JOURNAL OF AMERICAN MEDICAL SCIENCE & RESEARCH

Review Article
ISSN: 3041-5578
Journal homepage: https://medical.researchfloor.org/

Liquid Biopsy: A Review of Non-Invasive Frontier in Cancer Diagnosis and Management

Anenga RN[1], Ugwu IV[2], Umobong EO[3], Gbaa ZL*[4], Tsegha LJ[5], Ojo BA[6], Gbaa Fa[7] and Otene, Sa[8]

[1]*Department of Anatomical Pathology, Benue State University Teaching Hospital, Makurdi, Nigeria*
[2]*Department of Anatomic Pathology, Federal University of Health Sciences, Otukpo, Nigeria*
[3]*Histoconsult Laboratory, Abuja, Nigeria*
[4]*Department of Surgery, College of Health Sciences, Benue State University, Makurdi, Nigeria*
[5]*Department of Surgery, Benue State University Teaching Hospital Makurdi, Nigeria*
[6]*Department of Histopathology, Benue State University Teaching Hospital, Makurdi, Nigeria*
[7]*College of Health Sciences, Benue State University, Makurdi, Nigeria*
[8]*Department of Radiology, Federal University of Health Sciences, Otukpo (FUHSO), Benue State, Nigeria*

ABSTRACT

Background: *Although the gold standard for diagnosis, traditional tissue biopsies have several drawbacks, such as invasiveness, sampling bias, and the inability to track tumour progression in real time. A revolutionary, non-invasive substitute that provides a dynamic and thorough understanding of a tumor's biology from a straightforward blood sample is a liquid biopsy. The current knowledge of liquid biopsy and its clinical uses throughout the cancer care continuum is summarized in this academic review.*

Methods: *Using databases like PubMed, Web of Science, and Scopus, we carried out an extensive literature review of peer-reviewed publications released between 2020 and 2025. The following search terms were used: "liquid biopsy," "circulating tumour DNA," "ctDNA," "circulating tumour cells," "CTCs," "exosomes," "cancer diagnosis," "treatment monitoring," and "minimal residual disease." Articles were chosen for their clinical utility in a variety of cancer types, their relevance to technological advancements, and their emerging applications in both Western and sub-Saharan African contexts. To summarise the main conclusions, more than 20 articles including reviews, original research, and clinical trial reports were critically examined.*

Discussion: *Circulating tumour cells (CTCs), circulating tumour DNA (ctDNA), and exosomes are among the essential elements of liquid biopsy that are thoroughly covered in the review. The unique information that each biomarker offers is highlighted. From molecular profiling and early cancer detection to real-time treatment monitoring and the extremely sensitive detection of minimal residual disease (MRD) and imminent relapse, we examine the diverse clinical applications. The talk also covers the special advantages and difficulties of using liquid biopsy in places with limited resources, like sub-Saharan Africa, where it may be able to get past major diagnostic obstacles.*

Conclusion: *By facilitating a more individualized, proactive, and patient-centric approach to cancer management, liquid biopsy has the potential to completely transform oncology. Notwithstanding issues with cost and standardization, continued research and technical developments indicate that liquid biopsies will be a vital component of cancer treatment in the future.*

Keywords: *circulating tumour cells (CTCs), circulating tumour DNA (ctDNA), Liquid biopsy, Exosomes, Minimal residual disease (MRD), Precision oncology, Sub-Saharan Africa, biomarkers, Cancer diagnosis, and Treatment monitoring.*

Citation: Anenga RN, Ugwu IV, Umobong EO, Gbaa ZL, Tsegha LJ, Ojo BA, Gbaa FA and Otene, SA (2025). Liquid Biopsy: A Review of Non-Invasive Frontier in Cancer Diagnosis and Management.
Journal of American Medical Science and Research.
DOI: https://doi.org/10.51470/AMSR.2025.04.01.57

