Annals of *Research* in *Oncology*Vol. 5(3), 116-129, 2025

#### **REVIEW**

# POINT-OF-CARE TESTING: AN ALLY FOR PRECISION ONCOLOGY

Sima **Singh** <sup>1,\*</sup>, Panagiota M **Kalligosfyri** <sup>1</sup>, Antonella **Miglione** <sup>1</sup>, Ada **Raucci** <sup>1</sup>, Alessandra **Glovi** <sup>1,2</sup>, Gabriella **Iula** <sup>1</sup>, Michelino De **Laurentiis** <sup>3</sup>, Canio **Martinelli** <sup>4,5</sup>, Stefano **Cinti** <sup>1,\*</sup>

- <sup>1</sup> Department of Pharmacy, University of Naples Federico II, Naples, Italy
- <sup>2</sup> Scuola Superiore Meridionale, University of Naples Federico II, Naples, Italy
- <sup>3</sup> Department of Breast and Thoracic Oncology, Istituto Nazionale Tumori IRCCS Fondazione G. Pascale, Napoli, Italy
- <sup>4</sup> Sbarro Institute for Cancer Research and Molecular Medicine and Center of Biotechnology, College of Science and Technology, Temple University, Philadelphia, PA
- <sup>5</sup> Unit of Obstetrics and Gynecology, Department of Human Pathology of Adult and Childhood Gaetano Barresi, University of Messina, Messina, Italy
- \* Correspondence to: ✓ stefano.cinti@unina.it; sima.singh@unina.it

ABSTRACT: the future of cancer care will be based on precision oncology, which uses individual tumor molecular profiles to provide the correct drug to the appropriate patient at the appropriate time. This approach might deliver precise results with minimal side effects and enhanced treatment success rates. However, the vision fails to materialize in reality because current tools remain centralized and needs advanced infrastructure together with specialized/trained staff and prolonged procedural time. The lack of laboratory capabilities in healthcare settings can be addressed through Point-of-Care (POC) testing which enables diagnostic methods to be performed near or at the site of patient care thus linking laboratory capabilities to practical healthcare delivery. The technology is capable of delivering specific diagnostic tests at bed-side, and in particular in remote areas. The implementation of POC testing enables precision oncology to become practical allowing for prompt medical decisions. POC systems allow for continuous tracking of relapse, resistance and response. POC testing serves as an essential component of precision oncology because it enables personalized care more quickly and directly to patients. This review synthesizes current and emerging POC platforms for oncology, evaluates their analytical performance, clinical readiness, and regulatory landscape, and identifies unmet needs that must be addressed to enable routine adoption for diagnosis and monitoring.

Doi: 10.48286/aro.2025.113

**Impact statement:** The possibility of reaching precision oncology solutions cannot be considered apart from a quick monitoring of therapeutic efficacy. In order to tailor therapies for cancer patients, the development of point-of-care devices would open to easy and quick response by specialists and patients, also strengthening the concept of telemedicine.

**Key words:** precision oncology; POC testing; molecular diagnostics; liquid biopsy; sensors.

Received: Mar 03, 2025/Accepted: Sept 10, 2025

Published: Oct 14, 2025

# INTRODUCTION

Cancer treatment followed under a "one-size-fitsall" model for many decades because it relied on standardized protocols that used tumor histology, anatomical site, and clinical staging as guidance (1). These techniques show effectiveness for treating initial-stage cancer, yet fails to handle molecular complexity, heterogeneous nature and its dynamic evolutionary changes (2).

The field of tumour-genome profiling has experienced significant advancement during the last twenty years. The first wave started with commercial next-generation sequencing (NGS) in 2005 (3).

The implementation of hybrid-capture panels in 2013 enabled clinical-grade whole-exome/large-target sequencing to become a standard practice in oncology (4). Single-cell RNA/DNA sequencing followed in 2015, revealing intratumoral heterogeneity at cellular resolution (5). The landscape evolved further with the introduction of Long-read high-fidelity (HiFi) sequencing technology in 2019 that enables the detection of intricate structural variations which short reads fail to identify. Ultra-deep error-suppressed assays which started in 2021 provide part-per-million sensitivity for plasma-based minimal residual disease monitoring (6, 7). The conventional cancer classification system's limitations led to a new approach of molecular profiling which triggered successive genomic innovations that shifted oncology from histology-based treatment to biology-driven precision care.

Rapid advancements in genomic research have accelerated the adoption of precision oncology as a standard treatment approach for cancer patients. Precision oncology uses multiple biomarkers to determine the appropriate therapy intensity based on tumor biology: (i) The use of genomic markers like activating Epidermal Growth Factor Receptor (EGFR) mutations in non-small-cell lung cancer (NSCLC) leads patients to receive tyrosine-kinase inhibitors (TKI) instead of standard chemotherapy treatment (8); (ii) the presence of Human Epidermal Growth Factor Receptor 2 (HER2) overexpression as a proteomic marker enables doctors to identify breast cancer patients who need trastuzumab treatment while preventing its use in patients without HER2-positive tumors (9); (iii) the presence of MGMT promoter methylation in glioblastoma serves as an epigenetic marker to predict improved temozolomide response thus requiring more intense treatment (10) and (iv) multi-analyte expression panels such as the 21-gene Oncotype DX test stratify early-stage, hormone-receptor-positive breast cancer so that low-risk patients safely omit adjuvant chemotherapy, reducing overtreatment without compromising outcomes (11, 12). Such advancements demonstrate how precision tools both direct treatment escalation and provide safe de-escalation treatment which establish a foundation for individualized care.

Precision medicine has transformed oncology by moving away from standard treatments to personalized care which has reshaped both the objectives and organization of the field and improved treatment effectiveness through better response rates, reduced unnecessary treatment, and individualized choices (13). Yet the real-world implementation of precision oncology practices exists in a state of significant inequality and operational inefficiency. Centralized diagnostic workflows that need advanced laboratory infrastructure and expensive sequencing platforms and highly specialized personnel create delays of up to three weeks between biopsy and therapeutic decision-making (14-16). The time spent waiting for test results is crucial for patients with fast-moving cancers because tumor biology changes, patient health worsens, and treatment opportunities decrease with each passing hour. Cancer diagnostic facilities exist mainly in urban high-income countries which prevents their use by rural populations and low and middle-income countries where cancer cases are increasing quickly (17, 18). Even in well-resourced settings, the process of sample collection, transport, sequencing and analysis creates delays that result in therapeutic decision delays of days to weeks especially for aggressive or late-stage cancers (19).

