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Review

Blood Cancer Detection using Quantum Dot based Electrochemical Sensors

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Abstract- Quantum dot (QD)-enabled electrochemical sensors are emerging as a promising technology for the early diagnosis and continuous monitoring of blood-related cancers, including leukemia and lymphoma. These nanomaterials exhibit exceptional optical features, customizable fluorescence, and a large surface-to-volume ratio, making them highly effective for the sensitive and selective identification of cancer-specific biomarkers. Their ability to detect multiple analytes simultaneously enhances diagnostic efficiency by enabling the recognition of various biomarkers or circulating tumor cells (CTCs), which is vital for early-stage detection and tracking minimal residual disease (MRD). However, potential cytotoxicity, limited biocompatibility, and regulatory hurdles must still be addressed. Ongoing research is directed toward creating safer, non-toxic QDs, refining sensor functionality, and incorporating these sensors into portable diagnostic platforms. Furthermore, integrating optical and electrochemical detection methods—alongside innovations in surface chemistry and signal amplification—is anticipated to improve both sensitivity and clinical reliability. QD-based electrochemical sensors are expected to become essential tools for early, non-invasive blood cancer diagnostics and individualized patient care as these technologies evolve.

Keywords- Quantum dots; Electrochemical biosensors; Hematologic malignancies; Leukemia; Lymphoma; Cancer markers; Circulating tumor cells (CTCs); Minimal residual disease (MRD)

1. INTRODUCTION

Timely diagnosis and accurate monitoring of blood cancers, including leukemia and lymphoma, are essential for improving prognosis and enabling early treatment [1-6]. Conventional approaches like imaging and biopsies are often invasive, time-consuming, and require complex data analysis. As a result, there is an increasing need for diagnostic solutions that are non-invasive, fast, and capable of detecting cancers at early stages while also tracking disease progression and therapeutic effectiveness [3]. In this regard, electrochemical sensors—especially those enhanced with quantum dots (QDs)—have emerged as a cutting-edge alternative with the potential to transform cancer diagnostics [2,7-10]. Figure 1 illustrates the electrochemical detection strategies and mechanisms used for identifying blood cancer cells through QD-modified electrodes.

Quantum dots (QDs) are nanoscale semiconductor materials known for their exceptional optical characteristics, primarily resulting from quantum confinement effects [4,5]. Their size-dependent fluorescence, large surface-to-volume ratio, and chemical resilience make them highly suitable for biosensing applications [11]. Functionalization of QDs with specific biomolecules—such as antibodies, DNA strands, or aptamers—enables targeted interactions with cancer-associated biomarkers or abnormal cells, particularly beneficial in the diagnosis of hematological malignancies [7]. One of the standout advantages of QDs is their tunable emission, which facilitates the simultaneous detection of multiple biomarkers in a single assay—an essential feature for comprehensive cancer diagnostics [3].

Recent innovations in QD-based electrochemical sensors have demonstrated exceptional sensitivity in detecting trace amounts of cancer indicators, including surface proteins like CD19, CD20, CD34, and CD45, as well as circulating tumor cells (CTCs) found in blood samples, even at early disease stages [8-13]. These sensors operate based on the electrochemical behavior of QDs and their specific interactions with biomolecules, which manifest as measurable shifts in electrical parameters such as current, voltage, or impedance [12]. The combination of electrochemical readouts with QD technology offers several advantages: rapid analysis, affordability, user-friendly formats, and potential deployment in point-of-care diagnostic settings.

Nonetheless, challenges persist in the path toward clinical adoption. Key among these are concerns about the biocompatibility and potential toxicity of QDs, particularly those composed of heavy metals like cadmium [14-16]. To address these safety concerns, researchers are actively developing safer alternatives, such as carbon-based and silica-coated QDs, which maintain functional performance while reducing toxicity risks [10,15,16]. Securing regulatory approval for these sensors also presents a barrier, as stringent clinical standards must be met [14].

