Oncology, Nuclear Medicine and Transplantology

Review Article

The Role of Liquid Biopsies in Tracking Tumor Evolution and Overcoming Therapeutic Resistance in Cancer

Tosin Ayodeji Oladosu[1], Chinaecherem Peace Okafor[2], Patrick Chinazam Nwosu[3], Ayo Ebunolorun Ibukunoluwa[4], Uduh Ifeoma Monica[5], Tosin Abiodun Aderanti[6]

[1]*Department of Chemistry and Biochemistry, University of Minnesota Duluth, Duluth, MN, USA*
[2]*Department of Biochemistry, Federal university of Technology, Owerre, Imo State, Nigeria*
[3]*Clinical Lead Rehabilitation and Quality Department, San Ramo Nursing and Rehabilitation Center, Garland, TX, USA*
[4]*Department of Nutritional Sciences, Auburn University, Auburn, AL, USA*
[5]*Department of Dentistry, University of Port Harcourt, Port Harcourt, Rivers State, Nigeria*
[6]*Department of Chemical and Environmental Sciences, Babcock University, Ilishan-Remo, Ogun State, Nigeria*

Received: Oct 01, 2025
Accepted: Oct 01, 2025

Corresponding author's email:
olado012@d.umn.edu

Abstract:
Liquid biopsies have developed as a revolutionary technique in cancer diagnosis, treatment evaluation, and the detection of therapeutic resistance. Unlike traditional tissue biopsies, which are invasive and limited to a single temporal analysis, liquid biopsies offer a non-invasive, real-time evaluation of tumour dynamics through the analysis of biomarkers such as circulating tumour DNA (ctDNA), circulating tumour cells (CTCs), exosomes, and microRNAs. This approach enables continuous monitoring of tumour advancement, allowing for the early detection of cancer, the tracking of minimal residual disease, and the identification of emerging resistance mutations. As cancers advance and acquire resistance to therapies, liquid biopsy provides critical information that enables clinicians to customise treatment strategies and improve outcomes. Despite challenges such as sensitivity limitations in early-stage cancers and the necessity for standardised testing protocols, technological advancements, including next-generation sequencing (NGS), CRISPR, and AI-driven analytics, are enhancing the precision and accessibility of liquid biopsies. Through ongoing validation and cost-reduction efforts, liquid biopsies are set to become essential to precision oncology, offering a transformative approach to cancer therapy that could improve patient outcomes and foster equitable healthcare globally.

Keywords: Liquid Biopsy; Circulating Tumor DNA (ctDNA); Therapeutic Resistance; Minimal Residual Disease (MRD); Precision Oncology

Introduction

Overview of Liquid Biopsy

Non-invasive liquid biopsy examines blood, urine, or saliva to identify and track malignancy. Liquid biopsies offer real-time genetic profiling of tumours without the need for invasive surgery. This approach focusses on biomarkers such as ctDNA, CTCs, exosomes, and microRNAs derived from bodily fluids. Liquid biopsy can identify mutations, track disease progression, and inform customised treatment without the need for repeated invasive procedures, rendering it highly favoured in oncology [1].

Relevance to Tumor Evolution and Therapeutic Resistance

Cancer cells undergo genetic and epigenetic evolution to promote disease progression, metastasis, and resistance to therapy. These modifications can transpire rapidly, leading to resistant subclones that obstruct chemotherapy, targeted therapies, and immunotherapy. Liquid biopsy facilitates the monitoring of tumour evolution and the understanding of genetic alterations and clonal dynamics that contribute to therapeutic resistance. Liquid biopsy enables clinicians to monitor disease development and identify resistance mutations in real time, facilitating adjustments to treatment programs. Enhanced patient outcomes rely on non-invasive tumour monitoring [2].

Objective of the Review

Liquid biopsies may facilitate the monitoring of tumour growth and address resistance to cancer therapies. This review will examine ctDNA, CTCs, and exosome liquid biopsies, along with their clinical applications in mutation identification, therapy response assessment, and therapeutic decision-making. The review will examine the existing limitations of liquid biopsy technologies and potential advancements that may enhance their therapeutic efficacy. This thorough review investigates the impact of liquid biopsies on oncology and the provision of novel tailored cancer treatment alternatives.

Background

Traditional Biopsy Limitations

Although crucial for cancer diagnosis and monitoring, traditional tissue biopsy possesses considerable limitations. The primary disadvantage of surgery to excise tissue samples is the potential threat it poses to patients, particularly those with advanced or metastatic cancers. Tissue biopsies are typically performed singularly, complicating the monitoring of tumour activity such as mutations or clonal evolution throughout treatment. Tumours exhibit heterogeneity, as distinct subclones possess varying molecular characteristics; therefore, a single biopsy may not comprehensively represent the genetic diversity. This limitation may hinder the identification of resistant mutations or the advancement of cancer in reaction to treatment [3].