Researchers have previously addressed the translational gap through laboratory-based molecular innovations. Liquid biopsy stands out as a minimally invasive and repeatable tissue biopsy alternative which allows researchers to study circulating tumor DNA (ctDNA), RNA, extracellular vesicles (EVs) and circulating tumor cells (CTCs) from biofluids, including blood, urine and (20-22). EVs are broadly classified by size and origin into exosomes (30-150 nm, endosomal origin), microvesicles (100-1000 nm, plasma membrane budding), and apoptotic vesicles (50-5000 nm, released during cell death) (23). However, liquid biopsy offers real-time insights and operational flexibility, the analytical accuracy depends on biological and pre-analytical variability which can hide true tumor signals.

Recent evidence shows that the absolute amount of circulating biomarkers can fluctuate substantially within the same individual, even when tumour burden is biologically constant, because of short-term physiological factors. Acute shifts in plasma volume caused by dehydration or strenuous exercise produce multi-fold transient rise in total cell-free DNA (cfDNA) concentration that ctDNA assays report (24). Independent time-series studies have also revealed diurnal oscillations: CTC counts in mouse and human models peak at the onset of the rest/ night phase, suggesting endocrine regulation of tumour-cell egress (25). Finally, pre-analytical variables-plasma vs serum matrix, occult haemolysis,

and delays in tube processing - can shift total cfDNA or EVs yield by an order of magnitude, with direct consequences for mutation calling and quantitative trending (24). Collectively, these hydration, circadian and matrix-driven effects underscore the need for active normalisation strategies whenever liquid biopsy is decentralised to the point of care (POC). The clinical adoption of liquid biopsy faces challenges because it depends on complex centralized laboratory infrastructure and sophisticated assay platforms (26). Liquid biopsy technologies need adaptation to achieve their maximum potential for POC implementation. The POC testing model transforms healthcare by providing decentralized rapid and clinically actionable diagnostics directly at or near patient care locations (27, 28). The POC systems provide quick biomarker results which enable fast diagnostic-treatment intervals and immediate therapeutic alignment (29). The time advantage is essential in oncology because urgent medical interventions have major effects on patient outcomes. The promise of precision oncology requires technological innovation to develop compact diagnostic tools that are both sensitive and clinically adaptable for POC settings.

The detection of cancer biomarkers has undergone a transformation through new smart tools that combine compact design with ultra-sensitivity and decentralized adaptability. Electrochemical biosensors now enable the real-time detection of ctDNA at femtomolar concentrations using small sample volumes (30). By integrating nanostructured electrodes with surface-functionalized aptamers or DNA probes, these platforms can achieve analytical performance similar to that of centralized laboratories through rapid POC testing (31, 32). The integration of multiple functions, including isolation, enrichment, and downstream biomarker analysis, onto a single microfluidic platform enables microfluidic lab-on-chip systems to perform multiplexed analysis of liquid biopsy. The integrated design of these systems decreases the complexity of sample handling and reduces both bioanalyte loss and contamination risks when compared to traditional benchtop laboratory procedures (33). CRISPR-based diagnostics offer programmable nucleic acid detection through user-friendly readouts, including colorimetric, luminescent and lateral-flow assays for rapid POC testing (34). The clinical adoption of nanoparticle-enhanced sensors depends on solving manu-

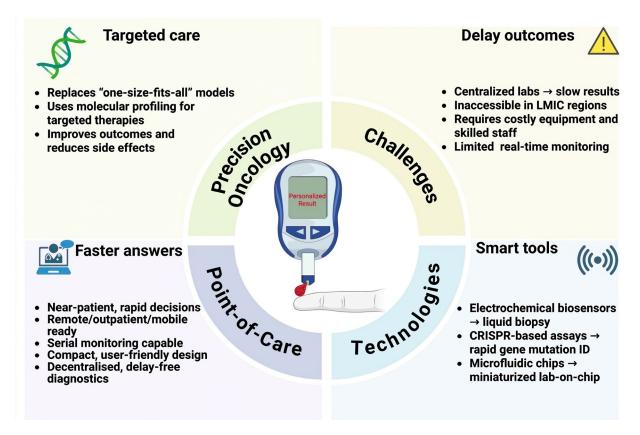


Figure 1. From bottlenecks to bedside, smart tools accelerate precision oncology.

facturing scalability issues, cost reduction, regulatory approval, and workflow integration challenges (35). These innovations create a vital pathway for implementing precision oncology outside clinical laboratory settings. The conceptual framework in **Figure 1** demonstrates how POC testing functions as a vital component of real-time patient-centered precision oncology.

The evidence from this review demonstrates that POC technologies possess the technical ability to detect molecular signatures for precision oncology; however, their full potential requires coordinated action. The combination of nanomaterial-enhanced electrochemical sensors, CRISPR diagnostics, and fully integrated microfluidic "lab-on-a-chip" platforms enables bedside assays to reduce the biopsy-to-decision window from weeks to minutes, thus enabling therapeutic choices that match the speed of tumor detection/management. The implementation of global POC precision oncology demands essential steps, including the development of affordable devices that are validated in the field and the establishment of adaptive regulations that match innovative approaches with context-based validation. Further implementation of scalable training programs and ethical safeguards is required to protect privacy and ensure equitable access. Collectively, these measures will establish bedside genomics as a standard medical practice.

# PRECISION ONCOLOGY AND THE URGENCY OF DECENTRALISED TESTING

Modern precision oncology depends on continuous measurement of highly dynamic biomarkers like single-nucleotide variants, gene fusions, circulating microRNAs, exosomes, oncoproteins, and even intact circulating tumor cells (27, 33). The foundational idea is that treatment is most effective when tailored to the unique molecular profile of a patient's cancer (36). However, this vision is difficult to realize due to several limitations of current centralized diagnostic systems. These systems are labor-intensive, slow, and often fail to capture the spatial and temporal heterogeneity of malignancies (37). Traditional assays lack the sensitivity, speed, and multiplexing capabilities required for early detection, continuous monitoring, and precise treatment stratifi-

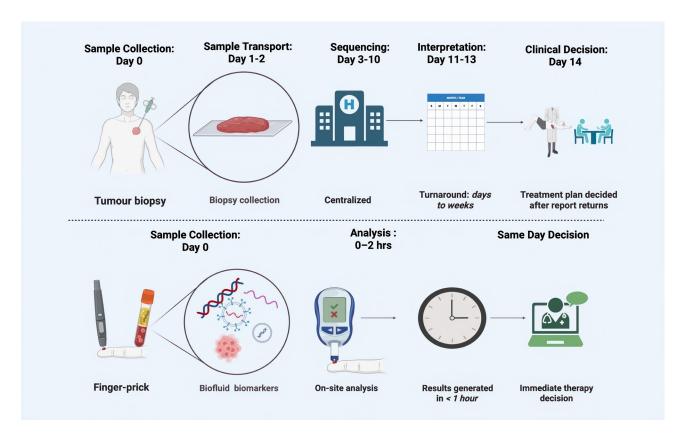


Figure 2. Comparative timelines for centralized laboratory testing versus on-site diagnostics in precision oncology.

cation-critical needs, especially for fast-progressing cancers. As a result, actionable biomarkers often cannot be exploited effectively in clinical practice due to logistical delays, infrastructure deficits, and access inequities inherent in the central-lab (38, 39). To overcome this translational gap, diagnostic platforms must not only deliver high analytical precision but also function with operational flexibility across diverse healthcare settings. The transition from centralized laboratory workflows to rapid near-patient testing is illustrated in **Figure 2**.

