary based on population demographics and detection platforms.

In breast cancer, liquid biopsies are being utilized to detect tumor-derived genetic material, such as ctDNA and RNA. These biomarkers can provide insights into the molecular characteristics of tumors, aiding in early detection and personalized treatment strategies. Clinical trials have demonstrated the efficacy of liquid biopsies in detecting early-stage breast cancer, enhancing the potential for timely intervention and improved patient outcomes (Tao, *et al*., 2024).

Still, other studies emphasize variability in ctDNA levels based on tumor burden and hormonal subtypes, which may necessitate complementary imaging or biomarker panels for robust diagnostics.

Prostate cancer detection has also benefited from liquid biopsy technology. Biomarkers like prostate-specific antigen (PSA) combined with CTC analysis can improve the accuracy of early detection. The integration of liquid biopsy into routine screening programs can help in identifying high-risk individuals earlier, thus facilitating early treatment and potentially reducing mortality rates (Tao, *et al*., 2024). However, clinical utility is still under debate in low-risk prostate cancer, where overdiagnosis may occur—highlighting the need for better stratification using liquid biopsy data.

Several case studies and clinical trials have underscored the effectiveness of liquid biopsies. For instance, a clinical trial involving the use of liquid biopsies for the detection of early-stage lung cancer showed that ctDNA analysis could identify cancerous mutations with a high degree of accuracy. Similar success has been reported in trials for colorectal and breast cancers, highlighting the robustness of this technology in various clinical settings (Tao, *et al*., 2024; Shen, *et al*., 2022). Yet across these trials, differences in sequencing sensitivity and patient tumor characteristics introduce variability in reported detection rates, stressing the importance of protocol harmonization.

The integration of liquid biopsies into routine screening programs is a promising development. These tests can be conducted alongside existing screening methods to provide a more comprehensive assessment of cancer risk. By incorporating liquid biopsies, healthcare systems can enhance the early detection of cancers, leading to better prognosis and survival rates for patients (Tao, *et al*., 2024).

MONITORING DISEASE PROGRESSION AND TREATMENT RESPONSE

Liquid biopsies have revolutionized the monitoring of disease progression and treatment response in oncology, offering a non-invasive method to detect minimal residual disease (MRD), recurrences, and metastasis. One key application is in tracking MRD, where liquid biopsies can detect trace amounts of cancer cells that remain post-treatment, potentially leading to early interventions before full relapse occurs (Bankó, *et al*., 2019). Studies in breast cancer have shown that the presence of CTCs is a strong predictor of recurrence, highlighting the utility of liquid biopsies in ongoing patient monitoring (Ignatiadis & Reinholz, 2011). However, some studies show inconsistency in the predictive value of CTCs in low-burden disease, suggesting that integrating multiple biomarkers (*e.g*., ctDNA + CTCs) may yield better prognostic accuracy.

Detecting recurrence and metastasis is another critical application of liquid biopsies. For instance, in lung cancer, liquid biopsies have shown high sensitivity in identifying metastatic spread and local recurrences, often before they are visible on imaging scans (Souza, *et al*., 2023). This capability allows for timely changes in therapeutic strategies, improving patient outcomes. Similarly, in colorectal cancer, ctDNA levels are used to monitor for metastatic disease, providing a minimally invasive alternative to traditional methods (Trapp, *et al*., 2019). Nonetheless, inter-patient variability in ctDNA levels and differences in tumor shedding rates can limit universal application, underscoring the need for case-specific interpretation.

Assessing treatment efficacy and resistance mechanisms is also facilitated by liquid biopsies. These tests can detect mutations associated with resistance to specific therapies, enabling clinicians to adjust treatment plans in real-time. For example, in breast cancer, tracking ctDNA has been used to monitor the effectiveness of chemotherapy and identify the emergence of resistance mutations, thus informing subsequent therapeutic decisions (Pierga, *et al*., 2015). That said, false negatives due to transient ctDNA suppression during therapy are possible, warranting repeat sampling or combination with imaging.

Furthermore, the ability to conduct real-time monitoring of tumor evolution is a significant advantage of liquid biopsies. This continuous monitoring can capture the dynamic changes within a tumor's genetic landscape, allowing for a more tailored and responsive treatment approach. In prostate cancer, for example, serial liquid biopsies have been employed to track genetic alterations over time, providing insights into tumor behavior and helping to guide precision medicine (Goodman, *et al*., 2018). This longitudinal approach has yielded promising insights, though some studies caution about sequencing error accumulation over time, highlighting the importance of using error-correction algorithms.