Introduction of Liquid Biopsies

Liquid biopsies serve as a non-invasive alternative to tissue biopsies, mitigating the associated downsides. Liquid biopsies, introduced in the early 2000s, diagnose and monitor cancer through the use of biomarkers such as ctDNA, CTCs, and exosomes in blood samples. Liquid biopsies are simple to obtain, may be performed often without causing patient discomfort, and may provide superior insights into tumour dynamics. Advancements in next-generation sequencing (NGS) and microfluidics enhance the precision of liquid biopsy procedures, rendering them effective for early cancer detection, monitoring, and tracking therapy resistance [4].

Tumor Heterogeneity and Resistance

Cancer is complex and heterogeneous, exhibiting diverse genetic and epigenetic patterns across distinct tumour regions or metastases. Clonal evolution generates subclones exhibiting varying treatment sensitivities or resistances as a result of mutations. As cancers progress, they frequently acquire resistance to therapies, rendering previously effective treatments ineffective. Cancer's dynamic nature necessitates continuous surveillance for mutations and clonal alterations. Liquid biopsies provide the real-time identification of cancer evolution and resistance mutations by capturing genetic material shed from tumours into the circulation, thereby informing treatment decisions and enhancing patient outcomes [5].

Types of Liquid Biopsies

Circulating Tumor DNA (ctDNA)

Liquid biopsy depends on circulating tumour DNA (ctDNA), which consists of fragmented DNA released by cancer cells into the bloodstream. ctDNA analysis can identify mutations, genetic alterations, and resistance mutations in tumours without the need for tissue biopsies. The primary function of ctDNA in liquid biopsy is to represent the tumor's genetic composition and monitor cancer growth. ctDNA can contemporaneously monitor cancer genetic mutations in response to treatments, elucidating therapeutic efficacy and resistance mechanisms.

One of the primary advantages of ctDNA is its exceptional sensitivity in identifying minimal residual disease (MRD), the minute quantity of cancer cells that persist post-therapy and have the potential to return. Circulating tumour DNA (ctDNA) is crucial for early-stage cancer screening and post-treatment surveillance, as it can be identified even with a modest tumour burden. ctDNA analysis can identify residual disease prior to clinical signs of relapse, facilitating early intervention and tailored treatment [6].

In certain cancers or patients with modest tumour burden, the sensitivity of ctDNA may be compromised by inadequate circulation. The kind of tumour and the ctDNA extraction technique can influence the identification of certain mutations, highlighting the necessity for standardisation and enhancement.

Circulating Tumour Cells (CTCs)

Circulating tumour cells (CTCs) are individual cancer cells or small clusters that have detached from the primary tumour or metastases and have entered the bloodstream. Circulating tumour cells (CTCs), a promising liquid biopsy biomarker, indicate cancer dissemination, progression, and therapeutic resistance. Through the extraction and analysis of circulating tumour cells (CTCs), physicians can identify cancer dissemination, metastatic disease, and genomic characteristics of CTCs to inform personalised treatment strategies [7].

Circulating tumour cells (CTCs) can identify therapeutic resistance by revealing real-time genetic and phenotypic changes in the cancer. When a medicine reduces tumour size but CTC analysis reveals resistance mutations, physicians may modify the treatment. Real-time resistance monitoring decreases treatment delays and enhances outcomes [8].

Circulating CTCs are few, complicating investigation. Circulating tumour cells (CTCs) are infrequent, particularly in early-stage malignancies characterised by confined illness, hence complicating their detection and separation. Microfluidics and immunomagnetic capture technologies enhance circulating tumour cell (CTC) isolation; however, obtaining high-quality CTCs for subsequent molecular analysis remains challenging [9].

Exosomes and MicroRNAs

Exosomes transport proteins, lipids, and nucleic acids from the tumour to the bloodstream. These vesicles communicate between cells and promote tumour growth, metastasis, and therapy resistance. Exosomes carry tumor-specific mutations and non-coding RNAs, making them useful liquid biopsy biomarkers. Cancer liquid biopsies have focused on exosomal miRNAs as biomarkers [10].

Cancer commonly alters miRNAs, tiny non-coding RNAs that influence gene expression. Exosomal miRNAs reveal tumour features, progression, and treatment resistance pathways. MiRNAs are persistent in body fluids and less prone to degradation, making exosome identification a dependable and non-invasive technique to monitor cancer dynamics.

Exosomes and miRNAs are still being tested as liquid biopsy indicators. Isolating exosomes from complicated bodily fluids and standardising their characterisation techniques are difficult. Exosome-based liquid biopsies may be useful for real-time cancer monitoring, but additional study is needed to validate and standardise methods [11].

Other Emerging Biomarkers

Besides ctDNA, CTCs, and exosomes, various indicators are being studied for liquid biopsy. Long non-coding RNAs (lncRNAs) regulate gene expression and are linked to cancer start and progression. LncRNAs are persistent in plasma and serum and may reveal tumour behaviour and therapy response [12].

