



Review Article

Harnessing Nanorobotic Technology for Precision Cancer Treatment: A Comprehensive Review

Queeny Wilcy Noronha¹, Ramdas Bhat^{2*}

¹PG scholar, Department of Pharmacy Practice, Srinivas College of Pharmacy, Valachil, Farangipete Post, Mangalore, Karnataka, India. 574143

²Associate Professor, Department of Pharmacology, Srinivas College of Pharmacy, Valachil, Farangipete Post, Mangalore, Karnataka, India. 574143

Article Info

Abstract

Article history:

Manuscript ID:

IJPHI2022132024

Received: 20- July-2024

Revised :22-August-2024

Accepted: 13-September-2024

Available online: September
2024

Keywords:

Nanorobotics, Precision cancer treatment, Targeted drug delivery, Theranostics, Nanomedicine.

***Corresponding Author:**

ramdas21@gmail.com

This review explores the emerging field of nanorobotics and its applications in precision cancer treatment. Nanorobots, engineered devices ranging from 0.1-10 micrometers in size, offer unprecedented capabilities for targeted drug delivery, diagnostics, and therapeutic interventions at the cellular level. We examine the key types of nanorobots - organic, inorganic, and hybrid - highlighting their unique properties and potential applications. The review discusses critical features of nanorobots including size, targeting mechanisms, multifunctionality, biocompatibility, and controllability. Various fabrication techniques, from top-down to bottom-up approaches, are outlined. The paper provides a comprehensive overview of nanorobot applications in cancer treatment, including targeted drug delivery, diagnostics, therapeutic interventions, and surgical applications. Current research and early-phase clinical trials are reviewed, showcasing the progress and challenges in translating nanorobotic technologies from laboratory to clinic. Technical, biological, and ethical challenges are addressed, along with regulatory considerations. Finally, we explore future prospects and emerging trends, including advanced materials, AI integration, and Theranostics capabilities. This review underscores the transformative potential of nanorobotics in cancer treatment while acknowledging the hurdles that must be overcome for widespread clinical implementation.

@2024 IJPHI All rights reserve



This work is licensed under the Creative Commons Attribution 4.0 International License. To view a copy of this license, visit <http://creativecommons.org/licenses/by/4.0/> or send a letter to Creative Commons, PO Box 1866, Mountain View, CA 94042, USA

INTRODUCTION

Cancer remains one of the leading causes of death worldwide, with conventional treatments often limited by their lack of specificity and associated side effects [1]. The advent of nanotechnology has opened new avenues for cancer treatment, and its convergence with robotics has given rise to the promising field of nanorobotics [2]. This review article aims to provide a comprehensive overview of how nanorobotic technology is being harnessed for precision cancer treatment.

Nanorobots, also known as nanobots or nanomachines, are engineered devices or robots ranging in size from 0.1-10 micrometres, capable of performing specific tasks at the nanoscale [3]. In the context of cancer treatment, these miniature machines offer the potential for targeted drug delivery, precise surgical interventions, and real-time diagnostics at the cellular level. The integration of nanorobotics in cancer treatment aligns with the goals of precision medicine, which aims to tailor medical treatment to the individual characteristics of each patient [4]. By leveraging the unique properties of nanomaterials and the programmability of robotic systems, nanorobots can potentially overcome many of the limitations associated with traditional cancer therapies [5].

This review will explore the current state of nanorobotic technology in cancer treatment, discussing its applications, challenges, and future prospects. We will examine various types of nanorobots being developed for cancer therapy, their mechanisms of action, and the results of preclinical and early clinical studies. Additionally, we will address the technical, biological, and ethical challenges that need to be overcome for the widespread clinical implementation of this technology.

TYPES OF NANOROBOTS

Nanorobots are cutting-edge microscopic devices designed for various medical applications [2]. The Pharmacy, a 1-2 μ m medical nanorobot, can carry drugs and target

specific areas using molecular markers or chemotactic sensors. It's powered by glucose and oxygen from its environment and can be removed via centrifuge nanopheresis. The Respirocyte, an artificial oxygen carrier, mimics red blood cells but provides 236 times more oxygen to tissues. It uses endogenous serum glucose for power and efficiently manages oxygen and carbon dioxide transport through its onboard nano computer. Colonocytes are artificial mechanical platelets that achieve near-instant haemostasis, working 100-1000 times faster than the natural system. They use a biodegradable fiber mesh to stop bleeding rapidly and efficiently [5,6].

