HIGH SCHOOL EDITION
Journal of Student Research
Volume 13 Issue 4 (2024)

Nanotechnology in Early Cancer Detection and Treatment

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ABSTRACT

Breast cancer is one of the leading causes of cancer deaths worldwide. Diagnosis and treatment are usually quite challenging. The standard techniques of diagnosis, like MRI and CT scans, often lack the ability to detect the disease in its early stages, while invasive ones like biopsy may include certain discomfort and risks. Nanotechnology, a type of technology that operates at the molecular level, offers solutions to these challenges. It talks about the application of nanotechnology in the detection and treatment of early-stage breast cancer, focusing on nano-enabled biosensors and nanoparticles. Nano-enabled biosensors can detect cancer biomarkers in body liquids, providing a non-invasive alternative to the conventional techniques of imaging. At the same time, nanoparticles enhance treatment efficacy owing to their potential for precise targeting of cancer cells, which reduces the side effects compared to conventional chemotherapy. This review also explores recent preclinical and clinical studies discussing the latest advances, such as bifunctional nanoprobes, fluorescent nano sensors, and ultra-pH-sensitive nanoparticles. Despite these advances, certain challenges remain regarding both biocompatibility and long-term safety. Continued research and exploration will be necessary fully to utilize the potential of nanotechnology in improving the detection and treatment of breast cancer. Basically, nanotechnology represents a huge step in the development of early detection and effective treatments, which can ensure happier and healthier patients.

Introduction

Cancer is a diagnosis that can change one's life forever. It is a disease in which some cells grow uncontrollably and can spread across the entire body. Anyone can develop cancer regardless of gender, race, or place of habitation. Specifically, breast cancer is prominent in every single country. This type of cancer is mainly found in women, but men aren't an exception either, as anyone with breast tissue can be diagnosed with breast cancer. It doesn't affect one ethnicity or race more than the other, but studies show that African American women have a higher death rate from breast cancer, due to a triple-negative diagnosis, which is the most lethal type of breast cancer. The global incidence number of breast cancer as of 2022 was 2.3 million diagnoses, and the global mortality number was 670,000. In countries with a high human development index, 1 in 12 women will be diagnosed with breast cancer, and 1 in 71 women will die of it. In countries with a low human development index, 1 in 27 women will get breast cancer, and 1 in 48 women will die of it. In the United States, there is a 13% (1 in 3) chance a woman will get breast cancer, and a 2.5% (1 in 39) chance she will die from it. (American Cancer Society, 2024). Cancer patients go through radiation therapy and chemotherapy, which are extremely physically and mentally arduous treatment processes. In this process, patients experience hair loss, constant fatigue, changes in mood, and memory loss. Chemotherapy can also cause long-term damage to the liver, heart, or lungs. It causes death in 25% of cancer patients and has hastened death in about 27% of cases (Megget et al., 2008).

When it comes to detecting cancer at its earlier stages, the current detection techniques have many limitations. For example, classic imaging techniques such as MRI scans, CT scans, or X-rays, fail to detect a tumor at its early stages. Sometimes, these methods may result in a false positive or negative, which quite literally means life or death for the patient. In addition, biopsies are incredibly invasive procedures and can be uncomfortable or dangerous for patients depending on where the tumor is located. There needs to be an alternative option when it comes to approaching cancer detection.

Nanotechnology, a new development in modern medicine, can be used for early cancer detection, treatment, and therapies. Nanoparticles are 100 - 10,000 times smaller than a human cell and can interact with the inside and outside of a biomolecule, a characteristic that is being exploited to develop novel early detection as well as therapeutic strategies for various types of cancer. Nanoparticles can also be used for tumor-targeted delivery of chemotherapeutic drugs to minimize undesirable side effects. This review article will examine the progress and development of nanotechnology, specifically focusing on the utilization of nano-enabled biosensors for the early detection and treatment of breast cancer, it will also explore ongoing preclinical and clinical studies in which nano-enabled biosensors are being applied in combination with other therapies for breast cancer.