Proteins and metabolites are promising liquid biopsy candidates. Tumor-derived proteins like CA-125 and EGFR can be found in the circulation and indicate tumour progression and therapy resistance. Circulating metabolites also reflect tumour metabolism, giving a non-genetic way to track tumour dynamics [13].

These developing biomarkers offer new liquid biopsy potential, but detection sensitivity, specificity, and clinical validation remain problems. As the science improves, multi-omics techniques with many biomarker types may improve liquid biopsies for cancer diagnosis and therapy monitoring.

Liquid biopsy methods based on ctDNA, CTCs, exosomes, and developing biomarkers have great potential for real-time cancer surveillance and personalised treatment. Each form of biomarker has its own limitations, but improved detection technologies and clinical relevance will certainly increase their use in oncology. Liquid biopsy is becoming a popular non-invasive cancer diagnostic, monitoring, and treatment tool. Fig 1 shows how liquid biopsy indicators such cfDNA, ctDNA, and CTCs monitor tumour state from diagnosis to treatment and recurrence [14].

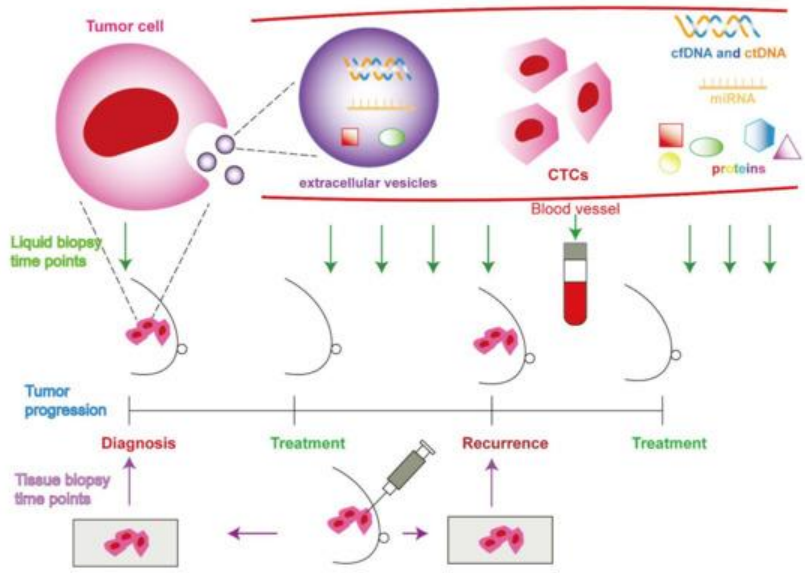

Fig 1 Liquid Biopsy and Tumor Progression Monitoring: A Visual Guide. This figure illustrates the key components involved in liquid biopsy for cancer monitoring, including tumor cells, extracellular vesicles, and circulating tumor cells (CTCs). The image highlights the use of cfDNA, ctDNA, miRNA, and proteins as biomarkers for tumor progression at various time points, such as diagnosis, treatment, and recurrence. The diagram also contrasts liquid biopsy with tissue biopsy, emphasizing its relevance at different stages of cancer management.Zhu, X., Wu, J., Xu, J., et al. (2020).

Mechanisms of Tumor Evolution and Therapeutic Resistance

Genetic Mutations and Clonal Evolution

Genetic mutations facilitate the evolution of cancer throughout time. Genetic alterations in cancer cells override normal cellular regulations, resulting in unchecked proliferation and spread. Errors in DNA replication and exposure to carcinogens induce genetic mutations. As cancer progresses, genetic heterogeneity increases, resulting in a diverse population of tumour cells, referred to as "clonal evolution." Mutations in tumour subclones can enhance proliferation, facilitate immune evasion, and confer treatment resistance [15].

Liquid biopsy is an effective technique for the real-time detection of genetic abnormalities. Liquid biopsy analyses circulating tumour DNA (ctDNA) from bodily fluids, providing insights into the tumor's genetic landscape and facilitating the identification of mutations, deletions, and amplifications linked to tumour evolution. As malignancies progress, specific mutations or genetic anomalies may become more pronounced, fostering resistance to therapies. In non-small cell lung cancer (NSCLC), mutations in the EGFR gene, such as exon 19 deletions or T790M, may develop over time, resulting in resistance to first-line EGFR treatments. Liquid biopsy facilitates the ongoing surveillance of these mutations, allowing for prompt intervention and modifications in treatment [16].

Tumor Microenvironment

The advancement of cancer and resistance to therapy are influenced by the tumour microenvironment (TME). The tumour microenvironment comprises non-malignant cells such as fibroblasts, immune cells, blood vessels, and extracellular matrix constituents that influence tumour cells. Modifying the TME can induce significant changes that promote resistance. Cancer-associated fibroblasts (CAFs) can shield cancer cells from chemotherapy-induced apoptosis, whereas tumor-infiltrating immune cells can enhance or inhibit tumour immunity.

