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Role of liquid biopsy in cancer prevention and treatment process – review paper

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ABSTRACT

Liquid biopsy is an insufficiently studied diagnostic method that detects cancer cells and other cancer biomarkers. It is a method that can be invasive, minimally invasive, or non-invasive and uses biological fluids such as blood, urine, saliva, cerebrospinal fluid, stool, semen, breast milk, or vaginal discharge, but usually blood. Its particular advantage is the ability to detect cancer at a very early stage. Detecting cancer at a lower stage increases the patient's chances of complete recovery, reducing the risk of complications and the overall cost of therapy. In addition to detecting cancer, a liquid biopsy can assess the effectiveness of anticancer therapy and detect minimal residual disease after treatment. After the method was introduced in 2010, the concept was widely developed, giving many opportunities for the future in oncology. Adhering to proper standardization protocols provides the chance to establish a universal screening test in the future. At the moment, a combination of both methods should be considered, as they can complement each other to provide the best outcome for patients.

Keywords: liquid biopsy, cancer screening, Cell-Free DNA, Circulating Tumor DNA, circulating tumor cells

1. INTRODUCTION

Biopsy, by definition, is a medical procedure performed by a doctor in which a sample of tissue or cells is taken and examined by a pathologist using histological, cytological, and sometimes molecular techniques. The primary purpose of a biopsy is to establish a definitive diagnosis by assessing tissue architecture and cellular morphology. There can be a needle-based biopsy (fine-needle aspiration and core needle biopsy) - the most common one, which remains a gold standard, endoscopic biopsy – that collects samples during colonoscopy, gastroscopy, bronchoscopy, cystoscopy, hysteroscopy etc., bone marrow biopsy, skin biopsy, and surgical biopsy - which may be either incisional or excisional depending on the clinical indication (Layfield & Gopez, 2019). It is a test done when a tumor or cancer is suspected. It identifies the tumor type (benign or malignant) and metastasis status, and facilitates treatment selection. Despite its central role in oncological diagnostics, traditional tissue biopsy has several limitations. It can be invasive, give discomfort or complications for the patient, and sometimes it cannot be repeated safely. Tissue biopsy provides only information from a single tumor site at a specific point in time, which may not fully reflect tumor heterogeneity.

First introduced in 2010, the concept of a liquid biopsy was to use a blood sample to detect circulating tumor cells (CTCs) (Pantel & Alix-Panabières, 2010). Recent advancements in molecular biology and technology (such as next-generation sequencing, digital polymerase chain reaction (PCR), and high-sensitivity analytical techniques) have enabled the detection of low levels of tumor cells in body fluids. This progress has improved the diagnostic capabilities of liquid biopsy for searching for cancer-related material in a person's blood or other fluids.

What started as a concept then is now, 15 years later, extended to other fluids that can be found in our body, such as urine, saliva, sputum, stool, semen, breast milk, and vaginal discharge - non-invasive sources—as well as cerebrospinal fluid, which requires the most invasive access (Reckamp et al., 2016; Patel et al., 2022; Qin et al., 2022; Diehl et al., 2008; Saitta et al., 2023; Cunningham & Turner, 2023; Zhu et al., 2022; Wang et al., 2024; Friedman et al., 2022).

Not only can it be used to search for CTCs, but new analysis methods allow us to detect parts of DNA such as circulating cell-free DNA (cfDNA), circulating cell-free RNA (cfRNA, miRNA, mRNA), circulating tumor DNA (ctDNA), metabolites, tumor-specific proteins, tumor-educated platelets, and exfoliated cancer cells (Edsjö et al., 2023). These biomarkers provide valuable information on tumor genetics, heterogeneity, disease progression, and treatment response, often in real time. A traditional biopsy, also called a tissue biopsy, involves invasive sampling of suspected tumor tissue to collect material for further examination. In contrast, a liquid biopsy provides information from an easily accessible fluid.

Aim of the study

This study aims to provide an overview of the subject, spreading knowledge about liquid biopsy and its role in clinical practice. This study aims to compare liquid biopsy with traditional tissue biopsy, marking the advantages and disadvantages of each.

In addition, the study seeks to highlight the current challenges and practical limitations of liquid biopsy in routine clinical settings, thereby contributing to a clearer understanding of its clinical value and areas requiring further improvement.