CHALLENGES AND LIMITATIONS

Liquid biopsies, despite their promising potential, face several technical and analytical challenges. One of the primary issues is the detection limits inherent to the technology. The low abundance of ctDNA and CTCs in early-stage cancers requires highly sensitive methods to detect and quantify these biomarkers accurately (Tsui, *et al*., 2020). Standardization of pre-analytical and analytical processes is crucial to ensure reproducibility and reliability of results. Variables such as the type of blood collection tubes, time to processing, and DNA extraction methods can significantly impact the quality and quantity of ctDNA obtained (Ghosh, 2022).

Biological variability also presents a significant challenge. The heterogeneity of tumors means that different regions of the same tumor may release different genetic materials into the bloodstream. Moreover, biological processes such as clonal hematopoiesis can lead to the presence of non-tumor-derived mutations in the blood, complicating the interpretation of liquid biopsy results (Deveson, *et al*., 2021). These factors necessitate the development of robust algorithms and reference standards to differentiate between true tumor-derived signals and background noise.

Regulatory and ethical considerations further complicate the widespread adoption of liquid biopsies. The regulatory landscape is still evolving, with differences in requirements between regions such as the United States and the European Union. The lack of standardized guidelines for the validation and clinical implementation of liquid biopsy tests means that their clinical utility and reliability can vary significantly between different assays and laboratories (Montagut, 2022). Ethical issues, including patient consent and data privacy, must also be addressed to ensure the responsible use of genetic information obtained from liquid biopsies.

Cost-effectiveness is another crucial factor influencing the clinical adoption of liquid biopsies. While these tests offer a less invasive and potentially more comprehensive assessment of the tumor genome compared to traditional tissue biopsies, they can be expensive. The high costs associated with advanced sequencing technologies and the need for repeated testing to monitor disease progression can limit their accessibility, particularly in resource-constrained settings (Cristiano, *et al*., 2019). A recent cost-effectiveness study found that incorporating liquid biopsy in colorectal cancer screening reduced late-stage diagnoses and saved an estimated $1,500 per patient annually (Cristiano, *et al*., 2019). Comprehensive cost-benefit analyses are required to determine the economic feasibility of integrating liquid biopsies into routine clinical practice.

FUTURE DIRECTIONS AND EMERGING TRENDS

The field of liquid biopsies is rapidly evolving, with several promising future directions and emerging trends. One such trend is the adoption of multi-omic approaches, which integrate different biomarkers to provide a more comprehensive view of cancer biology. By combining genomic, transcriptomic, proteomic, and metabolomic data from CTCs, cfDNA, and other analytes, multi-omic liquid biopsies can capture the complexity of tumor heterogeneity and evolution more accurately than single-analyte approaches (Hasin, *et al*., 2017).

Another key trend is the development of liquid biopsy-based companion diagnostics, which can guide treatment decisions by identifying specific mutations and other biomarkers that predict response to targeted therapies. For instance, liquid biopsy tests detecting EGFR mutations in non-small cell lung cancer are already used to select patients for EGFR inhibitor treatments (Kumar, *et al*., 2022). These companion diagnostics have the potential to make precision medicine more accessible and effective.

Artificial intelligence (AI) and machine learning (ML) are also playing an increasingly important role in liquid biopsy analyses. These technologies can handle the vast amounts of data generated by multi-omic approaches, identifying patterns and correlations that might be missed by traditional statistical methods. AI and ML can enhance the sensitivity and specificity of liquid biopsies, improve the interpretation of complex data sets, and enable real-time monitoring of tumor dynamics (Graves & Haystead, 2002).

The integration of liquid biopsies into personalized medicine strategies is another exciting frontier. Personalized medicine involves

tailoring treatment to the individual characteristics of each patient's disease. Liquid biopsies, with their ability to provide continuous, real-time insights into tumor genetics and dynamics, are ideally suited to support personalized treatment plans. This approach could lead to more effective and less toxic cancer therapies, as treatments can be adjusted based on the latest molecular information from the patient's tumor (Horgan & Kenny, 2011).

CONCLUSION

In conclusion, liquid biopsies represent a transformative advance in oncology, offering a minimally invasive means to detect, monitor, and guide the treatment of cancer. With technological advances such as next-generation sequencing and PCR-based methods, the sensitivity and specificity of these tests have significantly improved, enabling the detection of CTCs, cfDNA, and ctDNA. Despite challenges related to technical limitations, biological variability, and regulatory and ethical considerations, the potential for multi-omic approaches, the integration of artificial intelligence and machine learning, and the development of liquid biopsy-based companion diagnostics are paving the way for their broader application in personalized medicine. Despite their promise, barriers such as high test costs, lack of standardization, and limited reimbursement pathways hinder clinical adoption. Future research should continue to evaluate cross-study variability in biomarker performance, optimize assay consistency, and integrate clinical validation pipelines that address both sensitivity and population-level applicability. As the technology continues to evolve, liquid biopsies are poised to become a cornerstone in the early detection and continuous monitoring of cancer, significantly impacting patient outcomes and treatment strategies.

