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NANOBOT : NOVELTY IN CANCER TREATMENT

Nirant Institute of Pharmacy, Boramani ,Solapur

By

Miss. Giram Aarti Kashinath B. pharm.

Under the Guidance of

Mrs. R.R. Kotwal

1. INTRODUCTION

Nanorobotics is a branch of nanotechnology engineering dedicated to developing atomic, molecular, and cellular nanorobots with precise nanoscale manipulation capabilities. Their applications in oncology, especially in cancer detection, diagnostics, drug administration, and treatment, hold immense potential. Nanotechnology can enhance cancer imaging sensitivity, overcome medication resistance, and improve the treatment of metastatic cancer. However, the design cost and associated challenges present significant limitations. Extensive research is necessary to overcome these obstacles and fully exploit the potential of nanobots. In the next decade, it may become possible to infuse our bloodstream with microscopic nanorobots that aid in maintaining our health and even facilitate the transfer of our thoughts to a wireless cloud. Operating at the molecular level, these nanorobots would preserve our biological systems and ensure a healthy and prolonged life. While still in the

early stages of design and experimentation, patents are emerging, underscoring a promising future for nanotechnology and nanobots. (1)

Researchers have emphasised nanotechnology as an outstanding technological trend in the last few decades, and it is characterized by the fast proliferation of electronics for applications in communication, known as nanomedicine, and environmental monitoring. Studies are now being conducted on the scientific bottlenecks that affect the lifespan of the living, particularly humans. Among these constraints are illnesses with few or no alternatives for treatment and healing. A drug delivery system (DDS) refers to an alternative diagnosis and/or therapy that has been shown in the medical fraternity [2,3]]. Nanorobots are nanoelectromechanical systems (NEMS), a recently developed chapter in miniaturisation, similar to microelectromechanical systems (MEMS), which is already a multibilliondollar business. Designing, architecting, producing, programming, and implementing such biomedical nanotechnology are all part of nanorobotics and NEMS research. Any scale of robotics includes calculations, commands, actuation and propulsion, power, data-sharing, interface, programming, and coordination. There is heavy stress on actuation, which is a key prerequisite for robotics [2]. The similarity in size of nanorobots to that of organic human cells and organelles brings up a huge variety of its possible uses in the field of health care and environmental monitoring of microorganisms. Other potential uses, such as cell healing, may be possible if nanorobots are tiny enough to reach the cells. Furthermore, it is still to be realised that the tiny sensors and actuators' square measures are necessary for the growing concept of a strongly connected ascending information technology infrastructure; the envision of artificial cells (nanorobots) that patrol the cardiovascular system, thus, detecting and destroying infections in minute quantities. This might be a programmable system with approachable ramifications in medicine, creating a revolutionary replacement from therapy to bar [2]. Chemotherapeutic substances employed in cancer treatment measure disseminates non-specifically throughout the body, where they exert an influence on both malignant and normal cells, restricting the drug quantity feasible within the growth and also resulting in unsatisfactory medication due to excessive toxic hazards of the chemotherapy drugs on normal cells of the body. It is safe to say that molecularly focused medical care has evolved as a collaborative method to overcome the lack of specificity of traditional cancer therapy drugs [4]. With the help of nanotechnology, intercellular aggregation of the drugs in cancer cells can be increased while minimising the risk of unwanted drug toxicity in normal cells by utilising various drug targeting mechanisms [5].

2. REVIEW OF LITERATURE

This review article focuses on the recent advancements, technological growth, and expansion in the field of nanorobotics and nanotechnology and its application in the discipline of bio-healthcare systems, principally for the DDS in the medication of cancer. Existing research literature and relevant studies regarding the topic of concern were read and a detailed analysis was undertaken in the indexes of PubMed, Science Direct, MEDLINE, Scopus, and Google Scholar. Hardly any language or time constraints were applied. To obtain a detailed search, more articles, synonyms, and derivatives of the phrases were employed; the following evaluation phrases were used: “drug delivery”, “cancer”, “neoplasms”, and “cancer therapy”.

2.1. NANOROBOTS & THERE TYPES :

There are many different types of nanorobots .

2.1.1. Smallest engine ever created:

“A group of physicists from the University of Mainz in Germany recently built the smallest engine ever created from just a single atom. Like any other engine, it converts heat energy into movement — but it does so on a smaller scale than ever seen before. The atom is trapped in a cone of electromagnetic energy and lasers are used to heat it up and cool it down, which causes the atom to move back and forth in the cone like an engine piston.”(6)

2.1.2. 3D-motion nanomachines from DNA:

“Mechanical engineers at Ohio State University have designed and constructed complex nanoscale mechanical parts using ‘DNA origami’ — proving that the same basic design principles that apply to typical full-size machine parts can now also be applied to DNA — and can produce complex, controllable components for future nanorobots.(6)

2.1.3. Nanoswimmers:

"ETH Zurich and Technion researchers have developed an elastic
"nanoswimmer" polypyrrole (Ppy) nanowire about 15 micrometers (millionths of a meter) long and 200 nanometers thick that can move through biological fluid environments at almost 15 micrometers per second…The nanoswimmers could be functionalized to deliver drugs and magnetically controlled to swim through the bloodstream to target cancer cells, for example."(6)