Methodology

The objective of this review article is to focus on the different uses for nanotechnology regarding early cancer detection and treatment. This study will specifically focus on current cancer nano-therapies that are being produced in hopes of targeting biomarkers directly. Recent advancements in nanotechnology have shown an improvement in bone metastasis in breast cancer (Zhu, Yu et al., 2024). Different types of nanoparticles, such as polymeric micelles, liposomes, and dendrimers, have been created to effectively target bone metastases. By functionalizing these nanoparticles with ligands like alendronate, which have a strong affinity for bone tissue, they can selectively deliver drugs directly to the bone microenvironment (Chen et al., 2022). This review article will explore the differences in current methods of cancer detection and treatment compared to methods that incorporate nanotechnology. This study is a review of existing literature, focusing on research articles and observations about nanotechnology in early diagnoses, treatment and related biomarkers. It will involve analyzing previous research with help from two professors. Since the study doesn't involve new experiments or use physical tools, ethical issues are not a concern. To reduce biases, the study will use various online sources, cross-check information, and seek advice from the professors as needed.

Breast Cancer: Types, Symptoms, and Causes

Symptoms and Types of Breast Cancer

With the various types of breast cancer, there are also many symptoms that can raise questions. Every type of breast cancer has the following symptoms in common with each other; new lump in the breast or underarm, thickening/swelling of part of the breast, irritation/dimpling of breast, flaky skin or redness in nipple area, discharge or blood coming from nipple (does not include breastmilk), or over pain in nipple (CDC, 2024). There are 4 subtypes of breast cancer: luminal A, luminal B, human epidermal growth factor receptor 2-positive (HER2), and triple negative. Luminal A breast cancer (Group 1) involves tumors that are estrogen receptor (ER) and progesterone receptor (PR) positive, but HER2 negative. This means that those diagnosed with luminal A breast cancer are more likely to benefit from hormone therapy and chemotherapy. Luminal B breast cancer (Group 2) involves tumors that are ER and HER2 positive, but PR negative. Like luminal A, those diagnosed with luminal B breast cancer are likely to benefit from hormone therapy and chemotherapy, as well as HER2-targeted treatment. HER2-positive breast cancer (Group 3) includes tumors that are ER and PR negative, but HER2-positive. HER2-positive breast cancer patients are recommended to go through chemotherapy and HER2-targeted treatments. Finally, triple-negative breast cancer (Group 4, basal-like), the most lethal type of breast cancer, includes tumors that are ER, PR, and HER2 negative. Patients with triple-negative breast cancer are likely to benefit from chemotherapy (Mayo Clinic, 2022)

Causes of Breast Cancer

Breast cancer is initially caused by a genetic mutation. Women that have the inherited genetic mutation BRCA 1 or BRCA 2 (BRCA1/2) have an increased risk factor of 60% for developing breast cancer. Other causes of breast cancer include age, family/personal history of breast cancer, alcohol, obesity, a sedentary lifestyle, and not breastfeeding. BRCA is critical in identifying DNA damage (NCI, 2024). BRCA 1 is involved in initiating the repair process, while BRCA 2 initiates the binding of the RAD51 protein and single-strand DNA. This is part of homologous recombination, a process that permits repair and ensures that the DNA sequence is restored. If BRCA 1 or BRCA 2 is mutated during the process of repair, the homologous recombination process is diminished. This mutation causes the formation of other genetic mutations and abnormalities in the chromosome, leading normal cells to then transform into cancer cells. However, BRCA dysfunction is not sufficient to initiate tumor formation; apoptosis must be disrupted. Apoptosis (programmed cell death) is an imperative step for tumor suppression as it halts the growth of dysfunctional cells from proliferating; hence forming tumors. The main regulator in the process of apoptosis is the p53 gene. It triggers the cell cycle, a cycle of which involves apoptosis, if the damage done to a cell is too dangerous. If this gene is mutated, it causes a chain of reactions, ultimately leading to the proliferation of cancer cells, and in turn forming a tumor.

