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Advancements in nanobiosensors for early cancer detection, challenges, treatment, and future prospects: a comprehensive review

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Abstracts

Background Cancer is one of the leading causes of global mortality. To reduce treatment costs, improve quality of life and increase survival outcomes for an individual, early detection of cancer is crucial. Advances in nanobiosensors offer point-of-care detection with high specificity and sensitivity for biomarkers associated with tumour detection. Such biosensors also support personalised approaches to cancer treatment. Some nanosensors might be developed as theranostics, where they deliver therapeutic molecules or aid in therapy via mechanisms like photothermal ablation, sonodynamic therapy or precise targeting of therapeutic molecule to the tumor site. A comprehensive review is presented where the latest advances in nanoparticle based sensors are discusses.

Aim To examine emerging nanotechnology-driven biosensing approaches for cancer detection, a comprehensive review that encompass the detailed modus operandi and advantages and disadvantages and advancements in Nanoparticle-based biosensors, Paramagnetic nanoparticle-based biosensor, Quantum dots, Nano-shells-based biosensor, Gold nanoparticle-based biosensor, Nanowire-based biosensors, Nanorods, Carbon Nanotube Based Biosensors, Nanocantilever-based based biosensor, Nanocomposite based biosensors, NanoVelcro based biosensors, Nanozymes, and Amperometric Sensor is presented.

Method This review is based on a comprehensive analysis of published literature related to advanced nanomaterial-based biosensors for cancer diagnosis. Relevant research articles related to cancer detection, review papers, and reports were collected from scientific databases such as NCBI, PubMed, Web of Science, and Google Scholar. Keywords including nanobiosensors, nanocomposites, nanocantilevers, nanowires, carbon-nanotubes, cancer biomarkers, nanoparticles, aptamer-based sensors, nanomaterials, and nano-shells, were used to access literature. Articles which are published mainly within the last few years were prioritized to highlight recent advancements. Applications of various biosensors in detecting different cancer types also has been given. Only articles those are peer reviewed and published in English literature have been included.

Result Studies based on nanomaterials show that there is significant improvement in cancer detection. Additionally, the technology also enables early diagnosis, accurate imaging with the help of biomarkers, and targeted drug delivery. However, issues such as biocompatibility, clinical testing at a large scale, potential toxicity, and challenges related to its regulation remain some of its key limitations.

Conclusion Nanotechnology has significantly improved early cancer diagnosis via using highly sensitive and specific nanobiosensors. Despite challenges related to safety, cost, and clinical translation, continued research is essential to realize its full potential in cancer diagnostics and management.

Keywords Nanoparticle, Paramagnetic nanoparticle-based biosensor, Quantum dots, Nano shells, Gold nanoparticle, Nanowire, Nanorods, Carbon nanotube, Nanocantilever, Nanocomposite, NanoVelcro, Nanozymes, Amperometric sensor

1 Introduction

Cancer continues to pose a major global health burden, with increasing incidence and mortality rates despite advances in research and treatment [1, 2]. Early diagnosis is key to patient survival and the cost of cancer-related healthcare expenditures. Conventional imaging procedures and minimally invasive tissue sampling methods, such as fine-needle biopsy, often exhibit limitations in terms of sensitivity, specificity, and benign-versus-malignant discrimination and thus cannot deliver timely interventions [3]. Nanotechnology has emerged as a revolutionary strategy to address these problems and play a crucial role in two key areas: early diagnosis and treatment of cancer, based on the unique physicochemical properties of nanomaterials [4, 5]. Nanomaterials exhibit excellent biomedical performance due to their high surface-to-volume ratio, adjustable surface chemistry, and unique optical, electrical, and magnetic properties [5, 6]. Quantum dots (QDs), for example, have size-dependent fluorescence activity that can be used to image cancer biomarkers at an ultra-low concentration with a high contrast image [7]. Gold nanoparticles (AuN[8]Ps) have been extensively applied due to both their biocompatibility and ease of functionalization, permitting the enhanced amplification of signal in diagnostic assays and the programmed eradiation of tumor cells in photothermal therapy [9]. Carbon nanotubes (CNTs) have stimulated great interest because they possess extraordinary electrical conductivity and mechanical strength in addition to their ability to perforate cell membranes. These properties render them suitable candidates for biosensing platforms for various cancer biomarker detection as well as drug delivery to tumor loci [10]. Nanocomposites, consisting of more than one type of nanomaterial, could enable multifunctional benefits to combine diagnostic imaging with therapy. For instance, hybrid nanocomposites made by combining magnetic nanoparticles with fluorescent markers can be used for tracking of real-time drug delivery [11]. These innovative technologies are also used to detect circulating tumor cells, progression of disease, and response of a patient towards therapy [6, 12]. Instead of such advances, there are still some important gaps in the research that need more attention to fulfil. Only a few studies have evaluated nano-biosensors using real-time clinical sample data for point-of-care detection [13]. Consistent reproducibility, reliable calibration, and easy integration of these devices are still major hurdles [14]. Moreover, we often overlook concerns about toxicity, biocompatibility, and the environmental impact of nanomaterials [15]. Exosome-based nanosensors represent a promising direction for early cancer detection, making use of exosomes that carry tumor-specific molecular information. These

methods offer gentle, minimally invasive tests, allowing doctors to monitor disease progression over time [16]. Furthermore, combining nanotechnology with artificial intelligence in diagnosis becomes faster and more reliable, enabling medical professionals to provide better therapy to patients [8] .

2 Nanotechnology

Nanotechnology is an innovative approach to working with materials at an extremely tiny scale; their size is approximately one billion times smaller than a meter. Nanotechnology encompasses the creation and application of chemical, physical, and biological systems, as well as the integration of these resultant nanomaterials into larger systems. Nanotechnology can be defined as "atomic precision engineering." Within the subclassification of technology in colloidal science, chemistry, physics, biology, nanotechnology analyzes the matter at the nanoscale. Nanotechnology can play a crucial role in creating new products, upgrading existing production equipment, and developing advanced materials that function more effectively. This helps reduce the use of raw materials and energy, minimizes environmental damage, and also supports bioremediation [17, 18]. Nanomaterials are typically the most extensively investigated due to the variety of bioanalytical functions they offer in areas such as bioimaging, diagnosis, and drug delivery [19].

2.1 Nano-biosensors for cancer detection

In recent years, nano-biosensors have drawn significant attention as a promising approach for the early detection of cancer. Their strength lies in their ability to deliver highly sensitive and accurate results while relying on nanomaterials to detect important cancer biomarkers such as circulating tumor DNA, proteins, and exosomes. This enables clinicians to conduct diagnoses in a non-invasive manner and track changes in real-time [20, 21]. Liquid biopsy-based nano-biosensors have become increasingly important in cancer studies. These tools allow healthcare providers to follow the progress of tumors and evaluate patient responses to therapy, without subjecting patients to painful or time-consuming tests. Compared to older diagnostic methods, this approach is much more comfortable for the patient. Their usefulness has further increased with the application of different nanomaterials such as graphene, gold nanoparticles, and quantum dots. These materials have enhanced the sensitivity of the devices and also enabled the simultaneous study of multiple biomarkers in a single test [22]. This saves both time and resources while also giving more reliable results. Researchers are now examining these biosensors not only for quick and routine testing but also for their potential role in developing personalised treatment plans tailored to individual patients. As nanotechnology advances rapidly, biosensors will likely become a standard part of cancer care in the near future, particularly in enhancing diagnosis, monitoring, and overall disease management [23]. Figure 1 provides a visual overview of cancer cell growth and spread. Tumor clusters (shown in blue) begin to invade surrounding healthy cells, while new blood vessels form to supply them with nutrients through angiogenesis. Around a tumor, different immune cells such as natural killer (NK) cells, T-lymphocytes, B-lymphocytes, and macrophages gather to protect the body. When the basement membrane gets damaged or broken, the tumor cells can start moving into the surrounding tissues. This marks the initial stage of metastasis, where cancer cells first develop.

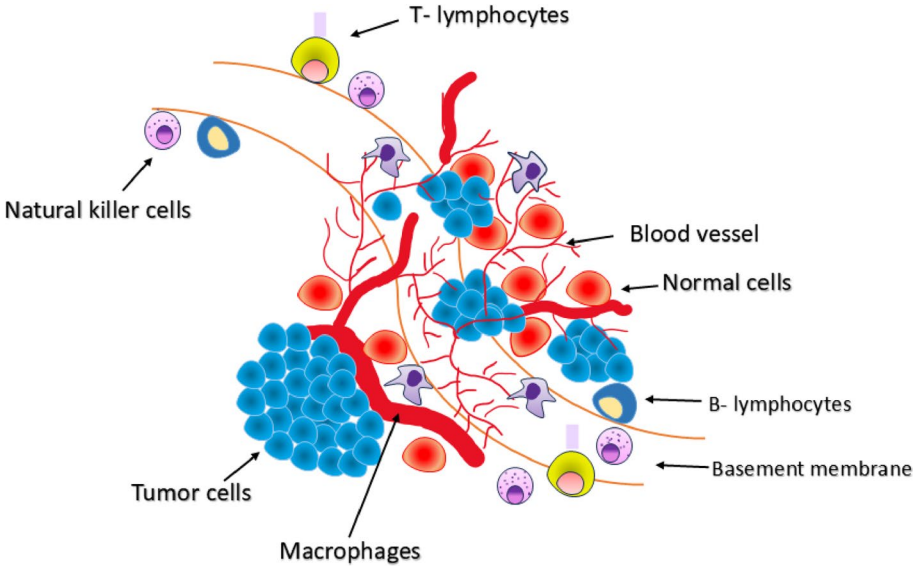

Fig. 1 The illustration shows tumour cell proliferation, invasion of normal cells, and blood vessel formation (angiogenesis) supplying nutrients

3 Biosensor

Nanosensors work at the molecular level, allowing extremely sensitive detection. They are made up of four main parts: a sensor, an analyte, a transducer, and a detector. The analyte interacts with the sensor surface, leading to changes in the transducer's physicochemical properties as shown in Fig. 2. This alters its optical or electronic characteristics, generating an electrical signal that can be detected and analysed [22, 23]. Based on how the components are attached or how the bio-recognition element (bioreceptor) is integrated with the transducer, biosensor evolution has been divided into three generations. The analyte and the bioreceptor, which diffuse to the surface of the transducer, result in the production of an electric response, which is measured by the biosensors in the first generation (Ist gen) as depicted in Fig. 2.

Another name for this kind of sensor is mediator-less amperometric biosensors [24–26]. In second-generation (IInd gen) biosensors, extra components are added to the biological layer to improve how well the sensor works. These may include helper enzymes or co-reactants, which act as mediators. Some of these mediators can be artificial or even slightly harmful nanomaterials. Such sensors are called mediator amperometric biosensors [26]. Third-generation (IIIrd gen) biosensors are more advanced. In these, the bioreceptor molecule is directly linked to the sensing element. This design eliminates the need for freely moving mediators in the solution and instead utilises enzymes and mediators fixed to the same electrode, making the sensor more efficient and reliable. Transferring electrons, a direct connection was formed between the enzymes and the electrode, with no intermediate steps needed, unlike with nanomaterials. The assistance of this generation of biosensors includes minimal cost of design and the ability to conduct repeated measurements [27–29]. The reading system then calculates the extent to which these alterations have changed [28]. A reading system in a biosensor can detect various types of physical changes. These include bending of the material, shifts in resonant frequency, alterations in optical properties, and electrochemical changes, such as changes in current or voltage. Biochips may hold several biosensors together. While each

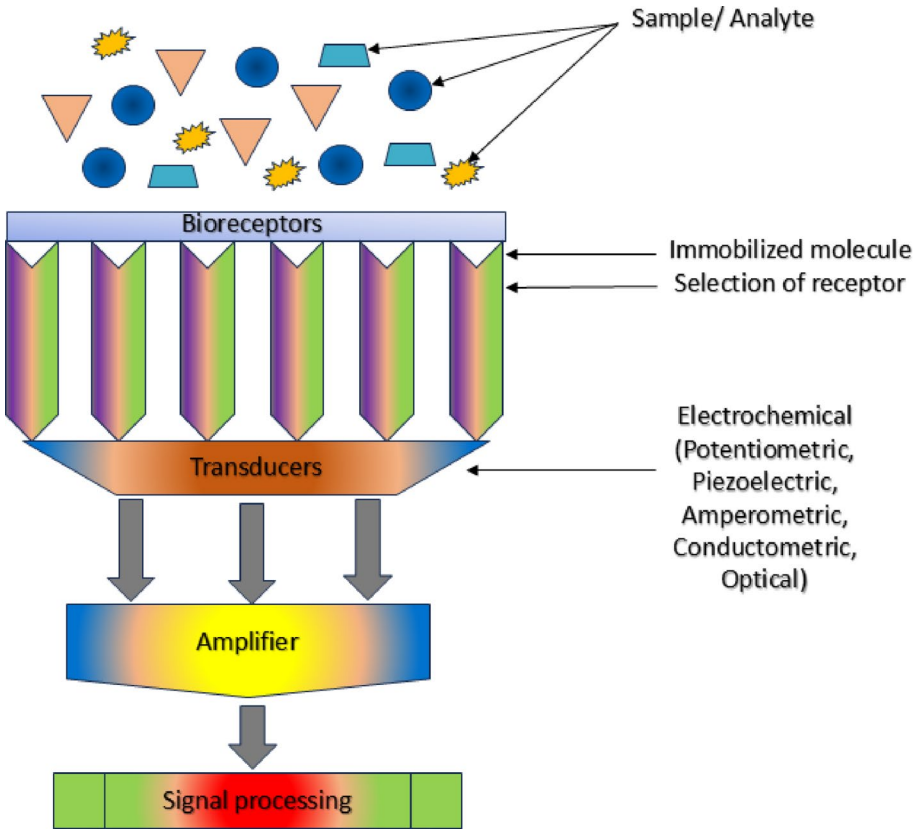

Fig. 2 The above diagram illustrates the working principle of a biosensor. A cell signal is generated when the ligand binds to its specific receptor. As the signal is detected, different types of transducer systems, such as electrochemical or optical systems, transform the signal. Successive to processing the amplification, the output is measured and analyzed

sensor operates independently, combining them enables the simultaneous detection of different analytes, allowing for the testing of multiple target substances at once [30]. Schematic illustration of IIIrd generation biosensors is given in Fig 3.

