ISSN Print: 2664-6536
ISSN Online: 2664-6544
Impact Factor: RJIF **5.4**
IJBB 2025; SP-7(2): 19-24
www.biosciencejournal.net
Received: 28-05-2025
Accepted: 30-06-2025

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Two-Days National Conference on Multidisciplinary Approaches for Innovation and Sustainability: Global solution for contemporary Challenges-NCMIS (DPG Degree College: 17 th-18th 2025)

Advancing cancer treatment: The role of liquid biopsy and personalised medicine in precision oncology

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DOI: https://www.doi.org/10.33545/26646536.2025.v7.i2a.125

Abstract
Liquid biopsy is a novel method in oncology that allows for the less invasive identification and investigation of cancer-related biomarkers in bodily fluids. This technology has transformed cancer management by allowing for convenient and consistent monitoring of cancer progression, early-stage detection, and assessment of therapy responses. With cancer accounting for approximately 10 million deaths worldwide in 2020, innovative diagnostic approaches are critical for improving patient outcomes. Despite its potential, liquid biopsy has major hurdles in integrating into ordinary clinical practices. These include challenges with standardization, sensitivity, specificity, and a lack of empirical data to demonstrate viability and efficacy in community-based settings. The relationship between survival outcomes and liquid biopsy-guided therapeutic decisions warrants additional exploration. This study assesses the therapeutic potential of liquid biopsy in guiding customised treatment options for advanced solid tumours. It examines current research on liquid biopsy technologies, including multiomic approaches, droplet digital PCR (ddPCR), and next-generation sequencing (NGS). Liquid biopsy enhances diagnosis accuracy by capturing tumour heterogeneity and providing real-time insights into cancer dynamics. It lessens the invasiveness of standard tissue biopsies while increasing early detection, treatment stratification, and follow-up monitoring. However, scarcity of ctDNA (circulating tumour DNA), contamination hazards, and accessibility issues limit its widespread utilisation. Liquid biopsy has great potential to revolutionize oncology through customised treatment. Addressing technical and accessibility issues may result in equitable benefits for all people. Future research should focus on improving detection technologies, incorporating artificial intelligence into data processing, and devising cost-effective protocols to maximise therapeutic value.

Keywords: Tumour heterogeneity, liquid biopsy, precision oncology, early cancer detection

Introduction
Cancer is a significant global health challenge. In 2020, the World Health Organization (WHO) estimated that around 10 million deaths were attributed to cancer, with new cases expected to reach 35 million by 2050 [1]. Ageing demographics and enduring risk factors, including tobacco use, obesity, and infections, fuel this growth. Cancer comprises a vast range of illnesses that differ greatly based on tissue origin and genetic factors. Contemporary sequencing has shown tremendous intertumoral heterogeneity, complicating therapeutic options and prognosis assessments. It is now universally recognised that no two patients' cancers are molecularly identical [2].

Imaging and tissue biopsies are two examples of traditional diagnostic techniques that have serious drawbacks. Despite being the gold standard, tissue biopsy is intrusive, only offers a moment in time, and is not appropriate for ongoing monitoring. Although imaging is helpful for staging, it does not have the molecular resolution required to direct targeted treatments. Dynamic tumour evolution, which may include the formation of therapy-resistant clones, is frequently missed by these approaches. Conventional therapies, such as radiation and chemotherapy, are non-specific, frequently causing harm to healthy tissue while omitting the distinct molecular drivers of the tumour [3, 4].

Precision oncology represents a paradigm change. This method employs genomic, proteomic, and transcriptomic profiling to adapt diagnosis and treatment to an individual's tumour biology. Advances in next-generation sequencing (NGS) and biomarker discovery have enabled the identification of actionable mutations across cancer types [5]. Notably, medicines that target HER2 in breast cancer or BCR-ABL in leukaemia have significantly improved outcomes. Tumours with comparable mutations, regardless of origin, may react to the same targeted therapy, increasing tissue-agnostic treatment approvals [2].

The liquid biopsy is a vital tool for allowing this transition. This minimally invasive approach detects tumour-derived materials (e.g., ctDNA, CTCs, and exosomes) in bodily fluids such as blood. Liquid biopsy enables real-time monitoring, early discovery of resistance mutations, and dynamic evaluation of minimal residual disease. Because it samples circulating material, it may provide a complete and more representative picture of tumour heterogeneity than a single biopsy [3].