Other ongoing challenges include enhancing the selectivity and sensitivity of these sensors within the complex matrix of human blood and mitigating background noise from non-target

components. Future advancements are focused on refining QD materials to make them safer and more biocompatible while preserving their optical and electrochemical strengths [15]. This includes adopting biodegradable materials and exploring newer generations of carbon and silica QDs [15].

Moreover, refining surface engineering techniques will enable more specific targeting of disease markers, while integrating QD sensors with complementary technologies—such as microfluidics—can lead to compact, portable lab-on-a-chip systems suitable for real-time diagnostics at the point of care [17-19]. The inclusion of artificial intelligence (AI) and machine learning tools to interpret sensor outputs could further elevate diagnostic precision, enabling personalized disease tracking based on biomarker trends and minimal residual disease (MRD) analysis [20,21].

In summary, QD-based electrochemical biosensors hold immense promise for revolutionizing blood cancer diagnostics. Continued research aimed at enhancing performance, ensuring safety, and streamlining device integration is expected to lead to powerful, non-invasive diagnostic tools capable of early detection and effective treatment monitoring in clinical environments.

2. EMERGING INNOVATIONS IN QUANTUM DOT-ENHANCED ELECTROCHEMICAL SENSORS FOR DETECTING BLOOD CANCER CELLS

Diagnosing blood cancers such as leukemia, lymphoma, and myeloma presents considerable difficulty, particularly in their initial stages when physical symptoms may not be apparent [22-30]. Detecting malignant cells early is vital for effective treatment and improved patient outcomes [23,25]. In recent years, quantum dot (QD)-based electrochemical sensors have emerged as a cutting-edge approach to enhance the sensitivity, accuracy, and speed of blood cancer diagnostics [2,7,9]. By leveraging the distinctive characteristics of QDs in conjunction with electrochemical techniques, researchers are developing diagnostic tools that are not only efficient and cost-effective but also capable of detecting blood cancer markers with remarkable precision [12,31-35].

2.1. Role of Quantum Dots in Electrochemical Detection of Hematological Cancers

Quantum dots are nanoscale semiconductor crystals with notable optical and electrical features, such as adjustable fluorescence based on size and large surface area [4,5,11,14]. These attributes make them excellent candidates for biosensor platforms. When conjugated with biological recognition elements like antibodies, peptides, or aptamers, QDs enable highly selective targeting of specific cancer-related markers and cells [7]. Within electrochemical sensing systems, QDs function as transducers—converting molecular interactions into measurable electrical signals [12]. The interaction of cancer markers or cells with the sensor surface triggers a detectable alteration in electrochemical properties, such as current, potential,

or impedance, which correlates with the concentration of the analyte, allowing for precise quantification [13].

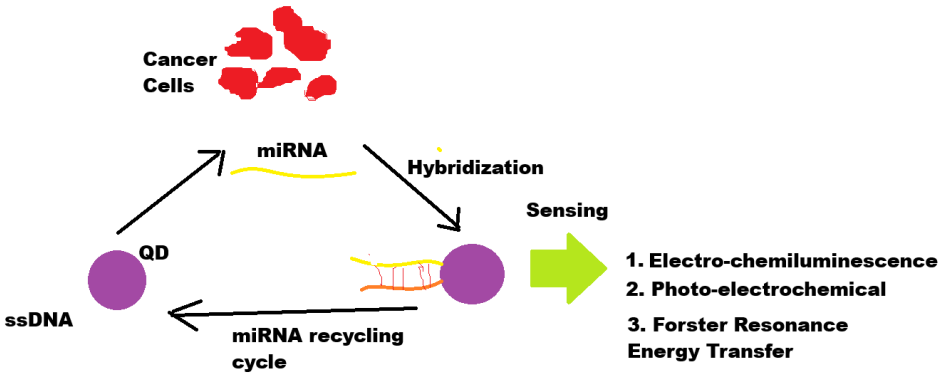

Figure 1. Quantum Dots in Cancers cell monitoring

2.2. Enhancing Sensor Performance with Nanomaterial Composites

The integration of QDs with advanced nanomaterials—such as graphene, gold nanoparticles (AuNPs), and carbon nanotubes (CNTs)—has led to notable improvements in signal strength, sensitivity, and detection thresholds [36-41]. These hybrid systems exhibit synergistic effects that enhance sensor functionality, particularly in detecting ultra-low levels of blood cancer biomarkers [36].

