

Applications of Nanorobots in Targeted Therapy for Cancer

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Abstract. Nanorobots have broad application prospects in the field of targeted cancer therapy. First, this paper summarizes the basic concepts of nanorobots, classifies and introduces their diverse species, and then summarizes the unique characteristics of nanorobots at the physiological level, especially the influence of their size and shape on the targeting mechanism, and the key role of material selection in biocompatibility. In view of the urgent need for cancer treatment, this paper analyzes the research route of nanorobots in this field in detail and discusses their application principles as targeted therapy tools. Nanobots provide new solutions for cancer treatment through precise targeting mechanisms and efficient drug loading and release strategies. In addition, this paper highlights innovations in the way nanorobots are driven and manipulated, especially their ability to move in a directional manner in response to external stimuli (e.g., magnetic, light, acoustic, or electric), which significantly improves the precision and efficiency of treatment. However, the application of nanorobots in targeted cancer therapy also faces many risks and challenges, including the limitations of real-time in vivo observation and imaging technology, and the safety of long-term use. These challenges are both a test of existing technologies and a key driver for the further development of nanorobotics. Finally, this paper looks forward to the future development of nanorobots and points out the importance of interdisciplinary cooperation and technological innovation to overcome existing problems and promote the vigorous development of nanomedicine. Nanorobots are expected to play a more important role in cancer treatment and other medical fields and make greater contributions to the cause of human health.

Keywords: Nanorobots; targeting mechanisms; driving mode; Drug carriers.

1. Introduction

Robotic systems have dramatically expanded human capabilities to perceive, interact, manipulate, and transform, especially in the medical field, where the convergence of technologies has led to revolutionary applications aimed at improving healthcare. Medical robots are different from industrial robots in that they emphasize miniaturized components and smart materials to adapt to precision medical operations and need to work efficiently with the human body. The development of this field is driven by advances in motor technology, control theory, advanced materials, medical imaging, and increased doctor-patient acceptance. For example, robotic surgical systems can accurately simulate surgeons' movements to perform minor internal surgeries. However, the current medical robots in minimally invasive applications are still limited by the size and rigidity of mechanical parts [1], and it is difficult to reach the depths of the human body. Therefore, the research and development of micro- to nano-scale multifunctional robots to achieve cell-level precision medicine has become a promising research direction.

Nanotechnology is gradually transforming the science fiction vision of the past into a realistic picture of medical practice. However, achieving this leap is by no means easy. It profoundly tests the innovative capabilities in micro-robot design, precision manufacturing, and efficient manipulation, and requires us to overcome unprecedented technical obstacles at the nanoscale. As the shining pearl of nanotechnology, the research and development of nanorobots requires a precise balance between structural complexity, biocompatibility, and operational efficiency to ensure that these micro "doctors" can operate safely in the human body without fear of immune response and side effects. At the same time, how to achieve precise navigation and control of these tiny machines so that they can

accurately reach the lesion and effectively perform treatment tasks has also become a key problem that needs to be overcome in the current scientific research field.

It is worth mentioning that the rise of micro-robotics technology, especially after the molecular machine won the Nobel Prize in Chemistry [2], has inspired endless imagination about its application potential around the world. In his groundbreaking speech, Richard Feynman used the metaphor of "plenty of room at the bottom" to envision a new era dominated by micro-robotics [2]. From the bold idea of "swallow the surgeon" to the fantastic scenes in the movie "Fantastic Voyage [2]", all of them indicate the broad prospects and unlimited possibilities of micro- and nano-robotics in the field of biomedicine.

In this paper, medical microrobots are introduced and analyzed, dedicated to developing and deploying a series of micro/nanorobots that are physically, chemically, or biologically driven, programmable, and reconfigurable. These high-tech products are designed to cope with the complex physiological environment of the human body and are intended to perform a variety of medical tasks including precise drug delivery, local hyperthermia treatment, targeted attacks on diseased cells, and cell-level microsurgery. Through the application of these cutting-edge technologies, medical microrobots are gradually leading the trend of innovation in medical treatment technology, bringing unprecedented hope and opportunities to improve the quality of life of patients.