Objective

This review explores how liquid biopsy and tailored treatment can help advance precision oncology. It discusses the limitations of traditional approaches, clinical applications for liquid biopsy, and how molecular profiling is changing therapy tactics. It also discusses current issues and future approaches, such as the potential of AI-enhanced multi-omics diagnostics.

Liquid Biopsy: Technologies and clinical applications

Detecting tumour-derived materials, including circulating tumour DNA (ctDNA), circulating tumour cells (CTCs), and exosomes, in body fluids, primarily blood, is a minimally invasive technique known as liquid biopsy. In contrast to tissue biopsy, it enables serial surveillance and the capture of real-time tumour evolution, thereby facilitating the diagnosis, prognosis, and selection of treatment [3].

Circulating tumour cells (CTCs) are intact neoplastic cells released into the bloodstream. Elevated numbers are associated with an unfavourable prognosis. Although infrequent, they can be quantified using instruments such as CellSearch®, but sensitivity continues to pose a barrier. ctDNA denotes diminutive DNA fragments originating from malignancies. Technologies such as digital PCR and next-generation sequencing (NGS) detect mutations, methylation patterns, and resistance indicators at low doses. Circulating tumour DNA (ctDNA) levels indicate tumour load and can inform real-time treatment modifications [3]. Exosomes are extracellular vesicles that comprise proteins, DNA, and RNA. They are plentiful and consistent in blood, presenting diagnostic potential; however, clinical applications remain exploratory [6].

Clinical applications

1. **Genomic Profiling:** When tissue samples are unavailable, ctDNA testing can detect actionable alterations. For precision therapy, FDA-approved tests such as FoundationOne Liquid CDx and Guardant360 examine hundreds of genes [7].
2. **Treatment Selection:** Targeted medications or immunotherapies are used based on molecular profiling. Clinicians can modify treatment strategies in response to new resistance by using real-time mutation tracking [3, 7].
3. **Monitoring and MRD Detection:** Before imaging, ctDNA and CTC levels are monitored in response and identify minimum residual disease (MRD), allowing for prompt interventions [3].
4. **Prognosis:** Unfavourable results are frequently linked to elevated baseline levels of ctDNA or CTCs. Additionally, while making decisions on immunotherapy, ctDNA-based tests can assess markers such as TMB and MSI [3][7].
5. **Clinical Trial Matching:** Patients can be matched to molecularly targeted trials like basket or umbrella studies thanks to the liquid biopsy's ability to identify uncommon mutations [7].

Personalised medicine in oncology: trials, targeting and stratification

Personalised oncology tailors therapy based on a patient's molecular profile rather than the tumour site alone. This transition is supported by innovative clinical trial designs. Basket trials evaluate a single drug for multiple cancer types with a shared mutation (e.g., BRAF, NTRK). In umbrella studies, patients with the same cancer type are assigned different treatments based on distinct biomarkers (e.g., EGFR, ALK) [8].

Large-scale efforts like NCI-MATCH screen thousands of patients to match them with specific treatments, expediting drug development and approval. Beyond genomics, multidisciplinary molecular tumour boards (MTBs) analyse sequencing results alongside clinical context to recommend medications, trials, or combinations. Studies suggest that MTB-guided treatment improves survival relative to empirical treatment. Approved targeted therapies include HER2 inhibitors (breast/gastric), BRAF inhibitors (melanoma), and AR inhibitors (prostate). Immunotherapies, e.g., checkpoint inhibitors like PD-1/PD-L1 or CTLA-4, require biomarkers such as TMB, MSI, or PD-L1 expression for optional patient selection. Stratification incorporates molecular, clinical, and logistical variables. Even with a targetable mutation, a frail patient may be ineligible for aggressive treatment. Emerging tools merge multi-omics and AI to facilitate such sophisticated decision-making [9].

Integration of liquid biopsy into personalised medicine

Workflows in precision oncology increasingly include liquid biopsies. A typical procedure consists of:

1. Tissue or, if unavailable, plasma ctDNA tumour profiling.
2. MTB evaluation of molecular results for trial matching or treatment.
3. Using ctDNA for serial monitoring to monitor response or new resistance.
4. The use of ultrasensitive assays for MRD identification and early relapse warnings.

In NSCLC, plasma-based EGFR mutation testing is typical when tissue is scarce. FDA recommendations encourage tissue confirmation for negative liquid biopsy results to avoid false reassurance. MTBs incorporate liquid biopsy findings to match patients with approved medications or trial options, including off-label combinations. Even when no mutations are discovered, data suggest further steps, such as different medications or additional testing. For patients

undergoing targeted or immunotherapy, regular liquid biopsies assist in assessing efficacy. Rising ctDNA signals resistance, while reductions reflect a good reaction. Importantly, clinical trials increasingly accept liquid biopsy data for inclusion, especially in tissue-agnostic research. This expands access to novel treatments based on blood-derived genetic data [3, 7].