2.1.4. Ant-like nanoengine with 100x force per unit weight:

"University of Cambridge researchers have developed a tiny engine capable of a force per unit-weight nearly 100 times higher than any motor or muscle. The new nano-engines could lead to nanorobots small enough to enter living cells to fight disease, the researchers say. Professor Jeremy Baumberg from the Cavendish Laboratory, who led the research, has named the devices 'actuating nanotransducers' (ANTs). 'Like real ants, they produce large forces for their weight…' "(6)

2.1.5. Sperm-inspired microrobots:

"A team of researchers at the University of Twente (Netherlands) and German University in Cairo (Egypt) has developed sperm-inspired microrobots, which can be controlled by oscillating weak magnetic fields." They will be used in complex micro-manipulation and targeted therapy tasks.(6)

2.1.6. Bacteria-powered robots:
"Drexel University engineers have developed a method for using electric fields to help microscopic bacteria-powered robots detect obstacles in their environment and navigate around them. Uses include delivering medication, manipulating stem cells to direct their growth, or building a microstructure, for example."(6)

2.1.7. Nanorockets:

"Several groups of researchers have recently constructed a high-speed, remote-controlled nanoscale version of a rocket by combining nanoparticles with biological molecules…The researchers hope to develop the rocket so it can be used in any environment; for example, to deliver drugs to a target area of the body."(6)

2.2. CHEMOTHERAPY DRUG DELIVERY USING NANOROBOTS IN CANCER TREATMENT :

2.2.1. Mechanisms of Cellular Targeting

For effective cancer therapy, it is essential to develop or engineer a drug or gene delivery system that has an excellent ability to target tumor cells sparing the normal healthy cells. It enhances therapeutic efficacy, thereby shielding normal cells from the effect of cytotoxicity. It can be achieved by the well-organized delivery of NPs into the tumor microenvironment (TME), indirectly targeting cancer cells. These nanoformulations should pass through numerous physiological and biological barriers. These barriers are complex systems of several layers (epithelium, endothelium, and cellular membranes) and components (mechanical and physicochemical barriers and enzymatic barriers). These facts impose specifications with respect to the size, biocompatibility, and surface chemistry of NPs to prevent unspecific targeting. However, mere cytosolic internalization of an NP drug molecule does not mean it reaches its subcellular target. Specific engineering and optimization are mandatory to enable cellular or nuclear targeting.

Several studies have been carried out so far and several more are in progress to discover NP-based drug targeting design. These nanocarriers typically should possess certain fundamental characteristics such as

1) ability to remain stable in the vascular system (blood) until they reach their target, TME,
2) to escape the reticuloendothelial system (RES) clearance,
3) escape mononuclear phagocyte system (MPS),
4) accumulate in TME via tumor vasculature,
5) high-pressure penetration into the tumor fluid, and
6) reach the target and only interact with tumor cells [6]. The vital aspects such as surface functionalization, physicochemical properties, and pathophysiological characteristics regulate the process of NP drug targeting.

Generally, NPs considered apt for cancer treatment have a diameter range of 10–
100 nm. In order to understand the process of interaction and crosstalk between NP carriers and cancer cells and tumor biology, it is important to address the targeting mechanisms. The targeting mechanisms can be broadly classified into two groups, passive targeting and active targeting.

2.2.1.1. Passive Targeting

The observation of preferential accumulation of few macromolecules in cancer cells was found in the late 1980s. The first macromolecule to be reported to accumulate in the tumor was poly(styrene-co-maleic acid)-neocarzinostatin (SMANCS) by Matsuura and Maeda [6]. On further studies, this preferential distribution was attributed to the occurrence of fenestrations that are found in the damaged tumor blood vessels and to the poor lymphatic drainage, the amalgamation of which is known as “enhanced permeation and retention effect.”

Under certain conditions such as hypoxia or inflammation, the endothelium layer of the blood vessels becomes more permeable [7]. Under hypoxia situations, the rapidly growing tumor cells tend to put in action more blood vessels or engulf the existing ones to cope up. This process is known as neovascularization. These new blood vessels are leaky as they have large pores that lead to poor perm-selectivity of tumor blood vessels compared to the normal blood vessels [8,9]. These large pores or fenestrations range from 200 to 2000 nm depending on the cancer type, TME and localization [10]. This rapid and defective angiogenesis provides very little resistance to extravasation and permits NPs to diffuse from such blood vessels and ultimately collect within cancer cells.

In normal tissues, the drainage of ECF (extracellular fluid) into lymphatic vessels frequently happens at an average flow velocity of 0.1–2 μm/s, which maintains constant drainage and renewal [11]. When a tumor is formed, the lymphatic function gets derailed, which results in minimal interstitial fluid uptake [12]. This feature contributes to the NPs retention as they are not cleared and hoard in the tumor interstitium. This process denotes the enhanced retention part of the EPR effect. This exceptional feature does not apply to molecules with short circulation time and gets washed out rapidly from the cancer cells. Hence, to improve such situations, encapsulating these small molecules in nanosized drug carriers is routinely carried out to enhance their pharmacokinetics, provide tumor selectivity and reduce side effects [13].

