# Role of Nanotechnology in Cancer Diagnosis: An Advance Approach

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## ABSTRACT

Worldwide, cancer is one of the main causes of mortality and low life expectancy. There is still a gap in the effectiveness of various cancer treatments, despite the fact that several methods have been developed to lower mortality, lessen chronic pain, and enhance quality of life. Early cancer cell diagnosis and high-specificity medication administration to minimize toxicities are essential elements in providing the best possible cancer treatment. Owing to the heightened systemic toxicity and refractoriness associated with traditional cancer diagnostic and treatment instruments, alternative approaches, such as nanotechnology, are being utilized to enhance detection and alleviate the intensity of the disease. Nanotechnology-based immunotherapeutic drugs have been employed for many cancer types throughout the years to lessen the invasiveness of malignant cells while protecting normal cells at the targeting site. This review discusses the various types of nanotechnologies that are commonly used in cancer diagnosis.



## KEY-WORDS

Nanotechnology, Cancer, Nanoparticles, Endoscopy, Dendrimers


## INTRODUCTION

The first line of defense in the battle against cancer is early detection. However, the fundamental or traditional methods employed to diagnose various cancer types impede this early identification. The screening procedure is generally delayed by the one or more limitations of conventional approaches, which postpones the early initiation of a patient's therapy.[1] Currently, the following traditional techniques are employed to detect cancer:

***1. Histopathology and Cell-Cytology***

To identify cancer at an early stage, cytology and histopathology cannot be used efficiently and independently alone.

***2. Imaging Techniques***

X-rays, magnetic resonance imaging (MRI), computed tomography (CT), endoscopy, and ultrasound, among others, may only identify cancer when an observable alteration in the tissue is present.[2]

The diagnostic ability of these techniques is strong however, they have two big drawbacks: Firstly, these approaches are unable to distinguish between benign and malignant tumors. Hence it becomes really difficult to obtain the proper detection as early as possible. Secondly, they can only be used when visual changes start to take place in the tissues or cells and by that time it gets late to treat or operate cancer in patients' bodies. As a result, developing methods to identify cancer at an early stage, before it spreads, is a huge issue.[3] It certainly is a big challenge to develop early detection techniques that are accurate, sensitive and very specific in their task. Therefore much of the research work has been focused on better diagnosing techniques for early recognition of cancerous cells in patients. The best emerging field is" *NANOTECHNOLOGY".* [4]

The conventional diagnosing techniques are either being combined with nanotechnology to evolve new novel nano-techniques or replaced with various devices of nano range to help in better diagnosis of cancer. Bioconjugated particles and technologies are also being developed for the detection of early cancer in bodily fluids such as blood and serum.[5] These nano-scale devices work by selectively catching cancer cells or target proteins. Sensors are often used by covering them with a cancer-specific antibody or other bio-recognition ligands, allowing capture of the certain electrical, mechanical, or optical signal which is produced by a cancer cell or target protein to detect. Such nano techniques are considered to be more sensitive and specific.[6] They help in multiple measurements and hence are useful for the detection of extracellular cancer biomarkers and cancer cells, as well as for in vivo imaging. This review helps you to develop a good understanding of how the application of nanotechnology is helpful in the detection of different types of cancers in patients as compared to the conventional as well as current techniques in use.[7]

## NANOTECHNOLOGIES USED IN CANCER DIAGNOSIS

There are many nano-structures as well as nanodevices that help to detect cancer at a very early stage. These may include:

***1. Nanoparticles***

At least half of the particles in the number size distribution must have a particle size of 100 nm or less. The majority of nanoparticles are composed of only a **N**few hundred atoms. A nanoparticle is a tiny entity that, in terms of movement and characteristics, behaves like a full unit. With the numerous applications of nanoparticles in diverse sectors, nanoparticle research is now the most researched branch of science.[8] The particles might have a wide range of uses in biological, optical and electrical domains. Nanoparticles are used in biology and medicine for a variety of reasons:

- ❖ Developing fluorescent biological labels for essential biological markers and substances used in disease research and diagnostics.
- ❖ Drug administration systems.
- ❖ In gene therapy, gene delivery techniques are used using nanoparticles.
- ❖ For the biological identification and diagnosis of disease-causing organisms.
- ❖ Helpful in protein detection.
- ❖ In researches related to biological substances and tumor cell isolation and purification.
- ❖ DNA structure investigation about cancer.
- ❖ Tissue and genetic engineering.
- ❖ Tumors are destroyed using medications or heat.
- ❖ In MRI research.
- ❖ In pharmacokinetic research area.

Nanoparticles are being used in cancer detection to collect biomarkers such as cancer-associated proteins, circulating tumor DNA, circulating tumor cells, and exosomes. One significant advantage of using nanoparticles for cancer detection is their high surface area to volume ratio in comparison to other heavy materials. [9] Because of this feature, antibodies, small molecules, peptides, aptamers, and other moieties can be thickly coated on nanoparticle surfaces but with special care to still maintain their sizes in nano ranges.

These target recognizing components when added with nano-size particles can attach to and identify certain cancer molecules. Multiplicative effects can be obtained by providing multiple bindings of ligands to cancer cells, which further increases the specificity and sensitivity of such nano particles.[10] These nanoparticles can be made up of various kinds of materials (metals) corresponding to the formation of different types of nanoparticles like gold, silver, magnetic, etc.

***a. GOLD-Nanoparticles***

Because of their tiny size, strong biocompatibility, and high atomic number, gold nanoparticles are a suitable contrasting agent. They target cells in both active and passive ways as illustrated according to researches. Because of the permeability tension effect (EPR) in tumor tissues, the principle of passive targeting is guided by the collecting of gold nanoparticles to increase imaging. Gold nanoparticle's active targeting of tumor cells is achieved by combining these nanoparticles with tumor-killing targeted medicines, such as EGFR monoclonal antibodies. [11]

***b. MAGNETIC-Nanoparticles***

Over recent decades, a variety of narrow size distribution magnetic nanoparticle preparations have been created. The particles are prepared from gold and iron oxide which help to incorporate magnetic properties in them. These are small size particles that respond to the magnetic field and hence can easily be used for diagnostic purposes not only in cancer but also in other disorders. Magnetic nanoparticles play a major role in cancer treatments by helping in the early detection of tumors and cancerous cells in the body fluids.[12] These nanoparticles are conjugated with the peptides and made more advantageous for helpful. They are used for angiogenesis imaging, cancer staging, immune cell tracking (cells such as monocytes/macrophages, T cells), and molecular and cellular targeting. Such particles represent a high degree of biocompatible nature as well as low toxicity. [13]

***2. Quantum Dots***

Quantum dots are nano-sized crystalline particles, more appropriately known as nanocrystals. They are made up of semiconductor materials as a basic component that entraps an inorganic element at its center and a metal forms a shell around them. QDs have sizes ranging from 2 to10 nm. Quantum dot's size and composition may be varied between 400 and 2,000 nm. They have the property of showing various colors in presence of different wavelengths.[14] Hence using varying wavelengths, quantum dots may be tuned to any hue, allowing for the detection and tracking of differently labeled biomarkers with a single light source emitting different wavelengths. Spectral imaging techniques have been used to separate signals from various fluorescent markers in cells or tissues, but the inability of visible spectrum imaging to penetrate things restricts its application.[15] To address this issue, quantum dots that produce fluorescence in the near-infrared range starting from 700nm to 1000nm have been developed, making them more suited for imaging colorectal cancer, liver cancer, pancreatic cancer,.and lymphoma. To improve cancer imaging, a subsequent near-infrared (NIR) window "NIR-ii", ranging from 900-1700 nm with greater tissue incursion power and superior spatial and temporal resolution has been created. Silver rich quantum dots including sulphur source has been made and have been reported to enable the observation of higher spatial resolution pictures throughout a broad infrared spectrum. In the context of multi-photon microscopy, fluorescence-tagged quantum dots provide multicolor bright imaging in live tissues.[16] Quantum dots show attractive properties which add to the advantages for their utilization such as:

- On simple excitation they show stable fluorescence
- Can easily be tuned to multiple spectra.
- High sensitivity and specificity
- Absence of the need for lasers.