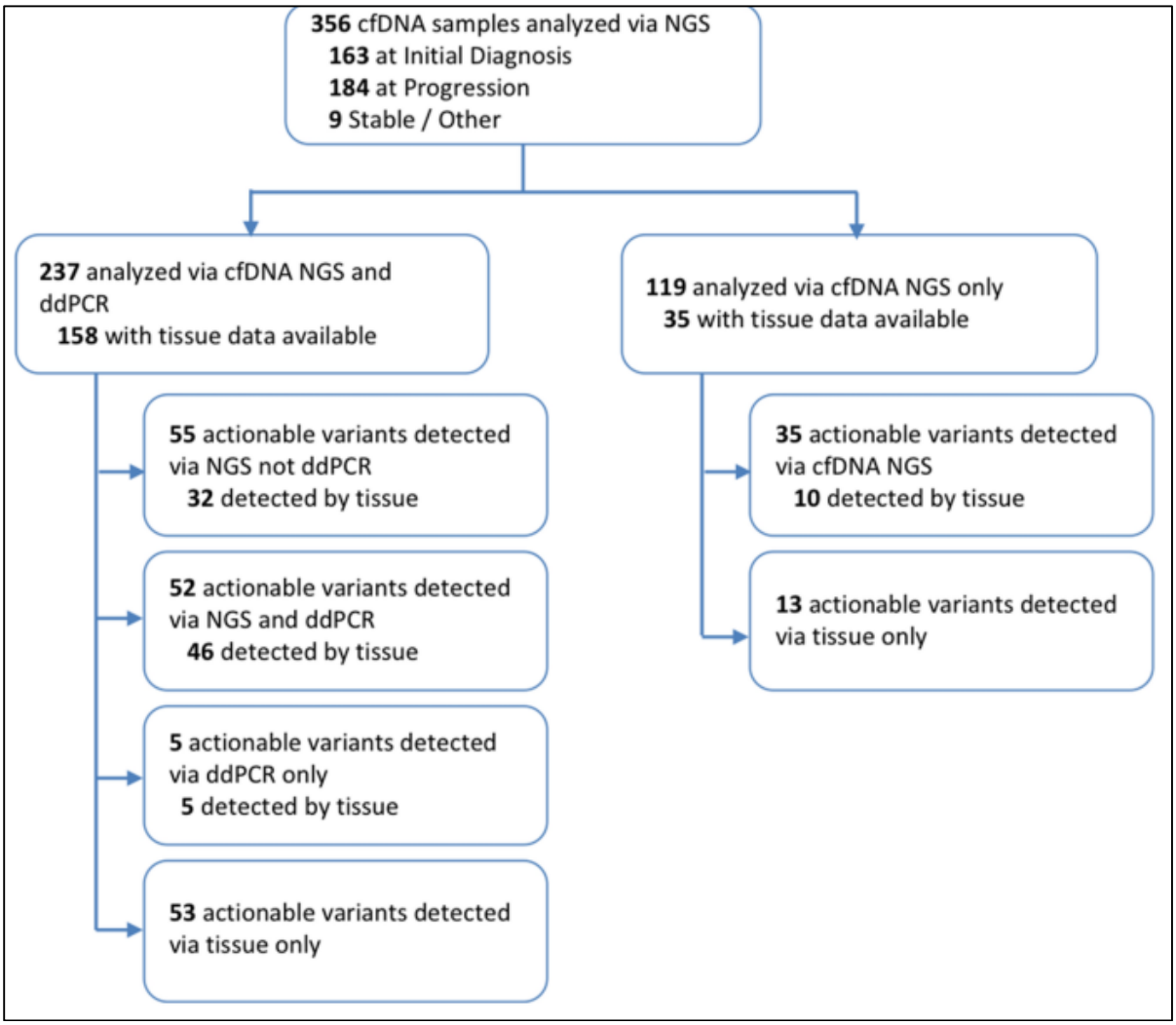

Fig 1: A flow chart summarizing the types of tests conducted; adapted from Garcia *et al*., (2021) [22]

Methodology

To assess the function of liquid biopsy and personalised medicine in precision oncology, a systematic narrative literature review was performed. To find research published in English between January 2000 and May 2025, several important databases were searched, including PubMed/Medline, Embase, Scopus, Web of Science, and the Cochrane Library. MeSH headings and free-text phrases such as "liquid biopsy", "ctDNA", "circulating tumour cells", "precision oncology", and "targeted therapy" were combined in the search terms. The search was narrowed down using Boolean operators [10].