Other types of nanorobots include the Chromalloy, which can replace entire chromosomes in individual cells, potentially reversing genetic diseases and preventing aging. These repair machines examine the cell's contents and structure, working molecule-by-molecule to repair the entire cell. Lastly, cellular repair nanorobots are being developed to perform precise surgical procedures at the cellular level, potentially minimizing damage compared to traditional surgical methods. These various nanorobots represent the forefront of nanotechnology in medicine, offering unprecedented possibilities for targeted drug delivery, enhanced oxygen transport, rapid healing, genetic repair, and microsurgery [6].

KEY FEATURES OF NANOROBOTS FOR CANCER TREATMENT

Nanorobots designed for cancer treatment possess several key features that make them uniquely suited for this application. First and foremost is their size and scale, which allows them to operate at the cellular level. These nanoscale devices, typically ranging from 0.1 to 10 micrometres, can interact directly with cancer cells and penetrate tumor tissues [6]. This small size enables them to navigate through the body's complex vasculature and overcome biological barriers that often hinder conventional therapies. Moreover, their scale

allows for precise targeting of cancer cells while minimizing damage to healthy tissues, a crucial advantage in cancer treatment. Another critical feature of nanorobots is their targeting mechanisms, which can be both active and passive. Active targeting involves the use of specific ligands or antibodies on the nanorobot's surface that can bind to receptors overexpressed on cancer cells. This approach ensures a high degree of specificity in targeting tumor tissues. Passive targeting, on the other hand, takes advantage of the enhanced permeability and retention (EPR) effect often observed in tumor vasculature. The leaky blood vessels and poor lymphatic drainage in tumors allow nanorobots to accumulate preferentially in these areas. These targeting strategies, combined with the multifunctionality of nanorobots, enable them to perform various tasks such as diagnosis, drug delivery, and therapy monitoring, all within a single platform [6,7].

Biocompatibility and controllability are two additional crucial features of nanorobots for cancer treatment. Design considerations to ensure minimal toxicity and immune response are paramount, as these devices need to operate within the body without causing adverse effects. Materials used in nanorobot construction are carefully selected and engineered to be non-immunogenic and biodegradable when possible. Controllability is achieved through external control mechanisms such as magnetic fields, light, or ultrasound, which allow for guided navigation and activation of the nanorobots. This feature enables precise control over the location and timing of therapeutic interventions, further enhancing the efficacy and safety of nanorobot-based cancer treatments. These combined features make nanorobots a promising tool in the development of more effective and personalized cancer therapies [6-8].

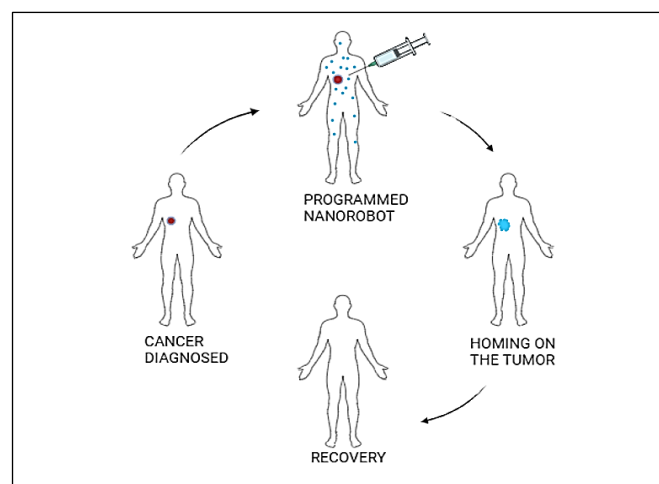


Fig. 1: Working methodology of Nanorobotics.

FABRICATION TECHNIQUES

The fabrication of nanorobots for cancer treatment employs a variety of techniques, broadly categorized into top-down, bottom-up, and hybrid approaches. Top-down approaches, including lithography and microfabrication techniques, start with larger materials and sculpt them down to the desired nanoscale structures, offering precise control over shape and size [8]. Bottom-up approaches, on the other hand, rely on the self-assembly of molecular components, leveraging the inherent properties of materials to form complex nanostructures. This method is particularly useful for creating organic nanorobots like DNA origami structures [8,9]. Hybrid approaches combine elements of both top-down and bottom-up methodologies, allowing for the creation of more complex and sophisticated nanorobot designs [10,11]. These hybrid techniques often involve using top-down methods to create templates or scaffolds, which are then populated or modified using bottom-up self-assembly processes. This combination of approaches enables the fabrication of highly functional and versatile nanorobots capable of meeting the diverse requirements of cancer treatment applications [9,11].