This paper delves into the specific applications of different technologies in the field of micro and nano robotics. From multiple dimensions such as optics, magnetics, acoustics, radiology, and integrated imaging, this paper analyzes in detail the different driving mechanisms of micro and nano robots, the core principles of imaging technology, the unique imaging characteristics, and the current practical application cases in medical exploration and scientific research.

This paper not only emphasizes the advantages of various imaging technologies in improving the operation accuracy of micro-nano robots and realizing real-time monitoring in vivo, but also objectively points out the current technical limitations, such as the penetration depth limitation of optical imaging, the need to improve the positioning accuracy of magnetic field imaging, and the signal interference problem of ultrasound imaging in specific environments, which points out the direction of optimization and breakthrough for subsequent scientific research [3].

In addition, the paper also looks forward to the future development trend of the integration of micro and nano robots and medical imaging technology and emphasizes the great potential of this cross-border integration in promoting precision medicine and early diagnosis and treatment of diseases. In short, the deep integration of micro and nano robots and medical imaging technology is gradually opening a new chapter in precision medicine, indicating broad development prospects and infinite possibilities.

2. Principles and Characteristics of Nanorobots

2.1. Basic Concepts and Types of Nanorobots

Robotics plays a key and diverse role in manufacturing and everyday life, with an unprecedented range of applications. Its rapid progress is not only a strong driving force for social modernization but also an important milestone in development. Robotics is known for its flexibility and adaptability, with a wide variety of applications spanning the micro to the macro domains. From nanorobots at the micro level, which show their skills in precision manufacturing and medical care, to macro industrial robots, which play an important role in automobiles, logistics, construction, and other fields, there are different types of robots with different functions. Its popularity has significantly improved production efficiency and product quality, reshaped the way people work and live, and demonstrated the great promotion and far-reaching impact of robotics technology on social development.

Nowadays, as the size of robots continues to shrink, the core feature of micro-nano robots, as the outstanding achievements of modern technology at the micro-scale, is that its size dimension is strictly defined at the sub-millimeter or smaller level, which is specifically subdivided into micro-nano operation robots focusing on micro-operations and tasks, and micro-nano scale exploration

robots aimed at exploring extreme scale phenomena. These sophisticated micro-mechanical systems, which integrate the essence of micro-nano technology, are the hallmark of robotics science diving deep into the microscopic world.

These untethered micro/nanorobots are seen as innovative alternatives to traditional invasive medical robots and passive drug carriers and are expected to have a profound impact in multiple areas of medicine. Specifically, their application potential can be grouped into four broad categories: targeted drug delivery, precision surgical assistance, real-time monitoring of biological targets, and toxin removal in vivo [1]. As confirmed by the latest proof-of-concept study, these micro/nanorobotics technologies are maturing and provide an exciting blueprint for the future of medicine.

2.2. Physiological Characteristics

The research, development, and application of micro-nano robots profoundly reflect the deep integration and cross-innovation of multidisciplinary knowledge such as physics, chemistry, materials science, bioengineering, precision mechanical engineering, information science and technology, and advanced control theory [4]. They are not only an extension and expansion of traditional robotics technology, but also an important driving force to promote the development of these basic disciplines.

In terms of scientific exploration, micro-nano robots, with their small size and excellent manipulation capabilities, have become a key tool to reveal the unique properties and behavior of matter at the nanoscale. They are capable of performing difficult tasks including but not limited to nanoscale material manipulation, exploration of cell internal structure and function, and biomolecule-level interaction studies, providing unprecedented precision and depth for scientific research.

At the level of technical application, micro-nano robots have shown a wide range of application potential and social value. In the field of advanced manufacturing, they can achieve high-precision and high-flexibility micro-nano processing, and promote the development of manufacturing in a more refined and intelligent direction; In the field of medical and health care, micro-nano robots can be used for precision medicine, targeted drug delivery, and even minimally invasive surgery in vivo, contributing to improving the level of medical care and ensuring human health. In addition, other high-tech fields such as environmental protection, information and communication, aerospace, and other high-tech fields, micro-nano robots also have huge application potential and market prospects.

