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Perspective

Liquid Biopsy Approaches in Precision Medicine

George Papadopoulos*

Department of Molecular Medicine, University of Athens, Athens, Greece.

ABOVE THE STUDY

Liquid biopsy has emerged as one of the most transformative innovations in precision medicine, fundamentally changing how we detect, monitor, and understand disease-particularly cancer. In my view, its greatest strength lies in its ability to provide real-time molecular insights from a simple blood sample, eliminating many limitations of traditional tissue biopsy, such as invasiveness, sampling bias, and inability to capture tumor heterogeneity. As precision medicine continues to evolve, liquid biopsy is increasingly positioned as a cornerstone technology for dynamic, patient-specific decision-making.

At its core, liquid biopsy refers to the analysis of tumor-derived components circulating in bodily fluids. These include Circulating Tumor Cells (CTCs), exosomes, microRNAs, and other cell-free nucleic acids. Each of these components provides a different layer of biological information. ctDNA reflects the genetic alterations of tumor cells, CTCs provide intact cellular material for morphological and functional studies, while exosomes and RNA species capture regulatory and signaling dynamics. In my opinion, the integration of these multiple analytes is what truly elevates liquid biopsy from a diagnostic tool to a comprehensive molecular surveillance system.

One of the most impactful applications of liquid biopsy is in early cancer detection. Tumors release small amounts of DNA and other biomolecules into circulation even at early stages, allowing for potential identification before clinical symptoms appear. Although sensitivity remains a challenge, especially in early-stage disease, advances in highly sensitive sequencing technologies and digital are steadily improving detection thresholds. The concept of detecting cancer through a "molecular fingerprint" in blood is particularly compelling because it shifts the paradigm from reactive diagnosis to proactive screening.

Another major strength of liquid biopsy lies in its ability to capture tumor heterogeneity. Solid tumors are not uniform; they consist of multiple subclonal populations with distinct genetic and epigenetic profiles. Traditional biopsies sample only a small portion of the tumor, often missing this diversity. In contrast, ctDNA in the bloodstream can originate from multiple tumor sites, offering a more comprehensive overview of the disease landscape. In my view, this ability to overcome spatial sampling bias is one of the most clinically significant advantages of liquid biopsy.

Liquid biopsy also plays a crucial role in monitoring treatment response and detecting Minimal Residual Disease (MRD). Changes in ctDNA levels can reflect how a tumor is responding to therapy in near real time, often before radiological changes become apparent. Persistent or rising ctDNA after treatment may indicate residual disease or early relapse. This dynamic monitoring capability allows clinicians to adjust therapeutic strategies more rapidly, potentially improving patient outcomes.

In precision medicine, liquid biopsy is increasingly being used to guide targeted therapies. By identifying actionable mutations such as *EGFR*, *KRAS*, or *ALK* alterations clinicians can select therapies tailored to a patient's specific tumor profile. Furthermore, serial sampling enables detection of resistance mutations that emerge during treatment, allowing for timely modification of therapeutic regimens. In my opinion, this iterative feedback loop between molecular profiling and treatment adjustment represents the true essence of precision oncology.

Despite its promise, several challenges remain. One of the most significant is the low abundance of tumor-derived material in early-stage disease, which can limit sensitivity. Biological noise from normal cell-free DNA also complicates interpretation. Additionally, standardization of pre-analytical and analytical workflows is still lacking, leading to variability across laboratories. Another concern is cost and accessibility, as advanced sequencing platforms may not yet be widely available in resource-limited settings.

Ethical considerations are also becoming increasingly relevant. Liquid biopsy can reveal incidental findings, germline mutations, and incidental disease risks, raising questions about patient consent, data privacy, and psychological impact. Proper

Correspondence to George Papadopoulos Department of Molecular Medicine, University of Athens, Athens, Greece. E-mail: george.papadopoulos@uoa.gr

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counseling and regulatory frameworks are essential to ensure responsible clinical use.

Looking ahead, the integration of liquid biopsy with artificial intelligence, multi-omics profiling, and digital health platforms is likely to further enhance its clinical utility. Machine learning algorithms can identify complex biomarker patterns, improving diagnostic accuracy and predictive power. Additionally, combining liquid biopsy with imaging and clinical data may enable truly holistic patient monitoring systems.

In conclusion, liquid biopsy represents a paradigm shift in precision medicine by enabling non-invasive, real-time, and comprehensive molecular profiling of disease. In my view, its continued development will redefine how we detect, monitor, and treat cancer and other complex diseases. While technical and clinical challenges remain, the trajectory of innovation strongly suggests that liquid biopsy will become an indispensable tool in future healthcare systems.