Gold Nanoparticles (AuNPs): Pairing QDs with AuNPs significantly boosts electron transfer rates and enhances electrochemical signal output [41,42]. This combination expands the sensor's surface area for functionalization with targeting molecules like aptamers or antibodies, thereby increasing the efficiency of capturing specific cancer indicators, including circulating tumor cells (CTCs) [43].

Graphene: Due to its excellent electrical conductivity and compatibility with biological systems, graphene is often combined with QDs to improve sensor responsiveness [31,44-46]. Graphene-QD composites exhibit enhanced charge transport, enabling quicker and more sensitive identification of disease markers such as CD19 and CD33, which are key indicators in leukemia and lymphoma detection [2,48].

Carbon Nanotubes (CNTs): CNTs serve as effective signal amplifiers when integrated with QDs, providing high conductivity and expansive surface areas [46-48]. This combination strengthens detection signals and supports the stable anchoring of diagnostic biomolecules on the sensor’s surface, which is essential for accurate and consistent performance.

2.3. Multiplexed Detection of Blood Cancer Biomarkers

A major advancement in the field of quantum dot (QD)-based electrochemical sensors is their ability to perform multiplexed detection—identifying multiple biomarkers simultaneously

within a single assay [3,46-51]. This capability is particularly valuable in diagnosing blood cancers such as leukemia, lymphoma, and myeloma, where different biomarkers must be tracked to determine cancer subtype, monitor disease evolution, or evaluate the effectiveness of treatment [22,24].

(i) Size-Dependent Emission for Multiple Target Detection: Quantum dots exhibit size-dependent fluorescence (Figure 2), allowing them to be engineered to emit light at specific wavelengths [5,11]. This tunable optical behavior makes them ideal for concurrently detecting several cancer-related biomarkers within one sample [47]. For instance, biomarkers such as CD19, CD33, CD34, CD45, and CD47—commonly linked to various blood cancers—can be detected in a single test [8,35]. This multiplexing capability enhances diagnostic accuracy and supports more tailored and dynamic treatment strategies [3,51].

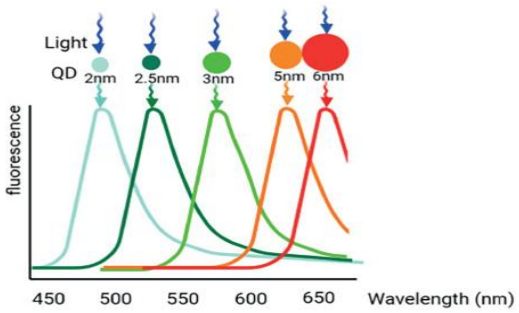

Figure 2. Size Dependent Emission in QDs

(ii) Dual-Mode Detection Using Fluorescence and Electrochemical Signals: Combining fluorescence imaging with electrochemical readouts offers a synergistic approach for improved sensitivity and reliability [52-55]. Fluorescent QDs enable real-time visualization of biomolecular interactions, while the electrochemical component delivers quantitative measurements of biomarker concentrations [12,54]. This dual-mode strategy not only ensures greater detection accuracy but also facilitates robust analysis of cancer cells and their molecular signatures [51].

A schematic representation of this integrated detection technique is illustrated in Figure 3.