Cell-free DNA (cfDNA) and RNA from the tumour microenvironment (TME) can be obtained using liquid biopsy, elucidating the influence of the TME on resistance mechanisms. Both cancerous and non-tumor cells release cfDNA, which can signify abnormalities in the tumour microenvironment, such as hypoxia, angiogenesis, and immunological modulation. Exosomal RNA from the cancer and adjacent stromal cells provide essential insights on the tumor's therapeutic response and developing resistance mechanisms. Through liquid biopsy, clinicians can identify genetic modifications in the tumour as well as the dynamic interactions between the tumour and its environment that lead to therapeutic resistance [17,18].

Therapeutic Resistance Mechanisms

Tumours often acquire resistance to chemotherapy, immunotherapy, and targeted medicines, making cancer treatment difficult. Mutations, TME changes, and compensatory signalling

pathways drive these resistance mechanisms. One prevalent [19] cause of chemotherapy resistance is the selection of tumour cells with mutations in genes involved in drug metabolism, efflux, or DNA repair. Mutations in the TP53 gene, which encodes the tumour suppressor p53, often cause cisplatin resistance in many malignancies [19]. Mutations can be detected by liquid biopsy, identifying people at risk for poor treatment outcomes.

- Immunotherapy Resistance: While immunocheckpoint inhibitors (ICIs) like pembrolizumab and nivolumab have revolutionised cancer treatment, not all patients respond. Mutations in genes like PD-L1 or tumour antigen presentation abnormalities can cause immunotherapy resistance. Liquid biopsy can predict immunotherapy response by detecting immune-related gene changes such PD-L1 expression or tumour antigen-presenting machinery mutations [20].
- Targeted Therapy Secondary mutations that bypass the blocked route cause targeted therapy resistance. The T790M mutation in the EGFR gene hinders first-generation EGFR inhibitors from attaching to NSCLC cells, causing resistance. Similar to colorectal cancer, KRAS mutations can cause EGFR-targeted therapy resistance. Liquid biopsy can detect ctDNA resistance mutations in real time, guiding therapeutic changes and detecting resistant clones.

Genetic mutations, TME alterations, and adaptive signalling pathways constitute the complicated mechanisms of cancer treatment resistance. Liquid biopsy can identify these changes, enabling tumour evolution tracking and personalised treatment adjustments. Liquid biopsy helps overcome therapeutic resistance and improve clinical outcomes by detecting genetic alterations, immune-related indicators, and extracellular variables [21].

Fig 2 shows the intricate interactions that affect tumour immune evasion and cancer therapy efficacy. It classifies these components as tumor-intrinsic, tumour microenvironmental, and host-related, each contributing to cancer therapy's dynamic immune response.