APPLICATIONS OF NANOROBOTS IN CANCER TREATMENT

Nanorobots offer a wide range of applications in cancer treatment, with targeted drug delivery being one of the most promising. These nanoscale devices can be engineered to carry and deliver therapeutic payloads directly to cancer cells, significantly reducing systemic toxicity. The drug delivery mechanisms of nanorobots involve sophisticated encapsulation and release techniques, often utilizing stimuli-responsive systems that can be triggered by factors such as pH changes, temperature fluctuations, or specific enzymatic activity in the tumor microenvironment. Active targeting strategies, employing cancer-specific biomarkers, further enhance the precision of drug delivery. Numerous preclinical and early clinical studies have demonstrated the potential of nanorobotic drug delivery systems in improving treatment efficacy while minimizing side effects [2,12].

In addition to drug delivery, nanorobots show great promise in cancer diagnostics and monitoring. These tiny machines can be designed for in vivo imaging and biosensing, enabling early detection of cancerous growths and real-time monitoring of treatment response. Nanorobots can also be utilized for detecting circulating tumor cells in the bloodstream, potentially allowing for earlier diagnosis and more effective tracking of metastatic spread. Furthermore, they offer the capability for molecular profiling of tumors, providing valuable information for personalized treatment strategies [12,13].

Beyond drug delivery and diagnostics, nanorobots can actively participate in cancer treatment through various therapeutic interventions. Photothermal and photodynamic therapies utilize nanorobots to generate localized heat or reactive oxygen species upon light activation, selectively destroying cancer cells. Nanorobots can also enhance the effectiveness of radiotherapy by increasing the sensitivity of tumor cells to radiation. In the realm of gene therapy, nanorobots serve as efficient vectors for delivering therapeutic

genes or RNA interference molecules to cancer cells. Additionally, nanorobots show potential in revolutionizing cancer surgery, enabling minimally invasive tumor removal, precise identification of tumor margins, and even microsurgery on blood vessels supplying tumors. These surgical applications, coupled with the ability to monitor post-surgical sites and deliver localized treatments, highlight the versatility of nanorobots in comprehensive cancer care [13,14].

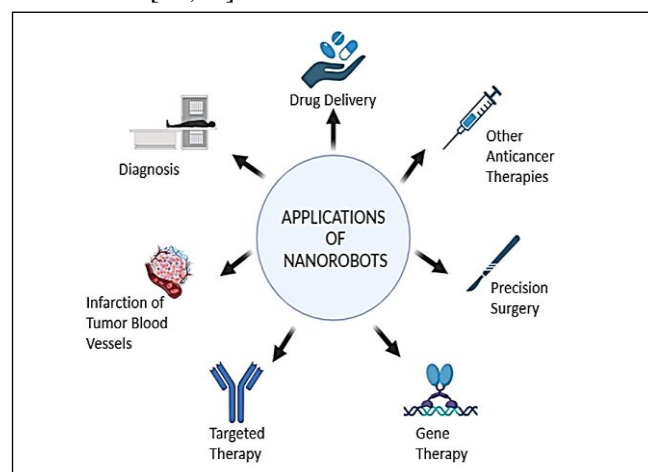


Fig. 3: Applications of nanorobots.

CURRENT RESEARCH AND CLINICAL TRIALS

The landscape of current research and clinical trials in nanorobotics for cancer treatment is characterized by a complex interplay of multidisciplinary approaches, cutting-edge technologies, and intricate biological interactions. Preclinical studies are delving into increasingly sophisticated nanorobotic systems that exploit the intricate molecular machinery of cancer cells. For instance, researchers have developed DNA-based nanorobots capable of autonomous logic-gated activation in response to specific molecular signatures of cancer cells. These nanorobots can distinguish between target and non-target cells with remarkable precision, releasing their therapeutic payload only when multiple cancer-specific markers are detected simultaneously. Another groundbreaking study has demonstrated the potential of hybrid organic-inorganic

nanorobots that combine the programmability of DNA origami with the photothermal properties of gold nanoparticles. These nanorobots can be remotely controlled using near-infrared light to perform complex tasks such as drilling into cell membranes for enhanced drug delivery or inducing localized hyperthermia [12,15].