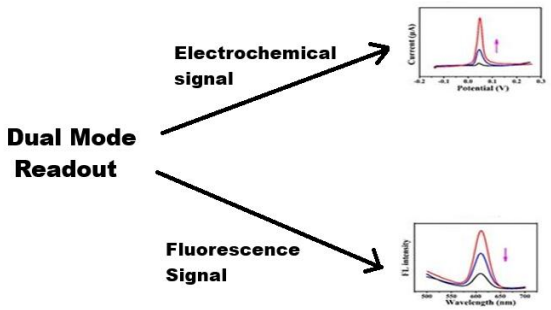

Figure 3. Dual-Mode Detection Using Fluorescence and Electrochemical Signals

2.4. Signal Amplification for Detecting Ultra-Low Concentrations

A defining advantage of quantum dot (QD)-based electrochemical sensors is their ability to detect extremely low levels of blood cancer biomarkers or circulating cancer cells [37]. Innovations in this area have concentrated on enhancing signal amplification methods, allowing for the identification of even trace biomarker quantities present in blood samples [56]. Figure 4 shows molecularly imprinted polymer-based sensors for cancer biomarker detection

(i) Enzyme-Driven Signal Enhancement: Common enzymes such as horseradish peroxidase (HRP) and alkaline phosphatase (AP) are frequently utilized to amplify the electrochemical signals in QD-based biosensors [57,58]. When a target biomarker binds to the functionalized QD surface, the enzyme catalyzes a reaction that produces a stronger electrochemical response [57]. This amplification method significantly boosts the sensor's sensitivity, enabling detection of minimal amounts of cancer biomarkers [58].

(ii) Polymerization-Based Amplification: Signal enhancement can also be achieved through the polymerization of conductive polymers [59,60]. When a biomarker interacts with the sensor, it initiates a chain reaction that forms conductive polymers at the sensor surface, enhancing the electrochemical output [59]. This method is especially effective for detecting cancer markers at very low concentrations [60].

(iii) Use of Magnetic Nanoparticles for Improved Sensitivity: Incorporating magnetic nanoparticles into QD electrochemical sensors helps improve target capture and signal strength [61]. These particles attract and localize rare cancer cells, such as circulating tumor cells (CTCs), onto the sensor's detection area [62]. This increases the signal-to-noise ratio and makes it easier to isolate cancer markers from complex samples like blood [61,62].

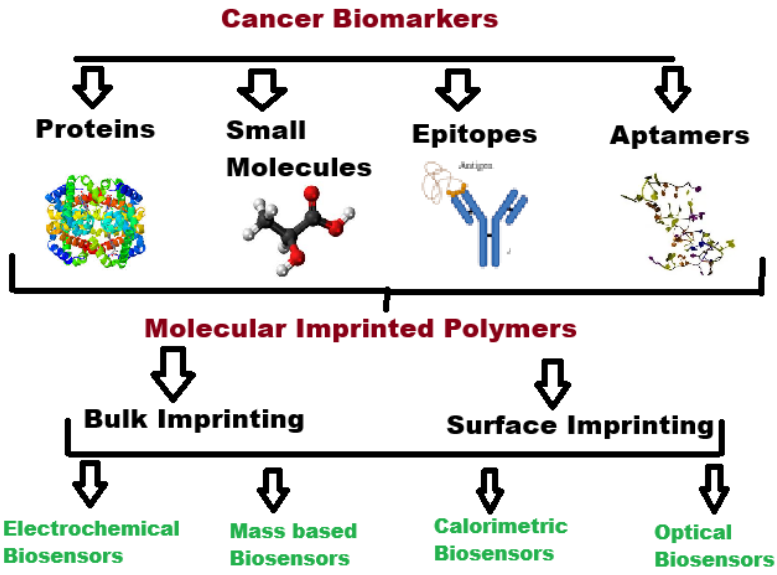

Figure 4. Molecularly imprinted polymer-based sensors for cancer biomarker detection

2.5. Integration with Microfluidics for Point-of-Care Applications

The combination of QD-based electrochemical sensors with microfluidic systems has opened new possibilities for point-of-care (POC) cancer diagnostics. Microfluidics enable precise handling of small sample volumes and rapid analysis, which is especially useful in clinical or low-resource environments.

(i) Lab-on-a-Chip Systems: Embedding QD sensors into microfluidic chips allows for better control over fluid dynamics, such as flow rate and sample volume. These systems can isolate CTCs from whole blood more efficiently, offering quicker diagnostic results and facilitating real-time disease monitoring. A conceptual design of such a system is shown in Figure 5 [63,64].