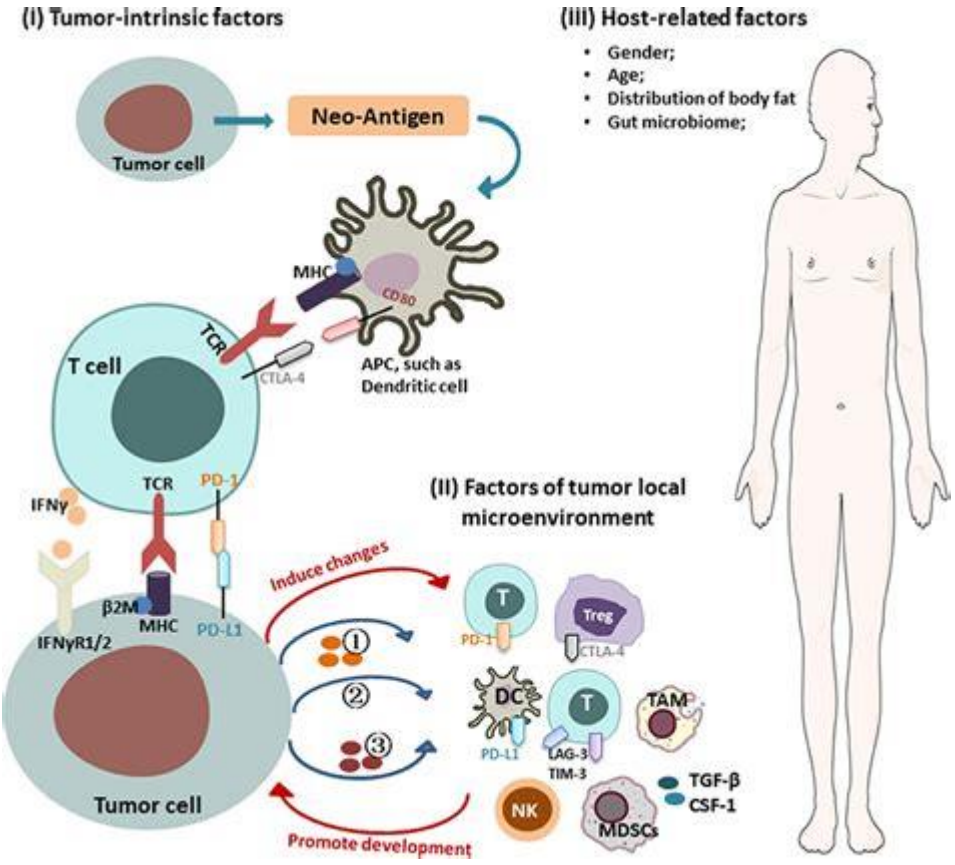

Fig 2: **Mechanisms of Cancer Resistance to Immunotherapy**" by Rilan Bai et al., published in *Frontiers in Oncology* in 2020. This figure visually summarizes the multifaceted mechanisms through which tumors resist immune checkpoint inhibitors (ICIs), categorizing them into tumor-intrinsic factors,

tumor-extrinsic factors, and host-related factors.Bai, R., Chen, N., Li, L., Du, N., Bai, L., Lv, Z., Tian, H., & Cui, J. (2020).

Clinical Applications of Liquid Biopsies

Early Detection and Diagnosis

As a non-invasive alternative to imaging and tissue biopsy, liquid biopsies seem promising for early cancer detection. Liquid biopsies can detect cancer-related genetic changes in asymptomatic or high-risk individuals before clinical signs develop, which is a major benefit. Studies have shown that ctDNA can be found in early-stage cancer patients' blood even when tumours are too tiny to image. Early cancer detection allows for faster interventions and better treatments, improving survival rates.

Recent clinical trials have used liquid biopsies to screen lung cancer. In 2020, JAMA Oncology reported that ctDNA screening in high-risk lung cancer patients detected disease mutations early, enabling early therapies that improved patient outcomes. In colorectal, breast, and ovarian cancers, liquid biopsies may be useful for early screening, especially in hard-to-screen populations [22].

Monitoring Tumor Evolution

Liquid biopsy facilitates real-time monitoring of tumour progression and therapy efficacy. Conventional tissue biopsies capture the tumor's genetic landscape at a specific moment, although they fail to detect dynamic changes. As cancers advance, new mutations, metastasis, and treatment resistance may arise. Liquid biopsy facilitates continuous observation of these changes, disclosing tumour progression throughout therapy [23].

In breast cancer and melanoma, ctDNA analysis monitors tumour mutations and clonal evolution in real time. Nature Medicine published findings on utilising ctDNA to monitor patients with metastatic melanoma during treatment. Alterations in ctDNA levels forecasted disease progression or remission and correlated with tumour response to treatment. By monitoring these alterations through liquid biopsy, clinicians can implement more informed treatment modifications to provide patients with optimal therapy tailored to their tumour profile [24].

Tracking Therapeutic Resistance

A primary clinical application of liquid biopsies is the monitoring of therapy resistance. Chemotherapy, targeted treatments, and immunotherapies reduce tumours; nonetheless, resistance leads to recurrence or disease progression. Clinicians can modify treatment protocols by identifying resistance mutations in real time by liquid biopsy.

Monitoring ctDNA in non-small cell lung cancer exemplifies the role of liquid biopsy in tracking resistance. Secondary mutations, such as the T790M mutation, can render epidermal growth factor receptor (EGFR) therapy ineffective for patients with non-small cell lung cancer (NSCLC). Liquid biopsy can identify this ctDNA mutation, enabling clinicians to transition to a third-generation EGFR inhibitor prior to the manifestation of clinical resistance. Early discovery of resistance mutations enhances patient outcomes by facilitating prompt therapy adjustments to halt disease progression [13,16].

Minimal Residual Disease and Monitoring Metastasis

MRD is the small amount of cancer cells that remain after treatment and might induce relapse. Patients in remission or needing extra treatment are identified by MRD detection. MRD detection requires liquid biopsy in haematologic malignancies like leukaemia, where ctDNA and CTCs can track small quantities of cancer cells in the bloodstream.

The Lancet Oncology examined acute lymphoblastic leukaemia patients for MRD using ctDNA. The study found that rising ctDNA levels required intervention before clinical recurrence. High-risk patients may receive targeted therapy or stem cell transplants before illness recurrence.

In addition to MRD, liquid biopsy can track metastases. Cancer metastasis can be indicated by CTCs or ctDNA in the blood. CTCs follow breast cancer's liver and lung spread. CTCs and ctDNA levels enable clinicians track cancer progression, assess treatment efficacy, and adjust treatment based on metastasis [25].

Liquid biopsy detects early detection, tumour evolution, medication resistance, minimal residual disease, and metastasis, revolutionising cancer care. By providing real-time, non-invasive genetic and molecular insights into cancer, liquid biopsy improves patient outcomes and personalised treatment. Advanced liquid biopsy technology and clinical validation will boost their cancer management stance.