To this, POC diagnostics are designed to move molecular testing from centralized laboratories to locations where patients receive care i.e. infusion suites, operating rooms, outpatient clinics, or even the home. In oncology this decentralization is uniquely valuable because actionable biomarkers (mutations, miR-NAs, proteins, circulating tumour cells/exosomes) can evolve rapidly under therapeutic pressure; short "sample-to-answer" times therefore translate directly into faster treatment adjustments and, potentially, improved outcomes (40).

POC liquid-biopsy technologies are beginning to close the "temporal gap" between sample collection and clinical decision-making by generating actionable molecular read-outs fast enough to guide therapy adjustments in real time. A good illustration is the integrated exosome isolation and detection system (EXID system) microfluidic cartridge that isolates tumor-derived exosomes, labels the immune-checkpoint protein PD-L1 on-chip, and quantifies the signal in <2 h. In a pilot cohort of 16 lung-cancer patients the assay distinguished post-treatment from pre-treatment samples and from healthy controls, with a limit of detection of 10.76 exosomes µL<sup>-1</sup>-demonstrating its utility for tracking emerging resistance to anti-PD-1/PD-L1 therapy at the chair-side rather than in a distant reference laboratory (41). Researchers have used a herring-bone microfluidic chip to monitor 24 patients with metastatic pancreatic ductal adenocarcinoma over multiple chemotherapy cycles. The device captured over 80% of samples as CTC-positive and produced per-patient "CTC/CSC trajectories" that mirrored radiological progression or response, providing a quantitative relapse signal weeks before routine imaging results were available (42). A 2025 study in triple-negative breast cancer introduced a disposable, pen-printed paper chip that detects exosomal miRNA-21 directly in serum. The self-contained strip, coupled with enzyme-free signal amplification, reaches a 1.2 nM limit of detection and delivers results in 30 minutes using a handheld potentiostat. This low-cost, home-based monitoring of treatment response and recurrence between clinic visits is particularly useful in aggressive TNBC (43). Taken together, these sensor shows how decentralised testing can capture rapidly evolving oncologic biomarkers at the POC, enabling much earlier detection of relapse than is possible with traditional, centrally run assays.

# SMART TOOLS: TECHNOLOGICAL CONVERGENCE IN PRECISION ONCOLOGY

A new generation of "smart" POC devices is emerging from the synergistic fusion of four previously independent innovation streams: (i) microfluidic labon-chip architectures that automate sample-to-answer workflows on disposable cartridges (33); (ii) biosensor transduction schemes-electrochemical that now achieve femtomolar-attomolar limits of detection for circulating proteins, exosomes, and nucleic acids (27). Further the integration of nanomaterial-enhanced signal amplification with CRISPR-based molecular recognition, microfluidic automation and miniaturized electronics to create deployable POC systems (44–46).

Electrochemical biosensing has become a cornerstone of molecular precision oncology due to its high analytical sensitivity with low-power, chip-scale instrumentation that can be mass-manufactured at minimal cost. By transducing the binding or cleavage of tumor-derived analytes-circulating-tumor DNA fragments, exosomal RNA cargoes, or oncoproteins-into voltammetric or impedimetric signatures, these platforms provide linear quantitative readouts across at least five orders of magnitude, with limits of detection routinely (47–49).

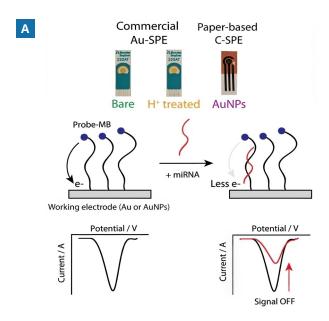
Such modular devices are operable in outpatient infusion suites, peri-operative theaters, or resource-constrained field clinics, thereby eliminating the geographic and temporal separation between specimen collection and molecular insight. The result is a compressed diagnostic-treatment loop that recasts precision oncology as a real-time discipline rather than a retrospective laboratory exercise, enabling clinicians to adjust targeted therapies at the pace of tumor evolution.

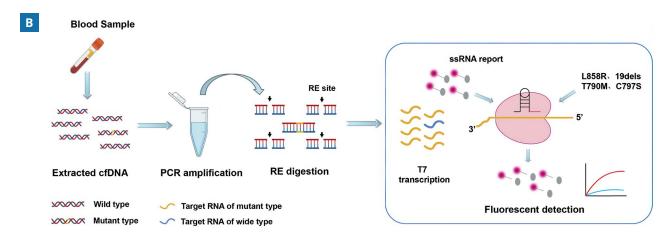
The integration of nanomaterials boosts sensor performance through faster electron transfer rates, increased biomarker capture surface area, and enhanced signal-to-noise ratio. The development of highly sensitive electrochemical biosensors has been made possible by recent advances in nanostructured material fabrication techniques. The effective surface area of the electrodes increases through the use of gold nanoparticles (AuNPs), which also enhances conductivity and provides a dense platform for stable biorecognition element immobilization (48, 50). Research findings from recent studies confirm that electrochemical biosensors show great potential for POC oncology testing. Raucci et al. (2024) demonstrated that acid treated commercial gold electrodes and AuNPs modified paper-based screen-printed electrodes can detect the lung-cancer biomarker miR-2115-3p with a methylene blue based electrochemical biosensor. The commercial gold platform achieved a slightly lower detection limit (≈1 nM), but the paper-based alternative offered comparable analytical performance at a much lower cost and with a more sustainable material profile. Both configurations maintained high selectivity against non-target miRNAs and functioned directly in human serum (Figure 3A) (50).

