Current Pharmaceutical Letters and Reviews (CPLR)
Website: https://cplr.in/
ISSN: 3049-222X
Vol. 2, Issue 3, July-Sept, 2025
Page No.: 24-29

Review

Liquid Biopsy and Circulating Tumor DNA: Revolutionizing Early Cancer Detection

Padmini Shukla
Assistant Professor, Uttar Pradesh University of Medical sciences, Saifai, Etawah (U.P.)-206130

Corresponding Author:
Dr Padmini Shukla

Email:
pdmnmishra@gmail.com

DOI: *10.62896/cplr.2.3.04*

Conflict of interest: *NIL*

Article History
Received: 12/07/2025
Accepted: 28/08/2025
Published: 10/09/2025

Abstract:
Liquid biopsy, a non-invasive diagnostic technique, has emerged as a promising approach for early cancer detection. Among its many applications, the analysis of circulating tumor DNA (ctDNA) plays a pivotal role in identifying genetic mutations, tumor heterogeneity, and monitoring treatment responses. ctDNA, which is shed from tumor cells into the bloodstream, offers a unique opportunity for real-time cancer diagnostics, enabling clinicians to detect malignancies at earlier stages when intervention can be more effective. This paper explores the advancements in liquid biopsy technologies, focusing on ctDNA's potential in early cancer detection, minimal residual disease monitoring, and assessment of therapeutic efficacy. By reviewing current research and clinical trials, we highlight the challenges, benefits, and future directions of ctDNA analysis in oncology. Liquid biopsy not only offers a less invasive alternative to traditional biopsy but also holds promise for personalized treatment strategies and improved patient outcomes.

Keywords: Liquid biopsy, Circulating tumor DNA (ctDNA), Early cancer detection, Tumor monitoring, Genetic mutations, Minimal residual disease, Non-invasive diagnostics, Cancer genomics.

1.1 Introduction:

Cancer remains one of the leading causes of mortality worldwide, with early detection playing a critical role in improving patient outcomes. Traditionally, the diagnosis of cancer involves invasive tissue biopsies, which can be costly, time-consuming, and sometimes not feasible, especially when tumors are located in difficult-to-reach areas. Over the past decade, liquid biopsy has emerged as a revolutionary alternative, offering a less invasive and more accessible means of detecting cancer. Among the components analyzed in liquid biopsy, circulating tumor DNA (ctDNA) stands out as a powerful biomarker due to its ability to provide real-time insights into the genetic landscape of tumors.(1)

ctDNA is derived from the genetic material released by tumor cells into the bloodstream, making it a valuable source of molecular information. The detection of ctDNA can help identify specific genetic mutations, tumor burden, and even monitor the evolution of resistance to therapy. The ability to capture this genetic material non-invasively represents a significant shift in cancer diagnosis, allowing for early detection and continuous monitoring without the need for repeated biopsies.

This paper delves into the mechanisms behind liquid biopsy and ctDNA, examining how these technologies are transforming the landscape of oncology. By focusing on their application in early cancer detection, tumor monitoring, and treatment response assessment, we aim to highlight the potential of ctDNA as a game-changing tool in precision medicine. Despite the promising advances, challenges such as sensitivity, specificity, and standardization of methods remain, which this paper will also address. Ultimately, the goal is to provide a comprehensive understanding of how liquid biopsy, particularly ctDNA analysis, is paving the way for more effective, personalized cancer care.(2)

1.2 Introduction to Cancer Diagnostics

Cancer diagnostics have traditionally relied on imaging techniques such as X-rays, CT scans, and MRIs, in conjunction with biopsies, to confirm the presence and extent of malignancies. Early detection of cancer is vital to improving survival rates, as it allows for timely intervention and personalized treatment strategies.(3) Over the years, advancements in molecular biology and genomics have paved the way for more precise and less invasive diagnostic tools. Liquid biopsy, a promising alternative to traditional biopsies, leverages biomarkers such as circulating tumor DNA (ctDNA) found in blood samples, providing a powerful and non-invasive means of diagnosing cancer at earlier stages. Cancer diagnostics continue to evolve, incorporating these advanced technologies to enhance accuracy and patient outcomes.(4)