3.1 Features of biosensors

Improving the performance of biosensors is essential if they are to be used in commercial applications, as this ensures both efficiency and reliability. The following factors play a significant role in enhancing biosensor functionality [31–34]

3.1.1 Selectivity and sensitivity

An ideal bioreceptor clearly identify the target molecule among other compounds. Along with the specificity, it should be sensitive enough to measure the analyte at very low concentrations, even in nanograms or femtograms per millilitre. The g-C_3N_4/chitosan-based biosensor demonstrated excellent selectivity towards flutamide, with a significantly higher signal response even in presence of interfering compounds like glucose, lactose, and urine. In complex biological matrices, the system has demonstarted strong specificity with minimal cross-reactivity [31].

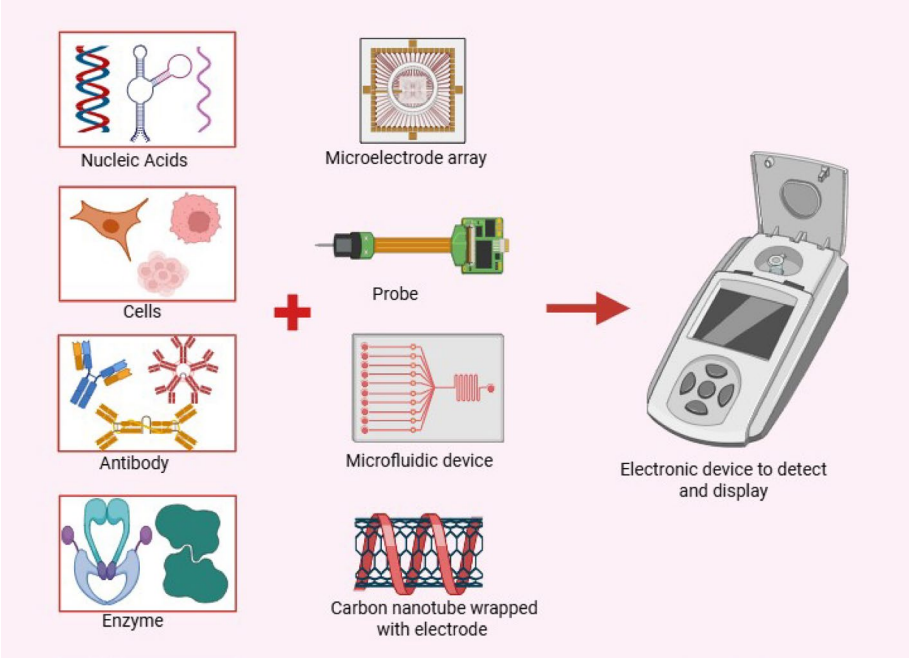

Fig. 3 Schematic illustration of the third-generation nanosensors

3.1.2 Linearity and limit of detection (LOD)

Accurate measurement is achieved in presence of a clear linear relationship between analyte concentration and sensor response. Also when the detection limit is low, it enables the identification of diseases in their early [35].

3.1.3 Reaction time and reproducibility

An ideal biosensor's reaction time is low and shall achieve nearly 95% of its full signal in a short period, making it suitable for real-time monitoring. Along with sensitivity and specificity, reproducibility is equally important, that indicates that the sensor is providing reliable, consistent results when the same measurement is repeated under similar conditions. For dependability, reproducibility is an imperative feature.

3.1.4 Stability

Stability is a crucial factor for the long-term use of biosensors. When bioreceptors are used they are prone to degradation and thus need to be sturdy enough to withstand degradation and remain unaffected by normal environmental fluctuations. In the study of Nasiri et al., 2025, the developed sensor demonstrated stable performance, with only 3% variation in signal across multiple measurements taken during the day at room temperature. Such reproducibility indicates that the combination of g-C_3N_4 and chitosan provided strong structural support and protection, helping the sensor retain both its function and reliability under standard conditions [31].

3.2 Architectural design of biosensor

The development of high-performance biosensors relies on the selection of advanced materials and the design of their structures. Transition metal oxides and conductive polymers (CPs) can create a superior biosensor with enhanced features. Recently, CPs

have been produced using different methods, including chemical, biological, and electrochemical synthesis techniques [36–38]. CPs are also involved in the design of the redox enzyme glucose oxidase [Gox], a glucose biosensor. As per the findings of several studies, GOx sensors are employed as biocatalysts in developing various CPs, such as polypyrrole and polythiophene. Some limitations associated with conventional bioanalytical tools, such as ELISA (enzyme-linked immunosorbent assays), include their expense and short-term usage, despite also offering benefits like precision in monitoring the target molecule. Affinity sensors can be employed to compensate for this complexity. Additionally, affinity sensors can be grouped into four main types. The first type uses natural or artificial materials, the second is based on molecularly imprinted polymers, the third relies on antibodies, and the fourth uses DNA aptamers [36, 39]. MXenes and transitional metal oxides have evolved. Two-dimensional materials with either metallic conductivity or super-semiconducting properties, or a combination of both, are used for the construction of biosensors and architectural design. There is closeness in the structural properties of MXenes and graphene (2D material). Since MXenes offer good flexibility, they are considered the ideal material for designing biosensors [39–41].

4 Selected modalities to detect cancer

Detecting cancer early is crucial for effective treatment. Various modalities are employed for cancer detection, as shown in Fig. 4. Here are some key methods.

4.1 Nanotechnology based biosensors

Biosensors based on different nanoscale tools are very helpful to diagnose and cure cancer by improving selectivity and sensitivity.

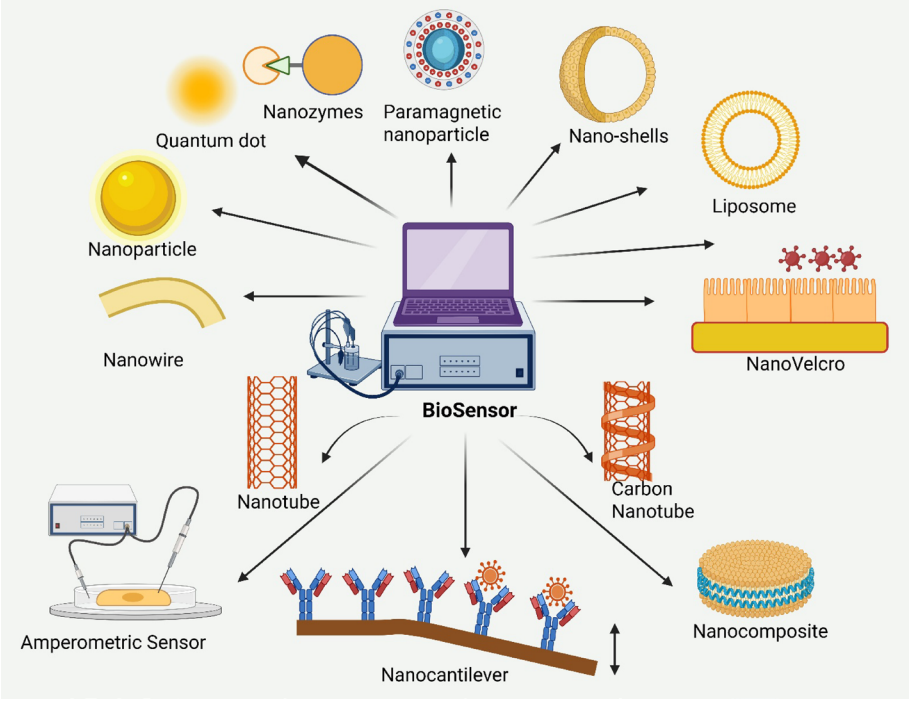

Fig. 4 The above illustration shows a biosensor platform integrated with different nanotools

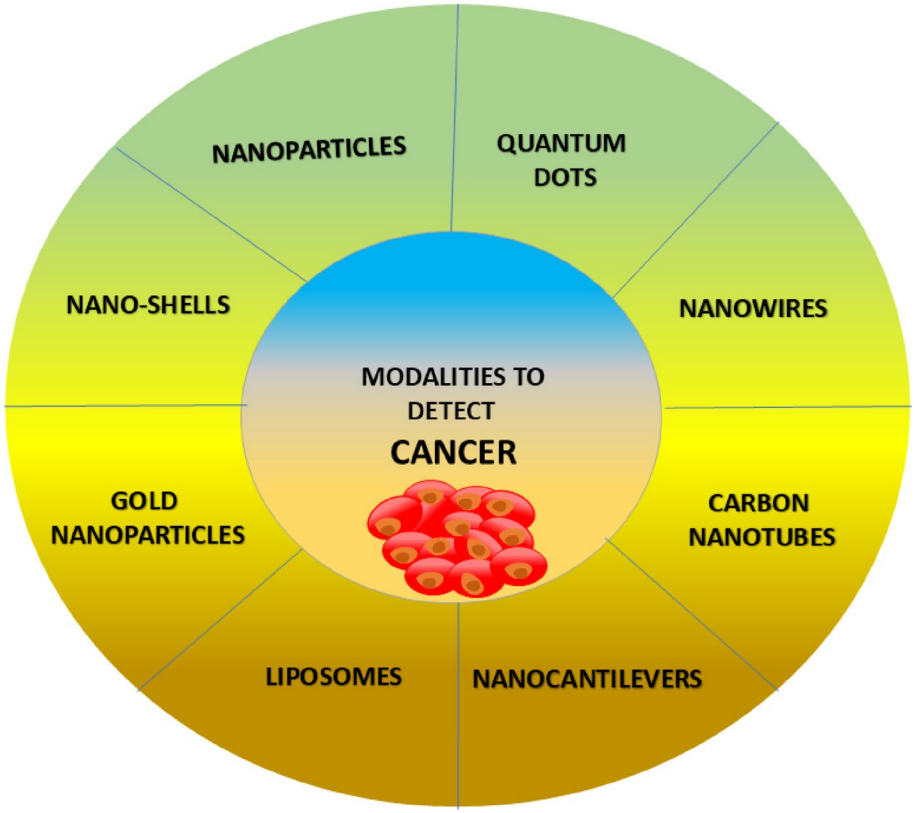

Fig. 5 The figure highlights several nanotechnology-based methods used in cancer detection. Among them are nanoparticles, quantum dots, nanowires, carbon nanotubes, liposomes, nanocantilevers, gold nanoparticles, and nanoshells. Each method adds its own benefits-some improve sensitivity, others provide clearer signals, or help detect minimal amounts of biomarkers

4.2 Nanoparticle-based biosensors

Ongoing advancements in nanoparticle-based biosensors have improved the accuracy of cancer detection and treatment by increasing the sensitivity and specificity of the test. For more accurate diagnosis, gold nanoparticles combined with aptamers have been used to differentiate between Burkitt's lymphoma cells and leukemia cells [34]. The Nano-Interfaced Microfluidic Exosome (nano-IMEX) biosensor is formed by utilising nanostructured materials in microfluidic devices, which are employed in the early diagnosis of ovarian cancer [35]. Cancer detection becomes more feasible and precise by using gold nanoparticles with biomarkers that have special optical properties [36]. One of the new and promising approaches in cancer diagnosis is the use of plasmonic biosensors, which utilise phase singularity along with two-dimensional nanomaterials to achieve better results. This remarkable approach creates a significant shift in lateral position, enabling the detection of cancer biomarkers even at extremely low concentrations in the sample. A theranostic platform has been developed that utilises Raman spectroscopy in conjunction with photodynamic therapy to detect cancer. This approach enables real-time cancer detection and simultaneously allows clinicians to track how patients respond to tailored treatments [37]. Simultaneously, a graphene-based brain–computer interface is being evaluated in clinical trials for use in surgical oncology. It aids surgeons in separating tumor tissue from normal brain tissue, improving precision and supporting improved patient outcomes [38]. At the same time, the paper-in-polymer-pond (PiPP)

device-a simple, affordable paper-based biosensor-can detect colorectal and prostate cancers within an hour, offering a practical solution for resource-limited settings [39].

4.3 Quantum dot-based biosensors

Quantum dots (QDs) are light-emitting molecules which makes them especially valuable for cancer studies. These are able to produce clear and precise images, thereby helpful in tracking the tumor development both in vitro and in vivo. More recently, multifunctional theranostic QD platforms have been developed, both detect disease and carry therapeutic agents to the tumor site [40]. Their application includes detection of circulating tumour markers, including tumour cells and nucleic acids, that has improved liquid biopsy approaches [41]. Quantum dots (QDs) are when combined with therapeutic molecules, they are able to transport drugs directly into tumors for precise targeting and protecting healthy cells from detrimental impact of treatment modalities [42]. In aggressive cancers such as TNBC, QD-based biosensors have opened new avenues for accurate diagnostics and tailored treatment [43]. Small, biosensing chips have been developed those are capable of detecting cancer markers in real-time, enabling timely action by healthcare professionals [44]. Additionally, cadmium-free QDs reduce environmental and patient risks while maintaining the optical features essential for detection [45]. QDs integrate imaging, treatment, and follow-up in a single system [46]. Inclusion of hydrogels with QDs makes them biocompatible which can be used to detect cancer markers in body fluids including blood, saliva, and urine [47]. QDs conjugated with antibodies and peptides, may target cancer cells more precisely. These advances highlight the value of QDs in superior imaging and precise detection. Therapeutic molecules can be carried straight to tumors, helping doctors to accurately kill cancer [48]. With QD-based biosensors, cancer care in the future can become safer, more precise, and less stressful for patients.

4.4 Paramagnetic nanoparticle-based biosensor

Paramagnetic nanoparticle-based biosensors have revolutionised cancer detection and treatment. They make the process more precise, less invasive, and highly effective. One approach, known as magnetic particle spectroscopy (MPS), examines the relaxation behaviour of magnetic nanoparticles. This enables the detection of cancer biomarkers with high sensitivity, eliminating the need for complex washing steps [49]. Another advance is the use of polyethylenimine-coated superparamagnetic iron oxide nanoparticles (SPIONs). With this method, chemotherapy drugs reach only to the tumor cells and are released there, causing less damage to the rest of the body [50]. Biosensors based on superparamagnetic nanoparticles have shown strong promise for point-of-care cancer testing [51]. Magnetic tools such as Magseed and Magtrace are found very useful in surgical oncology, where surgeons are getting help in locating tumors and map lymph nodes more precisely. This not only improves surgical clarity and reduce the chances of healthy tissue removal [52]. Also exosomal RNA can be identified, including cancer-related microRNAs and mRNAs, which makes early cancer diagnosis more feasible [53]. Magnetic nanoparticles are also being applied as imaging contrast agents and in hyperthermia treatment, which further highlights the wide role of nanomaterials in advanced cancer care [54].