2.2.1. Effects and shape

It is particularly noteworthy that in some specific scenarios, such as in vivo interventional diagnosis and treatment, large robots are unable to meet the high requirements for the manipulation of very small objects due to their size limitations. That's why scientists have conceived and designed a revolutionary solution – a targeted robot that can actively and intelligently carry chemotherapy drugs. Their most striking feature is their highly intelligent stimulus response capability, which can accurately sense and respond to a variety of external environmental stimuli, including pH changes, ion concentration differences, light signals, and magnetic fields [5]. They are distinguished by superior flexibility, strong adaptability, a high degree of robustness, and amazing accuracy. It is based on this unique ability that they have been given the reputation of "stimulus-responsive micro/nanorobots".

By using these precise stimulus-response mechanisms, these robots can navigate complex biological environments, deliver chemotherapy drugs to the lesion area with precision, and intelligently adjust the rate and volume of drug release to maximize treatment outcomes. At the same time, they can significantly reduce the damage to healthy tissues and toxic side effects, providing a safer and more effective treatment option for cancer patients. This innovative design not only opens a new avenue for cancer treatment but also brings unprecedented hope and opportunities to the medical field.

2.2.2. Effects of the material on biocompatibility

Biocompatibility plays a crucial role in the design and development of biomaterials, as it is a prerequisite for ensuring the safe and effective use of materials *in vivo*. The core of the concept of biocompatibility covers two aspects: histocompatibility and hem compatibility. Histocompatibility is concerned with the interaction and adaptability between the biomaterial and the surrounding biological tissue. A variety of factors work together to act on this process, including but not limited to the physical properties of the material (e.g., Young's modulus, hardness, etc.); The microscopic topography of the surface of the material is as critical as the internal atomic structure, and in addition, the strict control of impurities in the material is also indispensable, even trace amounts of harmful substances may trigger the body's immune mechanism or allergic reaction, which in turn interferes with the normal application of the material.

Hem compatibility focuses on the interaction of biomaterials with the circulatory system. When the material comes into direct contact with the blood, it must be ensured that it does not cause negative manifestations such as abnormal aggregation of platelets, coagulation reactions, thrombosis, or hemolysis [6]. These phenomena will not only reduce the effectiveness of the use of materials and the therapeutic effect but also may cause serious and even irreversible damage to the human body. Therefore, the design of biomaterials with high hem compatibility requires a deep understanding of the mechanism of the interaction between blood and the surface of the material, and effectively inhibits the occurrence of these adverse reactions by optimizing the chemical composition, surface properties, and interfacial microenvironment of the material.

3. Technical Route of Nanorobots for Targeted Therapy of Cancer

3.1. Principles of Application of Nanorobots in Targeted Cancer Therapy

Precision drug delivery technology has long been one of the core challenges in pharmaceutical research, where the ideal state is to deliver the exact dose of drug required for treatment directly to the target organ, tissue, or cell to achieve the best therapeutic outcome. However, this vision is difficult to achieve with traditional drug delivery models, as drugs are often absorbed, metabolized, or excreted by the rest of the body before they reach their target.

The introduction of nanotechnology has revolutionized the field of drug delivery, and nanocarrier-based drug delivery systems are seen as a promising solution to this problem. Nanocarriers can significantly improve the solubility of drugs and optimize their distribution pathways *in vivo*, making them more inclined to aggregate towards the target region. At the same time, by precisely adjusting the structure and design of the nanocarrier, the drug release rate can be finely adjusted, to achieve continuous release of the drug or release according to the present time-concentration curve to meet different treatment needs. In addition, nanocarriers can also protect drug molecules to a certain extent from being destroyed or inactivated before reaching the target, further improving the bioavailability and therapeutic effect of the drug.

3.1.1. Targeting mechanisms

It is well known that the core mechanism of drug delivery, whether constructed using passive targeting or active targeting strategies, is highly dependent on the blood circulatory system to achieve a wide distribution of the drug in the body. In the treatment of tumor tissues, due to the unique physiological characteristics of tumor tissues, especially the abnormality and high permeability of their vascular structure, molecules of specific sizes can more easily aggregate in the lesion area, and this process is significantly enhanced by enhanced permeability and retention (EPR) effect [7], thereby promoting the enrichment of passively targeted nanodrugs to tumor sites.