Peer-reviewed studies about human cancer patients and the clinical or translational use of liquid biopsy or customised medicine strategies were considered for inclusion. Original research, systematic reviews, and narrative reviews were all regarded as eligible study types. Editorials, conference abstracts, animal studies, and grey literature were all excluded [10].

Screening adhered to PRISMA criteria. Duplicates were deleted with reference management software. Two reviewers independently reviewed titles and abstracts, and entire texts were evaluated for eligibility. Disputes were addressed via conversation or third-party arbitration. The selection process was documented using a PRISMA flow diagram [11].

The data was extracted using a standard template. Important details included study design, patient population, cancer type, biopsy modality (e.g., ctDNA, CTCs, exosomes), analytical methodologies, primary outcomes (e.g., diagnostic accuracy, predictive value), and conclusions. Thematic synthesis divided findings into broad categories such as methodology, clinical applications, problems, and future potential. Due to the review's narrative character, no formal quality assessment or meta-analysis was undertaken [11].

The methodology emphasised transparency, reproducibility, and relevance, relying on best practices in biomedical narrative reviews.

Results

Early studies, conducted between 2005 and 2010, established liquid biopsy's clinical importance. Cristofanilli *et al*. (2005) found that breast cancer patients with ≥5 circulating tumour cells (CTCs) per 7.5 ml had considerably lower survival rates [12]. Similarly, Cohen *et al*. (2008) found

that metastatic colorectal cancer patients with greater CTC levels had shorter progression-free and overall survival [13]. Diehl *et al*. (2008) found that ctDNA levels were substantially linked with tumour burden and clinical progression in colorectal cancer, indicating the potential for real-time surveillance [14].

Significant technical advancements took place between 2011 and 2015. More than 75% of patients with advanced malignancies and 48-73% of individuals with localised tumours have ctDNA, according to Bettegowda *et al*. (2014). Research revealed that ctDNA had a high sensitivity and specificity for detecting colorectal cancer mutations such as KRAS. Regulatory support resulted from these findings: when tissue was not available, the European Medicines Agency and Chinese specialists authorized plasma ctDNA for EGFR mutation testing in NSCLS. Expanded mutation panels and the detection of low-frequency variations were made possible by concurrent advancements in digital PCR and NGS [15].

Clinical implementation accelerated between 2016 and 2020. The Cobas EGFR Mutation Test v2 for ctDNA-based EGFR identification in NSCLC was approved by the FDA. A 44.6% response rate was attained in a large Chinese research study that used digital PCR to guide Osimertinib therapy and detect EGFR T790M mutations with greater sensitivity than ARMS-PCR. With FDA approval, multi-gene NGS tests like FoundationOne Liquid CDx and Guardant360 CDx become commonplace instruments for non-invasively profiling hundreds of genes, enabling targeted and immunotherapy choices for a variety of tumour types [7, 16].

Recent research (2021-2025) emphasizes the liquid biopsy's function in monitoring and therapy selection. The DYNAMIC study demonstrated that ctDNA-guided treatment for stage II colorectal cancer reduced chemotherapy use while maintaining recurrence-free survival. In advanced NSCLC, variations in ctDNA levels throughout therapy predicted overall survival, with persistent ctDNA associated with poorer results. A 2025 meta-analysis indicated that ctDNA clearance was associated with considerably prolonged life across regimens [17, 18].

Beyond mutations, other indicators such as methylation patterns and exosomal RNAs are emerging. Combining them with TMB and MSI increases detection and customization. Liquid biopsy has now been introduced into standard practice and clinical trials, showing its evolution from an experimental tool to a critical component of precision oncology [17, 18].

Table 1: Summary of key studies in liquid biopsy

Author (Year)	Cancer Type	Sample	Biomarker	Method	Key Outcome
Cristofanilli (2005) [12]	Breast	Blood	CTCs	CellSearch	CTC ≥5 predicts worse OS
Diehl (2008) [14]	Colorectal	Plasma	ctDNA	BEAMing	ctDNA tracks tumor burden
Bettegowda (2014) [15]	Pan-cancer	Plasma	ctDNA	Digital PCR	Detected in >75% of advanced cancers
Tie (2022) [17]	Colon	Plasma	ctDNA	NGS	Guided chemo reduces toxicity

Discussion

Traditional diagnostic approaches, such as tissue biopsy and imaging, provide only a partial, static image of cancer, often failing to account for its complexity and heterogeneity. A single biopsy can miss crucial alterations present in other tumour locations or fail to detect growing resistance throughout therapy. Repeated biopsies are invasive and impractical for continual monitoring. As a result, many patients continue to use broad chemotherapy regimens, which are less effective and often produce considerable side effects [19].