Received 26 April 2025
Revised 22 May 2025
Accepted 20 June 2025

Corresponding Author: ***Gbaa LZ***
Email Address: ***zulumgbaa@gmail.com***

Introduction

With an estimated 19.3 million new cases and almost 10 million deaths in 2020 alone, cancer is still one of the leading causes of death worldwide [1]. Invasive tissue biopsy is the conventional "gold standard" for molecular profiling and cancer diagnosis. Despite its value, this procedure is frequently constrained by its risks, which include the possibility of complications, discomfort for the patient, and the difficulty of sampling tumours in anatomical locations that are difficult to reach [2]. Furthermore, a tissue biopsy only offers a static image of a tumour at a particular moment in time; it is unable to record the dynamic cellular and genetic alterations that take place during the course of the disease, metastasis, and the emergence of treatment resistance. In the age of personalized medicine, where real-time tracking of tumour progression is essential for successful treatment, this intrinsic limitation is a significant obstacle. Liquid biopsy (LB), a groundbreaking noninvasive diagnostic paradigm, has arisen in response to these difficulties. Tumor-derived biomarkers from bodily fluids—most frequently blood, but also urine, saliva, and cerebrospinal fluid—are analyzed using this method. Without requiring an invasive procedure, liquid biopsy offers a dynamic, thorough, and repeatable window into the biology of the tumour by identifying and examining these circulating components [3]. The fundamental idea is that cancer cells constantly release different substances into the bloodstream, such as extracellular vesicles, DNA fragments, and entire cells. A major benefit over static tissue biopsies is the ability to serially sample these biomarkers, which enables ongoing monitoring of disease progression and treatment response.

Method

This review systematically examines global, Western, and sub-Saharan African literature on liquid biopsy and its oncology

applications. A comprehensive search of PubMed/MEDLINE, Web of Science, Scopus, and Google Scholar identified peer-reviewed English-language studies published between January 2020 and August 2025, focusing on ctDNA, CTCs, exosomes, treatment monitoring, and minimal residual disease. Opinion pieces, non-cancer studies, and pre-2020 publications were excluded. Two reviewers independently screened and extracted data on study design, clinical applications, methodologies, and geographic context. The review synthesizes key trends, methodologies, and controversies, emphasizing biomarker isolation and analysis, and explores their role in diagnosis, treatment monitoring, early detection, MRD assessment, resistance mechanisms, and future integration into clinical care.

Liquid Biopsy Components

Circulating tumour cells (CTCs): Whole cancer cells that have shed from primary or metastatic tumours and made their way into the peripheral circulation. These cells are potent prognostic markers and a physical representation of metastasis. Since CTCs contain the entire genetic and proteomic signature of the original tumour, their analysis yields a wealth of information [4]. (Figure 1)

Isolation and Analysis: Because CTCs are so uncommon—an estimated one CTC per billion normal blood cells isolation and analysis present a substantial technical challenge(4). The most popular technique for CTC enrichment is the CellSearch® system, which captures cells expressing the epithelial cell adhesion molecule (EpCAM) using antibody-coated magnetic beads. The incapacity of EpCAM-based platforms to identify CTCs that have undergone epithelial-mesenchymal transition (EMT), a process in which cancer cells lose their epithelial traits in order to become more migratory, is a significant drawback. To get around this, newer techniques that are less dependent on particular surface markers are being developed, such as size-based filtration and micro fluidic technologies [5].

Clinical Significance: It is commonly acknowledged that the presence and count of CTCs serve as prognostic biomarkers. A higher CTC count is consistently linked to a lower progression-free and overall survival in a number of cancers, such as colorectal, breast, and prostate cancers. Analyzing CTCs presents a special chance to track the development of drug resistance and tumour evolution in real time [14].

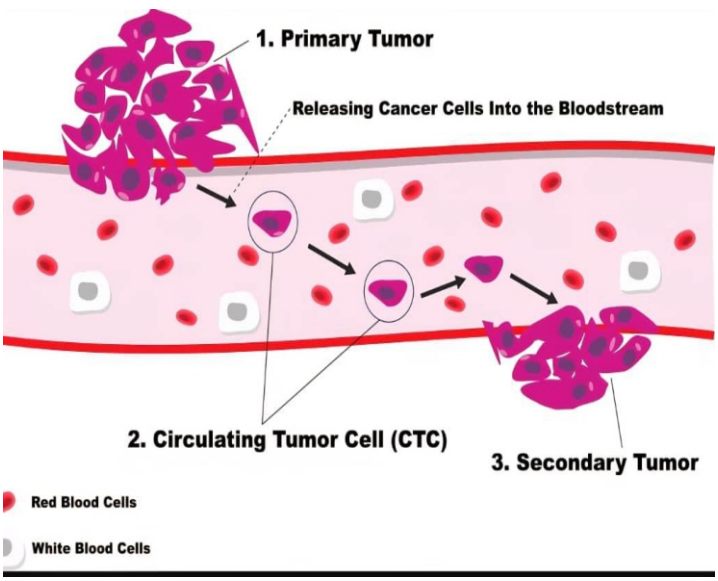

Figure 1: Circulating Tumor Cells (CTCs)