(ii) Portable Diagnostic Devices: The development of compact, user-friendly devices that incorporate QD-based sensors now allows cancer detection to take place outside of laboratory settings. These portable tools offer an affordable, non-invasive solution for regular screening and real-time monitoring during treatments like chemotherapy, enabling more accessible and frequent patient evaluations [65,66].

2.6. Biocompatibility and Safety Aspects of Quantum Dots

When employing quantum dots (QDs) in biomedical settings, ensuring their biocompatibility and minimizing toxicity are essential factors. Traditional QDs, particularly those containing cadmium, have drawn attention for their potential cytotoxic effects. In response, recent innovations have focused on developing safer alternatives—such as carbon-based QDs and QDs encapsulated with silica—that offer reduced toxicity while maintaining the necessary optical and electrochemical characteristics for effective biosensing [67–69].

(i) Carbon Quantum Dots (CQDs): CQDs, composed primarily of carbon, present a more environmentally friendly and biologically safe option compared to heavy metal-based QDs. They exhibit excellent fluorescence stability, high surface functionality, and can be easily modified for specific biomedical purposes, including blood cancer detection. Additionally, their natural biodegradability lowers the risk of long-term accumulation in the body, making them preferable for clinical use.

(ii) Silica-Coated Quantum Dots: Applying a silica layer to conventional QDs acts as a protective barrier, significantly limiting the release of toxic metal ions. This surface modification enhances the overall safety and biocompatibility of QD-based sensors. Such coated nanostructures are increasingly considered suitable for integration into clinical diagnostic systems due to their improved biosafety. Detailed data on the types of QDs used, including their limits of detection (LOD) and linear dynamic ranges (LDR), are presented in

Table 1.

Table 1. Data of type of QDs and their LOD with LDR

Type of QDs	**LOD**	**LDR**
CdSe/ZnS QDs [70]	0.1 nM	0.1-100 nM
GO QDs [71]	0.5 nM	0.005 – 50nM
CQDs [72]	2.3nM	2.3- 150 nM
InP/ZnS QDs [73]	1.2 nM	1-100 nM
AgInS2 QDs [74]	10 nM	10-200 nM
ZnO QDs [75]	0.5 nM	0.5 – 75 nM
Perovskite QDs [76]	3 nM	3-120 nM
Si QDs [77]	8 nM	8 -160 nM

3. RESEARCH DIRECTIONS FOR ADVANCING QUANTUM DOT ELECTROCHEMICAL SENSORS IN CANCER CELL DETECTION

Quantum dot (QD) electrochemical sensors hold significant promise for cancer cell detection due to their distinctive optical and electronic attributes. However, their successful application in clinical settings requires overcoming several obstacles. These challenges involve issues related to biocompatibility, sensitivity, selectivity, signal transduction, stability, and the development of practical, cost-effective devices [78-85]. Key research areas focused on addressing these issues are outlined below:

3.1. Enhancing Biocompatibility and Reducing Toxicity

A primary concern for QD-based sensors, particularly in clinical uses like in vivo cancer detection, is their potential toxicity and lack of biocompatibility. Traditional QDs, often composed of inorganic materials such as cadmium, can release toxic substances into the body, posing risks to health.

Research Directions are as follows:

(i) Surface Passivation: Modifying the QD surface is a key strategy to mitigate toxicity. Current research emphasizes developing biocompatible coatings that passivate QDs, preventing the release of harmful ions. Applying materials like silica, polyethylene glycol (PEG), or other biocompatible substances can effectively reduce toxicity and improve QD stability in biological environments.

(ii) Development of Eco-Friendly QDs: A promising alternative involves creating "greener" QDs from less toxic elements like copper, zinc, or silicon. These QDs can maintain beneficial optical properties while minimizing adverse health effects.

3.2. Improving Sensitivity and Detection Limits

Although QD-based sensors exhibit high sensitivity, detecting cancer cells at low concentrations, especially within complex biological samples like blood or urine, remains difficult. Achieving high sensitivity for early cancer diagnosis is essential [23].