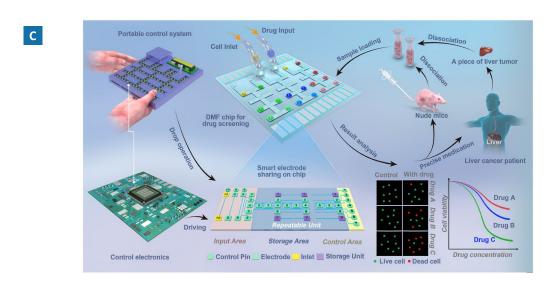
Nagdeve et al. created a sensor that measures microRNA-31 which serves as a recognized oral-cancer biomarker, while achieving detection limits of 70 pg mL<sup>-1</sup> in buffer solutions and 700 pg mL<sup>-1</sup> in diluted serum solutions, thus meeting the requirements for early cancer screening and diagnosis (53). This study demonstrates how electrochemical biosensors can transform precision oncology by detecting clinically relevant biomarkers in small sample volumes with high precision. These devices possess compact dimensions, affordable prices, and smartphone-readable functionality, making them appropriate for decentralized healthcare operations in limited-resource environments. The successful clinical implementation of these devices requires addressing three main challenges which include biofouling, signal drift and calibration stability through systematic materials development and thorough validation procedures (54). The integration of electrochemical sensors into wearable devices would allow for the continuous tracking of circulating tumour DNA which could serve as an early warning system for cancer relapse in colorectal and other cancer types. The analyte detection range of electrochemical devices is mainly limited to predefined targets, although they show high sensitivity for detecting proteins and small-molecule biomarkers. A complete real-time molecular surveillance system for oncology can be developed by combining CRISPR-based assays with electrochemical devices because CRIS- PR-based assays provide sequence-specific amplification-free nucleic acid detection.

CRISPR-based diagnostics, such as the SHERLOCK platform, detect nucleic acid biomarkers through Cas enzyme sequence-specific cleavage activity at single-molecule resolution for point-of-care oncology testing. Gootenberg et al. demonstrated in their research that SHERLOCK detects KRAS oncogenic mutations at attomolar concentrations through Cas13a recognition, which leads to collateral reporter cleavage, thus enabling non-invasive mutation detection in bodily fluids (55). SHERLOCK demonstrated 88.1% sensitivity and 100% specificity in detecting EGFR T790M mutations from NSCLC liquid biopsies, which led to osimertinib therapy decisions in clinical practice (Figure 3B) (51). This technology allows for the rapid detection of BRAF V600E mutations in melanoma plasma samples in a short time, supporting the timely selection of targeted treatments (56). CRISPR tools serve dual purposes beyond diagnostic applications, as they help track drug responses and monitor drug resistance. A research study showed that CRISPR/Cas13 technology enables the evaluation of the biological role of vlincRNAs in drug response, thus demonstrating CRISPR's capability for monitoring treatment effectiveness (57). CRISPR-based screening platforms identify essential protein-drug interactions, leading to the discovery of novel therapeutic targets. CRISPR-based systems work alongside traditional biosensors to detect ctDNA and RNA sequences with high sensitivity, which expands the capabilities of POC testing in oncology. The proposed cloud-based CRISPR analytics system would simplify the process of mutation profiling for tracking treatment resistance. The advanced detection capabilities of CRISPR diagnostics require microfluidic platforms to integrate multiple detection methods for complete POC testing applications.

Microfluidic devices or lab-on-a-chip platforms operate with nanoliter fluid volumes to perform sample preparation, amplification, and detection functions, making them suitable for low-sample-volume applications, such as blood or saliva analysis. Microfluidic systems have been used in cancer diagnostics to detect various cancer-diagnostic factors while creating suitable nanoparticles for drug delivery, demonstrating their dual role in cancer diagnosis and treatment (58). The detection and characterization of CTCs represent a fundamental application of microfluidics technology because it helps monitor metastasis and treatment response. Fachin *et al.* developed a microfluidic chip to detect and ana-







**Figure 3.** Schematic overview **(A)** the electrochemical assay for miRNA detection was performed using a commercial gold electrode, an acid treated gold electrode, and a paper based carbon electrode decorated with gold nanoparticles (50); **(B)** the HiCASE assay for the detection of cfDNA sample (51); **(C)** the digital microfluidic (DMF) system was used for drug screening of biopsy samples from MDA-MB-231 breast cancer xenograft mouse model and patients with liver cancer (52).

**Table 1.** A comparative analysis of essential biomarkers together with detection principles, validated specimen, cancer applications, analytical sensitivity, specificity and LOD to demonstrate each platform's translational status and diagnostic potential.

BIOMARKERS	PRINCIPLE OF DETECTION	CLINICAL / VALIDATED SPECIMEN	TYPE OF CANCER DETECTED	SENSITIVITY	SPECIFICITY	LOD	REFERENCES
BCR-ABL1 & PML-RARA fusions (APL/CML)	CRISPR	EDTA blood / dried spots	Leukemia	100 %	100 %	NA	(61)
Glycoprotein Tumor Biomarkers	Electrochemically controlled Atom Transfer Radical Polymerization (eATRP)	Human serum samples	General ( <i>e.g.</i> , Alpha- fetoprotein)	High	High	0.32 pg/mL	(62)
EGFR L858R, T790M (Cas12a DETECTR)	Cas12a trans- ssDNA collateral cleavage	Plasma	NSCLC (lung)	100	100	0.005 % MAF	(63)
Cas13, Cas12a, and Csm6	SHERLOCK-v2 multiplex panel	Plasma & contrived cfDNA	General liquid-biopsy demonstration	High	High	2 aM nucleic acid	(55)
CEA	Probe-integrated electrochemical immunosensor	Human serum samples	Colorectal Cancer	High	High	4 pg/mL	(64)
AFP (Alpha- Fetoprotein)	Homogeneous Electrochemical Immunoassay	Diluted human sera of hepatocellular carcinoma (HCC) patients	Hepatocellular Carcinoma	High	High	5 pg/mL	(65)
QGY-7701; QGY-7703	Competitive Electrochemical Sensing	Cancer cell	General Cancer	High	High	20 cells/mL & 35 cells/mL	(66)
Soluble HER2- ECD	Screen- printed ELISA immunosensor	Patient serum	Breast cancer	NA	NA	4 ng mL <sup>-1</sup>	(67)
Exosomes expressing CD63 & EpCAM	Microfabricated aptasensor combining CD63 capture, EpCAM aptamer bridging, HCR signal amplification, and HRP-TMB electrochemical readout	Serum samples from lung cancer patients (early- & late-stage), plus cultured cell-line exosomes	Lung cancer	High	High	5 × 10 <sup>2</sup> exosomes/ mL	(68)

lyze CTCs in the blood of cancer patients. The chip successfully captured 95% of EpCAM-positive cells, allowing genomic analysis for direct trastuzumab therapy. The microfluidic system proved superior to CellSearch systems through its enhanced sensitivity and faster operation, which shows its capability for real-time metastasis tracking (59). Zhai *et al.* developed a portable digital microfluidic platform  $(23 \times 16 \times 3.5 \text{ cm}^3)$  that performs par-