Over the EPR effect, TME is a vital feature in passive targeting. One of the important metabolic features of rapidly proliferating tumor cells is glycolysis. It is the chief energy source for cell division [14] and makes the surrounding environment acidic. This lowered pH of TME can be exploited to use pH-sensitive NPs that release drugs at low pH [15].

This type of tumor-targeting is termed as “passive.” Passive targeting mainly relies on different tumor biology (vascularity, leakiness) and carrier characteristics (size and circulation time). This type of tumor-targeting does not possess a specific ligand for certain types of tumor cells. The EPR effect greatly relies on the fundamental tumor biology, such as

1) the degree or extent of angiogenesis and lymphangiogenesis,
2) the extent or degree of perivascular tumor invasion, and
3) intratumor pressure. These factors, combined with physicochemical characteristics of NPs, determine the efficiency of NP drug delivery system .

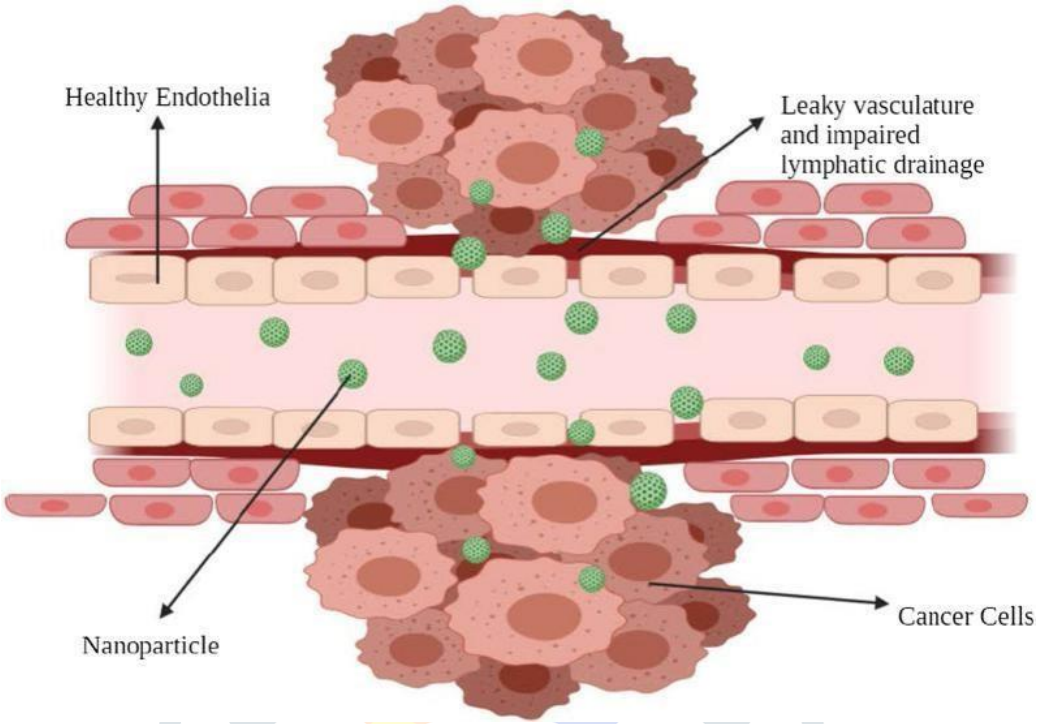


Fig 1 : Passive Targeting

Example of Passive Targeting

Taxanes are one of the most successful drug groups that are used in cancer treatment. Paclitaxel has shown great potency against a broad range of cancers. Breast cancer, lung cancer (small cell and non-small cell), and ovarian cancer are the most treated histologies with taxanes. US-FDA, in 2005, approved Abraxane® (albumin-bound paclitaxel, Abraxis Bio-Sciences), which is used for advanced or metastatic breast cancer (MBC).

2.2.1.2. Active Targeting

Active targeting depends on specific ligands or molecules, like transferrin and folate, which binds to molecules or receptors that are specifically expressed or over-expressed on the target cells (diseased organs, tissues, cells or subcellular domains) [16]. This type of targeting is called ligand-mediated targeting [17]. Here, the NPs that possess ligand with specific functions such as retention and uptake need to be in the target's proximity so that there is greater affinity. This strategy