Liquid biopsy offers a minimally invasive solution to these difficulties. By evaluating circulating tumour DNA (ctDNA), tumour cells (CTCs), or exosomes, doctors can track tumour progression over time. This technique enables the early diagnosis of resistance mutations, dynamic assessment of treatment response, and identification of relapse far before clinical signs develop. For example, ctDNA has been demonstrated to detect minimal residual disease (MRD) months ahead of radiographic findings [20].

Importantly, liquid biopsies also offer a scalable, repeatable approach for genetic profiling, particularly when tumour tissue is inaccessible or insufficient. FDA-approved technologies such as Guardant360 and FoundationOne Liquid CDx have already shown robust performance in finding actionable mutations across a spectrum of malignancies, enabling precision therapy selection [21].

Table 2: Comparison table-traditional biopsy vs liquid biopsy

Feature	Traditional Biopsy	Liquid Biopsy
Invasiveness	High	Low
Repeatability	Limited	High
Detection of heterogeneity	Limited to sample location	Captures systemic tumor DNA
Temporal monitoring	No	Yes
Cost	Variable	Decreasing with tech advances

Limitations

Despite its potential, liquid biopsy has limits in both sensitivity and interpretation. ctDNA concentrations can be exceedingly low, particularly in early-stage or slow-growing malignancies. Inadequate tumour shedding or poor sample quality may make detection difficult. False negatives frequently necessitate confirmatory tissue biopsies. Furthermore, identifying tumour derived mutations from background noise, such as clonal hematopoiesis, is difficult and necessitates extensive bioinformatics [3].

Liquid biopsy provides a partial view of tumour biology. It detects specific molecular changes but does not consider spatial context, the tumour microenvironment, or immune infiltration. As a result, it cannot fully substitute tissue biopsy in all situations. There is also a lack of large-scale evidence supporting outcome improvement. While

numerous studies show feasibility, few randomized trials reveal that liquid biopsy-driven decisions increased survival. Furthermore, a tiny number of individuals have actionable mutations, which limits immediate usefulness [3, 7].

Implementation problems include a lack of common test quality standards, sensitivity heterogeneity across platforms, and access inequities. Insurance coverage remains patchy, particularly in low- and middle-income areas [7].

Future Prospects

To increase the accuracy of liquid biopsy, future developments in cancer diagnostics will concentrate on multi-omics integration, which combines ctDNA with transcriptomics, proteomics, and methylomics. Predictive modelling and signal identification are being advanced by AI-driven technologies. The goal is to increase accessibility through the development of affordable, portable, and smartphone-compatible diagnostics. Assays for multi-cancer early detection (MCED) have promise for screening people who don't exhibit any symptoms. To scale these technologies across various healthcare systems, international cooperation and supportive legislation are crucial.

Conclusion

In the age of precision oncology, liquid biopsy has become a potent instrument that allows for real-time, minimally invasive tumour dynamics monitoring. It helps with treatment response, minimal residual illness, and early detection of resistance mutations by identifying circulating tumour DNA, cells, and exosomes. This method overcomes the drawbacks of conventional biopsies and provides more freedom in directing customised treatments.

However, issues like inconsistent test performance, false negatives, and low sensitivity in early-stage malignancies need to be addressed. Currently, liquid biopsy is used in conjunction with tissue biopsy rather than in substitution for it, particularly where histological and geographic context are important.

In the future, combining liquid biopsy with artificial intelligence and multi-omics data will improve patient classification and diagnostic precision. These advantages might soon be extended to larger populations thanks to technologies like low-cost, portable diagnostics and multi-cancer early detection kits.

In conclusion, liquid biopsy is becoming more and more useful in clinical settings, despite certain limitations. It is positioned to become a fundamental component of standard cancer care and a pillar of personalised medicine with further innovation, validation, and fair access.

Acknowledgement

I gratefully thank Dr. Asha Rani from the Department of Zoology, DPG Degree College, Gurugram, for her essential mentorship, direction and ongoing encouragement throughout this review. I also acknowledge the utilisation of resources from PubMed, Scopus, and other databases, which were important in the literature review process.

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