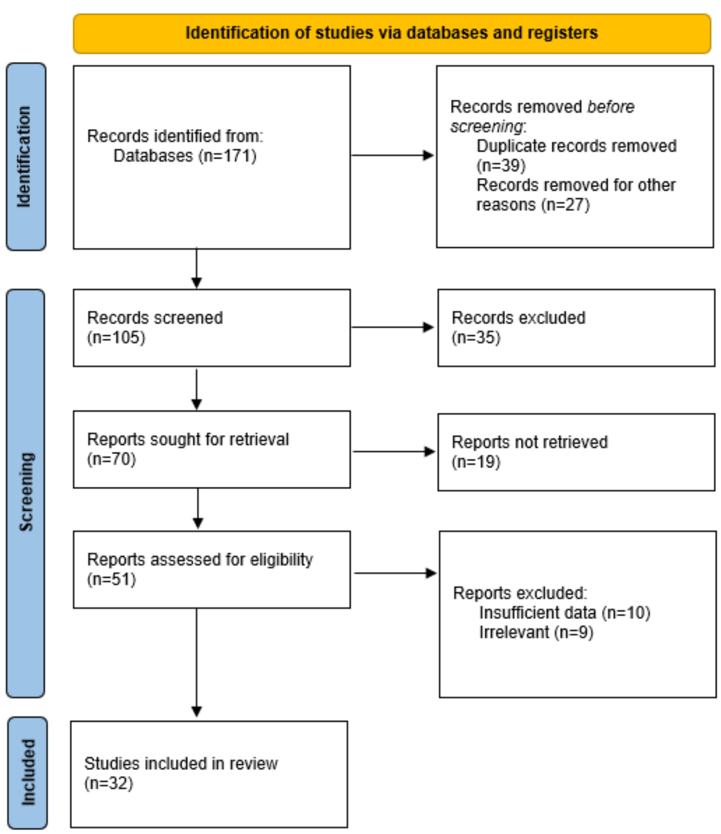

Figure 1. PRISMA CONSORT chart

2. REVIEW METHODS

This study was a narrative review of the existing literature on liquid biopsy and its clinical applications. The review paper was based on articles and pages available online, such as on PubMed, Google Scholar, medical websites, and Google. Relevant publications were identified through targeted keyword searches related to liquid biopsy, circulating biomarkers, cancer diagnostics, and clinical implementation.

When selecting eligible articles, we sought the latest innovations in liquid biopsy, including new applications, the range of sample types that can be used, and the types of cancer it can detect. Only English-language articles available online were included, mainly those published after 2020 to provide up-to-date, clinically relevant information. Older articles were chosen to provide a brief historical background and to describe the subject's origin and early development.

The selected literature was analysed and synthesized to compare liquid biopsy with traditional tissue biopsy, evaluate their respective advantages and disadvantages, and identify current challenges related to the clinical use of liquid biopsy. The article screening process followed the PRISMA guidelines (Figure 1).

3. RESULTS & DISCUSSION

What are the differences between traditional biopsy and liquid biopsy?

Although both methods aim to provide diagnostic and prognostic information about cancer, their methodologies differ, as do the types of biological information obtained and their clinical applicability. Traditional biopsy provides information about the histopathologic type of tumour and its cellular morphology, whereas liquid biopsy provides indirect molecular information derived from tumour-related components circulating in body fluids. These two approaches should be considered complementary, not mutually exclusive. (Siravegna et al., 2017; Wan et al., 2017).

Liquid biopsy results usually come in 1 week. Results from a traditional biopsy typically take 3-5 weeks. That is almost 20 days earlier, making it 3 times faster than traditional biopsy (Sehayek et al., 2022; Stergiopoulou et al., 2023). Shorter processing time is clinically significant, as it allows for earlier treatment initiation, faster adjustment in the event of resistance, and more timely clinical decision-making in advanced or rapidly progressing cancers.

There are already commercial companies that offer various liquid biopsy tests to screen for multiple cancer types. These commercially available assays reflect the growing integration of liquid biopsy into clinical practice; however, variability in test performance, cost, reimbursement policies, and regulatory approval remains a challenge and may limit widespread and equitable access.

What can we do to prevent ourselves from cancer?

Nowadays, worldwide cancer is the second most common cause of death, right after circulatory diseases. It is estimated that 1 in 5 people in the population will have cancer at some point during a lifetime, and approximately every tenth person will die from cancer. An 80% increase in cancer cases is projected by 2050 compared with the present (Bizuayehu, 2024). This expected rise highlights the urgent need for new, more effective, less time-consuming, and economically sustainable approaches to cancer prevention, early detection, and management.