Challenges and Limitations

Sensitivity and Specificity

Clinically, liquid biopsies' sensitivity and specificity for biomarkers such ctDNA and CTCs are problematic. Although promising for cancer identification and medication resistance monitoring, liquid biopsies can be insensitive in early-stage malignancies or patients with low tumour load. Sometimes circulating ctDNA or CTCs are too low to detect. Early-stage cancers or small tumours may release insufficient ctDNA into the bloodstream, reducing liquid biopsy sensitivity. A false positive or negative might misrepresent disease state and lead to unnecessary treatments or missed early intervention.

For pancreatic or glioblastoma, liquid biopsies are less sensitive than lung or colorectal ones. This limitation is especially obvious in mild metastatic activity, where tumor-derived DNA or cells are infrequently discharged. Clinical study attempts to increase liquid biopsy test sensitivity by increasing sequencing depth or CTC separation [26].

Technical and Standardization Issues

Laboratory standardisation hinders liquid biopsy uptake. There is no standard liquid biopsy protocol, hence results vary. Sample collection, processing, DNA extraction, and sequencing vary amongst labs, lowering accuracy and reproducibility. Different ctDNA or CTC separation methods can impact sensitivity, and sequencing or bioinformatics analysis tools can affect data interpretation.

Unharmonised criteria make it difficult to compare study and clinical results. Liquid biopsy is unpredictable, making it challenging to employ clinically and diagnostically. From blood collection to molecular analysis, liquid biopsy workflows are being standardised to ensure consistent results across healthcare settings [26].

Cost and Accessibility

Liquid biopsies are rarely employed in low- and middle-income countries due to the high cost of sequencing technologies like NGS. Specialised equipment and skilled workers are needed to process liquid biopsy samples, increasing costs. Due to liquid biopsy limitations, resource-limited patients may not have access to advanced diagnostic procedures. High sequencing costs limit the number of tests, making routine monitoring or screening problematic, especially for low-detection tumours or remission patients. Make liquid biopsy technologies more affordable and lower sequencing costs to make them more accessible. Cheaper sequencing platforms and easier tumor-derived DNA or cell extraction could solve these issues [22].

Ethical and Regulatory Barriers

Ethical and regulatory difficulties with liquid biopsy include genetic data privacy and test regulation. Privacy, consent, and usage issues arise when liquid biopsies show a person's genetic vulnerability to cancer and other diseases. Patients' genetic data must be securely stored, communicated, and used ethically for liquid biopsies to become common.

The FDA and EMA challenge fluid biopsy tests. Clinical validation ensures the accuracy, reliability, and clinical usefulness of regulatory-certified liquid biopsy assays. The lack of regulatory frameworks for liquid biopsies makes clinical use problematic.

In conclusion, liquid biopsies can diagnose, monitor, and treat cancer, but their sensitivity, standardisation, cost, and regulatory approval must be addressed. These restrictions must be solved by research, technology, and global collaboration to make liquid biopsies accessible, reliable, and standardised cancer tools [13,27].

Future Directions

Technological Advancements

NGS, CRISPR, and AI-driven analysis will shape liquid biopsies. By detecting even modest amounts of ctDNA, NGS has enhanced liquid biopsy sensitivity and depth, enabling earlier detection and more precise cancer evolution tracking. Liquid biopsies can detect more tumours and track resistance mechanisms as sequencing technology improves in speed, affordability, and accuracy.

CRISPR-based technologies, however new, could increase liquid biopsies' sensitivity and specificity. CRISPR may accurately change and enrich target DNA sequences, making medication resistance or minimal residual disease mutations easier to find. This method may boost sensitivity in low-tumor cases.

AI and ML for liquid biopsy data analysis is another intriguing improvement. AI algorithms can find complex patterns and subtle changes in vast sequencing and imaging datasets that people miss. AI-driven analysis could customise care, improve treatment, and discover cancer biomarkers [28].

Integration with Other Diagnostics

As a standalone diagnostic tool, liquid biopsy is promising, but combining it with additional methods could improve cancer surveillance. More accurate cancer diagnosis may result from liquid biopsy and MRI, CT, and PET scans. Imaging shows tumour size and location, while liquid biopsy shows evolution, metastasis, and treatment resistance. This multi-modal

strategy may improve clinician decision-making and patient outcomes.

In confusing or difficult tissue biopsy results, combining liquid biopsy with normal biopsies may increase therapeutic usage. These technologies could validate liquid biopsy's genetic mutations and clinical relevance, confirming its place in personalised medicine [29].

Global Implementation and Cost Reduction

Making liquid biopsies more economical and accessible worldwide, especially in resource-limited settings, is crucial for their wider use. Increasing tumour marker detection efficiency and lowering sequencing costs will make liquid biopsy a realistic alternative for patients worldwide. Governments, academic institutions, and industry leaders are working together to cut liquid biopsy test costs and develop low-cost alternatives for usage in various healthcare settings.