The transition from preclinical promise to clinical reality is fraught with challenges, yet early-phase clinical trials are cautiously progressing, navigating the complex regulatory landscape and addressing critical questions of safety, biocompatibility, and efficacy in human subjects. A phase I/II trial is exploring the use of magnetically guided nanorobots loaded with a combination of chemotherapeutic agents and small interfering RNA (siRNA) for treating pancreatic cancer. This trial aims to overcome the notorious drug resistance of pancreatic tumors by simultaneously delivering conventional chemotherapy and silencing genes involved in drug resistance mechanisms. Another innovative trial is investigating nanorobots designed to enhance immunotherapy in melanoma patients. These nanorobots are engineered to deliver tumor antigens directly to antigen-presenting cells, potentially boosting the body's immune response against cancer cells. The complexity of these clinical endeavors is further amplified by the collaborative efforts between academic institutions, pharmaceutical companies, and regulatory bodies. These partnerships must navigate not only the scientific and medical challenges but also the intricate web of intellectual property rights, funding mechanisms, and ethical considerations surrounding the use of nanorobotic technologies in human subjects. As these trials progress, they are generating vast amounts of data on the pharmacokinetics, biodistribution, and long-term effects of nanorobots in the human body, necessitating advanced computational approaches for data analysis and interpretation [13-15].

CHALLENGES AND LIMITATIONS

Nanorobot navigation and control require exceptional precision to accurately target specific cells or tissues within the human body, a challenge compounded by the complexity of the biological environment and the need for real-time adjustments [16]. Power sources and energy efficiency are critical, as nanorobots must operate with limited power while maintaining functionality over extended periods, necessitating the development of compact and efficient energy solutions. Mass production and quality control also pose significant hurdles, requiring advanced techniques and rigorous standards to ensure consistency and reliability. Biocompatibility and immunogenicity are primary concerns, as nanorobots must be compatible with human tissues to avoid adverse immune reactions and long-term toxicity [17]. Overcoming biological barriers, such as the blood-brain barrier, is another challenge, requiring nanorobots to be designed to navigate these obstacles effectively. The heterogeneity of cancer further complicates the adaptability of nanorobotic systems, as tumors can vary widely between patients and even within the same patient, necessitating highly adaptable and responsive nanorobots. The regulatory landscape for nanorobotic medical devices is still evolving, necessitating clear frameworks to ensure safety and efficacy, with regulatory bodies balancing innovation with patient safety [18]. Ethical considerations include consent, autonomy, and potential unintended consequences, as well as privacy concerns related to in vivo monitoring, which could pose risks to patient confidentiality. Ensuring equitable access to nanorobotic therapies is another ethical challenge, as these advanced treatments could exacerbate healthcare disparities if not made accessible to diverse populations. Addressing these regulatory and ethical issues is essential for the responsible development and deployment of nanorobotic technologies in medicine [19-21].

FUTURE PROSPECTS AND EMERGING TRENDS

The future of nanorobotics is being shaped by groundbreaking advancements in biocompatible materials, 4D printing, stimuli-responsive materials, and artificial intelligence integration. These innovations are enhancing the safety, versatility, and precision of nanorobots in medical applications. Biocompatible and biodegradable materials ensure nanorobots can interact safely with human tissues and be eliminated from the body after completing their tasks. 4D printing and stimuli-responsive materials allow for the creation of nanorobots that can adapt their shape or properties in response to specific stimuli, expanding their potential applications. AI integration optimizes nanorobot design, navigation, and control, enabling real-time decision-making and autonomous operation within the body. The combination of nanorobots with conventional therapies offers synergistic benefits, achieving more effective and targeted interventions. Multi-modal nanorobots capable of simultaneous diagnosis and treatment provide a comprehensive approach to managing complex medical conditions.

Personalized medicine is advancing through tailored nanorobotic interventions based on individual patient profiles, targeting specific disease mechanisms and pathways to improve treatment efficacy while minimizing adverse effects. Real-time adaptation of treatment strategies is possible through AI-equipped nanorobots with continuous monitoring capabilities, ensuring treatments remain effective as disease states change. Theranostic nanorobots, combining diagnostic and therapeutic functions, represent a significant advancement in nanomedicine. They streamline disease management by performing simultaneous diagnosis and treatment, enhancing precision and efficiency in healthcare delivery. As research in nanorobotics progresses, we can expect to see more innovative applications emerge, from

early disease detection and precise drug delivery to microsurgery and tissue repair at the cellular level. While challenges remain in manufacturing, control, and regulatory approval, the future of nanorobotics in medicine promises more effective, less invasive, and highly personalized medical treatments, potentially revolutionizing healthcare as we know it.