4.5 Nano-shells-based biosensor

Nanoshells are tiny, engineered particles consisting of a non-conductive core, known as a dielectric core, coated with a very thin layer of metal, most commonly gold. Like quantum dots, their optical properties can be manipulated by changing the size of the shell and core. Hybrid nanostructures, like metal–organic and covalent–organic frameworks combined with gold nanoparticles, reached to ultrasensitive detection of biomarker. These nanosensors have detected breast cancer markers such as CA15-3 with higher precision and at low target concentrations, which is especially useful for early diagnosis [55]. Multiplex biosensors enables identification of several cancer biomarkers simultaneously without the need for labeling. When functionalized nanomaterials are used, sensors can amplify electrochemical signals, enabling real-time and high-throughput cancer screening [56]. In addition, by integrating electroactive nanomaterials, scientists have improved the sensitivity of electrochemical biosensors, allowing reliable cancer detection even with very small sample sizes [57].

4.6 Gold nanoparticle-based biosensor

In gold nanoparticle (AuNP)- based optical biosensors, the signals from biomolecules become much clearer and sharper, helping to detect cancer at an earlier stage [36]. Functionalization with antibodies or peptides makes them even more selective, and in biopsy samples these can be used to detect cancer without the requirement of invasive procedures [58]. Few AuNPs based biosensors gives the flexibility of detecting multiple markers simultaneously in blood or saliva. These tools work quickly, right at the point of care, and in some cases can be linked with AI systems to guide diagnosis [59]. There is also progress in using AuNPs and other metal oxide particles in saliva tests for oral cancer. The use of saliva in cancer detection offers a non-invasive method that is readily adaptable for patients and causes less inconvenience which increases the likelihood of successful recovery [60]. Besides their role in diagnosis, AuNPs are valuable in treatment too. Medicines could be coupled with the therapeutic molecules and delivered directly to the tumor site and strengthen photothermal therapy, leading to fewer side effects and more effective cancer care [61].

4.7 Liposome-based biosensor

Liposomes are small bubbles mimick with the plasma membrane of the cell and are often used to deliver drugs or imaging agents directly to the site of infection. Antibodies that recognize cancer markers, like EphA2 can be coupled with liposomes for precise and effective targeting. This method helps drugs like docetaxel to bind with tumor cells more effectively, reducing side effects and improving treatment results [54]. Scientists have developed specific liposomes responding to the specific tumor microenvironment. Shifts in pH levels or altered enzymatic activity can signal them to release their drug load right at the cancer site. In another approach liposomes can be loaded with more than one therapeutic strategy molecule, like combining chemotherapy with immune-boosting agents. Appling multiple mechanisms, help addressing drug resistance and improve patients' recovery prospects [62]. Beyond drug delivery, liposomes can also be coupled with contrast agents to enhance contrast in imaging. When liposomes carry these agents, clearer images of tumors are obtained, so that identification of them become easy [63]. Researchers have also started combining liposomes with other

nanomaterials to build what are sometimes called "smart" particles. These can react to outside signals, such as changes in temperature or magnetic fields, which allows drugs to be released in a more controlled manner. At the same time, they make it possible to see how well a treatment is working while it's happening [64]. Another promising step has been the addition of small molecules, known as ligands, to the surface of liposomes. This helps the carriers recognise and attach more strongly to cancer cells, so the therapy reaches the tumour more directly and causes fewer side effects for healthy tissues, as illustrated in Fig. 4 [65].

4.8 Nanowire-based biosensors

Silicon nanowire field-effect transistor (SiNW-FET) biosensors have demonstrated impressive sensitivity, capable of detecting tumour-derived exosomes at extremely low concentrations, which makes early cancer diagnosis, as illustrated in Fig. 4 [66]. Vertical arrays of silicon nanowires with surface functionalization can be used to capture circulating tumor cells (CTCs) from blood in liquid biopsies, providing a non-invasive approach to check progression of cancer [67]. In addition, hydrogel–nanowire composite biosensors have been developed, offering a biocompatible and environmentally friendly marker for cancer detection [68]. Additionally, scientists have been enhancing plasmonic biosensors by fusing them with two-dimensional nanomaterials. With the help of this technology, such sensors can detect biomarkers even at extremely low levels, as small as sub-attomolar concentrations [69]. Graphene-based brain–computer interface (BCI) devices are also being tested in clinical trials during tumor removal to help surgeons to differentiate between healthy brain tissue and cancer cells. The goal is to improve patient outcomes [38].

4.9 Carbon nanotube-based biosensor

Carbon nanotube (CNT)-based biosensors have opened new possibilities in detecting and treating cancer. Their special electrical, optical, and chemical properties allow researchers to design tools that work more precisely and effectively. By combining functionalized CNT arrays with artificial intelligence (AI), spotting of cancer at an early stage becomes easier, as shown in Fig. 4. These sensors utilise near-infrared light to mark cancer cells with unique patterns, and AI analysis improves the ability to distinguish between cancerous and normal tissue [70]. CNTs are useful for targeted drug delivery, carrying therapeutic agents straight to tumors [71]. Alongside this, CNT-based field-effect transistor (FET) biosensors are proving highly effective in spotting cancer biomarkers in body fluids. Very low concentrations of the sample are detected and real-time outcomes are provided [72]. Carbon nanomaterial biosensors have shown remarkable sensitivity and can be adapted for detecting multiple kinds of cancer making them strong candidates for next-generation diagnostic tools with wide-ranging clinical use [73]. Single-walled CNT optical biosensors are a major breakthrough, able to track tumour-related molecules like hydrogen peroxide and nitric oxide in real time. These provide insight towards the tumor growth and impact of treatment modalities thus provide more personalized approaches to cancer care [74]. CNTs are also playing a key role in photothermal therapy as they absorb near-infrared light and upon irradiation with near IR lights, generate localized heat causing photothermal ablation of cancer cells while leaving healthy tissue unharmed [75].

4.10 Nanocantilever-based based biosensor

Cantilevers exhibit mechanical and mass attributes that make them capable of performing biosensing when tiny probes vibrate naturally at a particular frequency range. The baseline frequency of the probe changes due to the binding of biological molecules to this nanoscale, tiny probe. Using electricity or differences in patterns of light deflection, the alteration can be measured. Different processes related to probe behaviour were detected using various nano-cantilever systems. There are four general types of probes. A schematic representation of each kind of nanocantilever-based detection is presented in Fig. 6. The first type of nanocantilever-based detection method involves the probe bending after a molecule binds to it. This bending is measured and converted into electrical signal (Fig. 6A). Second type of nanocantiliver is vibrating cantilever whose resonance frequency changes due to capture of target bio-molecules (Fig. 6B). In the third kind, after binding to the target, the displacement of the tip of the cantilever acts as an amplitude of bio-molecules concentration (Fig. 6C). In the fourth kind of nanocantilever system, voltage drop due to reduction in air space is counted (Fig. 6D) [76]. All the above processes are due to the net stiffness property of nanocantilever. Since nanocantilevers are cost-effective, they can be replaced by several detection methods, such as PCR reactions, etc. Nanocantilevers extend the functionality of microarray tools and are also used to monitor several cancer biomarkers [77, 78].

4.11 Nanocomposite

Nanocomposite-based electrochemical sensors offer a promising approach for diagnosing neurodegenerative diseases by enabling the highly sensitive and rapid detection of neurotransmitters, as illustrated in Fig. 4. Their special properties-such as high conductivity, stability, and a large surface area—help these sensors detect biomarkers even at very low concentrations. This enables early diagnosis, supporting timely interventions and improved disease management [79]. The new nanocomposite-based biosensor

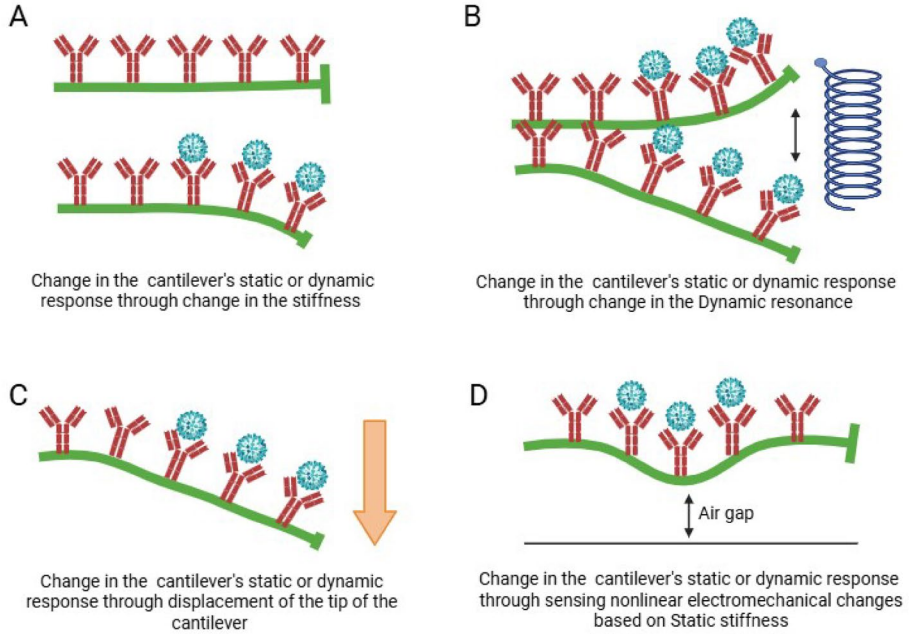

Fig. 6 Schematic illustration of the nanocantilever-based detection system

outperforms traditional gold thin layers, offering both high sensitivity and a wide detection range, making it a strong candidate for advanced biophotonic sensing applications [80]. The electrochemical sensor can detect sumatriptan (SUM) in water and human blood serum with very good sensitivity and selectivity. What helps is the electrochemical delamination of PGE, which makes the surface more porous. This allows the Zn(II)-MOF modifier to adhere more effectively and enhances electron transfer. The sensor reacts quickly—it takes only about 5 seconds—and can pick up SUM at very low levels, down to 0.29 μM. The sensor also shows excellent selectivity against common biological interferences, and high recovery rates of 96.6–111% demonstrate its reliability, highlighting its potential for practical biomedical applications [81].

4.12 NanoVelcro

One of the most advanced tools for cancer detection is the NanoVelcro CTC Assay. It can detect, capture, and study these cells, giving a clearer picture of how the disease is progressing. Over time, these assays have improved significantly. They can now count circulating tumour cells (CTCs), study and analyse their molecular details, and help in monitoring patients suffering from different solid tumours [12]. Here, the EpCAM antibodies are captured onto the SiNW-based cell capturing system, and this system shows enhanced capturing (45–65%) capacity for cancer cells compared to the flat Si nanoparticle (4–14%) surface fixed antibodies, suggesting that the 3D nanostructures offer more enhanced cell capturing abilities [82]. The phenomenon appears to be a tight attachment of fabric strips, similar to a Velcro fastener. The performance might be further enhanced by coupling it with microfluidic components. A SiNW-embedded microfluidic platform is developed using an overlaid PDMS chaotic micromixer, having a serpentine chaotic mixing channel. The chaotic micromixer enables the vertical flow of the cell suspension, thereby facilitating better interaction between the nanowire substrate and circulating cancer cells. A cell capture yield of 95% was achieved using an optimal flow rate of 1 mL/h. NanoVelcro Chips were able to capture more CTCs than the Cell-Search Assay [83]. Schematic representation of the same is illustrated in Fig 7.

4.13 2D nanozymes in modern biosensing

Graphene-based materials, MXenes, and metal–organic frameworks are common 2D nanozymes applied in biosensors. Because they have a large surface area, they can conduct electricity well and also act like enzymes; they can detect biomarkers quickly and accurately without the need of extra labels. These features make them ideal for point-of-care tests and compact lab-on-a-chip devices. On top of that, they are safe for biological use and can be manufactured on a large scale, which is encouraging their wider application in medical diagnostics as well as environmental monitoring [84]. An electrochemical biosensor based on enzyme nanosheets was designed for rapid and selective detection of aspartate present in fish. Although designed for aquaculture, this approach is relevant to cancer research, as abnormal aspartate metabolism is associated with tumor cell proliferation and diagnosis in cancers like glioma [85]. A lactate biosensor was developed using sturdy nanozyme-enzyme nanosheets to aid in the diagnosis of infections in fish. Lactate is important in cancer because tumor tissues often have higher lactate levels, making it a useful biomarker for detecting and tracking the disease [86]. The host receptor is valuable in diagnosis since, despite the mutations, the virus still

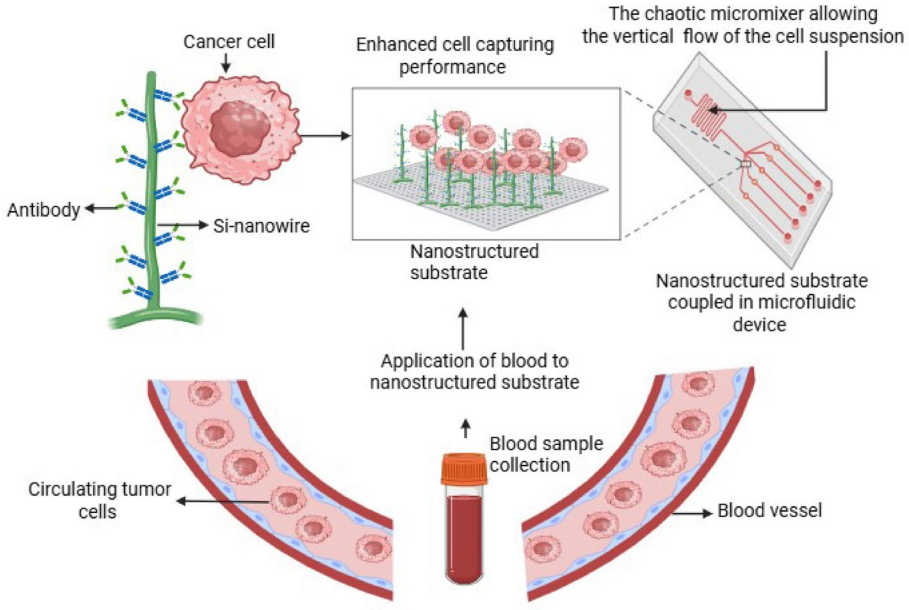

Fig. 7 Schematic representation of NanoVelcro circulating tumor cell assay

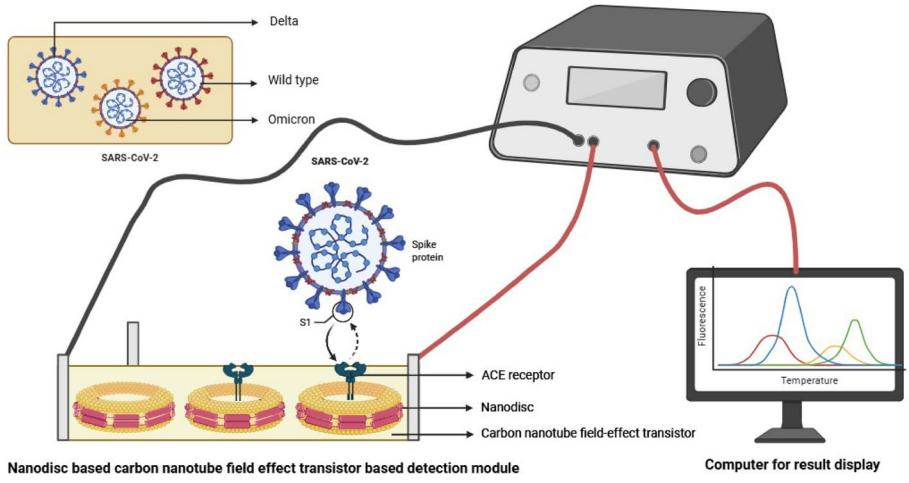

Fig. 8 Schematic illustration of a nanodisc-based nanotube field-effect transistor-based detection module

utilises the cell entry process using the same host receptors, thus can be used to detect the presence of the virus. The angiotensin-converting enzyme 2 (ACE2) receptor, which the SARS-CoV-2 virus uses to enter cells, is expressed in E. coli and embedded into a nanodisc platform, integrated with a carbon nanotube field-effect transistor (CNT-FET) sensor. The system can differentiate between SARS-CoV-2 wild-type and variants (Omicron, Delta) from other viruses, including ZIKA and MERS-CoV. Schematic illustration of the same is given in Fig 8. [87].