Quantum dots' red/infrared hues allow for whole blood tests. However, one issue with imaging normal healthy tissue in the past has been that it frequently shows auto-fluorescence, which interferes with the signal from malignant cells. Quantum dots have been made to exhibit fluorescent characteristics in the NIR spectrum, allowing them to reduce this interference to a large extent. Another issue with employing quantum dots in vivo is whether or not injection provides a hazardous danger. To reduce potential toxicity, changes have been made. [17]

***3. Dendrimers***

Dendrimers are engineered complex nanostructures with branched concentric layers encompassing an inward center. The shape, measure, surface functionalities, and branching length of a dendrimer may be controlled to perform distinctive capacities. The breadths of dendrimers run between 1nm to 10 nm.[18,19] Dendrimers are demonstrating to be especially proficient at serving as a flexible measured quality able of identifying several proteins, which are right now identified by performing a person's ELISA testing. In expansion, dendrimer nanoparticles have been made, which may be dually utilized for imaging utilizing MRI or NIR fluorescent modalities in a single test. This process has been utilized in the research works and has appeared to be successful in mice for mapping using soli-lipid nanoparticles. Dendrimers show various advantages such as: [20-22]

- Simplicity and ease of synthesis.
- Show excellent drug loading capacity.
- Show superb bio-degradable property.
- Transepithelial transport is improved.
- Gastrointestinal toxicity can easily be minimized.

Certain research studies have shown that in the case of colorectal cancer cells, SN38 (an antineoplastic agent) conjugated dendrimers had shown improved transepithelial transfer of anti-cancerous drugs with much lower colon and rectum toxicity to a large extent, suggesting that dendrimers have significant promise as carriers in the transport of anticancer medicines. They have also shown the results of increased oral bioavailability when used for the delivery of antitumor drugs. Various researchers have shown through their studies that polypropylene imine dendrimers can efficiently deliver tumor necrosis factor α-gene into colorectal adenocarcinoma cells to restrain the development of colorectal malignancy without causing toxic effects in the animals, signifying that dendrimers are an encouraging carrier for the delivery of target focused anti-tumor genes in treatment of cancer.[23]

***4. Nano-Hydrogels***

Hydrogels are networks at the nanoscale that have the ability to expand. They are produced by covalently cross-linking polymer chains or by non-covalent interactions, resulting in nano-sized hydrogels, or nanogels. Because of their enormous surface area to volume ratio, size tunability, regulated drug release profile, superior drug loading facility, and accessibility to environmental stimuli, nano-gels have drawn attention in medicine as imaging labels and targeted medication release while lowering systemic adverse [24] effects. There are several uses for nano-hydrogels, such as:

- ❖ They have a lot of consistency.
- ❖ They have a high level of blood compatibility.
- ❖ They are simple to link to targeted agents.
- ❖ Low cytotoxicity is demonstrated.
- ❖ When used as gene carriers, they perform admirably.
- ❖ Have the potential to be used in controlled delivery systems that are taken orally.