Research Directions are as follows:

(i) Signal Amplification: Employing signal amplification techniques is one method to enhance sensitivity. For instance, enzymatic amplification can be used to catalyze the conversion of specific cancer biomarkers into detectable signals. Additionally, amplification strategies using nanomaterials like gold nanoparticles or graphene can amplify the electrochemical signal [41,68].

(ii) Hybrid Nanomaterials: Combining QDs with other nanomaterials, such as graphene oxide, carbon nanotubes, or metal-organic frameworks (MOFs), presents a promising avenue. These hybrid materials can improve electron transfer rates, expand the interaction surface area with cancer cells, and enhance the overall electrochemical response [68].

(iii) Microfluidic Integration: Integrating QD sensors with microfluidic devices allows for the analysis of small sample volumes with reduced interference [63,64]. Microfluidics can also aid in the efficient isolation and concentration of cancer cells, leading to a better signal-to-noise ratio and increased detection sensitivity [62].

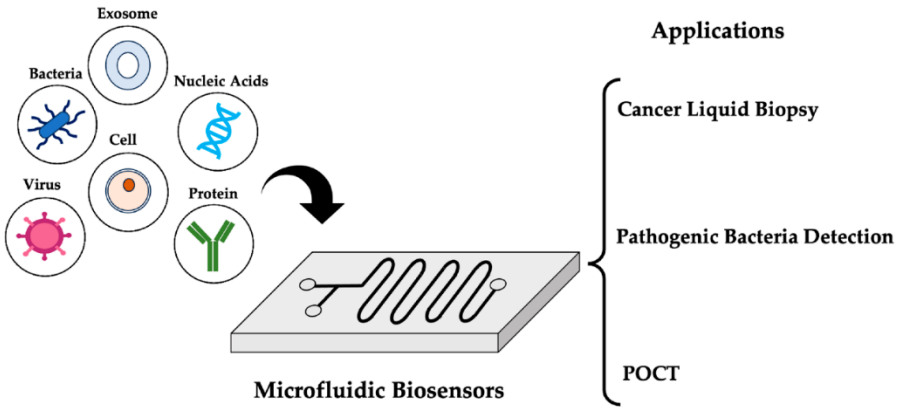

Figure 5. Microfluidic Biosensors

3.3. Achieving High Specificity in Cancer Cell Detection

For clinical applications, QD sensors must selectively detect cancer cells, avoiding interference from healthy cells or other biomolecules [7]. Non-specific binding can compromise sensor reliability by producing false positives or negatives [44].

Research Directions are as follows:

(i) Surface Functionalization: Enhancing selectivity relies on functionalizing QDs with specific targeting molecules like antibodies, aptamers, or peptides. These ligands should selectively bind to cancer cell surface biomarkers (e.g., HER2, EpCAM, or CD133). Current research focuses on optimizing the functionalization process to ensure the exclusive detection of cancer cells or specific cancer markers, even in complex samples [43].

(ii) Multi-Target Sensing: Employing QD-based sensors to detect multiple biomarkers simultaneously can further enhance specificity [3,46]. This multi-modal strategy increases

detection accuracy by minimizing interference from other cell types [51]. Researchers are developing multiplexed QD sensors capable of targeting various cancer-related biomarkers, thus improving diagnostic precision [45].

3.4. Enhancing Stability and Reproducibility

A significant challenge is the stability of QDs in biological samples [16]. QD degradation or aggregation can lead to decreased sensor performance over time, limiting the long-term applicability of QD-based sensors in cancer detection [67].

Research Directions are as follows:

(i) Stabilizing QD Structures: Strategies to enhance the physical and chemical stability of QDs in biological environments are being developed [16]. These include utilizing surface coatings or creating core-shell QD structures that offer better protection against degradation [67,69].

(ii) Ensuring Long-Term Reproducibility: To guarantee consistent performance over extended periods, QD sensors must maintain sensitivity through repeated use [10]. Achieving this requires developing highly reproducible sensor fabrication techniques and refining calibration protocols to maintain performance across multiple detection cycles [32].