enhances the changes of NPs binding to the cancer cell, enhancing the drug penetration. The foremost indication of the same was observed in 1980 with antibodies grafted in the surface of liposomes [13], followed by other various types of ligands like peptides, aptamers. Hence, the main method is intended at increasing the crosstalk between NPs and the target without fluctuating the total biodistribution [18]. The vital mechanism of active targeting or ligand-mediated targeting is ligand identification by the target substrate receptors. The illustrative ligands may include proteins, peptides, antibodies, nucleic acids, sugars, small molecules like vitamins, etc. [19]. The most commonly studied receptors are transferrin receptor, folate receptor, glycoproteins and the epidermal growth factor receptor (EGFR). Ligand-target interaction triggers infolding of the membrane and internalization of NPs via receptors-mediated endocytosis. There are various mechanisms by which active targeting takes place. The majority of tumor-targeting is done by the tumor cell targeting in general by NPs. This process improves cell penetration. As stated before, transferrin is one of the widely studied receptors. It is a type of serum glycoprotein that aids in transporting iron into cells. These receptors are found to be overexpressed in most tumor cells, especially solid tumors and are expressed at lower levels in healthy cells. Hence, we can modify the NPs with associated ligands that specifically target transferrin [20]. For instance, A2780 ovarian carcinoma cells overexpress transferrin. This feature is used by transferrin-modified PEGphosphatidyl-ethanolamine (Tf-Mpeg-pe) NPs that specifically target such cells [21]. Another alternative method is to target cells adjacent to cancer cells, such as angiogenic endothelial cells. These cells also have close contact with tumor blood vessels. This strategy makes it possible to create hypoxia and necrosis by reducing the blood supply to the cancer cells. It has been found out that tumor tissues are more acidic than normal ones. This has been extensively explained by the Warburg effect [22]. This explains the shift of cancer cell metabolism into glycolysis, forming lactic acid. When the lactic acid accumulates, the cell dies. To cope with this situation, the cells start overexpressing proton pumps that pump out excess lactic acid into the extracellular environment, making it more acidic.

Therefore, liposome-based pH-sensitive drug delivery system has been studied.

The multivalent nature of the NPs improves the crosstalk of ligand coated NPs with target cancer cells. The design of such NPs is complex as NP architecture and ligand-target chemistry influence the efficacy of the entire method. Other factors such as route of administration, physicochemical properties such as ligand density [23], and size of NPs contribute to the system's success ..

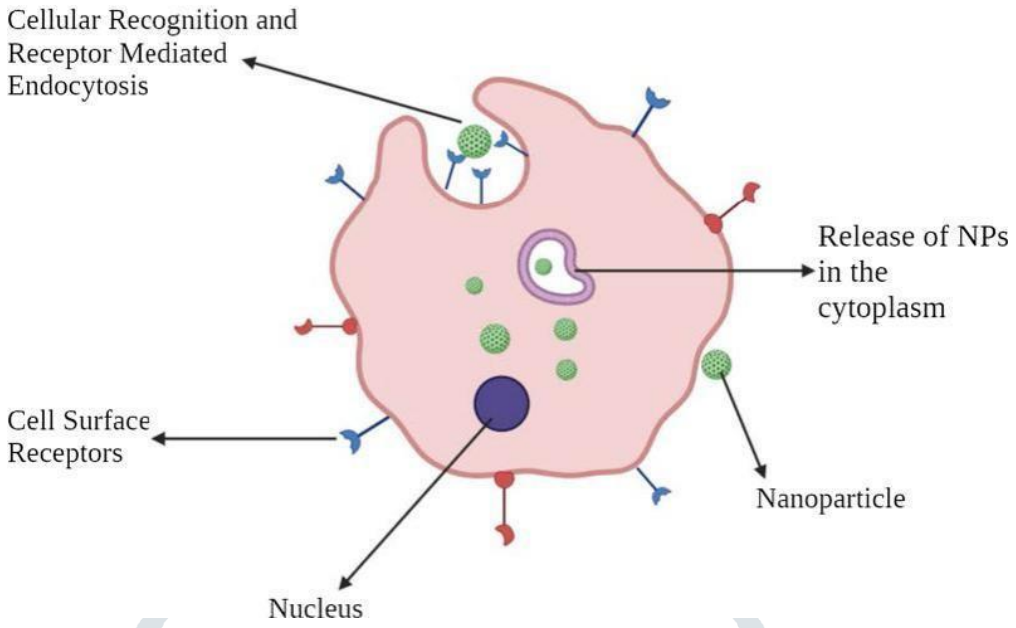


Fig 2 : Pictorial representation of active cellular targeting

Example of Active Targeting

Herceptin® is a therapeutic drug that targets human EGF receptor-2 (HER2) that is overexpressed on breast cancer cell surfaces. HER2-targeted PEGylated liposomal doxorubicin was developed to reduce cardiotoxicity, a known side effect of anthracyclines [24]

2.3. BENEFITS OF NANOTECHNOLOGY FOR CANCER

Modern medicine has significantly improved outcomes in cancer management, however the disease still causes over 600,000 deaths in the United States every year. While cancer treatments have advanced significantly, the need to increase their specificity and reduce systemic toxicity remains a challenge. As illustrated in the diagram below, nanotechnology presents opportunity to

(1) enhance earlier diagnosis through in vitro assays,

(2) enhance imaging capabilities for diagnosis and treatment monitoring, and

(3) improve therapeutic outcomes by refining targeting precision, augmenting localized drug efficacy, and minimizing systemic toxicity.[25]

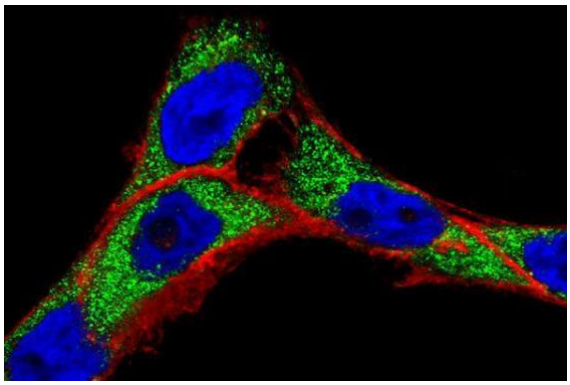


Fig 3 : Progress in cancer nanotechnology requires a better understanding of how molecularly-targeted nanoparticles interact with live cells.