The Journey and Clinical Significance of Circulating Tumour Cells (CTCs)*: This schematic illustrates the process by which CTCs are shed from a primary tumour, intravasate into the bloodstream, survive in the circulation, and ultimately extravasate to form distant metastases. CTCs are a heterogeneous population, and their analysis provides a "real-time" liquid biopsy snapshot of the tumour's biological state. The enumeration and molecular profiling of CTCs serve as valuable prognostic biomarkers for monitoring disease progression and assessing treatment response, particularly in metastatic settings. The figure also highlights the challenges of isolating these rare cells and the diverse molecular information, including genetic mutations and protein expression that they carry.*

Circulating tumour DNA (ctDNA): Small DNA fragments are released into the bloodstream by necrotic or apoptotic tumour cells. CtDNA is frequently more prevalent and can be a more sensitive indicator of tumour burden than CTCs, which are uncommon. Certain genetic mutations, chromosomal abnormalities, and epigenetic modifications found in the tumour can be found by analyzing the ctDNA [6].

Detection Techniques: The main difficulty in identifying ctDNA is separating it from the large amount of normal cell-free DNA (cfDNA). Extremely sensitive methods are needed, the most common of which are based on Next-Generation Sequencing (NGS). These include whole-exome and whole-genome sequencing for a more comprehensive picture of the genetic landscape of the tumour, as well as targeted gene panels for known cancer mutations [6]. A different, extremely sensitive technique for measuring particular mutations is digital droplet PCR (ddPCR).

Clinical Utility: Following surgery with a curative goal, ctDNA is being used more and more to detect minimal residual disease (MRD). After surgery, the presence of ctDNA is a reliable indicator of cancer recurrence and frequently appears months before radiographic evidence [7]. This makes it possible to start adjuvant therapy in high-risk patients on time. Additionally, the foundation of precision oncology is ctDNA analysis, which makes it possible to find targetable mutations to direct the choice of medications such as tyrosine kinase inhibitors. Cells, including cancer cells, secrete exosomes and extracellular vesicles (EVs), which are nanoscale lipid vesicles with a diameter of 30 to 150 nm. Encapsulating proteins, lipids, RNA, and DNA that mirror the molecular properties of their parent cell, they are a rich source of molecular cargo8. Exosomes are essential for intercellular communication because they affect the tumour microenvironment and promote metastasis.

Isolation and Analysis: Exosomes are difficult to isolate and characterize technically due to their small size and heterogeneity. Size-exclusion chromatography, immunoaffinity-based techniques, and ultracentrifugation are common approaches. Finding new biomarkers may be greatly aided by the examination of exosomal cargo, such as particular proteins or non-coding RNAs (miRNAs).

Clinical Potential: Exosomes are being studied for their potential as biomarkers for early diagnosis, especially in cancers that are difficult to detect, such as pancreatic cancer. In addition to being investigated as a drug delivery system, their distinct cargo offers information about the biological state of the tumor [9].

DOI: https://doi.org/10.51470/AMSR.2025.04.01.57

Other Biomarkers: Although exosomes, ctDNA, and CTCs have been studied the most, other circulating components are also being investigated. Emerging as promising new avenues for liquid biopsy research are circulating microRNAs (miRNAs), small non-coding RNA molecules, and tumor-educated platelets (TEPs), which absorb biomarkers derived from tumors [10].