4.14 Amperometric sensor for real-time detection

Researchers have designed a portable amperometric sensor composed of copper-doped mesoporous carbon, which acts as the enzyme tyrosinase (Cu–CMCS2). This material has a large surface area (104.2 m^2/g) and a good pore volume (0.224 cm^3/g), which

together help the sensor work more effectively. This structure enabled the rapid and real-time detection of catechol over a broad concentration range (1–1000 μM) with a low detection limit of 0.099 μM. The sensor is seamlessly integrated with a smartphone-connected potentiostat, offering accessible, high-throughput on-site testing [88]. A disposable enzyme-free amperometric sensor was created by drop-coating polyaniline-doped multi-walled carbon nanotubes (PANI-MWCNTs-2) onto screen-printed carbon electrodes. One biosensor was able to detect dopamine (DA) in ex vivo mouse brain tissue homogenates with a very low detection limit of 0.05 μM and a linear response from 1–200 μM [77]. Another sensitive electrochemical sensor, built from polyaniline and single-walled carbon nanotubes (SWCNTs), can detect purine metabolites—uric acid, xanthine, and hypoxanthine—with detection limits of 0.047 μM, 0.049 μM, and 0.052 μM, respectively. These metabolites are often elevated in cancers due to increased nucleic acid metabolism, making the sensor particularly helpful for more accurate cancer monitoring. The sensor showed strong antifouling ability, high conductivity (~4.18 S/cm), and worked effectively in serum and urine, making it suitable for point-of-care cancer diagnostics [78] (Table 1).

5 Applications of nano-biosensors in various cancer therapies.

Nano-biosensors have enhanced cancer treatment by facilitating faster diagnosis. It also helps in tracking the disease continuously and supporting personalized therapy as well. They can detect tumor biomarkers in different cancers, such as breast, lung, prostate, and colorectal [141, 142].

5.1 Prostate cancer

Prostate cancer can now be detected with more advanced methods beyond the routine PSA test. One is the Prostate Health Index (PHI), which combines total PSA, free PSA, and [– 2] proPSA into one score. It was approved by the FDA in 2012 and can detect serious prostate cancer more accurately. This helps avoid unnecessary biopsies [143]. Additionally, artificial intelligence is being increasingly utilised in the diagnosis of prostate cancer. AI can analyse MRI scans to help doctors and medical staff determine and verify lesions more precisely. It also makes the whole process quicker and helps plan better treatments [144].

5.2 Modalities for the diagnosis and therapy of prostate cancer

Diagnosis and treatment of prostate cancer are being transformed using nanoparticles enabled biosensors. These technologies enabled the detection in earlier stages and thereby improved the precision of detection. As a result, patients experience fewer side effects, and treatment outcomes can be much better.

5.2.1 Nanoparticles

The bio-barcode assay is a novel technology that can detect low levels of PSA in prostate cancer. In this procedure, gold nanoparticles functionalized antibodies specifically binds to PSA, along with DNA barcodes. Further, these are then combined with magnetic beads to help with separation and separated molecules are accurately measured. The test is almost 300 times more sensitive than conventional methods [145, 146]. A smartphone-based system measures the free-to-total prostate-specific antigen (f/t-PSA)

Table 1 Advantages and disadvantages of nanobiosensors-

S.No	Type of sensor	Advantages	References	Disadvantages	References
1	Nanoparticle-based biosensors Quantum dots	High sensitivity and low detection limits	[89]	Batch-to-batch variations in nanoparticle size, shape, and surface properties leading to inconsistent sensor performance and poor reproducibility across devices	[90]
		Very high surface-to-volume ratio enabling dense loading of molecules	[91]	Synthesis and complex functionalization is expensive	[92]
		Functionalization with a wide variety of bio-recognition molecules (antibodies, aptamers, molecularly imprinted polymers) is possible	[93]	Response times can lag in dynamic or high-throughput scenarios	[94]
		Readily integratable with microfluidics and lab-on-chip platforms	[51]	certain nanoparticles exhibit cytotoxicity, genotoxicity, or long-term accumulation in biological systems, thereby limiting in vivo or clinical applications	[95]
		Enhanced immobilization, biocompatibility and chemical and structural stability of biomolecules	[89]	Background noise, non-specific binding, and interferents in real samples leads to compromised sensitivity and specificity	[94]
		Integratable with low-cost readout systems (including handheld or smartphone-based readers)	[96]		
2		Broad absorption spectra coupled to narrow size-tunable photoluminescent emissions	[97]	Colloidal stability of Modified QDs limits the type and number of conjugatable to a single QD	[98]
		Exceptional resistance to photobleaching	[98]	Heavy metal cores (eg. CdSe, CdTe) release toxic ions	[99]
		Resistance to chemical degradation		Poor clearance from the body	[100]
		Iron oxide-based QD cores shows excellent biocompatibility, and minimal cytotoxicity	[101]	QDs exhibit random on–off switching in emission	[102]
3	Paramagnetic nanoparticle-based biosensor	Large specific surface areas	[103]	Batch-To-Batch Variation	[104]
		Low toxicity	[105]	Long-term accumulation via hepatobiliary/renal pathways may cause cytotoxicity risks	[106]
		Magnetic enrichment capabilities	[107]		
		Low-cost synthesis and scalability	[108]		

Table 1 (continued)

S.No	Type of sensor	Advantages	References	Disadvantages	References
4	Nano-shells-based biosensor	Hydrophilic character, high surface energies, chemical stability, thermal stability, and bio-compatible nature	[109]	During biosynthesis, a gradual increase in viscosity and molecular weight is observed	[110]
		Synergetic interaction of the core and shell material provides a tunable catalytic/electrocatalytic effect	[111]		
		The coating of an inert material usually improves the stability of core materials	[112]		
		Prevent photodegradation of the core nanoparticle, and render stability against aggregation	[113]		
5	Gold nanoparticle-based biosensor	Biocompatibility and low toxicity	[114]	Limited control over size of gold nanoparticle, and scalability; requires precise conditions	[114]
		Can be used within living organisms	[115]		
		Tunable optical properties	[116]	Gold nanoparticle aggregates easily	[117]
6	Nanowire-based biosensors	As electrodes enhance the sensitivity and selectivity of electrochemical biosensors	[118]	In vivo environment modulates the properties of nanowires	[119]
		Binding of even a few biomolecules results in high changes in conductance, leading to higher detection limits reaching to fM–aM levels	[120]	Limited stability of nanowires in-vivo	[121]
		High optical output	[122]	Coating strategies to prevent nanowire disintegration doesn't work for all the nanowires	[123]
		Controllable n-type conductivity			
		Unique thermal conductivity, transport and optical properties	[124]		
7	Nanorods	Higher surface plasmons lead to the enhancement of electrical field	[125]	Nanorod synthesis is costly	[126]
		High conductivity	[127]		
8	Carbon Nanotube (CNT)-Based Biosensors	High carrier mobility, excellent conductivity	[128]	Challenges include scalability, reproducibility, and long-term operational stability	[128]

Table 1 (continued)

S.No	Type of sensor	Advantages	References	Disadvantages	References
		Enhanced signal transduction when integrated into FET-based biosensors	[129]	Hydrophobic nature of CNTs restricts their utility in the field of medicine	[130]
		Its dimensions are suitable for electrostatic screening during physiological procedures	[130]		
9	Nanocantilever-based biosensor	Able to detect both charged and neutral bio-molecules	[131]	Sensing is based on the bending of the sensor upon binding of target to the receptor. Nonspecific binding might result into false positives	[132]
10	Nanocomposite based biosensors	Nanocomposite materials can be readily adapted for the 3D printing	[133]	Fine-tuning for composition, size, and surface characteristics are required for optimum composite and the target analytes interaction	[134]
		Exhibit enhanced electrical conductivity and colloidal stability			
		Exhibit superior electrical and mechanical properties	[135]		
		Long term biocompatibility and suitability of phosphorescence-based lifetime sensors in vivo	[136]		
11	NanoVelcro based biosensors	By depositing nonobrushes over nanosubstrate nanovelcro is prepared	[137]	Establishment of translational pipeline clinical validation and FDA approval is challenging	[137]
		High conductivity, stability, and a large surface area	[79]		
12	Nanozymes	Highly sensitive and low-biofouling	[138]	Stability and specificity are challenges for their wider application	[138]
				Susceptibility towards interference due to presence of other substances in the sample resulting in either false-positive or false-negative results	
13	Amperometric Sensor	Rapid analytical results	[139]	Immobilized enzymes might be denatured upon prolonged usage or using harsh immobilization techniques resulting in inappropriate result	[140]
		Parameters might be checked non-invasively and continuously			

ratio, which improved the accuracy of prostate cancer diagnosis. In the method a proximity-induced bio-barcode combined with a CRISPR/Cas12a assay is used. Here in the test, PSA is recognised by DNA and antibody probes, which causes the release of a small DNA barcode, which in turn activates the CRISPR/Cas12a system to release silver ions

(Ag^{+}). These silver ions interfere with the platinum nanoparticles, leading to change in the color, suggestive of presence of PSA. The change in color is monitored by the smartphone app, allowing the system to detect total PSA as less as 0.06 ng/mL. The assay's high sensitivity enables the distinction between prostate cancer and benign conditions [147].

5.2.2 Nanowires

Silicon nanowire (SiNW) based biosensors effectively sense prostate-specific antigen. Silicon nanowire (SiNW) field-effect transistors (FETs) functionalized with antibodies have been developed for ultralow-level detection of PSA. The detection limit was as low as 1 femtogram per millilitre (fg/mL) [145]. In a similar effort, Huang et al. designed a polysilicon nanowire FET biosensor integrated with microfluidics, for a label-free PSA detection in human serum [66]. Stern and his co-workers developed a two-step method where microfluidic purification chips is combined with silicon nanoribbon detectors. In this method several biomarkers can be directly captured and diagnosed directly from whole blood without purification step [146]. Additionally, Presnova and colleagues developed silicon nanowire FETs enabled silicon-on-insulator technology, for real-time label-free detection of PSA in human serum. [148].

5.2.3 Carbon nanotubes

Carbon nanotube (CNT) biosensors can help detect prostate cancer markers easily. In one study, gold nanoparticles (AuNPs) were coupled with CNTs. The CNT-AuNP combination detected the PSA antigen at a detection level as low as 0.1 ng/ml. Researchers also discovered that the sensor's performance is significantly affected by the size of the gold nanoparticles and smaller NPs are more reliable [143]. Additionally, chemically modified CNTs have been shown to eliminate the need for fluorescent agents and effectively diagnosing prostate cancer [144]. In addition, biosensors made of combination CNTs and graphene transistors are proving efficient cancer detection. Their special electrical and mechanical properties help them detect cancer markers more accurately [68].

5.2.4 Nanocantilevers

Recent advances show that piezoelectric nanomechanical cantilevers are highly effective for detecting prostate-specific antigen (PSA) through antibody–antigen binding. These sensors work by picking up small changes in resonance frequency that occur due to surface stress, rather than mass shifts. Because the method does not require labelling or fluorescent tags, it makes testing liquid samples much simpler. This approach is well-suited for point-of-care diagnostics and can be conveniently integrated into lab-on-a-chip platforms [149].

5.2.5 Nanocomposites

New advances in nanocomposite-based therapies are opening promising ways to manage prostate cancer. In particular, gold nanoparticles (AuNPs) linked with anti-androgen agents are being designed for androgen receptors that are highly active in prostate tumor cells. By targeting the tumor in this way, more of the medicine reaches the cancer cells while healthy tissues are less affected [150].

5.2.6 Portable amperometric biosensor

A portable amperometric biosensor was developed using a CS–PANI–mesoporous carbon nanocomposite to detect sarcosine, an essential biomarker for prostate cancer. The sensor showed high sensitivity (8.09 μA mM^{-1} cm^{-2}) and a very low detection limit of 0.077 μM, delivering results in less than a minute. Such biosensors are used in point-of-care testing due to certain features like reliability and smartphone connectivity [94]. Another advanced biosensor has been developed using screen-printed carbon electrodes coated with Prussian blue and polymer-dispersed rGO nanosheets, with the help of the enzyme sarcosine oxidase, which is attached to its surface. Such a biosensor is also disposable. This design enables the sensor to detect sarcosine quickly and with a high sensitivity of 9.04 μA mM^{-1} cm^{-2}. This design could detect very low levels of sarcosine, as small as 0.66 μM. Importantly, the sensor also worked excellently in real urine samples, showing its strong potential for practical medical use [151].