REFERENCES

Bankó, P., Lee, S.Y., Nagygyörgy, V., Zrínyi, M., Chae, C.H., Cho, D.H., and Telekes, A., 2019, Technologies for circulating tumor cell separation from whole blood, *Journal of Hematology & Oncology*, **12**(1), 48.

Bettegowda, C., Sausen, M., Leary, R.J., Kinde, I., Wang, Y., Agrawal, N., *et al.*, 2014, Detection of circulating tumor DNA in early- and late-stage human malignancies, *Science Translational Medicine*, **6**(224), 224ra24.

Cristiano, S., Leal, A., Phallen, J., Fiksel, J., Adleff, V., Bruhm, D.C., 2019, Genome-wide cell-free DNA fragmentation in patients with cancer, *Nature*, **570**(7761), 385–389.

Dao, J., Conway, P.J., Subramani, B., Meyyappan, D., Russell, S., and Mahadevan, D., 2023, Using cfDNA and ctDNA as Oncologic Markers: A Path to Clinical Validation, *International Journal of Molecular Sciences*, **24**(17), 13219.

Deveson, I.W., Gong, B., Lai, K., LoCoco, J.S., Richmond, T.A., Schageman, J., *et al.*, 2021, Evaluating the analytical validity of circulating tumor DNA sequencing assays for precision oncology, *Nature Biotechnology*, **39**, 1115–1128.

El Achi, H., Khoury, J.D., and Loghavi, S., 2019, Liquid Biopsy by Next-Generation Sequencing: a Multimodality Test for Management of Cancer, *Current Hematologic Malignancy Reports*, **14**, 358–367.

Goodman, C.R., Seagle, B.L., Friedl, T.W.P., Rack, B., Lato, K., Fink, V., 2018, Association of Circulating Tumor Cell Status With Benefit of Radiotherapy and Survival in Early-Stage Breast Cancer, *JAMA oncology*, **4**(8), e180163.

Graves, P.R., and Haystead, T.A., 2002, Molecular biologist's guide to proteomics, *Microbiology and Molecular Biology Reviews: MMBR*, **66**(1), 39–63.

Hasin, Y., Seldin, M., and Lusis, A., 2017, Multi-omics approaches to disease, *Genome Biology*, **18**, 83.

Heitzer, E., Haque, I.S., Roberts, C.E.S., and Speicher, M.R., 2019, Current and future perspectives of liquid biopsies in genomicsdriven oncology, *Nature Reviews Genetics*, **20**, 71–88.

Horgan, R.P., and Kenny, L.C., 2011, 'Omic' technologies: genomics, transcriptomics, proteomics and metabolomics, *The Obstetrician & Gynaecologist*, **13**(3), 189–195.

Ignatiadis, M., and Reinholz, M., 2011, Minimal residual disease and circulating tumor cells in breast cancer, *Breast Cancer Research*, **13**, 222.

Jensen, T.J., Goodman, A.M., Kato, S., Ellison, C.K., Daniels, G.A., Kim, L., *et al.*, 2019, Genome-Wide Sequencing of Cell-Free DNA Identifies Copy-Number Alterations That Can Be Used for Monitoring Response to Immunotherapy in Cancer Patients, *Molecular Cancer Therapeutics*, **18**(2), 448–458.

Ju, S., Chen, C., Zhang, J., Xu, L., Zhang, X., Li, Z., *et al.*, 2022, Detection of circulating tumor cells: opportunities and challenges, *Biomarker Research*, **10**, 58.

Kalluri, R., and LeBleu, V.S., 2020, The biology, function, and biomedical applications of exosomes, *Science*, **367**(6478), eaau6977.

Kumar, V., Garg, V.K., Kumar, S., and Biswas, J.K., 2022, Omics for Environmental Engineering and Microbiology Systems. In CRC Press eBooks. https://doi.org/10.1201/9781003247883

Lone, S.N., Nisar, S., Masoodi, T., Singh, M., Rizwan, A., Hashem, S., *et al.*, 2022, Liquid biopsy: a step closer to transform diagnosis, prognosis and future of cancer treatments, *Molecular cancer*, **21**, 79.

Milbury, C.A., Li, J., and Makrigiorgos, G.M., 2009, PCR-based methods for the enrichment of minority alleles and mutations, *Clinical Chemistry*, **55**(4), 632–640.