Table 1: Comparison of Liquid Biopsy Biomarkers

Biomarker	Description	Detection Methods	Advantages	Limitations
Circulating Tumor Cells (CTCs)	Intact cancer cells shed from tumors into the bloodstream.	Immunomagnetic enrichment (e.g., Cell Search), microfluidic devices, size-based filtration.	Provides a "live" cell for genomic, transcriptomic, and proteomic analysis; allows for real-time monitoring of tumor evolution.	Very rare (low abundance); isolation methods may miss certain subtypes (e.g., those undergoing EMT); not always present in early-stage disease.
Circulating Tumor DNA (ctDNA)	Fragments of tumor-derived DNA released into the blood from apoptotic or necrotic cells.	Digital droplet PCR (ddPCR), Next-Generation Sequencing (NGS), methylation analysis.	More abundant than CTCs; high sensitivity for detecting specific mutations; ideal for minimal residual disease (MRD) detection.	Short half-life; requires highly sensitive assays to distinguish from normal cell-free DNA (cfDNA); does not provide single-cell information.
Exosomes	Nanoscale extracellular vesicles secreted by tumor cells.	Ultracentrifugation, size-exclusion chromatography, immunoaffinity capture.	Carry a diverse cargo of DNA, RNA, and proteins; provides insights into tumor-stroma communication; stable in circulation.	Technical challenges in isolation and standardization; less established clinical utility compared to ctDNA.

Comparison of Liquid Biopsy Biomarkers*: This table provides a concise overview of the key biomarkers analyzed in liquid biopsies, their respective detection methods, and their distinct clinical advantages and limitations. The information synthesized here highlights the complementary nature of these biomarkers, underscoring the potential for multi-analyte liquid biopsies to provide a more comprehensive and accurate picture of a patient's tumour biology. This data is based on a critical review of recent literature and represents the current consensus on the utility of each biomarker [4-10].*

Clinical Uses in the Treatment of Cancer

Early Cancer Detection and Screening: The potential of liquid biopsy to detect cancer in asymptomatic individuals early on is its holy grail. Liquid biopsy tests have the potential to screen for cancer before it has reached an advanced stage by identifying low-abundance tumor-derived biomarkers in the blood. Multi-cancer early detection (MCED) tests are being validated through extensive clinical trials. One well-known example of this endeavour in Western nations is the GRAIL Galleri test, which examines methylation patterns in cfDNA. Liquid biopsy has enormous potential in sub-Saharan Africa, where diagnostic infrastructure is scarce. Research is looking into its potential for the quick diagnosis of endemic cancers like Burkitt's lymphoma and Kaposi's sarcoma, which are frequently detected too late because invasive biopsies are difficult to perform in environments with limited resources [11].

Diagnosis and Molecular Profiling: When a tissue biopsy is impractical or does not produce enough material, a liquid biopsy can be a potent tool for both initial diagnosis and molecular profiling in patients with a suspected cancer diagnosis. Clinicians can determine the precise genetic mutations causing the tumour by examining ctDNA, such as EGFR mutations in non-small cell lung cancer, which directly influences the selection of targeted treatments [12]. This analysis can be completed from a straightforward blood sample, which greatly speeds up diagnosis and enables a more individualized treatment plan.

Treatment Monitoring and Response Evaluation: Real-time treatment monitoring is one of the most direct and significant uses of liquid biopsy. Long before alterations are apparent on conventional imaging, changes in the amounts of ctDNA or CTCs can indicate how well the tumour is responding to treatment. For instance, a drop in ctDNA concentration after chemotherapy starts may be a sign of a good reaction, whereas an increase in concentration could indicate ineffectiveness or the emergence of resistance [13]. This makes it possible to promptly modify treatment plans, avoiding needless toxicity from ineffective medications.

Monitoring for Relapse and Minimal Residual Disease (MRD): After surgery or other curative measures, MRD may persist and cause relapse in the future. A very sensitive technique for identifying this MRD is liquid biopsy, especially ctDNA analysis. After a treatment that is thought to be curative, the presence of ctDNA is a strong indicator of relapse. CtDNA-positive patients have a markedly increased risk of recurrence and may benefit from more aggressive adjuvant therapy, according to numerous studies, including a sizable study on colorectal cancer from the Netherlands14]. By shifting from "wait and see" methods to more proactive, individualized care, this application has the potential to completely transform post-treatment surveillance. (Table 2)

Table 2: Clinical Applications of Liquid Biopsy across the Cancer Care Continuum.