***5. Nano-Shells***

Another widely used nanotechnology in cancer is nano-shells. Nano-shells are dielectric cores with diameters ranging from 10nm to 300 nm. They are frequently made of silicone and topped with a thin metal casing usually of gold.[25] Using UV-infrared emission/absorption arrays, these nano-shells convert plasma-mediated electrical energy into light energy signals that could easily be detected. Nano-shells are required because their imaging is devoid of heavy metal toxicity, despite their large size limiting their applicability.[26-28] Gold-coated nano-shells with a dimension of 120nm were employed by Rice University researchers to remove cancer tumors in mice. Nano-shells may be designed to attach to malignant cells found everywhere in the live body by attaching antibodies or peptides to their surfaces. Irradiating the location of the carcinoma clusters with an infrared laser beam, which penetrates through tissue without heating them helps in killing those cells perfectly The gold metal coated on the nanoshells is sufficiently heated to kill cancer cells when such nano-shells are bombarded on them. [29,30]

### *6. Nano-Cantilevers*

Cantilevers are small flexible beams placed in a row at the nanoscale. Cantilevers provide for biosensing because their small vibrations occur naturally at a frequency determined by mass properties and mechanics. The baseline probe frequency is often determined by a change in the probe's light deflection pattern, which may be readily recognized by the detectors or by other electrical means, when a biological molecule attaches to this nanoscale probe.[31–33] In atomic force microscopy (AFM) force feedback mode, cantilever vibrations are primarily deflected to provide real-time images. [34] Some of the cited advantages of using nanoscale cantilever devices in cancer diagnosis are as follows:

- They don’t need to be labeled with fluorescent or radioactive materials.
- They’re capable of detecting cancer in liquid samples.
- The technology can readily be transferred to “chips” to be utilized in test facilities helping in cancer providing cancer diagnosis.
- Because of their cheaper cost in terms of sample preparation, time, and materials, they’ve also been labeled a “simple replacement” for polymerase chain reaction techniques and detection technologies.
- Nanometre cantilever devices, in which cantilevers are coated with specialized receptors, might be utilized to detect disease-specific molecules like DNA or protein in a very sensitive and rapid way.

### *7. Carbon Nanotubes*

Another kind of nanodevice that may be utilized to find cancer biomarkers is carbon nanotubes. To transform carbon nanotubes into nanoscale marvels, researchers have frequently coated them with polymer coatings to make them biocompatible.[35] They have been investigated as imaging and medication delivery agents with potential for therapeutic application. According to researchers at Stanford University, carbon nanotubes retain their ability to attach remarkably well to a large range of medicinal and imaging compounds in a safe but reversible manner.[36,37] Single-walled carbon nanotubes have been employed by researchers as high-resolution tips for atomic force microscopy (AFM) to demonstrate that particular kilobase-size DNA topologies may be seen, especially from singlebase mismatch sequence patterns. The researchers also found that the therapeutic payload of carbon nanotubes was retained when they were dissolved in blood serum with a typical physiological buffer, but that the medication rapidly leaked out of the tubes in an acidic environment. Because the tumor cells also have an acidic environment, the medication from the nanotubes is easily released in them, which makes them effective in destroying cancer cells. Additionally, the researchers showed how tumor-targeting compounds and imaging contrast agents may be attached to nanotubes, opening the door for the development of multifunctional nanodevices that are capable of both diagnosing and treating cancer in live organisms.[38]

***8. Nano-Rods***

When cetyltrimethylammonium bromide, a cationic surface-active agent used in various synthesis, is completely covered on nano-rods, it accumulates on the cell surface over an identical amount of time, while when cetyltrimethylammonium bromide is carefully removed from nano-rods that have already been functionalized with folate, it internalizes into cells via a nonspecific uptake pathway within hours.[39–44] Therefore, when the nanorods are exposed to radiation at their longitudinal plasmon resonance, they increase the susceptibility of tumor cells to photo-thermal damage in both cases, causing a significant blebbing of the cell membrane. More and more studies have revealed that gold nanorods might be employed to make incredibly bright imaging agents. Georgia Institute of Technology researchers found that gold nanorods will align themselves in an ordered manner on the surface of cancer cells when they are linked to an antibody that binds to tumor cells. This will intensify the optical signal that the nanorods produce and give tumor cells a distinct optical signature.[45–49]