CONCLUSION

Nanorobotic technology holds transformative potential for precision cancer treatment, offering innovative solutions for targeted drug delivery, real-time diagnostics, and minimally invasive interventions. As advancements in materials, AI integration, and theranostic capabilities continue, nanorobots are poised to revolutionize personalized medicine. Addressing technical, biological, regulatory, and ethical challenges will be crucial for the successful clinical implementation of nanorobotic therapies. With ongoing research and development, nanorobots could become a cornerstone in the fight against cancer, significantly improving patient outcomes and advancing healthcare.

Conflict of Interest: None.

Financial support: None.

Ethical statement: None.

REFERENCES

1. Kashyap BK, Singh VV, Solanki MK, Kumar A, Ruokolainen J, Kesari KK. Smart nanomaterials in cancer theranostics: challenges and opportunities. *ACS Omega*. 2023;8(16):14290-320.
2. Kong X, Gao P, Wang J, Fang Y, Hwang KC. Advances of medical nanorobots for future cancer treatments. *J Hematol Oncol*. 2023;16(1):74.
3. Kukreti S, Ramawat S, Singh N, Dixit A. Strain-engineered thermophysical properties ranging from band-insulating to

- topological insulating phases in β -antimonene. *Nanoscale*. 2023;15(34):13997–4006.
4. Yadav R, Das PP, Sharma S, Sengupta S, Kumar D, Sagar R. Recent advancement of nanomedicine-based targeted delivery for cervical cancer treatment. *Med Oncol*. 2023;40(12):347.
 5. Aggarwal M, Kumar S. The use of nanorobotics in the treatment therapy of cancer and its future aspects: a review. *Cureus*. 2022;14(9).
 6. Patel S, Patel PN. A brief review on nanorobotics applications in medicine and future prospects. *Asian J Res Pharm Sci*. 2021;13(1):19–28.
 7. Pradeep P, Sonia MM, Kizhakkepeedika RD. Nanobots in cancer treatment—framing lung cancer. *J Adv Lung Health*. 2024;4(2):57-69.
 8. Elnaggar A, Kang S, Tian M, Han B, Keshavarz M. State of the art in actuation of micro/nanorobots for biomedical applications. *Small Sci*. 2024;4(3):2300211.
 9. Hayakawa T, Fukada S, Arai F. Fabrication of an on-chip nanorobot integrating functional nanomaterials for single-cell punctures. *IEEE Trans Robot*. 2013;30(1):59-67.
 10. Chen G, Zhu F, Gan ASJ, Mohan B, Dey KK, Xu K, et al. Towards the next generation nanorobots. *Next Nanotechnol*. 202;2(1):1-17.
 11. Wang Z, Xu Z, Zhu B, Zhang Y, Lin J, Wu Y, et al. Design, fabrication and application of magnetically actuated micro/nanorobots: a review. *Nanotechnology*. 2022;33(15):152001.
 12. Hu M, Ge X, Chen X, Mao W, Qian X, Yuan WE. Micro/nanorobot: a promising targeted drug delivery system. *Pharmaceutics*. 2020;12(7):665-6.
 13. Li J, Esteban-Fernández de Ávila B, Gao W, Zhang L, Wang J. Micro/nanorobots for biomedicine: delivery, surgery, sensing, and detoxification. *Sci Robot*. 2017;2(4):1-19.
 14. Sun L, Liu H, Ye Y, Lei Y, Islam R, Tan S, et al. Smart nanoparticles for cancer therapy. *Signal Transduct Target Ther*. 2023;8(1):418-9.
 15. Chehelgerdi M, Chehelgerdi M, Allela OQB, Pecho RDC, Jayasankar N, Rao DP, et al. Progressing nanotechnology to improve targeted cancer treatment: overcoming hurdles in its clinical implementation. *Mol Cancer*. 2023;22(1):169-70.
 16. Giri G, Maddahi Y, Zareinia K. A brief review on challenges in design and development of nanorobots for medical applications. *Appl Sci*. 2021;11(21):10385.
 17. Liu D, Guo R, Wang B, Hu J, Lu Y. Magnetic micro/nanorobots: a new age in biomedicines. *Adv Intell Syst*. 2022;4(12):1-19.
 18. Xu Y, Bian Q, Wang R, Gao J. Micro/nanorobots for precise drug delivery via targeted transport and triggered release: a review. *Int J Pharm*. 2022;616(1):121551.
- Singh AV, Chandrasekar V, Janapareddy P, Mathews DE, Laux P, Luch A, et al. Emerging application of nanorobotics and artificial intelligence to cross the BBB: advances in