3.5. Developing Cost-Effective and Scalable Manufacturing Techniques

The high cost of producing QD-based sensors, particularly when scaling up for clinical or commercial applications, is a major limitation [10]. Developing cost-effective and scalable manufacturing methods is essential for the widespread adoption of QD electrochemical sensors in cancer diagnostics [15].

Research Directions are as follows:

(i) Green Synthesis Methods: Traditional QD synthesis methods can be costly and environmentally harmful [15]. Researchers are exploring cost-effective, sustainable, and scalable synthesis alternatives, such as "green" synthesis techniques that minimize the use of toxic chemicals and simplify processes [10,72].

(ii) Roll-to-Roll Fabrication: For large-scale production, roll-to-roll (R2R) fabrication methods are being investigated to integrate QDs into sensor platforms [10]. This technology enables mass production of sensors with high uniformity and low cost, facilitating the large-scale manufacture of QD electrochemical sensors [80].

3.6. Integration with Wearable and Point-of-Care Devices

The widespread adoption of QD-based sensors in cancer diagnostics necessitates their integration into portable, user-friendly, and cost-effective devices suitable for point-of-care (POC) applications [19,65].

Research Directions are as follows:

(i) Wearable Platforms: Researchers are investigating the incorporation of QD-based sensors into wearable devices for real-time monitoring of cancer markers [27]. Such sensors could allow for continuous tracking of cancer progression or treatment effectiveness, reducing the need for frequent hospital visits [66].

(ii) Portable Detection Devices: Miniaturized electrochemical sensors utilizing QD technology can be integrated into portable diagnostic tools for on-site cancer cell detection [65,66]. These devices would be particularly valuable in resource-limited settings with limited access to advanced diagnostic equipment [18].

3.7. Real-Time Monitoring and Early Detection

Early-stage cancer diagnosis relies heavily on real-time cancer cell detection, as timely intervention significantly improves treatment outcomes [23,25]. QD-based electrochemical sensors must be optimized for rapid, real-time cancer cell detection [20].

Research Directions are as follows:

(i) Real-Time Sensing Systems: Efforts are underway to develop systems that enable continuous or real-time monitoring of cancer cells, particularly using non-invasive methods like blood or saliva samples [20,65]. These systems require high-speed signal processing to provide immediate results [21].

(ii) In Vivo Sensing: For enhanced early detection, QD-based sensors could be integrated into in vivo sensing platforms, allowing for direct cancer cell detection within the body [27]. This necessitates the creation of biocompatible, minimally invasive systems capable of operating in complex biological environments without compromising detection accuracy [67,82].

4. CONCLUSION

In summary, quantum dot (QD) electrochemical sensors represent a promising avenue for the early detection and diagnosis of blood cancers. Their unique optical properties, large surface area, and adaptability in surface functionalization make them highly effective for detecting low concentrations of cancer biomarkers and circulating tumor cells (CTCs). Despite their potential, challenges remain in areas such as improving sensitivity and specificity, ensuring biocompatibility, and addressing reproducibility and clinical integration.

Recent research has achieved notable progress in tackling these challenges through innovative strategies like signal amplification techniques, the development of biocompatible QDs, and the combination of QDs with nanomaterials and microfluidic platforms. These advancements have enhanced the performance of QD electrochemical sensors, making them more sensitive, reliable, and suitable for practical diagnostic applications.

Looking ahead, realizing the full potential of QD-based electrochemical sensors in cancer detection hinges on overcoming remaining obstacles related to clinical translation, cost-effectiveness, and scalability. Continued innovation in nanomaterial design, biosensor integration, and regulatory approval processes will be crucial. Ultimately, QD-based sensors offer the potential to transform early cancer detection by providing a rapid, non-invasive, and accurate alternative to current diagnostic methods, leading to more personalized and timely treatment strategies and contributing to improved outcomes for patients with blood cancers.

Declarations of interest

The authors declare no conflict of interest in this reported work.

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