5.2.7 AI-driven biomarker analysis

A recent study created an AI system to predict whether prostate cancer (PCa) could return after surgery to remove the prostate. Detailed images of prostate tissues are analyzed by the AI system called as whole-slide images (WSIs), Here both the obvious patterns and subtle changes that are difficult to discern are identified. It identifies specific areas, known as regions of interest (ROIs), which are linked to the cancer. By identifying these areas early, the system enables doctors and healthcare professionals to detect possible cancer recurrences sooner, making treatment plans easier and recovery more likely. Using the AI-generated scores, the system predicted 3-year recurrence with an accuracy (AUC) of 0.78, which is much better than the traditional Gleason Grade Group score of 0.62. This method demonstrates how AI is helping healthcare professionals in early identification of patients at higher risk of recurrence and supports more personalised treatment plans [152].

5.3 Breast cancer

Nanotechnology uses nanoparticles, making imaging techniques such as MRI and PET more transparent and accurate. The processes help medical professionals detect cancer in early stages and their analysis in a better manner [153]. Advances in nanotechnology made breast cancer care more targeted, more personalized and less invasive and it helps patients recover effectively [154]. Nanotheranostics combines both detecting and treating cancer in one step, giving doctors the ability to customize treatment plans for every patient [155]. As nanotechnology develops, it allows breast cancer therapies to be more precise and customized, giving patients better outcomes.

5.3.1 Modalities for the diagnosis and therapy of breast cancer

Nanotechnology is playing an increasingly important role in the detection and treatment of breast cancer. Nanoparticles and other nanoscale materials enable earlier and more accurate cancer detection, while also delivering treatment more precisely. The following explains how nanotechnology is helping in breast cancer care.

5.3.2 Nanoparticles

Recent developments in nanotechnology have greatly improved breast cancer detection and treatment. Quantum dot (QD)-based probes, in particular, offer highly sensitive detection of HER2-positive breast cancer cells, surpassing the accuracy of standard immunohistochemical methods. QD525 conjugated with HER2 monoclonal antibodies has been used to successfully detect HER2 in live and fixed SKBR-3 cells and breast cancer tissue samples [156]. Magnetic iron oxide nanoparticles, paired with trastuzumab (Herceptin), are also demonstrating significant potential for therapeutic applications. These nanoparticles allow drugs to reach tumors more effectively and also boost imaging contrast, making tumor detection more accurate. Recent Studies have shown that paclitaxel (PTX) and Herceptin-loaded MIONPs (PTX-Herceptin-MNPs-Fe_3O_4) demonstrate vigorous antitumor activity while boosting T2-weighted imaging contrast in tumor models, highlighting their potential as theranostic agents [157]. Additionally, improvements in MIONP functionalization increase their biocompatibility, imaging properties and targeting efficiency [158].

5.3.3 Nano-shells

Nano-shells are composed of a dielectric core covered with a thin gold layer. Similar to QDs, these can be designed to possess specific optical properties and absorption in near-infrared (NIR) region. To facilitate surgery in patients of breast cancer, sentinel lymph node mapping is essential. Generally two methods are employed: one is using radioactive technetium-99 m sulphur colloid, and the other is injecting crucial blue dyes. Both approaches have one or the other limitations [159]**.** Rare-earth nanoprobes are being used to find sentinel lymph nodes (SLNs) in breast cancer. These probes primarily accumulate in cancer cells, enabling surgeons to detect the disease's spread more clearly [160]. Albumin-bound paclitaxel nanoparticles (Abraxane®) are more soluble than the drug alone and deliver efficiently to tumor cells. Using this approach at lower doses strong treatment effects might be achieved with reduced side effects compared with standard paclitaxel therapy [161].

5.3.4 Nanowires

A liquid-gated graphene FET based biosensor has been developed which readily can detect ERα without the need for labels, reaching a detection limit as low as 2.62 femtomolar (fM). The system is able to differentiate ERα-positive from ERα-negative cells in just 30 minutes, making it well-suited for rapid clinical testing [162]. Vertically aligned silicon nanowire (vSiNW) based biosensors presented a sensitive method to detect estradiol. Sensors coated with estradiol receptor are able to measure estradiol concentrations between 1 and 100 ng/mL. The system is able to and distinguish estradiol from similar hormones, including androgens [163]. Electrochemical biosensors, such as carbon paste electrodes combined with graphene and mesoporous carbon, have been used to detect very small amounts of estrogen in human serum. Additionally, quantum dot-based sensors, which use tin selenide dots on gold electrodes, can accurately detect 17β-estradiol in the 1–8 nM range, providing dependable tools for both clinical applications and research [163, 164].

5.3.5 Nanotubes

Carbon nanotubes (CNTs) are being used as new approaches towards breast cancer therapy. Specific ligands are attached to multi-walled carbon nanotubes (MWCNTs), which specifically target receptors overexpressing on breast cancer cells. Carbon nanotubes (CNTs) apart targeting receptor, by illuminating with near-infrared light, can generate slight heat locally in the tumor tissue that is capable of destroying cancer cells [70, 165]. In addition, MWCNTs functionalized with aptamers may guide therapeutic molecules directly to the tumor site and also improve MRI imaging. This help an oncologist obtain a clear view for diagnosis. This method is helpful in locating tumor precisely, realtime monitoring the impacts of therapy, and increasing the impact of therapy [166]. A combination of carbon nanotube (CNT) photothermal therapy with immunotherapy using anti-PD-1 antibodies, is able to remove tumors and enhance the immune response, which has shown promise in treating metastatic breast cancer [167]. Furthermore, the use of CNTs in advanced drug delivery systems enhances drug solubility and absorption, allowing for controlled release and resulting in improved outcomes and fewer side effects for patients [168]. The blood of breast cancer patients, exosomes are isolated that contain miRNA21. For the detection of breast cancer exosomal miRNA21 a Field-Effect Transistor Biosensor (FET) has been developed. The CNT are functionalized with oligos probe complementary to miRNA21. A hybridization between the probe and miRNA-21 results in a change in the current flow, which is detected by the detector that senses minor even changes in the current. By this method, high specificity and a limit of detection of 0.87 aM have been obtained [169]. A Schematic representation of a field-effect transistor (FET) biosensor has been given in Fig. 9.

5.3.6 Nanocantilevers

Determining mutations in the BRCA1 gene can be useful for assessing a person's risk of developing prostate, breast, and ovarian cancers [170]. A cantilever tool was designed to monitor single-nucleotide polymorphism [SNP] for breast cancer, causing the BRCA1 gene. The advantages of this test are its excellent specificity and short duration time [3] for the steps of hybridization, washing and readout. Graphene oxide-coated nanocantilevers have enhanced detection sensitivity, enabling the identification of biomarkers at extremely low, femtomolar levels, which supports early breast cancer diagnosis [169].

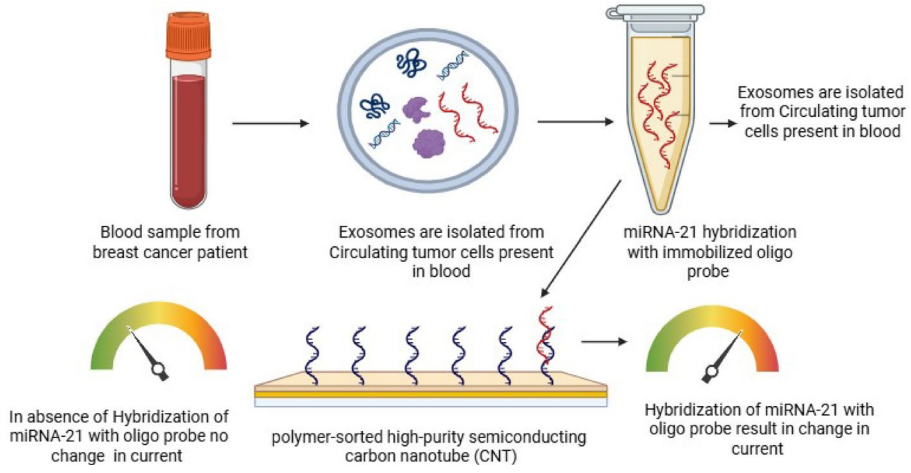

Fig. 9 Schematic representation of field-effect transistor (FET) biosensor for the detection of miRNA

Zinc oxide nanowire-coated cantilevers have also been used to detect BRCA1 mutations, showing strong selectivity and consistent performance across different concentrations [171]. Graphene-coated fibre-optic SPR sensors provide precise readings of BRCA1 hybridisation by monitoring small shifts in resonance angles [172]. Similarly, combining polyaniline nanofibers with reduced graphene oxide in cantilevers has greatly increased their sensitivity, making the detection of breast cancer biomarkers more reliable and accurate [173].

5.3.7 Nanocomposites

Breast cancer therapy has significantly benefited from the use of nano gels as drug delivery vehicles. Chitosan-based nano gels, for example, have been used to encapsulate chemotherapeutic drugs such as doxorubicin. With nanogels, the drug becomes more stable and easier to dissolve, and it is released gradually at the tumor site. This increases the effectiveness of therapy while minimizing harmful effects elsewhere [174].

5.4 Pancreatic cancer

The early stages of pancreatic cancer usually pass without warning signs, making timely diagnosis difficult and survival rates low. Most patients with pancreatic cancer will eventually pass away, either from local tumor growth of the superior mesenteric or celiac arteries or from metastasis to other organs; in either scenario, the illness is incurable at this point [163, 175].

5.5 Modalities for the diagnosis and therapy of pancreatic cancer

Pancreatic ductal adenocarcinoma (PDAC) is challenging to diagnose in its early stages, largely due to the absence of noticeable symptoms and the presence of a dense, fibrotic tumor microenvironment. It is difficult to treat pancreatic cancer since its recovery rates are often very low [176]. However, advances in nanotechnology provide new possibilities for its treatment. Nanoparticle-based based sensors are able to detect minor changes in protein quantities, making it possible to identify pancreatic ductal adenocarcinoma (PDAC) early using blood test samples [177]. Their structure helps them move through the dense stroma of tumors, allowing better drug penetration and improved outcomes [54, 178, 179].

5.5.1 Nanoparticles

Superparamagnetic nanoparticles (SPIONs) are small particles which are magnetic field reactive, offer a breakthrough in more precise tumor detection. Different targeting ligands are attached to the iron oxide nanoparticles, including folate and the surface receptor urokinase plasminogen activator receptor (uPAR), which is expressed more often on pancreatic tumour cells and the surrounding stromal cells, for making a detection module [180]. Beyond targeting uPAR, SPIONs immobilized with antibodies against alpha-enolase (ENO1), a protein abundantly expressed in pancreatic cancer cells, are able to bind to the tumor firmly, thus improve the MRI imaging and making it easier to detect pancreatic ductal adenocarcinoma (PDAC) [181]. Other nanoparticles such as carbon quantum dots (CQDs), are also being used for diagnostic and imagining [182].

5.5.2 Nanotubes

SiO2 nanoparticles encapsulated the secondary antibody in the sandwich ELISA immunoassay. This boosts the signal frequency and improves the sensitivity of the assay. The detection limit of the experiments using several concentrations of CA19-9 is 100 times lower than the existing ELISA standards used in practice [183]. Use of specialized multi-walled carbon nanotubes to generate mapping of genetic fingerprints for pancreatic cancer. To distinguish guanine and deoxyguanine triphosphate in the DNA of blood samples from the peripheral blood of a normal person and a person suffering from pancreatic cancer, a multi-walled carbon nanotube coupled with randomly amplified polymorphic DNA is used [175]. MWCNTs are not only useful for diagnostics but also show promise in treatment, especially in photothermal therapy. By attaching polyethylene glycol (PEG) to the nanotubes, they can concentrate specifically in tumor tissues. Exposing these PEGylated nanotubes to near-infrared laser light causes them to produce heat in the targeted area, which damages cancer cells and triggers their self-destruct. This method focuses treatment on the tumor while sparing nearby healthy tissues [184].

5.5.3 AI-driven biomarker analysis

A reliable multi-gene signature has been discovered for early PDAC detection. Machine learning analysis revealed nine gene pairs that can separate PDAC tissue and plasma from normal samples with high precision. A separate model combining circulating miRNAs (such as miR-20a, miR-21, miR-24, miR-25, miR-99a, miR-185, and miR-191) achieved an AUC of 0.99 for PDAC detection in serum samples [15].

5.6 Lung cancer

Lung cancer is the most fatal type of cancer. Differentiating between different kinds and subtypes of lung cancer as well as stage is crucial for lung cancer diagnosis and therapy choices since it plays a crucial role in treatment selection. Earlier and more precise identification of lung cancer with the use of nano-biosensor technology can have a significant impact on patient prognosis [183].

5.7 Modalities for the diagnosis and therapy of lung cancer

Nanotechnologies are showing significant promise in both the detection and treatment of lung cancer. Below are the key nano-modalities used for diagnosis and therapy:

5.7.1 Nanoparticles

Attempts are being made to develop reliable clinical screening tests for lung cancer. One method utilises gold nanoparticles to detect various volatile organic compounds (VOCs). The headspaces of many lung cancer cell lines were examined for volatile organic compounds (VOCs). A functionalized GNP-based array connected to gas chromatography-mass spectroscopy (GC-MS) was also utilized in additional research that demonstrated the ability to classify cancer patients based on their breath samples, including those with lung, breast, prostate, and colorectal malignancies [185]. Gas chromatography–mass spectrometry (GC-MS) can be used to analyze volatile organic compounds (VOCs) in the breath of a patient. These compounds act as biomarkers that help to detect the difference between lung cancer patients and healthy individuals [186]. Using GC-MS, volatile organic compounds (VOCs) can help distinguish lung cancer patients from healthy

individuals. Mass spectrometry has some limitations compared to nanotechnology-based methods. It needs costly instruments, longer sample preparation, and trained personnel to perform the analysis. In contrast, nano-biosensors make testing faster, easier, and more accessible [187].

5.7.2 Nanowires

Epithelial cell adhesion molecules (EpCAM) are overexpressed on the surfaces of lung cancer cells. A quartz nanowire array immobilized with antibodies targeting EpCAM was developed to detect lung cancer. The blood sample was used as test material and subjected to the microfluidic cell capture device. After binding of target cells to the nanowire, detection was done using laser scanning cytometry. Using this technique, it was possible to identify circulating tumour cells comprising just a few cells per millilitre of whole blood [188]. IL-10 and osteopontin (OPN) molecules also can be used for detecting lung cancer. To silicon nanowire a capture antibody against OPN or IL-10 is immobilized with secondary antibody linked to an enzyme called alkaline phosphatase. The system helps in detecting the presence of the cancer antigen through presence of colored compound generation [189]. Furthermore, metal-coated silica nanowires can act as substrates for surface-enhanced Raman scattering (SERS) [190]. Amplification of the Raman signals of target molecules allows sensitive detection of biomarkers like IL-10 in lung cancer model [191].