Application	Biomarker(s) of Interest	Rationale for Use	Examples and Clinical Impact
Early Detection/Screening	ctDNA (methylation patterns), Exosomes	To detect cancer-specific biomarkers in asymptomatic individuals before clinical symptoms appear.	**GRAIL Galleri test** for multi-cancer early detection; studies in pancreatic and ovarian cancer to identify high-risk individuals.
Diagnosis & Molecular Profiling	ctDNA, CTCs	To provide a genetic profile of the tumor when tissue biopsy is not feasible or fails.	Detecting **EGFR mutations** in NSCLC from a blood sample to guide targeted therapy; identifying actionable mutations in advanced cancer.
Treatment Monitoring	ctDNA, CTCs	To monitor changes in tumor burden and predict response to therapy in real-time.	Decreasing ctDNA levels correlate with positive response to chemotherapy; rising ctDNA may indicate the development of drug resistance.
Minimal Residual Disease (MRD)	ctDNA	To detect microscopic disease after curative-intent treatment, predicting risk of recurrence.	Post-operative ctDNA positivity in colorectal cancer is a strong predictor of relapse, guiding the use of adjuvant chemotherapy.
Relapse Monitoring	ctDNA, CTCs	To identify early signs of cancer recurrence long before they are visible on imaging.	Serial liquid biopsies can detect a rise in ctDNA, prompting earlier intervention and improving patient outcomes.

DOI: https://doi.org/10.51470/AMSR.2025.04.01.57

Clinical Applications of Liquid Biopsy across the Cancer Care Continuum: *This table summarizes the diverse and evolving clinical utility of liquid biopsy at different stages of a patient's cancer journey. It highlights how various biomarkers, particularly ctDNA and CTCs, are being applied to shift cancer management from a reactive to a proactive paradigm. The information presented reflects key advancements in personalized oncology, from screening and diagnosis to the crucial monitoring of treatment response and minimal residual disease (MRD) [11-14].*

Challenges: Despite its potential, a number of obstacles need to be removed before liquid biopsy can be widely used in clinical settings. Assay standardization is crucial because disparate platforms and approaches can produce inconsistent results, making it difficult to compare data from different studies and clinics[15]. Technical challenges are also brought on by the low abundance of biomarkers, especially in early-stage cancers, where there is a greater chance of false-negative results. The cost of the technology is still a deterrent, particularly in low- and middle-income nations where there is a greater need for non-invasive diagnostics. Lastly, to conclusively prove the clinical utility and cost-effectiveness of liquid biopsy in standard practice, extensive, prospective clinical trials are required for strong clinical validation. (Table 3)

Table 3: Research on Liquid Biopsies in Sub-Saharan Africa (SSA)

References	Cancer Type(s)	Biomarker(s) Studied	Key Findings	Challenges/Recommendations
[11]	Lymphoma (Burkitt's)	ctDNA	Demonstrated feasibility of liquid biopsy for rapid diagnosis in a resource-limited setting; showed high concordance with traditional biopsy.	High cost of technology; need for local validation and training; limited access to advanced lab infrastructure.
[17]	Hepatocellular Carcinoma	ctDNA	Validated ctDNA methylation markers for early HCC detection; highlighted potential for screening in at-risk populations (e.g., chronic hepatitis B).	Lack of standardized protocols; difficulty with sample storage in high-temperature environments.
[18]	Ovarian Cancer	Exosomes	Identified novel exosomal miRNA biomarkers for early detection; promising for overcoming late-stage diagnosis in the region.	Requires advanced technology not widely available; further validation needed in larger cohorts.
[16]	Various Cancers	General Review	Highlighted the potential of liquid biopsy to address diagnostic delays and improve outcomes in SSA; emphasized the need for a collaborative approach.	Infrastructure limitations; financial barriers; insufficient research funding for local studies.

Summary of Studies on Liquid Biopsy in Sub-Saharan Africa (SSA)*: This table outlines key research efforts exploring liquid biopsy in SSA. It highlights the potential of this technology to address regional challenges, such as diagnostic delays and limited infrastructure, while also acknowledging the hurdles of cost, technical validation, and standardization that must be overcome for widespread implementation. The studies listed demonstrate the growing body of evidence supporting liquid biopsy as a transformative tool in resource-constrained settings*.

Future Prospects for Liquid Biopsies

Key clinical and technological advancements will drive the dynamic and quickly changing landscape of liquid biopsy in the future. A key component of this advancement is expected to be the combination of machine learning (ML) and artificial intelligence (AI). These technologies are essential for analyzing the large and intricate datasets produced by multi-analyte liquid biopsies, allowing for the previously unheard-of level of precision in identifying subtle but clinically significant biomarker signatures. With this increased analytical capability, the field will advance from the detection of simple mutations to a thorough comprehension of the biological state of a tumour, including its heterogeneity and changing resistance mechanisms [16-18].