Over the years, our understanding of cancer risk factors has significantly improved. Factors are modifiable or non-modifiable. Modifiable factors can be influenced by lifestyle choices - diet containing high sugar, low-fibre or processed food, and alcohol consumption, smoking cigarettes or vapes, obesity and overweight, physical inactivity, and exposure to UV light. Other risk factors, including age, genetic mutations, and family history, are non-modifiable. Certain risks can be reduced through medical interventions; for example, infection-related cancers may be prevented through vaccination (such as human papillomavirus vaccination (HPV) for cervical cancer and hepatitis B vaccination for liver cancer) or antibiotic treatment (Helicobacter pylori infection, which is associated with gastric cancer).

Regular medical check-ups are essential in cancer prevention. These check-ups include routine blood tests, annual physical examinations, and screening programs at specific ages or in gender groups - mammography, colonoscopy, Pap smears, and prostate-specific antigen testing.

Early cancer detection through screening can improve overall outcomes. It can also reduce the mortality rate, but unfortunately, not every type of cancer can be detected by screening tests, and some can remain asymptomatic until an advanced stage. Emerging technologies, including liquid biopsy, artificial intelligence–assisted diagnostics, and molecular screening methods, hold promise for improving early cancer detection and prevention. These approaches may enable the identification of cancer-related changes at a molecular level even before clinical symptoms appear, allowing earlier intervention and personalized prevention strategies. Integrating traditional prevention measures with novel diagnostic technologies may represent a key step toward reducing the global cancer burden.

How does the liquid biopsy work?

Depending on the type of sample that was collected and the clinical purpose of the examination, different components are targeted. The process generally begins with collecting the sample (most commonly blood, but also urine, saliva, or cerebrospinal fluid). This process is followed by careful processing to preserve nucleic acids and other biomarkers. Using specialized lab techniques, it is possible to isolate specific components, such as CTCs, ctDNA, or circulating cell-free nucleic acids. These components are then analyzed to identify the tumor's molecular profile and to check treatment response and minimal residual disease (MRD) (Siravegna et al., 2017).

The most common techniques for analyzing liquid biopsy are PCR and NGS (next-generation sequencing) (Shegekar et al., 2023). Digital polymerase chain reaction is a very sensitive and accurate method. It detects point mutations in ctDNA at very low allele fractions.

There are some impressive techniques in PCR: droplet digital PCR (ddPCR) and beads, emulsions, amplification, and magnets called BEAMing. These methods are highly accurate at quantifying specific genetic changes, making them valuable tools in research and clinical settings (Elazezy & Joose, 2018).

On the other hand, NGS allows the analysis of multiple genes or genomic regions simultaneously and enables the detection of a range of genetic modifications, including point mutations, insertions, deletions, copy number variations, and gene fusions (Schwaederle et al., 2016).

The analysis method we choose depends on the purpose of the examination. PCR is often used for targeted mutation detection and for monitoring treatment. NGS is preferred for genomic profiling and the discovery of new changes. Together, these technologies make liquid biopsy an important tool in oncology. Table 1 summarizes the types of components found in sample materials.

Table 1. Types of components that can be found in sample materials

INVASIVENESS	SAMPLE	ISOLATED MATERIAL	TYPE OF CANCER
Invasive	Cerebrospinal fluid	ctDNA CTCs Circulating metabolites Tumor specific proteins	CNS tumors
Minimally invasive	Blood	ctDNA CTCs	Various types of cancers
Non-invasive	Urine	utDNA	Urothelial carcinoma
		Exfoliated cancer cells	Bladder and prostate cancer
		Circulating metabolites and proteins	Various types of cancers

	Saliva	ctDNA CTCs Circulating metabolites and proteins	Head and neck tumors
	Sputum	ctDNA CTCs Circulating metabolites and proteins	Respiratory tract tumors
	Semen	CTCs	Prostate cancer
	Stool	ctDNA	Colorectal cancer
	Breast milk	ctDNA	Breast cancer
	Vaginal discharge	cfRNA, ctDNA	Cervical cancer, ovarian cancer

What types of cancer can it target?