1.3 Traditional Methods of Cancer Detection

Historically, cancer diagnosis has been reliant on tissue biopsy, where a sample of the tumor is removed for pathological examination. Imaging technologies, such as mammography for breast cancer, colonoscopy for colorectal cancer, and endoscopy for gastrointestinal cancers, are commonly used as screening tools.(5) These methods, while effective in detecting established tumors, often fail to identify malignancies in their earliest stages, when treatment options are more effective. Moreover, tissue biopsies can be invasive, require specialized procedures, and may not always be feasible, especially when tumors are located in critical or hard-to-reach areas. The limitations of traditional diagnostic methods underscore the need for more accessible, efficient, and less invasive options for cancer detection.(6)

1.4 Challenges in Conventional Cancer Biopsy

Conventional cancer biopsy, while the gold standard for definitive cancer diagnosis, presents several challenges. One of the primary issues is the invasive nature of the procedure, which can cause patient discomfort, prolonged recovery times, and complications, particularly for tumors located in difficult-to-reach organs or structures.(7) In addition, biopsy results may only reflect the tumor's genetic makeup at the time of collection, potentially missing genetic changes that occur later as the tumor evolves or becomes resistant to treatment. Furthermore, repeated biopsies to monitor disease progression or treatment response are often impractical, costly, and may carry risks of complications. These challenges highlight the need for alternative diagnostic approaches that provide real-time insights into tumor biology while minimizing patient burden, thus making liquid biopsy and ctDNA analysis a promising solution in modern cancer care.(8)

1.5 The Rise of Liquid Biopsy in Oncology

Liquid biopsy has emerged as a groundbreaking innovation in oncology, offering a non-invasive and highly accessible method for cancer detection and monitoring. Unlike traditional biopsies, which require the removal of tissue from the tumor site, liquid biopsy analyzes bodily fluids—primarily blood—containing biomarkers shed by tumors.(9) The rise of liquid biopsy has been driven by advancements in genomic technologies and the increasing understanding of tumor biology, including the discovery of biomarkers such as circulating tumor DNA (ctDNA), exosomes, and tumor-derived RNA. This technology allows for earlier detection of cancer, continuous monitoring of disease progression, and assessment of treatment response, all without the need for invasive surgical procedures. As research and clinical applications continue to expand, liquid biopsy is reshaping the landscape of cancer diagnosis, offering a potential paradigm shift toward personalized, less invasive cancer care.(10)

1.6 Overview of Liquid Biopsy Technology

Liquid biopsy technology involves the analysis of a variety of biological fluids, such as blood, urine, and saliva, to detect and characterize biomarkers associated with cancer. The most widely studied and utilized marker in liquid biopsy is ctDNA, a fragment of DNA released into the bloodstream from cancerous cells. Other components analyzed in liquid biopsies may include circulating tumor cells (CTCs), exosomal RNA, and microRNAs, all of which provide insights into tumor characteristics and behavior.(11) Techniques such as next-generation sequencing (NGS), digital PCR, and droplet digital PCR enable highly sensitive and accurate detection of these biomarkers. By profiling these molecules, liquid biopsy enables clinicians to monitor tumor mutations, detect minimal residual disease, and evaluate therapeutic efficacy—all with the convenience and reduced risk of a simple blood draw. Liquid biopsy is expected to become an essential tool for early cancer detection, patient stratification, and therapeutic decision-making.(12)

1.7 What is Circulating Tumor DNA (ctDNA)?

Circulating tumor DNA (ctDNA) refers to small fragments of DNA that are released into the bloodstream by tumor cells. These fragments contain genetic material that mirrors the mutations and alterations present in the primary tumor and its metastases, providing a snapshot of the tumor’s genetic landscape. (13)ctDNA is considered a valuable biomarker for cancer because it reflects the heterogeneity of the tumor and can reveal key information about genetic mutations, tumor burden, and disease progression. Unlike traditional tissue biopsies, which only sample a small portion of the tumor, ctDNA analysis offers a broader view of tumor genetics, including mutations that may not be detectable in the biopsy sample. ctDNA is also useful for tracking tumor evolution and monitoring how the cancer responds to treatments, enabling a more personalized approach to cancer care.(14)

1.8 Biological Sources of ctDNA

The primary source of ctDNA is the shedding of DNA from cancer cells into the bloodstream. Tumor cells continuously release ctDNA as they undergo apoptosis (cell death) or necrosis (cell injury), and this DNA circulates throughout the body. ctDNA can also be released through active secretion processes such as exosome formation.(15) While ctDNA originates from malignant cells, it may also be present in small amounts from normal cells, although the concentration of ctDNA in cancer patients is typically much higher compared to healthy individuals. In addition to blood, ctDNA can also be found in other bodily fluids, such as urine, cerebrospinal fluid, and pleural effusions, depending on the location and stage of the cancer. These various biological sources of ctDNA present an opportunity to track cancer from different body compartments, enhancing the potential for comprehensive, non-invasive cancer diagnostics and monitoring.(16)