Current Treatments

Current standard therapies used to treat breast cancer include surgery, radiation, hormone therapy, chemotherapy, and immunotherapy. There are also other treatments being developed. HER2-targeted treatments, which destroys the HER2 protein, a protein which promotes cancer cell growth. Another type of targeted treatment are CDK4/6 inhibitors which targets the proteins that promote cell division. Immunotherapy involves checkpoint inhibitors, which are antibodies that target and remove the checkpoints that the tumors use to block activated immune cells. Cancer vaccines that can stimulate the immune system to fight against breast cancer are currently being researched. Gene therapy is another type of therapy that is being researched. Gene-editing technologies will be made to undo gene mutations that end up causing breast cancer. (Chehelgerdi, M., Chehelgerdi, M., Khorramian-Ghahfarokhi, M. et al. 2024). Nanotechnology based treatments solely target the cancer biomarker and have minimal effect on surrounding tissue. Nanoparticles deliver chemotherapy to the tumor cells only, which potentially leads to healthier and happier patients.

Current Detection Techniques

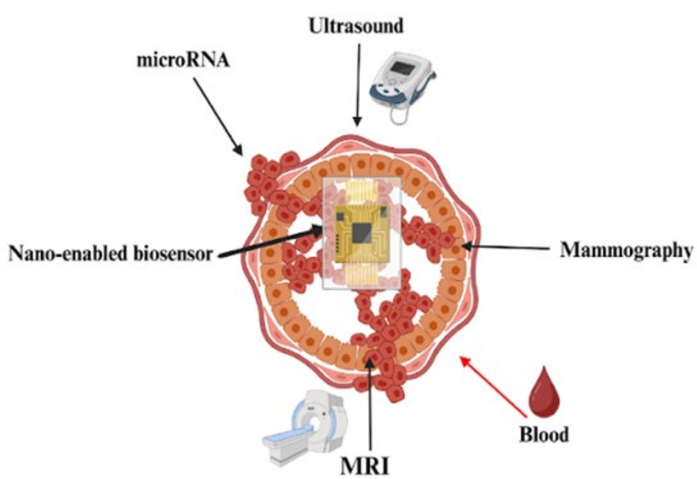

Figure 1. Early Detection Methods in Breast Cancer Cell (created by Lakshmi Trivedi using Biorender)

This figure shows current and common breast cancer imaging techniques. When it comes to the detection of breast cancer cells, mammography (screening/diagnostic) is the most used technique (Mayo Clinic, 2024). Screening mammograms use low dose X-rays to image and detect tumors. Diagnostic mammograms are used when symptoms of breast cancer show up, or the results in a screening mammogram involve something unusual. In second place comes the ultrasound, a tool that uses sound waves that produce images to help differentiate between masses and cysts. Last, is magnetic resonance imaging (MRI), which is used to explore areas that may inflict concern found by a mammogram. This non-invasive detection technique produces images that are precise and detailed due to its use of magnetic fields and radio waves. Functional MRI can detect nonmalignant tumors from a malignant tumor. Immunochemical techniques are used to detect microRNA and blood samples. Immunohistochemical techniques (IHC) are commonly used to detect breast cancer cells. IHC is done by taking a tissue sample from a breast biopsy and uses the antibodies that are specific to the HER2 protein (Seladi-Schulman et al., 2022). The results are based on how much the color changed in the tissue sample once the test has been fully conducted. The results help guide decisions about treatment, and whether one should use hormone therapy or targeted therapies.