5.7.3 Carbon- nanotubes

A sensor array composed of single-walled carbon nanotubes (SWCNTs) has been shown to distinguish between volatile organic compounds (VOCs) in the breath of lung cancer patients and those of healthy individuals, highlighting its potential in lung cancer diagnosis [192]. The accuracy and sensiyivity might be enhanced by coating the SWCNTs with non-polymeric organic coatings. This approach effectively recognizes lung cancer-specific breath patterns, advancing reliable breath-based non-invasive diagnostic tools [193].

5.7.4 AI-driven biomarker analysis

AI models have advanced biomarker discovery and diagnostic precision in lung cancer through both imaging and molecular data analysis. A systematic review and meta-analysis showed AI-driven approaches achieved pooled sensitivity and specificity of approximately 0.77 and 0.79, respectively, in predicting prognostic and predictive biomarkers [194].

5.8 Brain cancer

Brain tumours, both primary and metastatic, can result in disastrous outcomes. Although brain tumors are not a prevalent cause of cancer-related deaths in adults, they are the most common cause of cancer-related deaths in children. Additionally, the diagnosis and treatment of brain cancers are complicated by two unique issues: [1] the blood-brain barrier's (BBB) tight capillary endothelium junctions, and [2] the possibility of delicate structures being in close proximity to the tumor and potentially causing significant death if damaged [195–197].

5.9 Modalities for the diagnosis and therapy of brain cancer

The nanoscale tools also improve the accuracy of diagnostic tests and make therapies more precise and individualised to treat brain cancer.

5.9.1 Nanoparticles

The brain is a desirable target for nanoparticles to enhance therapeutic delivery and imaging agents for improved standards of diagnosis and detection. The blood-brain barrier (BBB) is unique since it only permits the passage of medications and tiny molecules into the brain parenchyma with a molecular mass of 400–500 Daltons and high lipid solubility [198]**.** Magnetic nanoparticles (MNPs) have remarkable potential for both imaging and treatment. These MNPs facilitate MRI scanning by improving the contrast [199]. They can also be designed to carry chemotherapy drugs straight to tumor sites, boosting treatment effectiveness. Carbon-based nanoparticles can cross the blood-brain barrier, deliver chemotherapy, and highlight tumor cells with fluorescent markers, allowing doctors to treat and monitor brain tumors at the same time [195].

5.9.2 Nanowires

Significant advancements have been made in the area of nanowire-based detection of brain tumours. For example, platinum nanowires of approximately 600 nanometers width can reach the blood vessels of the spinal cord to monitor electrical activity. Furthermore, flexible hydrogel microelectrodes, and Ultrasound-powered devices are some new forms of cancer tracking devices [188, 189, 192].

5.9.3 Carbon nanotubes

Carbon nanotubes (CNTs) are being studied for the early detection of brain tumors. Ligands might be attached to them to target the overexpressing molecules present on the surface of cancer cells. An electrochemical DNA biosensor has been built with multi-walled CNT arrays and has potential to be used in early cancer detection too [201]. Apart from their use in diagnostics, CNTs are also gaining attention for therapeutic applications. Studies have shown that CNTs can carry CpG oligodeoxynucleotides into cells, where these might enhance the body's immune response against glioma cells. Thus CNTs have proven themselves as candidate for both the detection and therapy and thus could represent a promising tool for monitoring as well as treating intracranial tumors [202].

5.9.4 Nanocomposites

Treating brain tumours is difficult because of the protective nature of the blood–brain barrier (BBB). To address this challenge, scientists made nanocomposites with cell-penetrating peptides and gold nanoparticles. These carriers deliver drugs straight to brain tumors, making treatment more accurate and safer for healthy brain tissue.

5.9.5 AI-driven biomarker analysis

AI has enhanced the speed and accuracy of intraoperative tumor diagnostics through the combination of deep learning and stimulated Raman histology (SRH) imaging. In a dataset of 278 patients, the algorithm diagnosed brain tumors with 94.6% accuracy

in just 150 seconds, matching-but vastly accelerating-the performance of traditional pathology workflows [203].

5.10 Leukemia

Acute lymphoblastic Leukemia (ALL) is still difficult to treat because leukemic cells strongly depend on the bone marrow micro environment for survival and growth. Such abnormal division is caused by the uncontrolled division of T- line and B-line cells lymphoid lineage cells. This shows higher prevalence in children which is around 80% and in adult around 20%. Nanodrug delivery systems (NDDSs) show great promising approach to treat this malignant disease progression. The presence of different cell populations within the same patient often leads to poor and uneven responses to clinical therapy. Furthermore, immune escape and drug resistance [204] reduce the effectiveness of current treatments [205, 206].

5.11 Modalities for the diagnosis and therapy of Leukemia

Advances in nanodrug delivery systems (NDDSs) are improving the diagnosis and treatment of leukemia. Nanotechnology based modalities allow earlier and more accurate detection of proliferated white blood cells. These strategies help lower side effects and improve overall treatment outcomes to improve survival rate.

5.11.1 Nanoparticles

The study identified CD13 as an important leukemia cell surface marker and designed a nanobody which is capable of selectively binding to this surface marker. TRAIL, a molecule known to induce programmed cell death or apoptosis, was conjugated onto AaLS-based protein nanoparticles to enhance anti-leukemic activity by inhibiting proliferation of white blood cells [207]. Additionally, Mn–Zn ferrite nanoparticles were shown to restore adriamycin responsiveness in resistant K562/ADR cells through ferroptosis induction pathway, highlighting their role in reversing tumor cells [208, 209].

5.11.2 Nanozymes

Functional nanomaterials that mimic natural enzymes are called nanozymes, overcoming limitations of conventional enzymes and showing strong potential in leukemia therapy. They can regulate reactive oxygen species (ROS) through activities such as peroxidase, catalase, superoxide dismutase, and oxidase making them useful to inhibit leukemia like cells [210]. For example, Fe3O4@Pt nanozymes combined with CXCR4 antagonists produce ROS in acidic environments which triggers killing of AML cells while safeguarding healthy cells [211]. Similarly, biomimetic nanozyme composites enhance effect of individualized therapy by increasing anti-leukemia effects due to generation of ROS and targeting the bone marrow to remove residual cancer cells [212].

5.11.3 Polymeric micelles

Doxorubicin-loaded polymeric micelles with FLT3-targeting peptides (CKR and EVQ) enhanced uptake of drug at target site and killing of AML stem-like cells compared to free doxorubicin, helping to overcome drug resistance to improve leukemia treatment [213]. Similarly, PEG-HPMA micelles carrying curcumin showed strong cytotoxic effects and were efficiently taken up by K562 leukemia cells [214]. In addition,

stimuli-responsive chitosan/heparin micelles were designed to release drugs like doxorubicin in response to tumor-specific conditions such as pH or redox changes, improving therapeutic efficacy while lowering toxicity.

5.11.4 Exosomes/extracellular vesicles

Exosomes are showing strong potential in leukemia treatment. Engineered exosomes (PRIME Exos) carrying antibodies and immune-activating proteins can simultaneously target Acute Myeloid Leukemia (AML) cells and stimulate T cells, boosting anti-leukemia immune responses in preclinical models to enhance immune response against leukemia, additionally they also serve as biocompatible as well as natural delivery system to target leukemia [215, 216]. Interference of CLL-derived exosomes with functioning of bone marrow in blood cell formation making them important to therapeutically target leukemia [217].

5.11.5 Nanogels

Nanogels have emerged as effective tools for leukemia therapy because they improve drug delivery and target leukemic cells precisely. Chitosan-based nanogels combine with curcumin induced stronger programmed cell death and higher cytotoxicity in K562 leukemia cells compared to free curcumin [218]. Multifunctional nanogels are stable and tunable, offering a safe and effective platform to deliver anticancer agents in leukemia treatment via reacting to signals of tumor microenvironment like Reactive oxygen species and pH [219, 220].

5.12 Cervical cancer

Cervical cancer remains a serious global health challenge with high morbidity and mortality despite conventional treatments [212]. Nanotechnology offers promising innovative solutions to improve diagnosis, drug delivery and targeted therapy [222]. Nano based tools used in photodynamic therapy enhance generation of reactive oxygen species (ROS) and tumor targeting, while nanocarriers sensitive to natural stimulus like pH or redox conditions allow controlled drug release at tumor sites [223–225].

5.12.1 Nanoparticles

Multi- functionalized gold nanoparticles Hyaluronic acid–chitosan targeting the CD44 receptor enhanced doxycycline drug uptake in cervical cancer cells, showing better therapeutic outcomes by enhancing cytotoxic effects than against cervical cancer cell [226, 227].

Photodynamic therapy and liposome mediated gold nanoparticles increased reactive oxygen species (ROS) production both in-vivo and invitro [221, 228].

5.12.2 Nanogels

Recent research shows that hydrogels are emerging as effective localized treatment systems for cervical cancer. An in-situ forming nanocomposite hydrogel loaded with an anti-PD-L1 inhibitor and the anti-angiogenic drug apatinib was able to suppress cervical tumor growth and improve survival by activating immune responses in cervical cancer models [229]. Another study developed a self-healing polymeric hydrogel carrying 5-fluorouracil, which showed strong and selective anticancer activity against HeLa cervical

cancer cells [230]. Along with this, a pH-responsive polymeric hydrogel delivering both 5-fluorouracil and heparin also demonstrated significant anti-metastatic effects in HeLa cells, indicating its potential for combination therapy [231].

5.12.3 Nanocomposites

A recent 2025 study reported manganese ferrite [$MnFe_2O_4$] /graphene oxide nanocomposite that showed novel therapeutic approach that supports strong anticancerous activity against HeLa cervical cancer cells by enhancing cellular uptake and generating high levels of reactive oxygen species, leading to apoptosis [232]. This hybrid magnetic–graphene structure was more effective than individual components, highlighting its potential as a targeted therapeutic approach. Parallel to this, recent studies on nanocomposites used in photodynamic therapy (PDT) show that these systems improve photosensitizer delivery, increase tumor selectivity, and light induced cytotoxicity of affected cervical cells [233].

5.12.4 Dendrimers as nanocarriers

Recent research highlights the growing role of dendrimers in cervical cancer therapy. A 2025 study reported a G4-PAMAM dendrimer system co-delivering methotrexate and curcumin, which showed higher cytotoxicity against cervical cancer cells than free drugs due to controlled release and increased ROS-mediated apoptosis [234]. In parallel, DNA dendrimer nanocarriers were developed for targeted and stimuli-responsive co-delivery of chemotherapeutic agents, offering a promising design framework for future cervical cancer applications [235]. Earlier studies also demonstrated dendrosome-based dendrimers could successfully deliver siRNA targeting HPV E6 and E7 oncogenes, supporting the potential of dendrimer-mediated gene therapy in cervical cancer therapy [234] (Table 2).

6 Challenges

Although nanotechnology can significantly aid in cancer care, several challenges remain for its practical use in clinics. Among these, the reliability of nanoparticle-based detection is a primary concern. Results must be consistent and accurate, but problems like clumping of nanoparticles, binding to the wrong targets, or detection errors can reduce their effectiveness [291]. These issues must be resolved to ensure their widespread use in diagnostic facilities. Another major obstacle is the large-scale production of highly sensitive and reproducible nanoprobes. While most nanoprobes are currently synthesised under meticulously controlled laboratory conditions, transitioning to mass production remains difficult [292]. This challenge becomes bigger when it is combined with the concerns of cot effectiveness, which is very essential to make these technologies accessible and practical for clinical settings. The nanoparticle-based diagnostic devices should be sensitive, reliable, user-friendly, and economically feasible. For nanotechnology to seamlessly integrate into routine clinical diagnostics, point-of-care devices must be designed to meet practical usability standards without compromising performance [293]. Furthermore nanoparticles could be toxic to the body, they might undergo long trem accumulation and may cause renal or hepatic malfunctioning with alteration in vital enzyme and levels in body. Before employing novel nanoparticle probes for in vivo imaging or therapeutic purposes, it is crucial to thoroughly evaluate their pharmacokinetics,

biodistribution, biodegradability, and possible toxic effects. Comprehensive toxicity assessments are required to ensure patient safety and the long-term viability of nanoparticle-based cancer treatments. For curbing toxicity various strategies like surface-functionalization strategies like PEGylation, protein capping, and zwitterionic coatings, have been shown to enhance biocompatibility and stability while reducing oxidative degradation [294]. Another concern is the scalability of nanoparticles. Screen-printed electrodes (SPEs) or electrodes that can be printed directly on the surface can be used to mitigate the issue of reproducibility and scalability [295]. Further in order to improve the uniformity and reliability of devices, standardized 3D printing methods are being developed [296]. These advances are actively working to overcome these issues linked with the applicability of nanomaterials and paving the way for safer and efficacious cancer care [297].

7 Discussion and future perspective

Nanotechnology has significantly enhanced cancer care by facilitating both detection and [86] treatment. Theranostics, which combines diagnosis with therapy, enables doctors to detect cancer and provide targeted treatment simultaneously [298]. This helps detect cancer quickly and directs drugs precisely to tumor cells, reducing harm to healthy tissues [299]. When combined with advanced imaging techniques, nanotechnology helps to monitor tumors easily [300]. Special nanoprobes also increase the accuracy and sensitivity of imaging, allowing for early and precise detection of cancer [301]. Nanotechnology has added advancements in cancer diagnostics and treatments, including chemotherapy, radiotherapy, and photothermal therapy, making them stronger and safer for healthy parts of the body [302]. Leading-edge nanoparticles those can act like delivery vehicle, imaging molecule as well as therapeutic moiety are requirement of time so that they can act all in one allowing more personalized treatment [303]. Smart nanoparticles are needed which reach and release therapeutic molecule on-site [304]. Safer an dbiodegradable molecules are required to reduce the risk of toxicity or long-term side effects. Tiny 2D particles, such as graphene derivatives, MXenes, and MOFs, can carry electricity and accelerate reactions, which helps detect cancer-related molecules, including aspartate and lactate, in real time [84–86]. For the usage of nanoparticle in clinics and hospitals experts from different fields need to work together, with clear guidelines, and government intervention. As research advances, these technologies could help detect cancer earlier, enhance treatment effectiveness, and enhance patient care and survival [305].