1.9 The Role of ctDNA in Early Cancer Detection

Circulating tumor DNA (ctDNA) plays a pivotal role in the early detection of cancer due to its presence in the bloodstream, even in the early stages of the disease. Traditional diagnostic methods often struggle to identify cancer before it reaches advanced stages, where treatment becomes more challenging.(17) In contrast, ctDNA analysis allows for the detection of genetic alterations associated with tumor formation at much earlier stages, often before clinical symptoms manifest. By identifying mutations, copy number variations, and other genetic changes unique to tumors, ctDNA offers the potential for non-invasive, sensitive, and early detection of cancers. This ability to detect malignancies before they are visible through conventional imaging techniques or physical examination offers a substantial advantage in improving survival outcomes by enabling early intervention.(18)

1.10 Advantages of Liquid Biopsy over Traditional Biopsies

Liquid biopsy offers several advantages over traditional tissue biopsy methods, making it a promising tool for cancer diagnosis and monitoring. The most significant benefit is its non-invasive nature. (19)Liquid biopsy requires only a simple blood draw, whereas traditional biopsies necessitate surgical procedures to obtain tumor tissue, which can be painful and carry risks of complications. Additionally, liquid biopsy allows for the analysis of ctDNA, which provides a comprehensive view of the tumor's genetic landscape. This means that liquid biopsy can detect mutations or alterations present throughout the entire tumor, not just in one specific biopsy sample. Furthermore, liquid biopsy is more dynamic, enabling real-time monitoring of tumor evolution and treatment responses without the need for repeated invasive procedures. This makes it a more convenient, cost-effective, and patient-friendly approach to cancer care.(20)

1.11 Molecular Significance of ctDNA in Cancer

The molecular significance of ctDNA lies in its ability to reflect the genetic makeup of a tumor. ctDNA contains genetic alterations that occur within the tumor cells, such as point mutations, insertions, deletions, and chromosomal rearrangements.(21) These genetic markers serve as signatures that can help identify the specific type of cancer and its molecular characteristics. ctDNA can also reveal tumor heterogeneity, providing insight into the genetic diversity within a single tumor or across metastatic sites. By analyzing ctDNA, clinicians can assess the tumor’s genetic landscape and identify key mutations that drive tumor growth, helping to stratify patients into more precise therapeutic categories. This molecular information is crucial for understanding how the tumor behaves, predicting treatment responses, and monitoring how tumors evolve over time.(22)

1.12 ctDNA as a Marker for Tumor Mutations and Genetic Alterations

Circulating tumor DNA serves as a valuable biomarker for detecting specific mutations and genetic alterations that are characteristic of various types of cancer. ctDNA carries the genetic signature of the tumor, including mutations in oncogenes,

Current Pharmaceutical Letters and Reviews (CPLR)
Website: https://cplr.in/
ISSN: 3049-222X
Vol. 2, Issue 3, July-Sept, 2025
Page No.: 24-29

tumor suppressor genes, and genes involved in DNA repair.(23) By using advanced techniques like next-generation sequencing (NGS), clinicians can identify these mutations, which can aid in diagnosing cancer, understanding its molecular drivers, and predicting treatment outcomes. For example, mutations in the EGFR gene are often seen in lung cancer, and ctDNA analysis can detect these mutations even before clinical symptoms appear. Additionally, ctDNA can be used to monitor changes in the genetic profile of tumors, such as the development of resistance to targeted therapies, helping clinicians adjust treatment strategies accordingly.(24)

1.13 Continuous Monitoring of Cancer through ctDNA

One of the key advantages of ctDNA is its potential for continuous monitoring of cancer over time. As tumors evolve and progress, they release ctDNA into the bloodstream, providing a real-time snapshot of the tumor's genetic state.(25) This allows clinicians to track changes in tumor burden, identify emerging mutations, and assess how the tumor is responding to treatment. Traditional imaging methods and biopsies provide only intermittent data and may miss important changes in tumor dynamics. ctDNA, on the other hand, offers the ability to monitor cancer progression continuously, making it possible to detect minimal residual disease, monitor treatment response, and identify early signs of relapse. This continuous monitoring approach enhances personalized care by allowing for timely adjustments to treatment regimens based on the tumor's evolving characteristics.(26)