Development of Nanotechnology for Detection & Treatment

Developments in nanotechnology for the detection and treatment of breast cancer have progressed over the past few decades. The first discovery of nanotechnology's potential to improve the study of medicine was in the 1980s, when it kicked off with the developments of cluster science and the scanning tunneling microscope (Brown et al., 2019). Then, researchers focused on using nanoparticles for drug delivery, and those theories were proven right in the 1990s, when the first experimental studies showed that nanoparticles can aid in drug delivery to tumors and cancer cells. Carbon nanotubes were also discovered during this time, which was a groundbreaking development for the field. This era of early research is what initiated the growth of nanoscience in the medical field in the 2000s. On September 13, 2004, the National Cancer Institute (NCI) launched the Alliance for Nanotechnology in Cancer - "a five-year initiative to integrate nanotechnology development into basic and applied cancer research to facilitate the rapid application of this science to the clinic." In the mid 2000s, the first nanoparticle-based drug, "Doxil" (Doxorubicin-loaded nanoparticles) was approved by the FDA, which showed better efficacy with reduced side effects in comparison to free doxorubicin treatment (Barenholz et al., 2012). Nanoscience research has grown exponentially in the 2010s. Incredible advancements in multifunctional nanoparticles, including imaging, therapies, and drug delivery, are made. Theranostics - a unique approach to diagnosing and treating cancer patients with the use of radiotracers (compound of radiation and chemicals that bind to a biomarker), is introduced (Hosseini et al., 2023). In the mid-late 2010s, highly sensitive nano sensors that can react to pH levels in a tumor's microenvironment were developed (Kumar, Um, Park et al., 2020) Currently, researchers are focused on improving the accuracy of nanoparticles' ability to specifically target a biomarker or cancer cells, and integrating technology with other treatments. In the future, nano scientists hope to develop something that can provide a precise approach to early cancer diagnosis and treatment, and in turn leading to more effective treatments and reduced side effects.

Recent and Ongoing Pre-Clinical and Clinical Studies Using Nano Sensors

Nano-enabled biosensors can be used to detect extracellular biomarkers, such as tumor DNA and extracellular vesicles. These biosensors are composed of 3 main components, which include bioreceptors, transducers, and nanomaterials. The 1st step is signal generation. The bioreceptor (a biological element) binds to the biomarker, which then induces a change that a transducer can detect. There are 3 forms that this change occurs in: electrical, optical, or mechanical. The 2nd step is signal transduction, where the transducer converts this interaction into a viable signal. The 3rd step is the processing of said signal. It is processed using a computer which displays an output which correlates with the target sample (Ramesh et al., 2023) Nano-enabled biosensors are more efficient than CT or MRI due to their ability to identify and bind cancer biomarkers at the molecular level. Any bodily fluid can be used as a sample, but it depends on the type of cancer. Furthermore, in cancer treatment and therapy, nanotechnology offers benefits beyond just drug delivery. Nanoparticles possess physical properties such as energy absorption and reradiation. These particles are also miniscule enough to amass at the site of the tumor, but are also sizable enough to hold pharmaceutical compounds, which can be used to fight the tumor directly. Some recent/ongoing studies on the use of nanotechnology in cancer detection or therapy are summarized in Table 1 and Table 2 below.

Table 1. Pre-clinical Studies using Nanotechnology in the detection or treatment for Breast Cancer

Institute	Type of Breast Cancer	Type of nanotech used	Biomarker or pathway	Therapy or detection
UNICAMP, Brazil.	Triple negative breast cancer	Bifunctional nanoprobe combined with photodynamic therapy	Does not specify	Therapy
Zhejiang University, China	MCF-7 Breast Cancer	Fluorescent nano sensor	Does not specify	Detection
University of Texas, Austin	Various types of breast cancer	Ultra-pH-sensitive polymeric nanoparticles	Biomarkers	Detection
University of Texas, Austin	Various types of breast cancer	Self functionalized 3D nano sensor	Stem cell pathways	Detection

A pre-clinical study conducted by the UNICA MP Institute in Brazil, explores bifunctional nanoprobes combined with photodynamic therapy to treat triple-negative breast cancer. This type of breast cancer excessively overexpresses the epidermal growth factor receptor (EGFR), which leads to a deficient prognosis, and higher risk of recurrence. The bifunctional nanoprobe in this study uses gold nanoparticles and Chlorine e6 to target the EGFR, and in turn increases the effectiveness of photodynamic therapy. The study showed that the bifunctional nanoprobe combined with photodynamic therapy improves selectivity to tumor tissue and tissue damage.