Nanoparticles, being one hundred to ten thousand times smaller than human cells, possess the unique ability to interact with biomolecules on both the surface and inside cells. This broad access across various organs holds the potential to change how we think about cancer detection and treatment, leading to a multitude of research publications (as depicted in the figure below, Carolina Salvador Morales and Piotr Grodzinski, WIREs Nanomedicine and NanobiotechnologyExit Disclaimer, 2023). The application of nanoscale materials in cancer research relies on their design flexibility and tunability. For example, gold nanoparticles can be readily decorated with different ligands on their surfaces to facilitate an understanding of how they interact with live cancer cells (as shown in the top right image). By enabling rapid and sensitive detection of cancer-related molecules, nanotechnology empowers scientists to detect molecular changes, even in a small percentage of cells. Moreover, nanotechnology has the potential to generate entirely novel and effective therapeutic agents. In addition, nanomaterials exhibit the ability to passively accumulate at the tumor sites, actively target cancer cells, and traverse physiological barriers such as the blood-brain barrier or the stomach epithelium.[25]

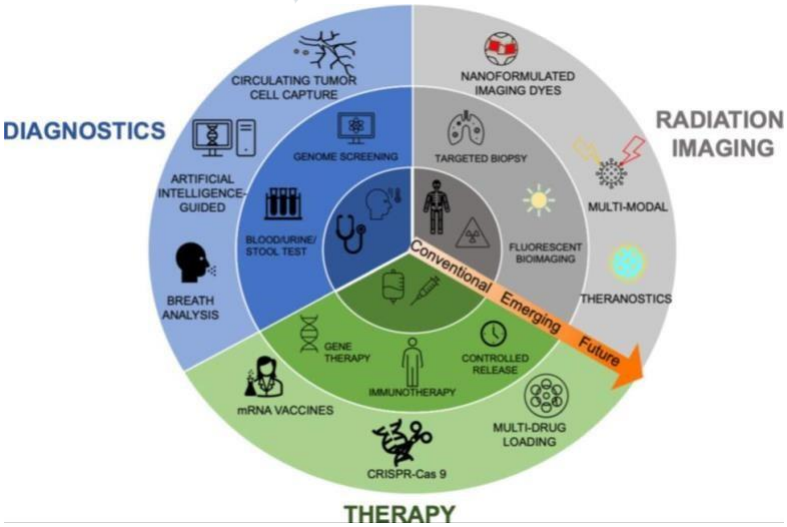
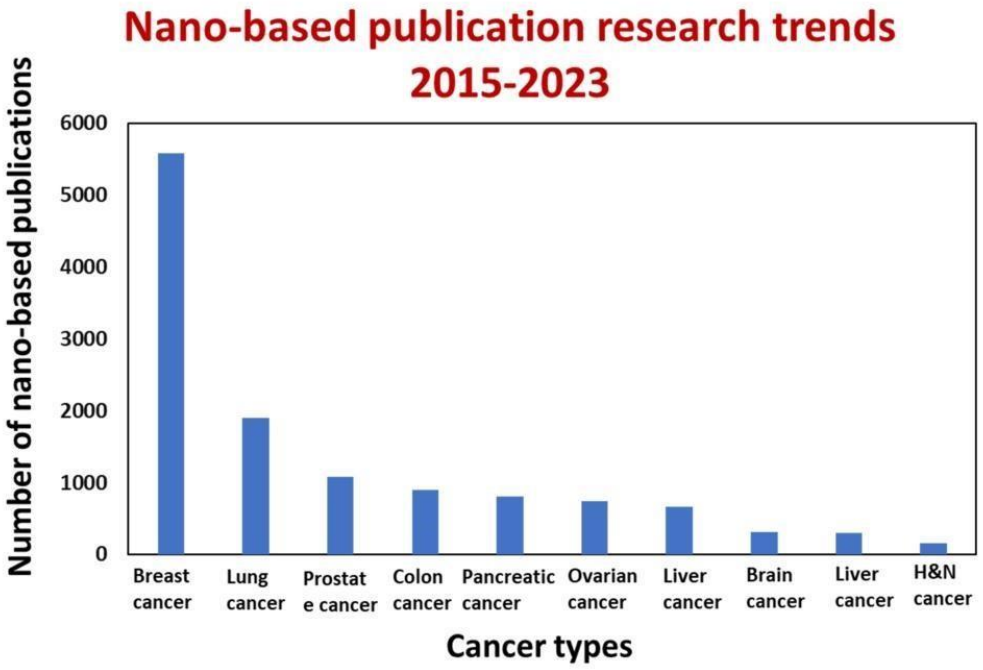


Fig 4 : Conventional cancer therapies, diagnostics, radiation treatments, and imaging can be significantly improved through nanotechnological applications. Source: Jessica A. Kemp and Young Jik Kwon, Nano Convergence, 2021