The introduction of liquid biopsy technology to disadvantaged people in low- and middle-income nations could revolutionise diagnostics. Simplifying sample collection and developing portable, point-of-care liquid biopsy analysis equipment could lower costs and enable global implementation. These developments could democratise cancer care by providing early detection and continuous monitoring through liquid biopsies in all locations [30].

Liquid biopsy's future lies in developing more sensitive technologies, integrating complementing diagnostic procedures, and lowering prices and increasing accessibility worldwide. As these advances continue, liquid biopsy will become increasingly important in cancer detection, monitoring, and therapy worldwide.

Conclusion

Real-time liquid biopsies can track cancer progression and medication resistance, revolutionising oncology. Liquid biopsies assess cancer progression, determine minimum residual sickness, and change treatment options using biomarkers such ctDNA, CTCs, and exosomes. Early-stage cancer detection and therapy response monitoring are substantial advances over standard diagnostics.

Liquid biopsies could transform cancer treatment by offering more tailored and accurate options. Liquid biopsies can detect genetic mutations and track cancer changes, enabling earlier detection, better metastatic monitoring, and speedier treatment. These innovations offer patient-centered, flexible care.

Clinical validation and incorporation into clinical practice are liquid biopsies' future. As technology advances and costs fall, liquid biopsies will shape cancer diagnosis, monitoring, and treatment worldwide.

Acknowledgement

Authors' Contributions: Tosin Ayodeji Oladosu conceptualized and supervised the study. Chinaecherem Peace Okafor and Patrick Chinazam Nwosu conducted the literature review and data synthesis. Uduh Ifeoma Monica and Ayo Ebunolorun Ibukunoluwa contributed to manuscript drafting and critical revisions. Tosin Abiodun Aderanti assisted in editing, referencing, and formatting. All authors reviewed and approved the final manuscript.

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Disclosures: The authors declare no competing interests or conflicts of interest related to this work.

References

1. Adhit KK, Wanjari A, Menon S, K S. Liquid Biopsy: An Evolving Paradigm for Non-invasive Disease Diagnosis and Monitoring in Medicine. Cureus. 2023 Dec 8;15(12):e50176. doi:10.7759/cureus.50176
2. Baldassarre G, Serna IL de la, Vallette FM. Death-ision: the link between cellular resilience and cancer resistance to treatments. Molecular Cancer. 2025 May 15;24:144. doi:10.1186/s12943-025-02151-7
3. Hirahata T, Quraish R ul, Quraish A ul, Quraish S ul, Naz M, Razzaq MA. Liquid Biopsy: A Distinctive Approach to the Diagnosis and Prognosis of Cancer. Cancer Informatics. 2022 Feb 7;21:11769351221076062. doi:10.1177/11769351221076062
4. Ma L, Guo H, Zhao Y, Liu Z, Wang C, Bu J, et al. Liquid biopsy in cancer: current status, challenges and future prospects. Signal