***9. Nano-Wires***

Another type of nanodevice utilized in cancer detection are nano-wires. They may be made from a wide range of materials, including as oxides and polymers with different compositions, as well as semiconducting, metallic, and magnetic materials. Nano-wires are coated with ligands to be employed as target-focused materials.[50,51] Very effective biological target detection is made possible by the unique interaction between the target and its capture molecules, which alters the charge density and changes it into quantifiable data in the electric field of the nano-wire devices. Silicon nanowires have been developed to identify certain DNAs.Various surface receptors on silicon nano-wire FETs have been created and joined into arrays to create nano-wires that are perfect for label-free, multiplexed, extremely sensitive, and selective biomarker tests. The amount of false positive results might be further reduced with the assistance of the integrated control nanowires. Without the need for repeated amplification steps, real-time telomerase activity tests using samples taken from just 10 tumor cells may be made possible using nucleic acid receptors embedded into arrays.[52–55]

***10. Nano-Barcodes***

A novel protein and nucleic acid detection method based on biobarcode amplification was described by the researchers. This method combines magnetic micro-beads and colloidal gold nanoparticles; the magnetic micro-particles include target capture strands, and the gold nanoparticles contain both target capture and bar code strands that are subsequently hybridized to bar code DNA.[56] When target DNA is present, gold nanoparticles and magnetic microbeads create sandwich structures. The target DNA is then magnetically separated from the solution and extensively cleaned to get rid of unhybridized bar code DNA.[57] The colorimetric approach is used to detect the barcodes. With comparable sensitivity to PCR, this capture and detection approach is four to six orders of magnitude more sensitive than conventional protein ELISA.[58]

## CONCLUSION AND FUTURE PERSPECTIVE

Over the years, nanotechnology has showed great promise in the treatment of cancer. Nanomaterials have improved cancer detection and therapy through their enhanced pharmacokinetic and pharmacodynamic characteristics. Because of their specificity, nanotechnology enables targeted medicine delivery in damaged tissues with minimal systemic toxicity. Nevertheless, much like other therapeutic alternatives, nanotechnology has some drawbacks and is not entirely free of toxicities. These drawbacks include systemic and specific organ toxicity, which might hinder the use of nanotechnology in clinical settings. Considering the limits of nanotechnology, further research and development is needed to enhance medicine delivery, optimize its effectiveness, and minimize its drawbacks. Better relationships between the physicochemical characteristics of the used nanomaterials can lead to the development of safer and more effective derivatives for cancer management in terms of both diagnostic and therapy. In conclusion, our goal was to draw attention to the main benefits of nanotechnology as well as its limitations when it comes to treating cancer clinical demands. Furthermore, the potential for therapeutic application of nanotechnology in additional illness states may arise from its therapeutic advantages and future improvements. These may include rheumatoid arthritis and ischemic stroke, which would need for the precise administration of an appropriate pharmaceutical agent at the location of the injury.

## CONFLICT OF INTEREST

The authors declare that the review was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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## REFERENCES

1. Y. Zhang, M. Li, X. Gao, Y. Chen, and T. Liu, “Nanotechnology in cancer diagnosis: Progress, challenges and opportunities,” J. Hematol. Oncol., vol. 12, no. 1, pp. 1–13, 2019.
2. A. Garg, G. S. Sharma, A. K. Goyal, G. Ghosh, S. C. Si, and G. Rath, “Recent advances in topical carriers of anti-fungal agents,” Heliyon, vol. 6, no. 8, p. e04663, 2020.
3. M. Verma and D. Ph, “Application Of Nanotechnology in Cancer,” vol. 7, no. 2, 2008.