allel screening of three anticancer drugs on a  $4 \times 4 \text{ cm}^2$  chip using primary tumour cells. The drugs that showed effectiveness on the chip device successfully reduced tumour growth in animal models during MDA-MB 231 breast cancer xenograft and patient-derived liver cancer specimen tests. The device demonstrated potential for precision medicine guidance through whole exome sequencing which confirmed that effective agents main-

tained their target genes (Figure 3C) (52). Multiplex microfluidic platforms enable the simultaneous measurement of multiple cancer biomarkers from microliter-scale samples, thereby supporting comprehensive diagnosis, early detection, and evidence-based therapy selection in precision oncology. Chen et al. used magnetic-bead capture with acoustic micromixing to measure prostate-specific antigen and carcinoembryonic antigen in under 20 minutes with detection limits of 0.028 ng mL<sup>-1</sup> and 3.1 ng mL<sup>-1</sup>, respectively. These results illustrate the feasibility of rapid, POC cancer diagnostics based on multi-analyte profiling (60). The integration of advanced diagnostic applications through microfluidics can transform precision oncology by closing therapeutic gaps. Research has demonstrated its effects on different cancer types, leading to better personalized treatments. This technology optimizes clinical operations to deliver enhanced cancer care worldwide.

To help synthesize the diverse technologies discussed, **Table 1** provides a summary of the major POC platforms mentioned, highlighting their clinical application potential. This comparative overview supports the preceding discussion by visually organizing the diagnostic scope, sensitivity, and implementation status of each tool.

# REGULATORY AND OPERATIONAL CHALLENGES

Despite the spectacular analytical sensitivity now achievable in precision oncology, very few tests have been validated in prospective (e.g. Guardant360 CDx for EGFR mutations in NSCLC), and global regulatory harmonization is lacking. Different regions (EU IVDR, US CLIA/FDA, ISO standards) apply varied thresholds for evidence and performance, slowing global deployment. All of which inflate cost and lengthen timelines for regulatory submission.

Rigid in-vitro-diagnostic (IVD) frameworks that were originally drafted around single-analyte infectious-disease strips do not map neatly onto multimarker oncology cartridges. The next-generation POC liquid-biopsy devices must still satisfy U.S. CLIA-waiver "simple test" criteria while simultaneously proving multiplex variant accuracy that normally requires high-complexity molecular laboratories, a mismatch that slows 510(k)/De Novo submissions and has left only a handful of cancer assays cleared to date (69).

Progress is further hampered by the absence of universally commutable reference materials for ctDNA, microRNA, and extracellular-vesicle targets. The integrated lab-on-a-chip review by Surappa *et al.* notes that most groups calibrate limits-of-detection with contrived spike-ins prepared in-house, making cross-platform performance claims difficult to harmonize and complicating multi-site reproducibility studies demanded by regulators (33).

Operationally, the most consistent pain points involve pre-analytical variability and supply-chain resilience. Paper-based liquid-biopsy platforms demonstrate how hemolysis, diurnal swings in EV release, and freeze-thaw cycles can each shift electrochemical readouts by more than one standard deviation, forcing manufacturers to integrate on-cartridge normalization controls and environmental sensors, which in turn raise cost and assembly complexity.

The implementation of POC testing has the potential to transform precision oncology through bedside biomarker analysis; however, its adoption remains limited by major technical challenges. POC devices must precisely measure trace tumor-derived analytes, including circulating nucleic acids, in complex biofluids while functioning in different environmental settings. The combination of temperature changes and sample contamination along with environmental disturbances leads to assay accuracy degradation which results in unreliable results when tests are performed outside laboratory control (70).

Finally, real-world deployment in low- and middle-income countries (LMICs) encounters infrastructure limitations-intermittent power, limited cold-chain capacity, and scarce biomedical-engineering support-that can erode field accuracy by up to 20 % relative to controlled settings. A 2025 review of oncology POC implementation in LMICs calls for locally manufactured consumables, solar-powered readers, and streamlined post-market surveillance to sustain diagnostic precision outside tertiary centers (71).

The solution to these barriers requires coordinated innovation efforts. The adoption process will speed up through platforms that are accessible to all and resilient and use unified data standards and adaptive risk-based regulatory pathways. The implementation of scalable workforce training and robust ethical frameworks will protect data security and ensure equitable access. The implementation of these pillars will enable POC diagnostics to redefine precision oncology by providing fast individualized care across the world.

Finally, the ecosystem necessary for the successful implementation of POC oncology diagnostics is inherently complex. It requires coordinated efforts among diagnostic developers, clinicians, regulatory authorities, payers, and standards organizations.

••••••••••••••••••••••••••••••••

FUTURE DIRECTIONS AND CONCLUSIONS

The next wave of POC precision-oncology devices is moving toward single-cartridge, ultra-sensitive and highly multiplexed platforms that couple CRISPR/ Cas recognition, nanomaterial signal amplification, and fully integrated microfluidics. In the coming 3-5 years, these lab-on-chip architectures are expected to converge with wearable biosensors-flexible electrochemical patches, microneedle fluidics, or smartphone-coupled optical readers, supporting continuous or immediate, on-demand cancer-biomarker surveillance outside formal clinic walls.

For clinical integration, engineering priorities are shifting toward closed, sample-to-answer system that run on finger-stick blood, urine, or saliva and can be operated by self, nurses or community health workers after minimal training. Bluetooth/FHIR-compliant connectivity will push results straight into electronic health records and multidisciplinary tumorboard dashboards, facilitating rapid therapeutic alignment and longitudinal monitoring without centralized laboratory dependencies.

Translational success, however, hinges on standardization and regulation. Achieving global health equity remains a pressing mandate. Although most commercial POC cancer tests are currently configured for high-resource markets, the greatest diagnostic gaps exist in LMICs. Future development must therefore emphasize low-cost readers with battery or solar power, lyophilized reagents stable at tropical temperatures, and open-source firmware that can be localized for language and connectivity constraints (71). Collectively, the literature paints a clear trajectory: POC diagnostics are poised to transform precision oncology by collapsing the temporal and geographic gap between biomarker measurement and clinical action. The technological capability to match centralized laboratories in sensitivity is emerging; the challenge now is to embed these advances into rigorous yet agile regulatory frameworks, pragmatic clinical workflows, and equity-focused distribution models. With sustained interdisciplinary collaboration and deliberate attention to global implementation, POC precision-oncology testing can redefine cancer care as a rapid, individualized, and universally accessible enterprise.

# COMPLIANCE WITH ETHICAL STANDARDS

### **Funding**

The research leading to these results received funding from AIRC under MFAG 2022-ID. 27586 project-P.I. Stefano Cinti. This project has received funding from the European Union's Horizon 2020 research and innovation program under the Marie Skłodowska-Curie grant agreement No. 101110684 SMART-Sima Singh. Alessandra Glovi has received funding from Scuola Superiore Meridionale (SSM) within the PhD program in Clinical and Translational Oncology (CTO).