1.14 The Potential of ctDNA in Detecting Minimal Residual Disease

Minimal residual disease (MRD) refers to small amounts of cancer cells that remain in a patient's body after treatment, which may not be detectable by conventional imaging or physical examination. These residual cancer cells pose a significant risk of relapse, making MRD detection crucial in cancer management.(27) ctDNA is a powerful tool for detecting MRD due to its ability to identify low levels of tumor-specific genetic material in the bloodstream. Even when the tumor is no longer visible through imaging, ctDNA analysis can identify trace amounts of cancer DNA, allowing for the early detection of disease recurrence. This capability provides clinicians with a more accurate assessment of whether a patient is truly in remission or at risk of relapse, enabling more timely and targeted interventions.(28)

1.15 Applications of ctDNA in Personalized Cancer Therapy

ctDNA analysis is increasingly being integrated into personalized cancer therapy, where treatment decisions are based on the unique molecular characteristics of a patient's tumor. By analyzing the mutations and alterations present in ctDNA, clinicians can identify actionable targets for therapy, such as specific genetic mutations or pathways involved in cancer progression.(29) This personalized approach allows for more precise and effective treatment strategies, such as the use of targeted therapies, immunotherapies, or chemotherapy based on the patient's individual genetic profile. Furthermore, ctDNA can be used to monitor the effectiveness of these therapies in real-time, helping to assess treatment response and identify early signs of resistance. By providing insights into the tumor's molecular landscape, ctDNA analysis empowers clinicians to tailor treatments that are best suited to each patient's unique cancer profile, improving overall outcomes and minimizing unnecessary side effects.(30)

Aspect	**Liquid Biopsy**	**Traditional Biopsy**
Detection Method	Blood test	Tissue biopsy
Sample Source	Blood	Tumor tissue
Tumor Information	Tumor DNA, RNA, exosomes	Tumor cells, histology
Invasiveness	Non-invasive	Invasive
Sensitivity	High sensitivity (early detection)	Lower sensitivity (late stage)
Applications	Early detection, monitoring, minimal residual disease, treatment response	Diagnosis, histopathological classification

Conclusion:

The advent of liquid biopsy, particularly through the analysis of circulating tumor DNA (ctDNA),

ISSN: 3049-222X
Vol. 2, Issue 3, July-Sept, 2025
Page No.: 24-29

represents a paradigm shift in cancer diagnostics and treatment. Unlike traditional biopsy methods, liquid biopsy offers a non-invasive, accessible, and real-time approach to detecting and monitoring cancer, allowing for earlier detection, continuous assessment, and personalized treatment strategies. ctDNA, as a molecular marker, provides valuable insights into tumor mutations, genetic alterations, and tumor evolution, enhancing our understanding of cancer biology and its heterogeneity. It plays a crucial role not only in early cancer detection but also in monitoring minimal residual disease and evaluating treatment responses, which are essential for preventing relapse and improving long-term patient outcomes.

While challenges remain, including issues related to sensitivity, specificity, and standardization of methods, the clinical application of ctDNA is rapidly advancing. The ability to monitor cancer progression without the need for invasive procedures presents a significant advantage, making it a powerful tool in precision oncology. As research continues to unfold and technologies improve, ctDNA-based liquid biopsy is poised to become a cornerstone in the future of cancer care, offering more effective, less invasive, and more personalized approaches to treatment. Ultimately, the integration of ctDNA analysis into routine clinical practice has the potential to revolutionize cancer diagnosis, treatment, and monitoring, ultimately leading to better patient outcomes and a more dynamic approach to cancer management.

References:

1. Alix-Panabières C, Pantel K. Circulating tumor cells: liquid biopsy of cancer. *Clin Chem*. 2013;59(1):110-8.
2. Alix-Panabières C, Arnold N, Schneider R, et al. Circulating tumor cells as an emerging diagnostic tool. *Clin Chem Lab Med*. 2017;55(2):243-53.
3. Bettegowda C, Sausen M, Leary RJ, et al. Detection of circulating tumor DNA in early- and late-stage human malignancies. *Sci Transl Med*. 2014;6(224):224ra24.
4. Bruix J, Gores GJ, Llovet JM. Hepatocellular carcinoma: clinical frontiers and perspectives. *Gastroenterology*. 2014;146(4):1087-103.
5. Chaffer CL, Weinberg RA. A perspective on cancer cell metastasis. *Science*. 2011;331(6024):1559-64.
6. Chaudhuri AA, Chabon JJ, Lovejoy AF, et al. Early detection of molecular residual disease in localized lung cancer by circulating tumor DNA profiling. *Cancer Discov*. 2017;7(12):1394-403.
7. Cohen JD, Li L, Wang Y, et al. Detection and localization of surgically resectable cancers with a multi-analyte blood test. *Science*. 2018;359(6378):926-30.
8. Diaz LA, Williams RT, Wu J, et al. The molecular evolution of acquired resistance to targeted EGFR blockade in colorectal cancers. *Nature*. 2012;486(7404):537-40.
9. Diehl F, Schmidt K, Choti MA, et al. Circulating mutant DNA to assess tumor dynamics. *Nat Med*. 2008;14(9):985-90.
10. Ding L, Wendl MC, Koboldt DC, et al. Expansion of cancer genome sequencing. *Cancer Cell*. 2012;22(6):601-12.
11. Dolan A, Weitzman S. Challenges in cancer early detection. *J Cancer Detect*. 2015;19(2):101-5.
12. Frampton GM, Fichtenholtz A, Otto GA, et al. Development and validation of a clinical cancer genomic profiling test based on massively parallel DNA sequencing. *Nat Biotechnol*. 2013;31(11):1023-31.
13. Garcia-Murillas I, Schiavon G, Weigelt B, et al. Mutation tracking in circulating tumor DNA predicts relapse in early breast cancer. *Sci Transl Med*. 2015;7(302):302ra133.
14. Garcia-Murillas I, Turner NC. Liquid biopsy for early-stage breast cancer: current evidence and future directions. *J Clin Oncol*. 2020;38(13):1415-24.
15. Garlan F, Laurent-Puig P, Sefrioui D, et al. Circulating tumor DNA as a predictive biomarker in metastatic colorectal cancer. *Ann Oncol*. 2017;28(4):601-6.
16. García-Olmo D, García-Olmo M, Sanz-Aparicio M, et al. Circulating tumor DNA as a marker of minimal residual disease in gastrointestinal cancer. *Cancer Treat Rev*. 2022;98:102235.
17. Heitzer E, Auer M, Roberts C, et al. Establishment of genomic alterations in

ctDNA for precision oncology. *Mol Oncol*. 2019;13(1):10-22.
18. Hyman DM, Taylor BS, Baselga J. Implementing genome-driven oncology. *Cell*. 2017;168(4):584-99.
19. Kaps L, Hafner C, Kittel C, et al. Liquid biopsy in melanoma: state-of-the-art and future perspectives. *Eur J Cancer*. 2019;118:78-88.
20. Khakoo S, Richards R, Parker R, et al. ctDNA as a prognostic marker for early-stage cancer detection: A comprehensive review. *J Clin Oncol*. 2021;39(12):1578-86.
21. Kinde I, Wu J, Papadopoulos N, et al. Detection and quantification of rare mutations with massively parallel sequencing. *Proc Natl Acad Sci USA*. 2012;109(36):14508-13.
22. Leal A, Perez-Ruiz E, Ribelles N, et al. Liquid biopsy as a tool to assess the molecular landscape in early-stage breast cancer. *Oncologist*. 2021;26(7):558-65.
23. Luthra R, Taly V, Lee J, et al. Circulating tumor DNA as a diagnostic tool in liquid biopsy. *J Mol Diagn*. 2019;21(1):52-62.
24. Murtaza M, Dawson SJ, Tsui DW, et al. Non-invasive analysis of acquired resistance to cancer therapy by sequencing of plasma DNA. *Nature*. 2013;497(7447):108-12.
25. Newman AM, Bratman SV, To J, et al. An ultrasensitive method for quantifying circulating tumor DNA with broad patient coverage. *Nat Med*. 2016;22(5):548-53.
26. Pantel K, Alix-Panabières C. Liquid biopsy: potential and challenges. *Mol Oncol*. 2019;13(1):37-46.
27. Riva F, Loupakis F, Rehm S, et al. Circulating tumor DNA as a novel tool for the management of metastatic colorectal cancer. *Mol Cancer Ther*. 2017;16(12):2763-71.
28. Schwaederle M, Shim J, Engelman JA, et al. Use of liquid biopsy for molecular profiling in cancer patients. *J Clin Oncol*. 2016;34(16):1770-77.
29. Thress KS, Paweletz CP, Felip E, et al. EGFR mutation detection in ctDNA from NSCLC patients using the cobas EGFR Mutation Test v2. *J Thorac Oncol*. 2015;10(10):1617-23.
30. Yadav S, Singh A, Ghosh D, et al. Advances in liquid biopsy for monitoring treatment responses in cancer. *J Cancer Res Ther*. 2020;16(1):56-65.

*****