4. A. Gdowski, A. P. Ranjan, A. Mukerjee, and J. K. Vishwanatha, "Nanobiosensors: Role in cancer detection and diagnosis," Adv. Exp. Med. Biol., vol. 807, pp. 33–58, 2014.
5. B. M. Biswal and Z. Yusoff, "Application of Nanotechnology in Cancer Treatment," Top. Mining, Metall. Mater. Eng., vol. 7, no. 2, pp. 269–311, 2017.
6. B. Meckes, "System for High Resolution Ion Sensing," no. March, 2014.
7. W. H. Gmeiner and S. Ghosh, "Nanotechnology for cancer treatment," Nanotechnol. Rev., vol. 3, no. 2, pp. 111–122, 2014.
8. X. Wang, L. Yang, Z. Chen, and D. M. Shin, "Application of Nanotechnology in Cancer Therapy and Imaging," CA. Cancer J. Clin., vol. 58, no. 2, pp. 97–110, 2008.
9. A. B. Chinen, C. M. Guan, J. R. Ferrer, S. N. Barnaby, T. J. Merkel, and C. A. Mirkin, "Nanoparticle Probes for the Detection of Cancer Biomarkers, Cells, and Tissues by Fluorescence," Chem. Rev., vol. 115, no. 19, pp. 10530–10574, 2015.
10. S. S. Davis, "Biomedical applications of nanotechnology - implications for drug targeting and gene therapy," vol. 7799, pp. 217–224.
11. B. Pan et al., "Dendrimer-Modified Magnetic Nanoparticles Enhance Efficiency of Gene Delivery System Dendrimer-Modified Magnetic Nanoparticles Enhance," pp. 8156–8163, 2007.
12. B. SUN, Y. FANG, Z. LI, Z. CHEN, and J. XIANG, "Advances in the application of nanotechnology in the diagnosis and treatment of gastrointestinal tumors," Mol. Clin. Oncol., vol. 3, no. 2, pp. 274– 280, 2015.
13. C. A. M. Jwa-Min Nam, C. Shad Thaxton, "Tiny Particles Flag Scarce Proteins," Science (80-. )., vol. 301, p. 1827, 1884.
14. C. A. Savran, S. M. Knudsen, A. D. Ellington, and S. R. Manalis, "Micromechanical Detection of Proteins Using Aptamer-Based Receptor Molecules," vol. 76, no. 11, pp. 3194–3198, 2004.
15. S. Song, Y. Qin, Y. He, Q. Huang, C. Fan, and H. Y. Chen, "Functional nanoprobes for ultrasensitive detection of biomolecules," Chem. Soc. Rev., vol. 39, no. 11, pp. 4234–4243, 2010.
16. C. Jin, K. Wang, A. Oppong-Gyebi, and J. Hu, "Application of nanotechnology in cancer diagnosis and therapy - A mini-review," Int. J. Med. Sci., vol. 17, no. 18, pp. 2964–2973, 2020.