Liquid biopsy can target many cancer types, yet it is the most used at the moment in urology to detect prostate cancer. Urinary liquid biopsy uses urine and searches for mainly two types of cancer: bladder and prostate cancer (Ionescu et al., 2022). It is a powerful tool in the management of prostate cancer that does not cause any complications and is entirely painless (Groen & Schalken, 2022). Depending on the sample used, it is possible to detect different types of cancers. Cerebrospinal fluid is used to detect cranial nervous system tumors such as gliomas, where traditional tissue biopsy is much more invasive. It requires more to perform (Otsuji et al., 2024). Saliva searches for head and neck tumors, and sputum searches for respiratory tract tumors. Semen is used to detect prostate cancer, male-specific reproductive system tumors, and urine for bladder, prostate, and renal cell carcinoma (Li et al., 2023). The blood sample can detect various types of cancers.

How can we apply liquid biopsy to cancer prevention?

Ultimately, what we would like to achieve is a universal screening test. By taking a simple blood sample, we aim to detect early cancer-related changes in the body, monitor precancerous lesions, and potentially intervene before full-blown cancer develops—all at a relatively low cost and within a short timeframe. Liquid biopsy could be applied across several prevention strategies, enabling early detection.

It is incredibly helpful for screening patients at higher risk for cancer, especially those with a family history or genetic predispositions. Additionally, it plays an important role in monitoring patients with precancerous conditions, such as Barrett's esophagitis or colorectal polyps. By identifying potential markers of cancer development early, we can make proactive decisions to improve health outcomes. Liquid biopsy could enable real-time control of minimal residual disease after treatment, providing early warning of recurrence and enabling timely therapeutic intervention.

The lower the stage of cancer at detection, the higher the chance of complete recovery, with significantly better treatment outcomes and survival rates (Liang et al., 2025). The cost of care increases with advancing stage - stage III or IV often requires multiple hospitalizations, complex surgeries, additional adjuvant therapy (chemotherapy, radiotherapy), and numerous imaging, laboratory, and pathology tests (Butnari et al., 2025). By contrast, early detection via liquid biopsy could reduce both the clinical and economic costs, enabling simpler, less invasive, and more effective interventions.

Despite promising advances in liquid biopsy for preventive purposes, challenges remain. One of these concerns is sensitivity and the potential for false-positive results, variations among platforms, and the need for validation in asymptomatic populations. Research is focused on addressing these challenges and developing standardized protocols to enhance the feasibility and reliability of preventive liquid biopsy as a tool in the near future.

Room for improvement

There are still weak points in mainstream testing. One of the biggest is a meager amount of ctDNA from a particular tumor in the bloodstream. The "ctDNA booster" - a priming agent administered before collecting a blood sample could prove helpful. That agent protects ctDNA from rapid clearance from the blood (Martin-Alonso et al., 2024). A low ctDNA count can increase the risk of false-negative test results. One of the disadvantages of liquid biopsy is its disability to obtain a histologic diagnosis - it cannot provide tumor properties, which are essential to define grading and staging, but it can narrow a search. Additionally, ctDNA can reveal a variant specific to many types of cancer, leading to misdiagnosis (Bettegowda et al., 2014).

4. CONCLUSION

Liquid biopsy revolutionizes the approach to cancer prevention, with the hope that someday a simple blood sample will be enough to detect any cancer at an early stage or as a tool in the fight against cancer. There are still areas in need of development, particularly in standardization protocols (pre-analytical and analytical), biomarker validation, and the establishment of clinical guidelines. That is essential for the broader acceptance and routine implementation of this method.

Future research should aim to enhance sensitivity and specificity, refine clinical thresholds, conduct prospective trials, and tackle issues related to cost-effectiveness and accessibility. Additionally, ethical considerations, such as the implications of false-positive results and the anxiety patients may experience concerning early cancer detection, need to be thoroughly assessed before liquid biopsy can be effectively implemented as a population-level screening tool.

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Author's Contribution:

Conceptualization, supervision, and project administration: Gabriela Krych, Aleksandra Rusak, Joanna Oklińska.
Methodology: Michał Skóra, Klaudia Jadczak.
Software, validation, formal analysis, investigation, resources, writing original draft preparation: Weronika Gniado, Bartłomiej Kazimierski, Dawid Mądry.
Writing, review editing, and visualization: Gabriela Krych, Aleksandra Rusak.
All authors have read and agreed with the published version of the manuscript.

Informed consent

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Ethical approval

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Conflict of interest

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Data and materials availability

All data associated with this study will be available based on reasonable request to the Corresponding Author.

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