Another pre-clinical study conducted by Zhejiang University in China, explores the use of fluorescent nano sensors for identifying cancer cells. The fluorescent nano sensor detects ascorbic acid (AA) and glutathione (GSH), both of which are the most intracellular reactive substances, and are commonly used as biomarkers for cancer cell detection. The nano sensor uses biocompatible fluorescent silicon nanoparticles (SiNPs), which are then quenched by Fe^{3+} ions, followed by a recovery after a redox reaction with the reductive substances. This preclinical study shows the importance of the proper identification of cancer cells among normal cells, and the strategy used in this study can improve the detection of cancer cells through imaging.

In another study, conducted by the University of Texas at Austin discusses the use of ultra-pH-sensitive polymeric nanoparticles that behave like transistors. These nanoparticles are specifically and meticulously made to react to minute changes in pH levels, as these changes can develop the growth of the tumor's microenvironment. They can also be used for drug delivery due to their extreme sensitivity. This study shows how the development of technology, specifically nanotechnology can be used for the improvement in cancer treatment.

The last study in this table, also conducted by the University of Texas at Austin is centered around the enhancement of liquid biopsy methods for cancer diagnoses. It uses a model of a novel 3D nano sensor combined with extracellular vesicles from cancer stem cells. The use of surface enhanced Raman spectroscopy (SERS) and machine learning is what aids in the highly specific cancer detection and diagnosis.

Table 2. Clinical Studies using Nanotechnology in the detection or treatment for Breast Cancer

Clinical trial number	Institute	Type of Breast Cancer	Type of nanotech used	Biomarker or pathway	Therapy or detection
NCT01525966	City of Hope Medical Center	Triple negative breast cancer	Carboplatin and Paclitaxel Albumin-Stabilized Nanoparticle	Does not specify	Therapy
NCT05512468	Fujian Medical University Union Hospital	Triple negative breast cancer	Nano-carbon	Pathway	Therapy

A clinical study conducted by City of Hope Medical Center explores the effectiveness of a carboplatin and paclitaxel (2 chemotherapy drugs) albumin-stabilized nanoparticle used in breast cancer treatment before surgery takes place. This study targets patients with locally advanced or inflammatory forms of triple negative breast cancer (TNBC).

The next clinical study, conducted by the Fujian Medical University Union Hospital also explores the use of a nanocarbon particle in treating triple negative breast cancer. The nanotechnology used delivers drugs and treatment directly to the cancer cells to reduce side effects.

Conclusion

Nanotechnology now plays a real role in fighting breast cancer, enabling new ways of detection and treatment that are more precise than ever. Innovations such as nanoscale materials and devices now enable researchers to spot cancer at times much earlier than was heretofore possible. Such an improvement in diagnostic capability helps even in developing treatments. Tumor imaging with the use of nanoparticles and nano sensors has changed many of our conventional understanding of tumor behavior and quick responsiveness by the doctors. Regarding the treatment, nanotechnology has come up with some very promising methods in targeting directly at cancerous cells without harming healthy tissue. Still, we are within a challenge to make sure that such technologies are not harming the long-term utilization. More research and collaborations are needed in the way forward to deal with these issues, so that these technologies bring maximum benefit to the patient. Overall, nanotechnology opens new horizons in the field of early detection and treatment of breast cancer. Further progress in research promises better outcomes and hope for those suffering from this disease.

Limitations

This review article does have a few limitations. First, this paper does not consist of any original research. It is based on existing literature and previously conducted studies, therefore limiting the ability of presenting original conclusions based on the data that has been collected. Second, this paper does not consider the cost and difficulty of maintaining nanotechnology in clinical practices. Third, this review article implements findings from specific studies, not considering widespread practice and how the efficacy of nanotechnology-based treatments can vary depending on the type of breast cancer, demographics, etc. Finally, it also does not touch on disparities in healthcare and how ethics plays a role in the usage and possession of such advanced equipment.

Acknowledgments

I would like to thank Dr. Prahlad Parajuli, Professor Virgel Torremocha, my Gifted Gabber mentor Srikha Manubolu, and Coach Jo for giving me the proper guidance and support throughout my research.

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