An important advancement is the creation of multi-analyte platforms. These platforms will get around the drawbacks of single-biomarker methods by measuring several circulating biomarkers at once, including ctDNA, CTCs, and exosomes. The sensitivity and specificity of detection are increased by this holistic perspective, which offers a more thorough and accurate picture of a patient's cancer. For example, a multi-analyte approach could better track metastasis and inform treatment choices by combining the single-cell information from CTCs with the high specificity of ctDNA [19].

Developments in Global Accessibility and Ultrasensitive Detection

Ultrasensitive detection techniques, which are essential for clinical applications, are being rapidly developed in the field of liquid biopsy. Extremely low concentrations of circulating tumour DNA (ctDNA) can now be detected thanks to the development of sophisticated techniques like improved digital PCR and improved next-generation sequencing (NGS) methods [20-21]. Two important uses for this increased sensitivity are the accurate monitoring of minimal residual disease (MRD) following treatment and the early detection of cancer in asymptomatic individuals. More timely and efficient clinical interventions are made possible by these developments, which allow physicians to detect microscopic disease or approaching therapeutic resistance much earlier than traditional imaging can [22].

The ultimate goal of these technological developments is not only better performance but also more accessibility and affordability. The widespread use of liquid biopsy in settings with limited resources is becoming a real possibility as the cost of these ultrasensitive technologies drops and laboratory procedures become more standardized. This is especially important in places like sub-Saharan Africa, where the high expense of traditional biopsies and the absence of sophisticated diagnostic infrastructure frequently result in delayed diagnoses and subpar patient outcomes. Liquid biopsy has the potential to significantly improve early diagnosis and management of cancer in these areas by providing a non-invasive, effective, and economical substitute [23].

Conclusion: As a dynamic and non-invasive substitute for conventional tissue biopsy, liquid biopsy has become a game-changer in oncology. Its ability to provide real-time insights into tumour biology through the analysis of CTCs, ctDNA, and exosomes has opened up new avenues for personalized medicine. From early detection and molecular profiling to monitoring treatment response and detecting minimal residual disease, the clinical applications of liquid biopsy are vast and

DOI: https://doi.org/10.51470/AMSR.2025.04.01.57

impactful. While challenges related to standardization, validation, and cost remain, the rapid pace of technological innovation suggests that liquid biopsy is on the cusp of becoming a cornerstone of cancer care. By enabling a more proactive, precise, and patient-friendly approach to diagnosis and management, liquid biopsy is not just a new tool it is a new frontier that is reshaping the future of oncology.

Recommendations: The review emphasizes the need for standardized protocols for liquid biopsy biomarker analysis to ensure reproducibility and clinical integration. It calls for large-scale international trials to validate early detection and MRD monitoring, along with global collaboration to improve accessibility in low- and middle-income countries through affordable platforms and pilot programs. The integration of AI and bioinformatics is recommended to enhance biomarker detection and prognostication, while ongoing biomarker discovery, including exosomes and tumor-educated platelets, is essential for advancing precision oncology.

Conflict of interest: There are no conflicts of interest.

Funding sources: For this review article, we did not receive any grants or funding.

References

1. Siravegna G, Mussolin B, Buscarino M, Corti G, Cassingena A, Crisafulli G, et al. Clonal evolution and resistance to EGFR blockade in the blood of colorectal cancer patients. Nat Med. 2015;21(7):795-801.

2. Bettegowda C, Sausen M, Leary RJ, Kinde I, Wang Y, Agrawal N, et al. Detection of circulating tumor DNA in early- and late-stage human malignancies. SciTransl Med. 2014;6(224):224ra24.

3. Wan JCM, Massie C, Garcia-Corbacho J, Mouliere F, Brenton JD, Caldas C, et al. Liquid biopsies come of age: Towards implementation of circulating tumour DNA. Nat Rev Cancer. 2017;17(4):223-38.

4. Alix-Panabières C, Pantel K. Liquid biopsy: From discovery to clinical application. Cancer Discov. 2021;11(4):858-73.

5. Bronkhorst AJ, Ungerer V, Holdenrieder S. The emerging role of cell-free DNA as a molecular marker for cancer management. Biomol Detect Quantif. 2019; 17:100087.

6. Crowley E, Di Nicolantonio F, Loupakis F, Bardelli A. Liquid biopsy: Monitoring cancer genetics in the blood. Nat Rev ClinOncol. 2013;10(8):472-84.