However, the effectiveness of the EPR effect is not unassailable in the intricate environment of organisms. It is challenged by strong clearance pressure from the mononuclear phagocytic cell system (MPS), efficient glomerular filtration in the kidneys, and physical resistance generated by the capillary wall, which combines to limit the efficiency of the EPR effect in nanoparticle aggregation

in tumor tissues, resulting in a significant increase in concentration compared to normal tissues, but still far from ideal, often no more than twice as much. To make matters worse, the proportion of nanoparticles that can actually accumulate and function inside the tumor is extremely low, accounting for only about 1% of the total amount of drugs administered.

In response to this limitation, scientists have developed actively-targeted nanoparticles as a solution. These nanoparticles cleverly bind themselves to a variety of targeted ligands that are carefully engineered based on significant differences in gene expression between target tumor cells and normal cells. These ligands include but are not limited to antibodies and their fragments targeting specific receptors (e.g., epidermal growth factor receptor), peptides that bind to specific molecules on the cell surface (e.g., transferrin), and small molecules with high affinity (e.g., folic acid), each of which has its own unique recognition mechanism to direct nanoparticles precisely to tumor cells [7], enabling more precise and efficient treatment.

3.1.2. Drug loading and release strategies

At present, micro- and nano-level drug carriers such as ferrofluids, magnetic liposomes, and magnetic microspheres are generally regarded as the most promising drug carriers [8]. For these carriers to achieve optimal application results, they need to meet a number of key properties: first, they should have a high drug loading to ensure efficient drug delivery; Secondly, the encapsulation efficiency needs to be high to reduce the loss of the drug outside the carrier; At the same time, there is also a need for simple and efficient preparation and purification methods to meet the needs of large-scale production. In addition, the carrier material must be biodegradable, and the toxicity needs to be kept low or completely non-toxic to ensure patient safety; appropriate particle size and particle shape are also factors that cannot be ignored, which directly affect the in vivo distribution and residence time of the carrier. Finally, having a long in vivo circulation time is crucial to improve the targeting efficiency and efficacy of drugs, as it can reduce the possibility of over-clearance of drugs by the reticuloendothelial system [8], thereby increasing the specific aggregation of drugs to the lesion site, and ultimately achieving a significant improvement in efficacy.

Red blood cell carriers are becoming the focus of attention in the pharmaceutical field due to their excellent biocompatibility, biodegradability properties, and high stability in vivo. This advanced drug delivery system can not only achieve sustained drug release, thereby prolonging the duration of drug action in the body and reducing the frequency of administration but also accurately target the reticuloendothelial system, greatly improving the accuracy and effectiveness of drug treatment. In addition, the biodegradability of the erythrocyte carrier means that after completing its drug delivery task, the carrier itself can be safely metabolized or excreted by the organism without additional clearance steps, further improving the safety of the treatment and patient comfort [9].

3.2. Driving and Controlling Model

At the core level, the emergence of micro- and nano-robots marks a revolutionary leap forward in the field of drug delivery. These micro/nanorobots are not only the crystallization of technology but also the product of multidisciplinary integration. They can move directionally in response to external stimuli, such as magnetic, light, acoustic, or electric fields [10]. Energy sources to design and develop micro/nanorobots for precise drug delivery are shown in Fig. 1. At the same time, it can also generate power autonomously through internal chemical reactions, showing a high degree of flexibility and adaptability.