17. C. Loo et al., “Nanoshell-Enabled Photonics-Based Imaging and Therapy of Cancer,” 2015.
18. A. Manuscript, “rsc.li/analyst,” 2018.
19. D. G. Van Der Poll et al., “Design , Synthesis , and Biological Evaluation of a Robust , Biodegradable Dendrimer,” pp. 764–773, 2010.
20. D. Kim, Y. Y. Jeong, and S. Jon, “A drug-loaded aptamer - Gold nanoparticle bioconjugate for combined ct imaging and therapy of prostate cancer,” ACS Nano, vol. 4, no. 7, pp. 3689–3696, 2010.
21. F. Siaw-debrah, M. Nyanzu, and Y. Zhang, Nanomaterial Applications for Neurological Diseases and Central Nervous System Injury. Elsevier Ltd, 2017.
22. Fan R, Heath JR et al. Integrated barcode chips for rapid, multiplexed analysis of proteins in microliter quantities of blood. Nat Biotechnol. 2008;26:1373-8.
23. D. A. Tomalia, “Dendrimers in biomedical applications — reflections on the field B So,” vol. 57, pp. 2106–2129, 2005.
24. G. J. Zhang and Y. Ning, “Silicon nanowire biosensor and its applications in disease diagnostics: A review,” Anal. Chim. Acta, vol. 749, pp. 1–15, 2012.
25. Gaster RS, Hall DA, Wang SX. nanoLAB: an ultraportable, handheld diagnostic laboratory for global health. Lab Chip. 2011; 7;11:950-6.
26. Haun JB, Castro CM, Wang R, Peterson VM, Marinelli BS, Lee H, Weissleder R. Micro-NMR for rapid molecular analysis of human tumor samples. Sci Transl Med. 2011;3:71ra16.
27. J. Hoon, K. Seon, J. Park, K. Hyun, D. Sung, and T. Song, “Immunoassay of prostate-specific antigen ( PSA ) using resonant frequency shift of piezoelectric nanomechanical microcantilever,” vol. 20, pp. 2157–2162, 2005.
28. J. Hu, W. Huang, S. Huang, Q. Zhuge, and K. Jin, “Magnetically active Fe 3 O 4 nanorods loaded with tissue plasminogen activator for enhanced thrombolysis,” vol. 9, no. 9, pp. 2652–2661, 2016.
29. D. S. Goldberg, N. Vijayalakshmi, P. W. Swaan, and H. Ghandehari, “G3 . 5 PAMAM dendrimers enhance transepithelial transport of SN38 while minimizing gastrointestinal toxicity,” J. Control. Release, vol. 150, no. 3, pp. 318–325, 2011.
30. A. Manuscript, “NIH Public Access,” vol. 39, no. 11, pp. 4326–4354, 201.

31. J. Li, M. Yao, Y. Shao, and D. Yao, “The application of bionanotechnology in tumor diagnosis and treatment: A view,” Nanotechnol. Rev., vol. 7, no. 3, pp. 257–266, 2018.
32. J. M. Nam, S. I. Stoeva, and C. A. Mirkin, “Bio-Bar-Code-Based DNA Detection with PCR-like Sensitivity,” J. Am. Chem. Soc., vol. 126, no. 19, pp. 5932–5933, 2004.
33. J. Wang, M. Sui, and W. Fan, “Nanoparticles for Tumor Targeted Therapies and Their Pharmacokinetics,” Curr. Drug Metab., vol. 11, no. 2, pp. 129–141, 2010.
34. Jiang et al. A comparison of isolated circulating tumor cells and tissue biopsies using whole-genome sequencing in prostate cancer. Oncotarget 2015.
35. K. K. Alharbi and Y. A. Al-sheikh, “Role and implications of nanodiagnostics in the changing trends of clinical diagnosis,” Saudi J. Biol. Sci., vol. 21, no. 2, pp. 109–117, 2014.
36. Lin et al. Nanostructure Embedded Microchips for Detection, Isolation, and Characterization of Circulating Tumor Cells. Accounts of Chemical Research 2014.
37. M. Cristofanilli, “Circulating Tumor Cells, Disease Progression, and Survival in Metastatic Breast Cancer,” Semin. Oncol., vol. 33, no. SUPPL. 9, pp. 9–14, 2006
38. M. Y. Shen, B. R. Li, and Y. K. Li, “Silicon nanowire field-effecttransistor based biosensors: From sensitive to ultra-sensitive,” Biosens. Bioelectron., vol. 60, pp. 101–111, 2014.
39. N. R. Jabir, S. Tabrez, G. M. Ashraf, S. Shakil, G. A. Damanhouri, and M. A. Kamal, “Nanotechnology-based approaches in anticancer research,” Int. J. Nanomedicine, vol. 7, pp. 4391–4408, 2012.
40. Y. E. Choi, J. W. Kwak, and J. W. Park, “Nanotechnology for early cancer detection,” Sensors, vol. 10, no. 1, pp. 428–455, 2010.
41. S. Alshehri et al., “Progress of cancer nanotechnology as diagnostics, therapeutics, and theranostics nanomedicine: Preclinical promise and translational challenges,” Pharmaceutics, vol. 13, no. 1, pp. 1–35, 2021.
42. Nam JM, Thaxton CS, Mirkin CA. Nanoparticle-based bio-bar codes for the ultrasensitive detection of proteins. Science. 2003; 26;301:1884-6.
43. Park et al., Molecular profiling of single circulating tumor cells from lung cancer patients. PNAS 2016.