8 Conclusion

Nanotechnology is playing an increasingly important role in cancer management, offering methods that allow earlier detection and more precise treatment. New nanobiosensors have improved diagnostics by accurately and specifically identifying cancer cells at an early stage. Nanostructures possess unique properties that enhance cancer treatment and can be utilised in conjunction with existing therapies or independently. Tools that pair advanced imaging with targeted therapy allow clinicians to treat tumours more effectively while minimising damage to healthy tissue. Even with these advantages,

Table 2 Examples of several cancer targets or biomarkers, their principles, and modalities that have been utilised for the diagnosis and treatment of different types of cancer

S.no.	Type of cancer	Biomarkers	Modality	Principle of Biosensor	References	Advantages	Disadvantages	References
1	Prostate Cancer	Prostate specific antigen test (PSA), f/t-PSA, CTCs (Circulating TumorCells)	Bio-barcode assay	Gold nanoparticles linked with PSA antibodies and DNA barcodes attach to magnetic beads. This setup gives a clear and highly sensitive signal, allowing more accurate detection than traditional tests	[145, 146]	Detects even very low concentration of PSA or CTCs, useful for quick diagnosis, reliable results	Requires precise imaging and accurate synthesis of nanoparticles, relatively on expensive side, needs careful validation	[236, 237]
			Photoacoustic flowmetry	Nanoparticles detect circulating tumor cells by producing acoustic signals when they bind to them. These signals help in identifying cancer spread at an early stage		Detect very low numbers of tumor cells, non-invasive, provides real-time monitoring of tumor cells	It requires precise and specialized imaging equipment, Depthness of tissue or background noise can affect signal, Expensive for routine screening	[238, 239]
			Smartphone-integrated CRISPR/Cas12a assay	DNA and antibody probes are combined with a CRISPR system. When PSA is present, ions are released that stop the reaction and cause a color change, which can be checked using a smartphone for accurate detection	[147]	Highly sensitive, portable, user-friendly, allows on-site testing without any need complex lab equipment	Sensitive designing of required probe, may need calibration for accurate quantification	[240]
			SiNW Field-Effect Transistor (FET)	By using PSA antibodies on silicon nanowires, the target is captured directly, achieving quick and accurate detection without any fluorescent labeling	[145]	Very rapid and highly sensitive detection, label-free measurement, real-time screening, suitable for early diagnosis	Performance can be affected by signal drift non,pecific binding may occur, fabrication is costly	[241]
			Silicon nanoribbon detectors	Microfluidic channels help isolate and capture biomarkers straight from whole blood, making detection more accurate	[66, 146, 148]	High sensitivity, works directly with whole blood, less sample preparation required, improved accuracy due to microfluidic control environment	Device fabrication is critical, signals can be influenced by blood matrix effects, Need careful and frequent calibration for clinical use	[242, 243],

Table 2 (continued)

S.no.	Type of cancer	Biomarkers	Modality	Principle of Biosensor	References	Advantages	Disadvantages	References
			CNT-based electrochemical sensors	Adding conductive materials to carbon nanotubes boosts the electrochemical response, making PSA detection highly sensitive	[72, 244, 245]	Very high sensitivity, rapid response, low detection limit, point-of-care devices	Signal interference occurs due to non-specific binding, surface fouling over time, requires careful electrode modification	[246, 247] [248]
			Nanomechanical cantilever sensors	When antibodies connect with antigens, the resulting change in resonance frequency allows PSA to be measured. This method works directly in liquid samples without using chemical labels	[149]	Label-free detection of sample, very sensitive to small molecular interactions	Thermal and mechanical sensitivity, requires precise instrumentation, surface fouling can affect long-term stability of equipment	[249, 250]
		Morphometric patterns (Whole-Slide Imaging)	AI-driven biomarker analysis	Applies artificial intelligence to analyze prostate tissue images, identifying recurrence risks with greater predictive accuracy than conventional grading systems	[150]	Improves prediction of disease recurrence, captures miniature features missed by human assessment conventionally	Limited transparency in AI decision-making, Dependency on large annotated datasets	[251]
		Sarcosine	Portable amperometric biosensor	Using a CS–PANI–mesoporous carbon nanocomposite increases the detection signal of sarcosine, with results easily readable on a smartphone		High sensitivity, portable and user-friendly, low-cost, suitable for point-of-care testing	Electrochemical signals may be affected by interference of metabolites, Drawback of long term use due to sensor surface stability, requires calibration for clinical samples	[252]
			Disposable amperometric biosensor	A screen-printed carbon electrode coated with Prussian blue and rGO nanosheets detects sarcosine by measuring the signals produced during its enzyme reaction	[151]	Simple, cost- effective design, good sensitivity, low contamination risk because of disposable nature	Enzyme activity can decrease over time, single-use increases material consumption	[253]

Table 2 (continued)

S.no.	Type of cancer	Biomarkers	Modality	Principle of Biosensor	References	Advantages	Disadvantages	References
2	Breast Cancer	HER2, Estrogen Receptor (ER)	Nanoparticles (Quantum Dots—QDs)	Quantum dots attached to HER2 antibodies bind to HER2-positive breast cancer cells. When exposed to light, they emit a signal that allows for sensitive detection	[156]	Very high sensitivity, strong and stable fluorescence, allows multiplex detection of multiple biomarkers simultaneously, useful for early and precise imaging	Potential toxicity of heavy metal components, photobleaching concerns in long term imaging, requires careful surface modification for clinical use	[254]
			Nanoparticles (Magnetic Iron Oxide Nanoparticles—MIONPs)	Trastuzumab-coated magnetic nanoparticles move to tumor sites. They help deliver drugs directly and make MRI scans sharper for better treatment and detection	[157, 158]	Targeted therapy improves drug accumulation at tumor site for effective treatment	Biocompatibility concerns, Drug effectiveness depends on uniform HER2 expression	[255]
		Sentinel Lymph Nodes (SLNs)	Nano-shells (Indocyanine Green—ICG)	Indocyanine green (ICG) lights up when exposed to certain light during operations, assisting surgeons in identifying sentinel lymph nodes without radiation	[159]	Non-radioactive and safe, accuracy of SLN detection, reduces surgical complications	Not clear fluorescence due to limited tissue penetration, signals can fade over time	[256]
			Nano-shells (Rare-Earth-Based Nanoprobes)	Nanoprobes for NIR-IIb imaging build up in sentinel lymph nodes. This gives sharp, detailed images and helps spot cancer spread early	[160, 161]	High spatial resolution and sharp images, facilitate precise detection of metastatic lymph nodes	Lack of long-term biocompatibility, requires specialized NIR-II imaging equipment	[160]
		Estradiol (ERα)	Nanowires (Graphene FET)	This method detects ERα quickly without using labels. It is very sensitive, even at femtomolar levels, which helps in the early detection of hormone-related breast cancer	[163, 164] [164]	Ultra-sensitive detection, label-free, rapid response, suitable for point-of-care testing	Device fabrication is complex, requires precise surface functionalization since signal can be affected by unwanted adsorption specialized lab equipment needed	[162]

Table 2 (continued)

S.no.	Type of cancer	Biomarkers	Modality	Principle of Biosensor	References	Advantages	Disadvantages	References
			Nanowires (Silicon Nanowire Arrays)	Silicon nanowires coated with specific molecules can detect estradiol very accurately. Their high selectivity makes them useful for sensitive clinical testing		High selectivity and sensitivity, label-free detection, compatible with clinical lab testing	Fabrication complexity, Inaccurate results due to surface fouling, requires precise functionalization and instrumentation, limited large-scale clinical validation	[188]
			Nanowires (Electrochemical Sensors)	Carbon paste electrodes, when modified, can measure estrogen levels in serum with high accuracy and can detect even very small amounts		High sensitivity and selectivity, rapid and cost-effective, suitable for clinical serum testing, can detect even very low hormone levels	Electrode surface fouling can affect signal stability, requires frequent calibration and maintenance, interference from other serum components may reduce accuracy and affect results	[257]
			Nanowires (Wearable Aptamer-Based Biosensor)	A wearable device uses a gold nanoparticle–MXene electrode to detect estradiol in sweat. It sends the data wirelessly, allowing continuous monitoring		Enables real-time, continuous monitoring, non-invasive, highly sensitive and selective, suitable for personalized health tracking and early detection of disease	Calibration over long-term use can be challenging, sweat composition variability may affect accuracy, requires wearable electronics and wireless readout systems	[257]
			Nanowires (Quantum Dot-Sensitized Sensors)	Tin selenide quantum dots can detect 17β-estradiol with high sensitivity, improving the accuracy of diagnosis		Ultra-sensitive detection, allows label-free or simple readout, potential for miniaturized or less sample, point-of-care testing	Quantum dot toxicity may be a huge concern, stability under prolonged use can be challenging, fabrication complexity, may require specialized or complex instrumentation	[258]

Table 2 (continued)

S.no.	Type of cancer	Biomarkers	Modality	Principle of Biosensor	References	Advantages	Disadvantages	References
		BRCA1 Mutations	Nanocantilevers (Conventional)	BRCA1 gene mutations are found by letting DNA strands bind together (hybridize). This binding changes the vibration of a cantilever, which can then be measured to detect SNPs	[169]	Label-free detection, high sensitivity for single nucleotide polymorphisms, less sample required, allows direct DNA analysis	Requires precise micro-fabrication, signal can be affected by temperature or non-specific binding, complex instrumentation	[259]
			Nanocantilevers (Graphene Oxide-Functionalized)	Incorporating graphene oxide allows the sensor to detect mutations at femtomolar levels, making early-stage detection possible		Ultra-sensitive detection at femtomolar levels, mutation can be identified at early stage, label-free detection, enhanced mechanical response due to graphene oxide, low sample requirement	Fabrication complexity, requires precise surface functionalization, signal can be affected by environmental factors or natural stimulus, complex lab equipment needed	[260]
			Nanocantilevers (ZnO Nanowire-Coated)	ZnO-coated cantilevers offer accurate and selective detection of BRCA1 mutations, performing well at many different concentration levels	[171]	High selectivity and sensitivity, works across variable concentration ranges, enhanced signal due to ZnO nanowire coating, label-free detection	Surface functionalization and nanowire uniformity are challenging, limited large-scale clinical validation	[260]
			Nanocantilevers (Fiber-Optic SPR)	Genetic mutations can be detected by observing changes in the resonance angle when DNA strands pair up	[172]	Label-free detection, real-time monitoring, high sensitivity for variable mutation detection, minimal sample required	Requires precise optical alignment and surface functionalization, required costly equipment, signal can be affected by non-specific adsorption	[261]
			Nanocantilevers (Polyaniline Nanofiber-Based)	Polyaniline nanofibers combined with graphene oxide increase the sensitivity of biomarker detection, helping in the accurate diagnosis of breast cancer	[173]	High sensitivity due to conductive nanofiber–graphene oxide, label-free detection, low sample requirement, enhanced signal-to-noise ratio	Complex fabrication, requires precise functionalization, environmental factors like temperature or pH may affect stability, limited clinical validation for large-scale use	[262]

Table 2 (continued)

S.no.	Type of cancer	Biomarkers	Modality	Principle of Biosensor	References	Advantages	Disadvantages	References
3	Pancreatic Cancer	uPAR (Urokinase Plasminogen Activator Receptor) ENO1 (Alpha-Enolase) CA 19–9 (Carbohydrate Antigen 19–9)	Nanoparticles (Superparamagnetic Iron Oxide Nanoparticles—SPIONs) (Carbon Quantum Dots—CQDs)	SPIONs coated with uPAR-targeting ligands attach specifically to pancreatic cancer cells and surrounding tissues. This makes MRI images clearer and helps in accurate tumor detection SPIONs linked with ENO1 antibodies show stronger binding to tumor tissues, giving sharper MRI images and improving the detection of pancreatic ductal adenocarcinoma (PDAC) Carbon quantum dots (CQDs) give strong fluorescence signals. They are applied in immunoassays to identify CA 19–9 markers in blood serum, enabling sensitive and non-invasive cancer testing	[180–182]	Improves MRI resolution and tumor localization, non-invasive, targeted imaging reduces false results Increased tumor specificity and MRI signal, enables early PDAC detection, minimally invasive High sensitivity, non-invasive, rapid detection, Carbon quantum dots (CQDs) can be integrated into point-of-care assays	Potential toxicity occurs if SPIONs accumulate in organs, requires careful surface functionalization, high cost, limited long-term safety data Requires precise antibody conjugation, nanoparticle aggregation can reduce signal quality Fluorescence can be affected by serum impurities, CQD synthesis complexity, possibility of photobleaching	[263] [263] [264]

Table 2 (continued)

S.no.	Type of cancer	Biomarkers	Modality	Principle of Biosensor	References	Advantages	Disadvantages	References
		CA 19–9 (Carbohydrate Antigen 19–9) Genetic Variations (Guanine and Deoxyguanine Triphosphate)	Nanotubes (Silica Nanoparticles—SiO_2) (Multi-Walled Carbon Nanotubes—MWCNTs)	SiO_2 nanoparticles are loaded with secondary antibodies, which boosts the sensitivity of sandwich ELISA. This allows CA 19–9 to be detected at very low levels, supporting early diagnosis Multiwalled carbon nanotubes (MWCNTs), when used with RAPD techniques, help compare DNA from healthy individuals and pancreatic cancer patients. This creates a clear genetic profile for accurate detection	[117, 123]	High sensitivity, supports early diagnosis, compatible with standard ELISA platforms, enhances signal amplification for better results Enables genotyping and mutation analysis, sensitive differentiation between healthy and cancerous DNA, label-free detection	Requires careful nanoparticle-antibody conjugation, potential cross-reactivity, cost and reproducibility challenges Fabrication complexity, potential toxicity of MWCNTs, requires specialized RAPD protocols, limited large-scale clinical validation	[265] [266]
			Nanotubes (MWCNTs for Photothermal Therapy)	PEG-coated carbon nanotubes go to tumor tissues. Near-infrared light makes them heat up, which damages cancer cell mitochondria and kills the cells, leaving healthy tissue unharmed	[184]	Highly targeted and minimally invasive therapy, strong photothermal conversion efficiency, reduced damage to normal tissues, effective against drug-resistant tumors	Potential long-term toxicity and poor biodegradability, uneven heat distribution in deep tumors, requires external NIR irradiation equipment, limited clinical translation so far	[267]
		Nine-gene-pair signature (multigene expression)	(AI driven analysis) Tissue and plasma analysis	By comparing gene expression, differences between pancreatic cancer (PDAC) samples and normal samples can be identified	[15]	High diagnostic accuracy, works with tissue and liquid biopsy samples, captures tumor heterogeneity better than single biomarkers, supports early and personalized diagnosis	Requires high-quality sequencing data, computational complexity, limited interpretability of AI models, needs large patient cohorts for validation before routine clinical use	[268]