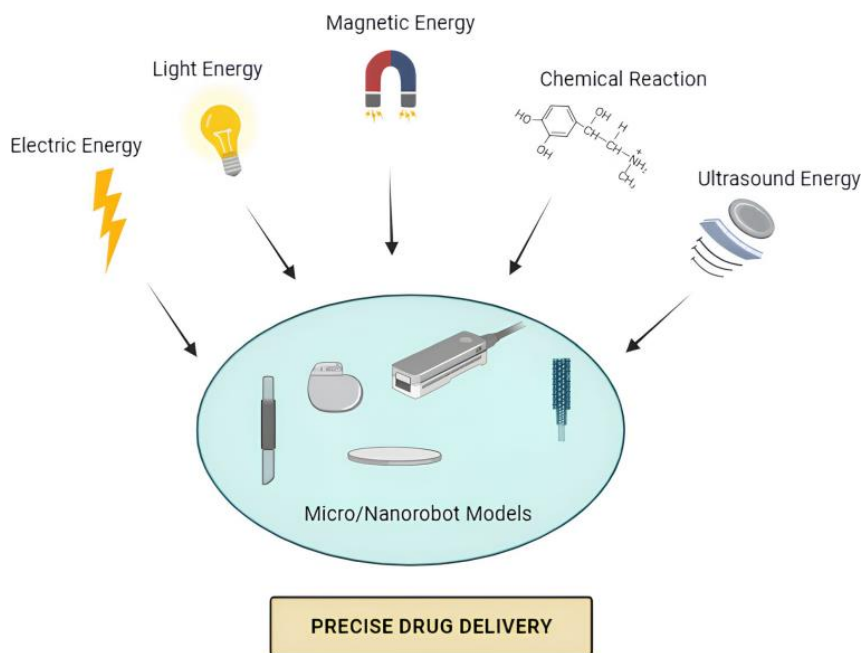


Fig 1. Energy sources to design and develop micro/nanorobots for precise drug delivery [10].

3.2.1. optical actuation

Light-driven micro-nano robots are shown in Fig. 2. These robots are facing the challenge of biocompatibility while pursuing efficient motion performance. These robots rely on the photothermal effect to achieve autonomous motion, i.e., by absorbing light energy and converting it into heat, the thermal gradient created by the heating of the material enhances the convection of the liquid [9], thus propelling the robot forward. However, it is important to note that hydrogen peroxide as an auxiliary medium is often required in light-driven processes [11], as well as irradiation with high-intensity light sources, which may adversely affect organisms in specific environments, thereby affecting their biocompatibility.

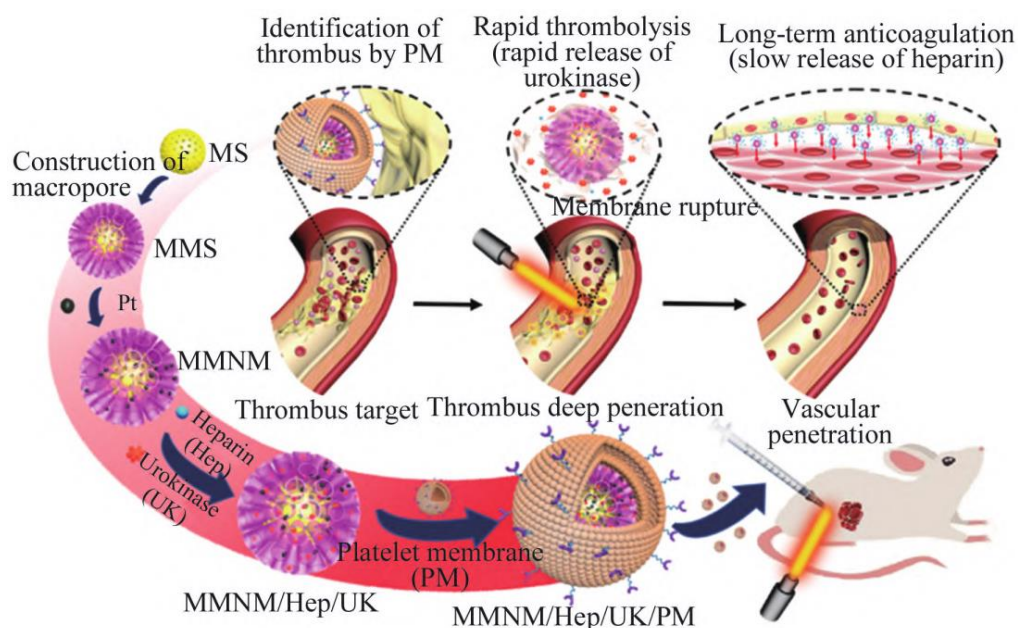


Fig 2. Light-driven micro-nanorobots for drug delivery and thrombus penetration [12].