Nanotechnology-based interventions in different cancers. A 2015-2023 analysis using “nanoparticles” and “cancer type” search terms via iSearch. H & N: head and neck. Adapted from Carolina Salvador Morales and Piotr Grodzinski, WIREs Nanomedicine and Nanobiotechnology, 2023 [25]

Credit: Carolina Salvador Morales and Piotr Grodzinski, National Cancer Institute Updated: October 1, 2023

2.4. FUTURE OF NANOTECHNOLOGY IN THE AREA OF MEDICINE

To bring in combination the required collaborative skills to produce these unique technologies, numerous conventional streams of science, such as medicine, chemistry, physics, materials science, and biology, have come together to form the expanding field of nanotechnology. Nanotechnology has a vast span of possible applications (Fig 5) [26], from improvements to current practices to the creation of entirely new tools and skills. The last few years have observed an exponential increase of interest in the topic of nanotechnology and research, which has led to the identification of novel

applications for nanotechnology in medicine and the emergence of an advanced branch called nanomedicine. It includes the science and technology of diagnosing, treating, and preventing illness, traumatic injury, and alleviating pain; conserving and enhancing human health using nanoscale architectured materials, biotechnology, and genetic engineering; Eventually, complex machine systems and nanorobots, known as “nanomedicine” (Fig 6 [27, 28].

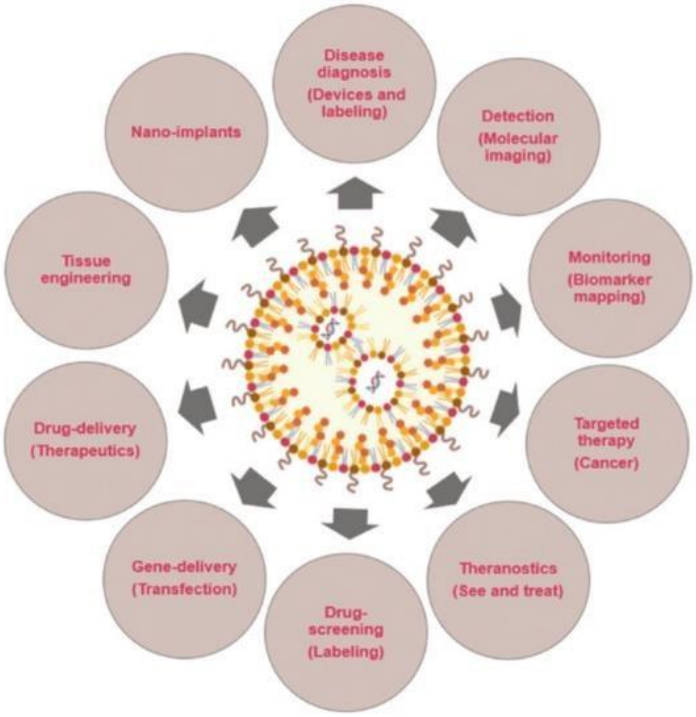


Fig 5: Illustration showing various other applications of nanotechnology in medicine.

The discovery of nanoparticles with the help of nanotechnology has led to its various uses in the area of medicine.

The nanoparticle so created can be employed for various uses like in the manufacturing of nano implants, tissue engineering for drug delivery systems, gene delivery systems, drug screening, theranostics, cancer therapy, Biomarker mapping, disease detection, and bio-imaging [26].

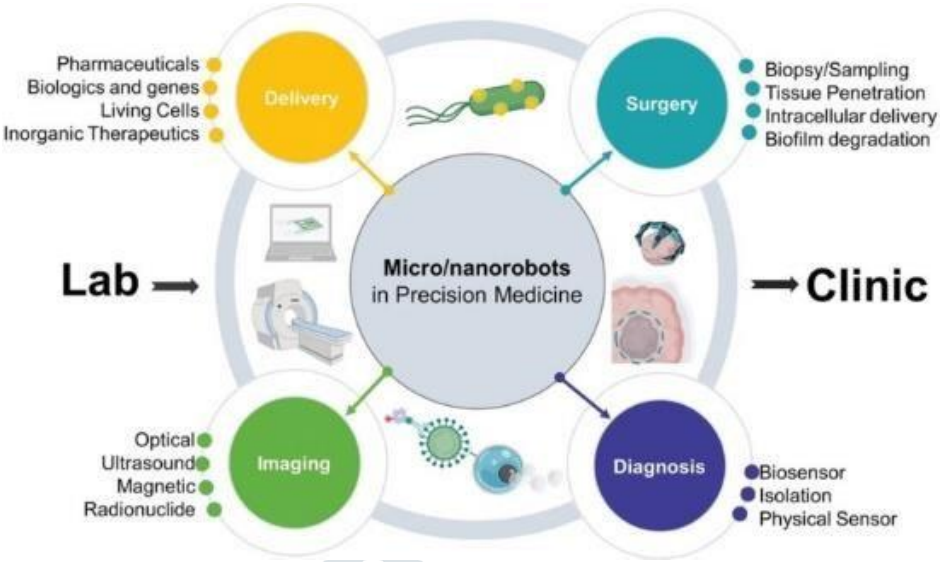


Fig 6: Schematic diagram of the current trends of Micro/nanorobotics in precision medicine.