7. Siravegna G, Marsoni S, Siena S, Bardelli A. Integrating liquid biopsies into the management of cancer. Nat Rev ClinOncol. 2017;14(9):531-48.

8. Murtaza M, Dawson SJ, Pogrebniak K, Rueda OM, Provenzano E, Grant J, et al. Multifocal clonal evolution characterized using circulating tumour DNA in a case of metastatic breast cancer. Nat Commun. 2015; 6:8760.

9. Merker JD, Oxnard GR, Compton C, Diehn M, Hurley P, Lazar AJ, et al. Circulating tumor DNA analysis in patients with cancer: American Society of Clinical Oncology and College of American Pathologists joint review. J ClinOncol. 2018;36(16):1631-41.

10. Underhill HR, Kitzman JO, Hellwig S, Welker NC, Daza R, Baker DN, et al. Fragment length of circulating tumor DNA. PLoS Genet. 2016;12(7): e1006162.

11. Cristiano S, Leal A, Phallen J, Fiksel J, Adleff V, Bruhm DC, et al. Genome-wide cell-free DNA fragmentation in patients with cancer. Nature. 2019;570(7761):385-9.

12. Dawson SJ, Tsui DWY, Murtaza M, Biggs H, Rueda OM, Chin SF, et al. Analysis of circulating tumor DNA to monitor metastatic breast cancer. N Engl J Med. 2013;368(13):1199-209.

13. Phallen J, Sausen M, Adleff V, Leal A, Hruban C, White J, et al. Direct detection of early-stage cancers using circulating tumor DNA. SciTransl Med. 2017;9(403): eaan2415.

14. Garcia-Murillas I, Schiavon G, Weigelt B, Ng C, Hrebien S, Cutts RJ, et al. Mutation tracking in circulating tumor DNA predicts relapse in early breast cancer. SciTransl Med. 2015;7(302):302ra133.

15. Abbosh C, Birkbak NJ, Wilson GA, Jamal-Hanjani M, Constantin T, Salari R, et al. Phylogenetic ctDNA analysis depicts early-stage lung cancer evolution. Nature. 2017;545(7655):446-51.

16. Parikh AR, Leshchiner I, Elagina L, Goyal L, Levovitz C, Siravegna G, et al. Liquid versus tissue biopsy for detecting acquired resistance and tumor heterogeneity in gastrointestinal cancers. Nat Med. 2019;25(9):1415-21.

17. Lee JH, Jeong SY, Lim Y, Kim JW, Kim NK, Lee WY, et al. Clinical application of circulating tumor DNA for colorectal cancer patients. Cancer Res Treat. 2021;53(2):349-59.

18. Siravegna G, Sartore-Bianchi A, Nagy RJ, Raghav K, Parseghian CM, Mussolin B, et al. Plasma HER2 (ERBB2) copy number predicts response to HER2-targeted therapy in metastatic colorectal cancer. Clin Cancer Res. 2019;25(10):3046-53.

19. Reinert T, Henriksen TV, Christensen E, Sharma S, Salari R, Sethi H, et al. Analysis of plasma cell-free DNA by ultradeep sequencing in patients with stages I to III colorectal cancer. JAMA Oncol. 2019;5(8):1124-31.

20. Tie J, Cohen JD, Wang Y, Christie M, Simons K, Lee M, et al. Circulating tumor DNA analysis guiding adjuvant therapy in stage II colon cancer. N Engl J Med. 2021;385(15):1374-83.

21. Heitzer E, Haesler P, Gecse K, Aubin F, Oellerich M, Pantel K, et al. Liquid biopsies for early cancer detection. Nat Rev ClinOncol. 2023;20(10):593-610.

DOI: https://doi.org/10.51470/AMSR.2025.04.01.57

22. Crowley E, Di Nicolantonio F, Loupakis F, Bardelli A. Liquid biopsy: Monitoring cancer genetics in the blood. Nat Rev ClinOncol. 2013;10(8):472-84.

23. Bii J, Obaj J, Ndung'u M, Otieno MW, Masika MM, Magogo CN, et al. A protocol to clinically evaluate liquid biopsies as a tool to speed up diagnosis of children and young adults with aggressive infection-related lymphoma in East Africa. BMC Cancer. 2022;22(1):475.

DOI: https://doi.org/10.51470/AMSR.2025.04.01.57