#### **Conflicts of interests**

The authors declare no competing interests.

### **Data availability**

All data generated or analyzed during this study are included in this article.

# **Author Contributions**

Conceptualization: SC and SS. Writing- Original Draft Preparation: SC and SS. Visualization and Figures: SS and AG. Critical Review and Editing: PMK, AM, AR, and Gl. Scientific Input and Guidance: SC, MDL, and CM. Funding Acquisition: SC, SS, and AG. All authors reviewed and approved the final version of the manuscript for submission.

## **Publications ethics**

# **Plagiarism**

Authors declare no potentially overlapping publications with the content of this manuscript and all original studies are cited as appropriate.

### Data falsification and fabrication

All the data corresponds to the real.

# **REFERENCES**

1. Lip S, Padmanabhan S. Introduction to precision medicine. Medicine. 2025;53(7): 476-482. doi: 10.1016/j.mpmed.2025.04.018.

- 2. Tsimberidou AM, Fountzilas E, Nikanjam M, Kurzrock R. Review of precision cancer medicine: evolution of the treatment paradigm. Cancer Treat Rev. 2020;86:102019. doi: 10.1016/j.ctrv.2020.102019.
- 3. Margulies M, Egholm M, Altman WE, Attiya S, Bader JS, Bemben LA, et al. Genome sequencing in microfabricated high-density picolitre reactors. Nature. 2005;437:376–80. doi: 10.1038/nature03959.
- 4. Frampton GM, Fichtenholtz A, Otto GA, Wang K, Downing SR, He J, et al. Development and validation of a clinical cancer genomic profiling test based on massively parallel DNA sequencing. Nat Biotechnol. 2013;31:1023–31. doi: 10.1038/nbt.2696.
- 5. Macosko EZ, Basu A, Satija R, Nemesh J, Shekhar K, Goldman M, et al. Highly parallel genomewide expression profiling of individual cells using nanoliter droplets. Cell. 2015;161(5):1202–14. doi: 10.1016/j.cell.2015.05.002.
- 6. Wenger AM, Peluso P, Rowell WJ, Chang PC, Hall RJ, Concepcion GT, et al. Accurate circular consensus long-read sequencing improves variant detection and assembly of a human genome. Nat Biotechnol. 2019;37:1155–62. doi: 10.1038/s41587-019-0217-9.
- 7. Kurtz DM, Soo J, Co Ting Keh L, Alig S, Chabon JJ, Sworder BJ, et al. Enhanced detection of minimal residual disease by targeted sequencing of phased variants in circulating tumor DNA. Nat Biotechnol. 2021;39:1537–47. doi: 10.1038/s41587-021-00981-w.
- 8. Lynch TJ, Bell DW, Sordella R, Gurubhagavatula S, Okimoto RA, Brannigan BW, et al. Activating mutations in the epidermal growth factor receptor underlying responsiveness of nonsmall-cell lung cancer to gefitinib. N Engl J Med. 2004;350(2):2129–39. doi: 10.1056/NEJMoa040938.
- 9. Slamon DJ, Leyland-Jones B, Shak S, Fuchs H, Paton V, Bajamonde A, et al. Use of chemotherapy plus a monoclonal antibody against HER2 for metastatic breast cancer that overexpresses HER2. N Engl J Med. 2001;344(11):783–92. doi: 10.1056/NEJM200103153441101.
- Hegi ME, Diserens AC, Gorlia T, Hamou MF, de Tribolet N, Weller M, et al. MGMT gene silencing and benefit from temozolomide in glioblastoma. N Engl J Med. 2005;352(10):997–1003. doi: 10.1056/NEJMoa043331.
- 11. Paik S, Shak S, Tang G, Kim C, Baker J, Cronin M, et al. A multigene assay to predict recurrence of

- tamoxifen-treated, node-negative breast cancer. N Engl J Med. 2004;351(27):2817–26. doi: 10.1056/NEJMoa041588.
- 12. Sparano JA, Gray RJ, Makower DF, Pritchard KI, Albain KS, Hayes DF, et al. Adjuvant chemotherapy guided by a 21-gene expression assay in breast cancer. N Engl J Med. 2018;379(2):111–21. doi: 10.1056/NEJMoa1804710.
- 13. Collins FS, Varmus H. A new initiative on precision medicine. N Engl J Med. 2015;372(9):793–5. doi: 10.1056/NEJMp1500523.
- 14. Singh S, Numan A, Cinti S. Electrochemical nano biosensors for the detection of extracellular vesicles exosomes: From the benchtop to everywhere? Biosens Bioelectron. 2022;216:114635. doi: 10.1016/j.bios.2022.114635.
- 15. Singh S, Raucci A, Cimmino W, Cinti S. Paper-based analytical devices for cancer liquid biopsy. Anal Chem. 2024;96(9):3698–706. doi: 10.1021/acs.analchem.3c04478.
- Singh S, Miglione A, Raucci A, Numan A, Cinti S. Towards sense and sensitivity-based electrochemical biosensors for liquid biopsy-based breast cancer detection. TrAC Trends Anal Chem. 2023;163:117050. doi:10.1016/j.trac.2023.117050.
- 17. Nnaji CA, Ezenwankwo EF, Kuodi P, Walter FM, Moodley J. Timeliness of diagnosis of breast and cervical cancers and associated factors in low-income and middle-income countries: a scoping review. BMJ Open. 2022;12(2):e057685. doi: 10.1136/bmjopen-2021-057685.
- 18. Pramesh CS, Badwe RA, Bhoo-Pathy N, Booth CM, Chinnaswamy G, Dare AJ, et al. Priorities for cancer research in low- and middle-income countries: a global perspective. Nat Med. 2022;28(4):649–57. doi: 10.1038/s41591-022-01738-x.
- 19. Heitzer E, Haque IS, Roberts CES, Speicher MR. Current and future perspectives of liquid biopsies in genomics-driven oncology. Nat Rev Genet. 2019;20(2):71–88. doi: 10.1038/s41576-018-0071-5.
- 20. Feng J, Li B, Ying J, Pan W, Liu C, Luo T, et al. Liquid biopsy: application in early diagnosis and monitoring of cancer. Small Struct. 2020;1(3):2000063. doi: 10.1002/sstr.202000063.
- 21. Cescon DW, Bratman SV, Chan SM, Siu LL. Circulating tumor DNA and liquid biopsy in oncology. Nat Cancer. 2020;1(3):276–90. doi: 10.1038/s43018-020-0043-5.
- 22. Singh S, Glovi A, De Laurentiis M, Cinti S. A novel point-of-care device for monitoring circulating miRNA-107 in prostate cancer: towards a