44. Phillips et al. Clinical translation of an ultrasmall inorganic optical PET imaging nanoparticle probe. Science Trans Med. 2016.
45. R. D. Loberg et al., "Detection and isolation of circulating tumor cells in urologic cancers: A review," Neoplasia, vol. 6, no. 4, pp. 302–309, 2004.
46. R. M. Kannan, E. Nance, S. Kannan, and D. A. Tomalia, "Emerging concepts in dendrimer-based nanomedicine : from design principles to clinical applications," no. 2009, pp. 579–617, 2014.
47. M. Gou et al., "Efficient Inhibition of C-26 Colon Carcinoma by VSVMP Gene Delivered by Biodegradable Cationic Nanogel Derived from Polyethyleneimine .pdf," vol. 4, no. 10, pp. 5573–5584, 2010.
48. R. Singh, "Nanotechnology based therapeutic application in cancer diagnosis and therapy," 3 Biotech, vol. 9, no. 11, pp. 1–29, 2019.
49. R. Toy, L. Bauer, C. Hoimes, K. B. Ghaghada, and E. Karathanasis, "Targeted nanotechnology for cancer imaging," Adv. Drug Deliv. Rev., vol. 76, no. 1, pp. 79–97, 2014.
50. S. Jia, R. Zhang, Z. Li, and J. Li, "Clinical and biological significance of circulating tumor cells, circulating tumor DNA, and exosomes as biomarkers in colorectal cancer," Oncotarget, vol. 8, no. 33, pp. 55632–55645, 2017.
51. J. R. Lee et al., "High-Resolution Analysis of Antibodies to Post-Translational Modifications Using Peptide Nanosensor Microarrays," ACS Nano, vol. 10, no. 12, pp. 10652–10660, 2016.
52. S. L. Troyan et al., "The FLARE Intraoperative Near-Infrared Fluorescence Imaging System : A First-in-Human Clinical Trial in Breast Cancer Sentinel Lymph Node Mapping," pp. 2943–2952, 2009.
53. S. Nie, Y. Xing, G. J. Kim, and J. W. Simons, "Nanotechnology applications in cancer," Annu. Rev. Biomed. Eng., vol. 9, pp. 257– 288, 2007.
54. C. Dufe, W. N. Keith, A. Bilsland, I. Proutski, I. F. Uchegbu, and A. G. Scha, "Synthetic Anticancer Gene Medicine Exploits Intrinsic Antitumor Activity of Cationic Vector to Cure Established Tumors," no. 18, pp. 8079–8085, 2005.
55. Shuhendler et al. Molecular Magnetic Resonance Imaging of Tumor Response to Therapy. Scientific Reports 2015.

56. T. R. Arunraj, N. Sanoj Rejinold, N. Ashwin Kumar, and R. Jayakumar, “Bio-responsive chitin-poly(l-lactic acid) composite nanogels for liver cancer,” Colloids Surfaces B Biointerfaces, vol. 113, pp. 394–402, 2014.
57. U. Yezdani, M. G. Khan, N. Kushwah, A. Verma, and F. Khan, “Aplication of nanotechnology in diagnosis and treatment of various diseases and its future advances in medicine,” World J. Pharm. Pharm. Sci., vol. 7, no. 11, pp. 1611–1633, 2018.
58. N. Y. Morgan et al., “Real Time In Vivo Non-invasive Optical Imaging Using Near-infrared Fluorescent Quantum Dots 1,” no. 1, pp. 313–323, 2005.