Table 2 (continued)

S.no.	Type of cancer	Biomarkers	Modality	Principle of Biosensor	References	Advantages	Disadvantages	References
		Circulating miRNAs (miR-20a, miR-21, miR-24, miR-25, miR-99a, miR-185, miR-191)	Serum-based liquid biopsy	An AI-based biosensor detects miRNA levels with very high accuracy, making diagnosis more reliable (AUC = 0.99)		Non-invasive and blood-based, extremely high diagnostic accuracy, early detection potential, captures complex miRNA patterns better than single biomarkers	miRNA expression can vary due to biological and technical factors, requires standardized sample handling, AI models need large datasets for robustness, limited routine clinical adoption so far	[269]
4	Lung Cancer	VOCs (Volatile Organic Compounds)	Nanoparticles (Gold Nanoparticles—GNPs)	GNP-based sensors detect unique chemical patterns in breath, which helps differentiate lung cancer patients from healthy individuals. When combined with GC–MS, this technique allows for non-invasive and affordable cancer detection	[185–187]	Completely non-invasive, rapid and affordable screening, suitable for early detection, high sensitivity to cancer-specific VOC patterns, potential for point-of-care use	VOC profiles can be influenced by smoking, diet, or environment, requires careful calibration and pattern analysis, standalone sensors may need GC–MS confirmation, limited large-scale clinical validation	[270]
		CTCs (Circulating Tumor Cells)	Nanowires (Quartz Nanowire Arrays)	Quartz nanowires coated with EpCAM antibodies can capture circulating tumor cells (CTCs) from blood using microfluidic devices. These rare cells are detected through laser scanning, aiding in the early diagnosis of lung cancer	[188]	Enables highly sensitive capture of rare CTCs, minimally invasive blood-based diagnosis, high surface area improves cell capture efficiency, suitable for early detection and disease monitoring	EpCAM-negative or EMT-transformed CTCs may escape detection, fabrication of nanowire arrays is technically complex, requires specialized microfluidic and imaging systems, limited large-scale clinical validation	[271]
		IL-10 (Interleukin-10), OPN (Osteopontin)	Nanowires (Silicon Nanowires)	Silicon nanowires coated with specific antibodies attach to target biomarkers. A linked enzyme reaction creates an electrical signal that reflects the biomarker level, enabling sensitive detection	[189, 191]	Extremely high sensitivity (femtomolar range), label-free or low-label detection, real-time electrical readout, small sample volume required, suitable for multiplexed inflammatory and cancer biomarker profiling	Enzyme stability may affect signal reproducibility, non-specific adsorption can cause background noise, requires precise surface functionalization, limited robustness in complex clinical samples without pre-processing	[272]

Table 2 (continued)

S.no.	Type of cancer	Biomarkers	Modality	Principle of Biosensor	References	Advantages	Disadvantages	References
		VOCs	Carbon Nanotubes (Single-Walled Carbon Nanotubes—SWCNTs)	SWCNT-based sensors with specific surface coatings can pick up lung cancer-related compounds in exhaled breath. They can detect very small concentrations, down to 6 ppb	[193]	Non-invasive breath-based detection, ultra-high sensitivity (ppb range), rapid response time, low power consumption, suitable for portable and point-of-care devices, potential for early-stage lung cancer screening	Limited specificity for single VOCs (pattern-based analysis needed), sensor drift over time, humidity interference in breath samples, requires calibration and AI/statistical algorithms for reliable clinical interpretation	[273]
		Prognostic and predictive biomarkers from imaging and molecular data	(AI driven analysis) Imaging data (radiomics) and molecular profiling	Data from imaging scans is combined with molecular biomarker information to help determine the diagnosis and the future course of the disease	[194]	Non-invasive or minimally invasive prognosis, captures tumor heterogeneity better than biopsy alone, improves prediction of treatment response, enables personalized medicine, supports early risk stratification and clinical decision-making	Requires large, high-quality annotated datasets, variability in imaging protocols affects reproducibility, complex models reduce interpretability, risk of overfitting, limited clinical validation in routine practice	[274]

Table 2 (continued)

S.no.	Type of cancer	Biomarkers	Modality	Principle of Biosensor	References	Advantages	Disadvantages	References
5	Brain Cancer	mRNA	Nanoparticles (Lipid-Based)	Lipid nanoparticles carry therapeutic mRNA across the blood–brain barrier to reach brain tumors, allowing the medicine to enter cells more efficiently than standard methods	[195, 198, 199]	Enables non-viral gene delivery, protects fragile mRNA, improves cellular uptake, allows transient and controllable protein expression, reduces risk of permanent genetic alteration, and shows potential for treating otherwise inaccessible brain tumors	Limited and variable blood–brain barrier penetration, possible immune activation, short duration of mRNA expression, challenges in precise tumor targeting, and need for repeated dosing; long-term safety in humans still under evaluation	[275]
			Nanoparticles (Magnetic—MNPs)	Magnetic nanoparticles improve MRI images to locate tumors precisely. When coated with targeting molecules, they can deliver chemotherapy drugs directly to tumors, treating them while keeping healthy tissue safe		Improves MRI sensitivity and tumor boundary visualization, enables targeted drug delivery, reduces systemic toxicity, allows image-guided therapy, and can be externally guided using magnetic fields for better tumor accumulation	Limited penetration across the blood–brain barrier, possible accumulation in liver and spleen, risk of iron overload at high doses, challenges in uniform tumor distribution, and incomplete clinical translation so far	[276]

Table 2 (continued)

S.no.	Type of cancer	Biomarkers	Modality	Principle of Biosensor	References	Advantages	Disadvantages	References
		Neural Signals	Nanowires (Platinum, Biodegradable Polymers, Hydrogel Microelectrodes)	Nanowire sensors and hydrogel microelectrodes monitor nerve signals and muscle activity. Flexible biodegradable polymer fibers can move through blood vessels to check tumors and nerve activity without invasive procedures	[196, 200]	High signal sensitivity, excellent tissue conformity, reduced mechanical mismatch with brain tissue, long-term stable recordings, minimal inflammation, and potential for minimally invasive neural and tumor monitoring	Limited long-term durability for biodegradable materials, challenges in precise positioning, gradual signal drift over time, complex fabrication, and regulatory hurdles for clinical translation	[277]
		Neural Stem/Progenitor Cells	Nanowires (Conductive Biomaterials)	Conductive materials combined with neural stem cells help the cells develop into working neurons. This supports nerve tissue repair and provides models to study the nervous system		Promotes efficient neural differentiation, improves formation of functional neuronal networks, supports nerve tissue repair, enables in vitro models for neuroscience studies, potential for bioelectronic interfaces	Requires careful control of electrical stimulation, potential cytotoxicity at high concentrations, scalability challenges for tissue engineering, long-term in vivo effects not fully known	[277]
		DNA Sequences (Multidrug-Resistant Genes)	Carbon Nanotubes (Multi-Walled—MWCNTs)	Electrochemical biosensors using MWCNT arrays can identify DNA sequences associated with early brain tumors, improving the accuracy and sensitivity of diagnosis	[201, 202, 278]	Ultra-sensitive detection of tumor DNA, high specificity for multidrug-resistant sequences, rapid analysis, minimal sample volume required, potential for early diagnosis and monitoring of therapy response	Requires careful probe design and immobilization, possible non-specific binding, signal drift over time, fabrication complexity, limited clinical validation	[279]
		Glioma Cells	Carbon Nanotubes (CNTs)	Carbon nanotubes (CNTs) help carry therapeutic molecules such as CpG oligodeoxynucleotides to glioma cells. This strengthens the immune response and allows both treatment and monitoring at the same time		Enables targeted therapy, enhances immune activation, potential for combined therapy and monitoring, reduces systemic toxicity, small doses required	Potential cytotoxicity of CNTs, possible accumulation in non-target tissues, challenges in consistent functionalization and delivery, long-term biocompatibility still under study	[280]

Table 2 (continued)

S.no.	Type of cancer	Biomarkers	Modality	Principle of Biosensor	References	Advantages	Disadvantages	References
		Glial Fibrillary Acidic Protein (GFAP), MGMT	Nanocomposites- MRI Imaging and Targeted Drug Delivery	Gold nanoparticles can cross the blood–brain barrier to deliver drugs directly to the target area	[195–197]	Enables combined imaging and therapy (theranostics), improves drug delivery across BBB, enhances MRI contrast, reduces systemic toxicity, allows targeted therapy to tumor site	Limited penetration for some BBB regions, potential long-term accumulation of gold nanoparticles, high production cost, clinical translation challenges	[281]
		Tumor histology patterns from stimulated Raman histology (SRH)	(AI driven analysis) Intraoperative SRH imaging	A deep learning system identifies the type of tumor from Stimulated Raman Histology (SRH) images with 94.6% accuracy in about 150 s	[203]	High diagnostic accuracy (94.6%), label-free imaging, fast intraoperative results, supports precision surgery, reduces need for frozen sections	Requires high-quality imaging data, complex AI training, may be limited by rare tumor types, depends on computational resources intraoperatively	[282]
6	Leukemia	CD13, Drug-resistant cells	Nanoparticles	Tiny particles carry drugs directly to leukemia cells, increasing their cytotoxicity and even make resistant cells sensitive again	[207, 208]	Enhances targeted therapy, reduces off-target toxicity, can overcome drug resistance, improves drug uptake, allows combination therapy	Potential immune clearance of nanoparticles, variable biodistribution, limited clinical translation, risk of nanoparticle accumulation in non-target organs	[207]
		CXCR4	Nanozymes	Artificial "enzyme-like" materials produce toxic molecules in cancer cells, selectively damaging tumors while leaving healthy cells unaffected	[210, 211] [212]	Targeted cancer cell killing, reduces systemic toxicity, can overcome drug resistance, enhances individualized therapy, works in acidic tumor microenvironments	Possible off-target ROS generation, stability in circulation may vary, potential immune response, challenges in large-scale synthesis and uniform activity	[211]
		FLT3	Polymeric Micelles	Smart carriers deliver therapeutic drugs to cancer stem cells and release drugs only when they reach tumor environments	[213, 214, 283]	Enhances targeted drug delivery, reduces systemic toxicity, overcomes drug resistance, improves uptake by leukemia stem cells, allows controlled and stimuli-responsive release	Limited stability under circulation, possible premature drug release, complex formulation, scale-up challenges, variable targeting efficiency in vivo	[284]

Table 2 (continued)

S.no.	Type of cancer	Biomarkers	Modality	Principle of Biosensor	References	Advantages	Disadvantages	References
		AML surface markers	Exosomes/ Extracellular Vesicles	Tiny vesicles mimic natural cell signals, activating the immune system to fight leukemia	[215, 216, 217]	Activates immune system against leukemia, reduces off-target toxicity, natural and biocompatible delivery, can target residual leukemia cells in bone marrow	Difficult to produce at scale, variability in exosome composition, potential immune overactivation, challenges in long-term stability and storage	[285]
		ROS, pH	Nanogels	Gel-like nanoparticles release drugs only under targeted tumor conditions, boosting stress inside cancer cells to trigger cytotoxicity of leukemia cells	[218, 219, 220]	Targeted and stimuli-responsive drug release, enhanced cytotoxicity in leukemia cells, reduced systemic toxicity, tunable and stable delivery platform	Possible premature drug leakage, variability in tumor microenvironment response, complex synthesis, limited in vivo clinical validation	[286]
7	Cervical Cancer	CD44 receptor[287]	Nanoparticles	Gold nanoparticles carry drugs straight into cancer cells, increase uptake, and create ROS to kill tumors	[221, 226, 227]	Targeted drug delivery, improved uptake, ROS-mediated cytotoxicity, reduced off-target toxicity, potential for combination therapy	Possible nanoparticle accumulation in non-target tissues, cytotoxicity at high doses, complex synthesis, limited clinical translation	[288]
		PD-L1	Nanogels	Hydrogels release drugs right at the tumor site, activate the immune system, and stop cancer cells from growing or spreading	[229–231]	Targeted and controlled drug release, activates immune system, reduces systemic toxicity, strong anti-metastatic effect, suitable for combination therapy	Limited penetration in some tumor regions, variability in pH response, long-term stability and biodegradation need further study, complex synthesis	[287]
		HeLa cells	Nanocomposites	Conjugated $MnFe_2O_4$/graphene oxide target cancer cells, generate ROS, trigger apoptosis, and improve light-based therapy	[289, 221]	Combines targeted therapy and ROS-mediated apoptosis, improves photodynamic therapy efficiency, higher cellular uptake, reduced off-target toxicity	Potential nanoparticle accumulation, complex synthesis, ROS may affect nearby healthy cells at high doses, limited clinical data	[289]

Table 2 (continued)

S.no.	Type of cancer	Biomarkers	Modality	Principle of Biosensor	References	Advantages	Disadvantages	References
		Dendrimers	HPV E6/E7	Tiny branched carriers deliver siRNA, boost programmed cell death specifically	[234, 235]	Targeted gene therapy, reduces off-target effects, enhances apoptosis in HPV-infected cells, can be combined with other therapies	Potential immune activation, limited in vivo stability, complex synthesis, delivery efficiency may vary, clinical translation still under study	[290]

problems such as potential toxic effects, high costs, and limited clinical adoption persist. Ongoing research is critical to fully realize the benefits of nanotechnology in cancer care.

Author contributions
SR: Writing—review and editing, Investigation, Formal analysis, Conceptualization. RK: Writing—review and editing, Writing—original draft, Supervision, Software, Project administration, Investigation, Formal analysis, Data curation, Conceptualization. TG: Writing—original draft, Visualization, Formal analysis, Data curation, Conceptualization. MAK: Writing—original draft, Supervision, Resources, Data curation, Conceptualization. PG: Writing—review and editing, Writing—original draft, Investigation, Formal analysis, Data curation, Conceptualization. AA: Writing—review and editing, Writing—original draft, Supervision, Investigation, Formal analysis, Data curation, Conceptualization. SAA: Revision, editing, review, writing, Figures; MEAZ: Revision, editing, review, writing, Figures.

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