- user-friendly liquid biopsy. Ann Res Oncol. 2025;5(2):95–114.
- 23. Tang P, Song F, Chen Y, Gao C, Ran X, Li Y, et al. Preparation and characterization of extracellular vesicles and their cutting-edge applications in regenerative medicine. Appl Mater Today. 2024;37:102084. doi: 10.1016/j.apmt.2024.102084.
- 24. Yuwono NL, Warton K, Ford CE. The influence of biological and lifestyle factors on circulating cell-free DNA in blood plasma. Elife. 2021;10:e69679. doi: 10.7554/eLife.69679.
- 25. Zhu X, Suo Y, Fu Y, Zhang F, Ding N, Pang K, et al. In vivo flow cytometry reveals a circadian rhythm of circulating tumor cells. Light Sci Appl. 2021;10(110). doi: 10.1038/s41377-021-00520-5.
- 26. Adhit KK, Wanjari A, Menon S, Siddhaarth K. Liquid biopsy: an evolving paradigm for non-invasive disease diagnosis and monitoring in medicine. Cureus. 2023;15(12):e50176. doi: 10.7759/cureus.50176.
- 27. Singh S, Podder PS, Russo M, Henry C, Cinti S. Tailored point-of-care biosensors for liquid biopsy in the field of oncology. Lab Chip. 2023;23:44–61. doi: 10.1039/D2LC00892K.
- 28. Moro G, Dalle Fratte C, Normanno N, Polo F, Cinti S. Point-of-care testing for the detection of microRNAs: towards liquid biopsy on a chip. Angew Chem Int Ed Engl. 2023;62(51):e202309135. doi: 10.1002/anie.202309135.
- 29. Lee S, Park JS, Woo H, Yoo YK, Lee D, Chung S, et al. Rapid deep learning-assisted predictive diagnostics for point-of-care testing. Nat Commun. 2024;15(1):1695. doi: 10.1038/s41467-024-46069-2.
- 30. Huang S, Liu S, Fang Y, Li H, Yang M, Wang W, et al. An ultra-sensitive electrochemical biosensor for circulating tumor DNA utilizing dual enzyme-assisted target recycle and hybridization chain reaction amplification strategies. Microchem J. 2024;204:111164. doi: 10.1016/j.microc.2024.111164.
- 31. Kumar V, Brent JR, Shorie M, Kaur H, Chadha G, Thomas AG, et al. Nanostructured aptamer-functionalized black phosphorus sensing platform for label-free detection of myoglobin, a cardiovascular disease biomarker. ACS Appl Mater Interfaces. 2016;8(35):22860–8. doi: 10.1021/acsami.6b06488.
- 32. Huang Z, Qiu L, Zhang T, Tan W. Integrating DNA nanotechnology with aptamers for biological and biomedical applications. Matter. 2021;4(2):461–89. doi: 10.1016/j.matt.2020.11.002.
- 33. Surappa S, Multani P, Parlatan U, Sinawang PD, Kaifi J, Akin D, et al. Integrated "lab-on-a-chip" microfluidic systems for isolation, enrichment,

- and analysis of cancer biomarkers. Lab Chip. 2023;23(13):2942–58. doi: 10.1039/d2lc01076c.
- 34. Kaminski MM, Abudayyeh OO, Gootenberg JS, Zhang F, Collins JJ. CRISPR-based diagnostics. Nat Biomed Eng. 2021;5(7):643–56. doi: 10.1038/s41551-021-00760-7.
- 35. Swierczewska M, Liu G, Lee S, Chen X. High-sensitivity nanosensors for biomarker detection. Chem Soc Rev. 2012;41(7):2641–55. doi: 10.1039/c1cs15238f.
- 36. Subbiah V, Kurzrock R. Challenging standard-of-care paradigms in the precision oncology era. Trends Cancer. 2018;4(2):101–9. doi: 10.1016/j.tre-can.2017.12.004.
- 37. Bamodu OA, Chung CC, Pisanic TR II. Harnessing liquid biopsies: exosomes and ctDNA as minimally invasive biomarkers for precision cancer medicine. J Liquid Biopsy. 2023;2:100126. doi: 10.1016/j.jolb.2023.100126.
- 38. Rodrigues M, Andrade I, Cruz R. Current point-of-care testing in cancer and future perspectives: a systematic review. Eur J Public Health. 2020;30(Suppl 2):ckaa040.033. doi:10.1093/eur-pub/ckaa040.033.
- 39. Benton DC, Al Maaitah R, Gharaibeh M. An integrative review of pursuing policy and political competence. Int Nurs Rev. 2017;64(1):135–45. doi: 10.1111/inr.12275.
- 40. Sandbhor Gaikwad P, Banerjee R. Advances in point-of-care diagnostic devices in cancers. Analyst. 2018;143:1326–48. doi: 10.1039/C7AN01687K.
- 41. Lu Y, Ye L, Jian X, Yang D, Zhang H, Tong Z, et al. Integrated microfluidic system for isolating exosome and analyzing protein marker PD-L1. Biosens Bioelectron. 2022;204:113879. doi: 10.1016/j. bios.2021.113879.
- 42. Varillas JI, Zhang J, Chen K, Barnes II I, Liu C, George TJ, et al. Microfluidic isolation of circulating tumor cells and cancer stem-like cells from patients with pancreatic ductal adenocarcinoma. Theranostics. 2019;9(5):1417–25. doi: 10.7150/thno.28745.
- 43. Glovi A, Kalligosfyri PM, Miglione A, Singh S, Iula G, Giordano A, et al. Towards liquid biopsy on chip for triple negative breast cancer: preliminary results on monitoring circulating miRNA-21 using portable diagnostics. Discov Oncol. 2025;16:1022. doi: 10.1007/s12672-025-02846-z.
- 44. Iannazzo D, Espro C, Celesti C, Ferlazzo A, Neri G. Smart biosensors for cancer diagnosis based on graphene quantum dots. Cancers (Basel). 2021;13(13):3194. doi: 10.3390/cancers13133194.