Nanorobots are being used in various domains of pre-clinical and clinical medicine. In pre-clinical medicine,Nanorobots are being employed in bioimaging and various delivery systems of drugs, gene therapy, living cells, and inorganic therapeutics. Similarly, nanorobots in clinical medicine are being extensively used in disease diagnosis and surgeries for biopsy, biofilm degradation, tissue collection, and sampling [28].

Image reprinted from [28] under Creative Commons Attribution 4.0 International License.

In vivo diagnostics, nanomedicine might create technologies that can act within the human body to diagnose ailments earlier and identify and measure toxic chemicals and tumour cells. In the surgical aspect, when launched into the body through the intravenous route or cavities, a surgical nanorobot controlled or led by a human surgeon might work as a semi-autonomous on-site surgeon. An inbuilt computer might manage the device's operations, such as looking for disease and identifying and fixing injury by nanomanipulation while maintaining communication with the supervising surgeon via coded Ultrasonic signals [30]. By transforming mechanical energy from bodily movement, muscle stretching, or water flow into electricity, scientists were able to design a new generation of selfsustained implanted medical devices, sensors, and portable gadgets [26]. Nanogenerators generate electricity by bending and then releasing piezoelectric and semiconducting zinc oxide nanowires. Nanowires may be produced on polymer-based films, and the utilization of flexible polymer substrates may one day allow portable gadgets to be powered by their users' movement [26]. Fluorescent biological labelling, medication and gene delivery, pathogen identification, protein sensing, DNA structure probing, tissue engineering, tumour

identification, separation and purification of biological molecules and cells, MRI contrast enhancement, and phagokinetic research are among the uses. The extended duration effect of nanomedicine study is to describe quantitative molecular-scale components called nanomachinery. Accurate command and manipulation of Nanomachinery in cells can lead to a more diverse and advanced gain in the interpretation of cellular processes in organic cells, as well as the creation of new technologies for disease detection and medication. The advantage of this research is the formation of a platform technology that will affect nanoscale imaging methodologies aimed to investigate molecular pathways in organic cells [27, 29].

3. AIMS AND OBJECTIVES

3.1. OBJECTIVES :

The goal of cancer treatment is to achieve a cure for your cancer, allowing you to live a normal life span. This may or may not be possible, depending on your specific situation. If a cure isn't possible, your treatments may be used to shrink your cancer or slow the growth of your cancer to allow you to live symptom free for as long as possible.

Cancer treatments may be used as:

- Primary treatment. The goal of a primary treatment is to completely remove the cancer from your body or kill all the cancer cells. Any cancer treatment can be used as a primary treatment, but the most common primary cancer treatment for the most common types of cancer is surgery. If your cancer is particularly sensitive to radiation therapy or chemotherapy, you may receive one of those therapies as your primary treatment.

- Adjuvant treatment. The goal of adjuvant therapy is to kill any cancer cells that may remain after primary treatment in order to reduce the chance that the cancer will recur.
  Any cancer treatment can be used as an adjuvant therapy. Common adjuvant therapies include chemotherapy, radiation therapy and hormone therapy.
  Neoadjuvant therapy is similar, but treatments are used before the primary treatment in order to make the primary treatment easier or more effective.

- Palliative treatment. Palliative treatments may help relieve side effects of treatment or signs and symptoms caused by cancer itself. Surgery, radiation, chemotherapy and hormone therapy can all be used to relieve symptoms. Other medications may relieve symptoms such as pain and shortness of breath.

Palliative treatment can be used at the same time as other treatments intended to cure your cancer.[31]

3.2. AIM :

Many cancer treatments are available. Your treatment options will depend on several factors, such as the type and stage of your cancer, your general health, and your preferences. Together you and your doctor can weigh the benefits and risks of each cancer treatment to determine which is best for you.

Cancer treatment options include:

- Surgery. The goal of surgery is to remove the cancer or as much of the cancer as possible.
- Chemotherapy. Chemotherapy uses drugs to kill cancer cells.
- Radiation therapy. Radiation therapy uses high-powered energy beams, such as X-rays or protons, to kill cancer cells. Radiation treatment can come from a machine outside your body (external beam radiation), or it can be placed inside your body (brachytherapy).
- Bone marrow transplant. Your bone marrow is the material inside your bones that makes blood cells from blood stem cells. A bone marrow transplant, also knowns as a stem cell transplant, can use your own bone marrow stem cells or those from a donor.
- A bone marrow transplant allows your doctor to use higher doses of chemotherapy to treat your cancer. It may also be used to replace diseased bone marrow.
- Immunotherapy. Immunotherapy, also known as biological therapy, uses your body's immune system to fight cancer. Cancer can survive unchecked in your

body because your immune system doesn't recognize it as an intruder. Immunotherapy can help your immune system "see" the cancer and attack it.

- Hormone therapy. Some types of cancer are fueled by your body's hormones. Examples include breast cancer and prostate cancer. Removing those hormones from the body or blocking their effects may cause the cancer cells to stop growing.

- Targeted drug therapy. Targeted drug treatment focuses on specific abnormalities within cancer cells that allow them to survive.