Mitchell, P.S., Parkin, R.K., Kroh, E.M., Fritz, B.R., Wyman, S.K., Pogosova-Agadjanyan, E.L., *et al.*, 2008, Circulating microRNAs as stable blood-based markers for cancer detection, Proceedings of the National Academy of Sciences of the United States of America, **105**(30), 10513–10518.

Nair, N., Camacho-Vanegas, O., Rykunov, D., Dashkoff, M., Camacho, S.C., Schumacher, C.A., *et al.*, 2016, Genomic Analysis of Uterine Lavage Fluid Detects Early Endometrial Cancers and Reveals a Prevalent Landscape of Driver Mutations in Women without Histopathologic Evidence of Cancer: A Prospective Cross-Sectional Study, *PLoS Medicine*, **13**(12), e1002206.

Ogt. (n.d.). Liquid biopsy: advantages, limitations & outlook | OGT blog. OGT. https://www.ogt.com/about-us/ogt-blog/liquid-biopsy-advantages-limitations-and-outlook/.

Pierga, J.Y., Petit, T., Lévy, C., Ferrero, J.M., Campone, M., Gligorov, J., *et al.*, 2015, Pathological response and circulating tumor cell count identifies treated HER2+ inflammatory breast cancer patients with excellent prognosis: BEVERLY-2 survival data, *Clinical Cancer Research*, **21**(6), 1298–1304.

Robertson, E.G., and Baxter, G., 2011, Tumour seeding following percutaneous needle biopsy: the real story!, *Clinical Radiology*, **66**(11), 1007–1014.

Shen, H., Jin, Y., Zhao, H., Wu, M., Zhang, K., Wei, Z., *et al.*, 2022, Potential clinical utility of liquid biopsy in early-stage non-small cell lung cancer, *BMC Medicine*, **20**, 480.

Siravegna, G., Marsoni, S., Siena, S., and Bardelli, A., 2017, Integrating liquid biopsies into the management of cancer, *Nature Reviews Clinical Oncology*, **14**, 531–548.

Souza, V.G.P., Forder, A., Brockley, L.J., Pewarchuk, M.E., Telkar, N., de Araújo, R.P., *et al.*, 2023, Liquid Biopsy in Lung Cancer: Biomarkers for the Management of Recurrence and Metastasis, *International Journal of Molecular Sciences*, **24**(10), 8894.

Staff, C.T., 2021, How Liquid Biopsies Can Complement Tissue Biopsies-American Association for Cancer

Research (AACR), American Association for Cancer Research (AACR). https://www.aacr.org/blog/2021/03/19/how-liquid-biopsies-can-complement-tissue-biopsies/.

Tao, X.Y., Li, Q.Q., and Zeng, Y., 2024, Clinical application of liquid biopsy in colorectal cancer: detection, prediction, and treatment monitoring, *Molecular Cancer*, **23**, 145.

Théry, C., Witwer, K.W., Aikawa, E., Alcaraz, M.J., Anderson, J.D., Andriantsitohaina, R., *et al.*, 2018, Minimal information for studies of extracellular vesicles 2018 (MISEV2018): a position statement of the International Society for Extracellular Vesicles and update of the MISEV2014 guidelines, *Journal of Extracellular Vesicles*, **7**(1), 1535750.

Trapp, E., Janni, W., Schindlbeck, C., Jückstock, J., Andergassen, U., de Gregorio, A., *et al.*, 2019, Presence of Circulating Tumor Cells in High-Risk Early Breast Cancer During Follow-Up and Prognosis, *Journal of the National Cancer Institute*, **111**(4), 380–387.

Tsui, D.W.Y., Blumenthal, G.M., Philip, R., Barrett, J.C., Montagut, C., Bramlett, K., *et al.*, 2020, Development, Validation, and Regulatory Considerations for a Liquid Biopsy Test, *Clinical chemistry*, **66**(3), 408–414.

Vidlarova, M., Rehulkova, A., Stejskal, P., Prokopova, A., Slavik, H., Hajduch, M., and Srovnal, J., 2023, Recent Advances in Methods for Circulating Tumor Cell Detection, *International Journal of Molecular Sciences*, **24**(4), 3902.

Wishart D.S., 2019, Metabolomics for Investigating Physiological and Pathophysiological Processes, *Physiological Reviews*, **99**(4), 1819–1875.

Zhu, W., Love, K., Gray, S.W., and Raz, D.J., 2023, Liquid Biopsy Screening for Early Detection of Lung Cancer: Current State and Future Directions, *Clinical Lung Cancer*, **24**(3), 209–217.