- 45. Yang QL, Zhong XY, Zhong LM, Zhang H, Hu SW. Advances in CRISPR-based biosensing strategies for cancer diagnosis. Cancer Screen Prev. 2024;3(1):61–71. doi: 10.14218/CSP.2023.00026.
- 46. Liu D, Wang Y, Li X, Li M, Wu Q, Song Y, et al. Integrated microfluidic devices for in vitro diagnostics at point of care. Aggregate. 2022;3(5):e184. doi: 10.1002/agt2.184.
- 47. Kumar S, Poria R, Kala D, Nagraik R, Dhir Y, Dhir S, et al. Recent advances in ctDNA detection using electrochemical biosensor for cancer. Discov Oncol. 2024;15:517. doi: 10.1007/s12672-024-01365-7.
- 48. Noreen S, Ishaq I, Saleem MH, Ali B, Ali SM, Iqbal J. Electrochemical biosensing in oncology: a review of advancements and prospects for cancer diagnosis. Cancer Biol Ther. 2025;26(1):2475581. doi: 10.1080/15384047.2025.2475581.
- 49. Raucci A, Cimmino W, Grosso SP, Normanno N, Giordano A, Cinti S. Paper-based screen-printed electrode to detect miRNA-652 associated with triple-negative breast cancer. Electrochim Acta. 2024;487:144205. doi: 10.1016/j.electacta.2024.144205.
- 50. Raucci A, Cimmino W, Romanò S, Singh S, Normanno N, Polo F, et al. Electrochemical detection of miRNA using commercial and handmade screen-printed electrodes: liquid biopsy for cancer management as case of study. ChemistryOpen. 2024;13(7):e202300203. doi:10.1002/open.202300203.
- 51. Wang L, Wen X, Yang Y, Hu Z, Jiang J, Duan L, et al. CRISPR/Cas13a-based supersensitive circulating tumor DNA assay for detecting EGFR mutations in plasma. Commun Biol. 2024;7(1):657. doi: 10.1038/s42003-024-06368-2.
- 52. Zhai J, Liu Y, Ji W, et al. Drug screening on digital microfluidics for cancer precision medicine. Nat Commun. 2024;15:4363. doi: 10.1038/s41467-024-48616-3.
- 53. Nagdeve SN, Suganthan B, Ramasamy RP. An electrochemical biosensor for the detection of microRNA-31 as a potential oral cancer biomarker. J Biol Eng. 2025;19:24. doi: 10.1186/s13036-025-00492-1.
- 54. Kozel TR, Burnham-Marusich AR. Point-of-care testing for infectious diseases: past, present, and future. J Clin Microbiol. 2017;55(8):2313–20. doi: 10.1128/JCM.00476-17.
- 55. Gootenberg JS, Abudayyeh OO, Kellner MJ, Joung J, Collins JJ, Zhang F. Multiplexed and portable nucleic acid detection platform with Cas13,

- Cas12a, and Csm6. Science. 2018;360(6387):439–44. doi: 10.1126/science.aaq0179.
- 56. Cheng L, Lopez-Beltran A, Massari F, MacLennan GT, Montironi R. Molecular testing for BRAF mutations to inform melanoma treatment decisions: a move toward precision medicine. Mod Pathol. 2018;31(1):24–38. doi: 10.1038/modpathol.2017.104.
- 57. Xu D, Cai Y, Tang L, Han X, Gao F, Cao H, et al. A CRISPR/Cas13-based approach demonstrates biological relevance of vlinc class of long non-coding RNAs in anticancer drug response. Sci Rep. 2020;10(1):1794. doi: 10.1038/s41598-020-58104-5.
- 58. Bargahi N, Ghasemali S, Jahandar-Lashaki S, et al. Recent advances for cancer detection and treatment by microfluidic technology: review and update. Biol Proced Online. 2022;24:5. doi: 10.1186/s12575-022-00166-y.
- 59. Fachin F, Spuhler P, Martel-Foley JM, Edd JF, Barber TA, Walsh J, et al. Monolithic chip for high-throughput blood cell depletion to sort rare circulating tumor cells. Sci Rep. 2017;7(1):10936. doi: 10.1038/s41598-017-11119-x.
- 60. Chen H, Chen C, Bai S, Gao Y, Metcalfe G, Cheng W, et al. Multiplexed detection of cancer biomarkers using a microfluidic platform integrating single bead trapping and acoustic mixing techniques. Nanoscale. 2018;10(43):20196–206. doi: 10.1039/C8NR06367B.
- 61. Vedula RS, Karp HQ, Koob J, Lim F, Garcia JS, Winer ES, et al. CRISPR-based rapid molecular diagnostic tests for fusion-driven leukemias. Blood. 2024;144(12):1290–9. doi: 10.1182/blood.2023022908.
- 62. Hu Q, Cao X, Li S, Liang Y, Luo Y, Feng W, et al. Electrochemically controlled atom transfer radical polymerization for electrochemical aptasensing of tumor biomarkers. Anal Chem. 2022;94(39):13516–21. doi: 10.1021/acs.analchem.2c02797.
- 63. Tsou JH, Leng Q, Jiang F. A CRISPR test for rapidly and sensitively detecting circulating EGFR mutations. Diagnostics (Basel). 2020;10(2):114. doi: 10.3390/diagnostics10020114.
- 64. Chen D, Luo X, Xi F. Probe-integrated electrochemical immunosensor based on electrostatic nanocage array for reagentless and sensitive detection of tumor biomarker. Front Chem. 2023;11:1121450. doi: 10.3389/fchem.2023.1121450.
- 65. Zhang JH, Liu M, Zhou F, Yan HL, Zhou YG. Homogeneous electrochemical immunoassay using an aggregation-collision strategy for alpha-fetopro-

- tein detection. Anal Chem. 2023;95(5):3045–53. doi: 10.1021/acs.analchem.2c05193.
- 66. Zhang X, Wang Z, Li X, Xiao W, Zou X, Huang Q, et al. Competitive electrochemical sensing for cancer cell evaluation based on thionine-interlinked signal probes. Analyst. 2023;148:912–8. doi: 10.1039/D2AN01599D.
- 67. Tallapragada SD, Layek K, Mukherjee R, Mistry KK, Ghosh M. Development of screen-printed electrode based immunosensor for the detection of HER2 antigen in human serum samples. Bio-electrochemistry. 2017;118:25–30. doi: 10.1016/j. bioelechem.2017.06.009.
- 68. Zhang W, Tian Z, Yang S, et al. Electrochemical micro-aptasensors for exosome detection based on hybridization chain reaction amplification. Microsyst Nanoeng. 2021;7:63. doi: 10.1038/s41378-021-00293-8.
- 69. U.S. Food and Drug Administration. Recommendations for dual 510(k) and CLIA waiver by application studies: guidance for industry and FDA staff [Internet]. Silver Spring (MD): FDA; [cited 2025 Aug 2]. Available from: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/recommendations-dual-510k-and-clia-waiver-application-studies.
- 70. Gubala V, Harris LF, Ricco AJ, Tan MX, Williams DE. Point-of-care diagnostics: status and future. Anal Chem. 2012;84(2):487–515. doi: 10.1021/ac2030199.
- 71. Gao W, Manning JC, Devaraj K, Richards-Kortum RR, McFall SM, Murphy RL, et al. Emerging trends in point-of-care technology development for oncology in low- and middle-income countries. JCO Glob Oncol. 2025;11:e2500142. doi: 10.1200/GO-25-00142.