- Cryoablation. This treatment kills cancer cells with cold. During cryoablation, a thin, wandlike needle (cryoprobe) is inserted through your skin and directly into the cancerous tumor. A gas is pumped into the cryoprobe in order to freeze the tissue. Then the tissue is allowed to thaw. The freezing and thawing process is repeated several times during the same treatment session in order to kill the cancer cells.

- Radiofrequency ablation. This treatment uses electrical energy to heat cancer cells, causing them to die. During radiofrequency ablation, a doctor guides a thin needle through the skin or through an incision and into the cancer tissue. High-frequency energy passes through the needle and causes the surrounding tissue to heat up, killing the nearby cells.

- Clinical trials. Clinical trials are studies to investigate new ways of treating cancer. Thousands of cancer clinical trials are underway.[31]

4. RESULT AND DISCUSSION

The development of immunotherapy has brought cancer treatment into a new era. NPs not only play an important role in delivery chemotherapy but have also shown great potential for applications in immunotherapy. Cancer immunotherapy is mainly achieved by activating the anti-tumor immune response (Zang et al., 2017). NP-associated immunotherapy includes

nanovaccines, artificial antigen-presenting cells (aAPCs), and targeting of the immunosuppressed tumor microenvironment (TME) (Zang et al., 2017).

Nanovaccines deliver tumor-associated antigens (TAAs) and adjuvants to APCs, such as dendritic cells (DCs) (Paulis et al., 2013). Additionally, NPs can be used as adjuvants themselves to increase APC antigen presentation and promote DC maturation, leading to the activation of the anti-tumor function of cytotoxic T cells (Shao et al., 2015; Yang et al., 2018). NPs, such as liposomes, gold NPs, PLGA NPs, micelles, and dendrimers all have the capability of cytoplasmic delivery of TAAs into DCs, thus enhancing the immune response against tumor cells (Guo et al., 2015). Among different types of NPs, inorganic NPs such as mesoporous silica and polymers such as acetylated dextran (AcDEX) have been shown to function as an adjuvant in immunotherapy, leading to a stimulation of the immune response (Fontana et al., 2017a, b). Unlike nanovaccines, artificial APCs function with MHCantigen complexes and co-stimulatory molecules that directly bind to T cell receptors (TCRs) and co-stimulatory receptors on T cells, respectively, resulting in T cell activation (Perica et al., 2014). Targeting the immunosuppressive TME is mainly achieved by targeting tumor-associated macrophages (TAMs), myeloid derived suppressor cells (MDSCs), and regulatory T cells (Tregs), all of which are important cell types in the TME (Shao et al., 2015). Furthermore, in order to minimize interactions with the reticuloendothelial system, NPs are usually modified with PEG (Zang et al., 2017).

In addition, the combination of chemotherapy and immunotherapy is a promising strategy of cancer treatment. For example, one study showed that co-loading of the chemotherapeutic agent Nutlin-3a and the cytokine GM-CSF in spermine-modified AcDEX NPs led to improved proliferation of cytotoxic CD8(+) T cells and stimulated immune response, leading to tumor cell death while avoiding toxicity in immune cells (Bauleth-Ramos et al., 2017). Alternative approaches of combined chemo-immunotherapy includes co-delivery of chemotherapeutics and monoclonal antibodies into porous silicon NPs, which have been effective in stimulating complement activation, antibody-dependent cell cytotoxicity (ADCC), and immune response against cancer cells (Li et al., 2018).

5. SUMMARY AND CONCLUSION

The main target of writing this review was to provide an outline of the technological development of nanotechnology in medicine by making a nanorobot and introducing it in the medication of cancer as a new mode of drug delivery. Cancer is described as a collection of diseases characterised by the unregulated development and spread of malignant cells in the body, and the number of people diagnosed every year keeps adding up. Cancer treatment is most likely the driving force behind the creation of nanorobotics; it can be auspiciously treated using existing medical technology and therapeutic instruments, with the major help of nanorobotics. To decide the prognosis and chances of survival in a cancer patient, consider the following factors: better prognosis can be achieved if the evolution of the disease is time-dependent and a timely diagnosis is made. Another important aspect is to reduce the side effects of chemotherapy on the patients by forming efficient targeted drug delivery systems. Programmable nanorobotic devices working at the cellular and molecular level would help doctors to carry out precise treatment. In addition to resolving gross cellular insults caused by non-reversible mechanisms or to the biological tissues stored cryogenically, mechanically reversing the process of atherosclerosis, enhancing the immune system, replacing or re-writing the DNA sequences in cells at will, improving total respiratory capacity, and achieving near-instant homeostasis, medically these nanorobots have been put forward for use in various branches of dentistry, research in pharmaceuticals, and aid and abet clinical diagnosis. When nanomechanics becomes obtainable, the ideal goal of physicians, medical personnel, and every healer throughout known records would be realized. Microscale robots with programmable and controllable nanoscale components produced with nanometre accuracy would enable medical physicians to perform at the cellular and molecular levels to heal and carry out rehabilitating surgeries. Nanomedical doctors of the 21st century will continue to make effective use of the body's inherent therapeutic capacities and homeostatic systems, since, all else being equal, treatments that intervene the least are the best.

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