Transduct Target Ther. 2024 Dec 2;9:336. doi:10.1038/s41392-024-02010-1
5. Zhang Y, Wang W. Advances in tumor subclone formation and mechanisms of growth and invasion. J Transl Med. 2025 Apr 21;23:461. doi:10.1186/s12967-025-05879-0
6. Yin H, Zhang M, Zhang Y, Zhang X, Zhang X, Zhang B. Liquid biopsies in cancer. Mol Biomed. 2025 Mar 20;6:18. doi:10.1186/s43556-025-00166-8
7. Lawrence R, Watters M, Davies CR, Pantel K, Lu YJ. Circulating tumour cells for early detection of clinically relevant cancer. Nat Rev Clin Oncol. 2023 Jun 2;1–14. doi:10.1038/s41571-023-00781-y
8. Labib M, Kelley SO. Circulating tumor cell profiling for precision oncology. Mol Oncol. 2021 Jun;15(6):1622–46. doi:10.1002/1878-0261.12988
9. Deng Z, Wu S, Wang Y, Shi D. Circulating tumor cell isolation for cancer diagnosis and prognosis. eBioMedicine. 2022 Aug 27;83:104237. doi:10.1016/j.ebiom.2022.104237
10. Javdani-Mallak A, Mowla SJ, Alibolandi M. Tumor-derived exosomes and their application in cancer treatment. J Transl Med. 2025 Jul 8;23:751. doi:10.1186/s12967-025-06051-4
11. Sychowski G, Romanowicz H, Ciesielski W, Hogendorf P, Durczyński A, Smolarz B. Diagnostic and Therapeutic Potential of Selected microRNAs in Colorectal Cancer: A Literature Review. Cancers. 2025 Jan;17(13):2135. doi:10.3390/cancers17132135
12. Saha D, Kanjilal P, Kaur M, Menon SV, Ashraf A, Kumar MR, et al. Transforming Cancer Diagnostics: The Emergence of Liquid Biopsy and Epigenetic Markers. MedComm (2020). 2025 Sep 14;6(9):e70388. doi:10.1002/mco2.70388
13. Pandey S, Yadav P. Liquid biopsy in cancer management: Integrating diagnostics and clinical applications. Pract Lab Med. 2024 Dec 24;43:e00446. doi:10.1016/j.plabm.2024.e00446
14. Wu HJ, Chu PY. Current and Developing Liquid Biopsy Techniques for Breast Cancer. Cancers. 2022 Jan;14(9):2052. doi:10.3390/cancers14092052
15. El Nachef L, Bouchet A, Bourguignon M, Foray N. When DNA Mutations Interplay with Cellular Proliferation: A Narrative History of Theories of Carcinogenesis. Cancers. 2024 Jan;16(11):2104. doi:10.3390/cancers16112104
16. Wang H, Zhang Y, Zhang H, Cao H, Mao J, Chen X, et al. Liquid biopsy for human cancer: cancer screening, monitoring, and treatment. MedComm (2020). 2024 May 28;5(6):e564. doi:10.1002/mco2.564
17. Asadi M, Zafari V, Sadeghi-Mohammadi S, Shanehbandi D, Mert U, Soleimani Z, et al. The role of tumor microenvironment and self-organization in cancer progression: Key insights for therapeutic development. Bioimpacts. 2024 Dec 7;15:30713. doi:10.34172/bi.2024.30713
18. Fatima S. Tumor Microenvironment: A Complex Landscape of Cancer Development and Drug Resistance. Cureus. 2025;17(4):e82090. doi:10.7759/cureus.82090
19. Lei Z, Tian Q, Teng Q, Wurpel JND, Zeng L, Pan Y, et al. Understanding and targeting resistance mechanisms in cancer. MedComm (2020). 2023 May 22;4(3):e265. doi:10.1002/mco2.265
20. Liu J, Cai Y, Liu J, Chen D, Wu X. Immunotherapy Resistance and Therapeutic Strategies in PD-L1 High Expression Non-Small Cell Lung Cancer. Onco Targets Ther. 2025 Aug 29;18:953–66. doi:10.2147/OTT.S503348
21. Wu J, Lin Z. Non-Small Cell Lung Cancer Targeted Therapy: Drugs and Mechanisms of Drug Resistance. International Journal of Molecular Sciences. 2022 Jan;23(23):15056. doi:10.3390/ijms232315056
22. Connal S, Cameron JM, Sala A, Brennan PM, Palmer DS, Palmer JD, et al. Liquid biopsies: the future of cancer early detection. J Transl Med. 2023 Feb 11;21:118. doi:10.1186/s12967-023-03960-8
23. Ma L, Guo H, Zhao Y, Liu Z, Wang C, Bu J, et al. Liquid biopsy in cancer: current status, challenges and future prospects. Sig Transduct Target Ther. 2024 Dec 2;9(1):336. doi:10.1038/s41392-024-02010-1
24. Bartolomucci A, Nobrega M, Ferrier T, Dickinson K, Kaorey N, Nadeau A, et al. Circulating tumor DNA to monitor treatment response in solid tumors and advance

precision oncology. NPJ Precis Oncol. 2025 Mar 24;9:84. doi:10.1038/s41698-025-00663-3

25. Song M, Pan W, Yu X, Ren J, Tang C, Chen Z, et al. Minimal Residual Disease Detection: Implications for Clinical Diagnosis and Cancer Patient Treatment. MedComm (2020). 2025 May 15;6(6):e70193. doi:10.1002/mco2.70193
26. Ma L, Guo H, Zhao Y, Liu Z, Wang C, Bu J, et al. Liquid biopsy in cancer: current status, challenges and future prospects. Sig Transduct Target Ther. 2024 Dec 2;9(1):336. doi:10.1038/s41392-024-02010-1
27. Qureshi Z, Altaf F, Khanzada M, Safi A, Asghar Z, Warraich D, et al. Liquid biopsies for early detection and monitoring of cancer: advances, challenges, and future directions. Ann Med Surg (Lond). 2025 May 21;87(6):3244–53. doi:10.1097/MS9.0000000000002859
28. Lin C, Liu X, Zheng B, Ke R, Tzeng CM. Liquid Biopsy, ctDNA Diagnosis through NGS. Life (Basel). 2021 Aug 28;11(9):890. doi:10.3390/life11090890
29. Neagu AN, Bruno PS, Josan CL, Waterman N, Morrissiey H, Njoku VT, et al. In Search of Ideal Solutions for Cancer Diagnosis: From Conventional Methods to Protein Biomarkers in Liquid Biopsy. Proteomes. 2025 Dec;13(4):47. doi:10.3390/proteomes13040047
30. Shegekar T, Vodithala S, Juganavar A. The Emerging Role of Liquid Biopsies in Revolutionising Cancer Diagnosis and Therapy. Cureus. 2023;15(8):e43650. doi:10.7759/cureus.43650