3.2.2. Chemical actuation

Chemically driven micro-nanorobots are shown in Fig. 3, which move autonomously with energy generated directly through chemical reactions, and often exhibit faster speeds than other drive methods. This internal drive mechanism eliminates the need to rely on complex external equipment,

simplifying operational processes and reducing costs, which is a significant advantage. However, chemical drives also come with their own set of challenges [13]. First, it lacks inherent directional movement ability, resulting in the movement trajectory of micro and nano robots in three-dimensional space is often random and difficult to control accurately. Second, the duration and efficiency of chemical drives are severely limited by the content of fuels, such as hydrogen peroxide, N_2H_4 , hydrochloric acid, and sodium hydroxide [11], which are toxic and pose a potential threat to the environment but may also affect the safety of their application in living organisms. In addition, fuel is easily consumed by the environment of non-lesional sites, further reducing the effective drive time.

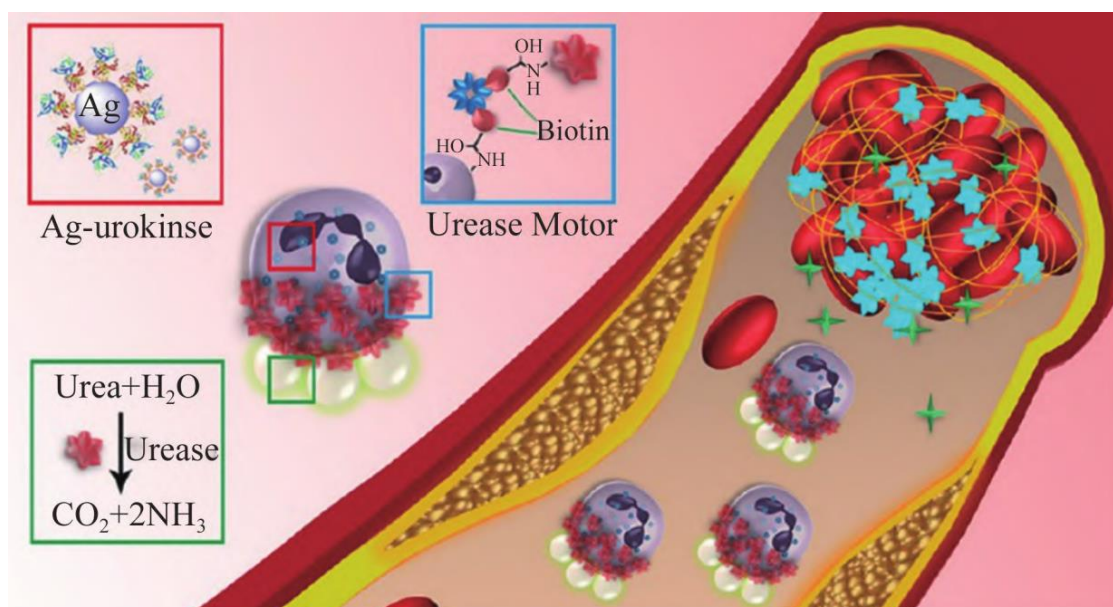


Fig 3. Chemically driven Janus nanomotors for targeted drug delivery [14].

3.2.3. Magnetic actuation

Magnetically driven micro- and nano-robots significantly overcome many of the limitations inherent in other propulsion mechanisms, and their unique advantages are described below: Magnetic fields as a driving force provide an unprecedented non-invasive means for micro/nanorobot operation, completely freeing from the need to rely on liquid fuels. This feature greatly simplifies the handling process and reduces the complexity of the operation [11], while ensuring the safety of the treatment process and the comfort of the patient. The use of low-intensity and low-frequency magnetic fields to drive magnetic micro/nanorobots can not only safely penetrate complex biological tissues and reach deep lesion areas, but also does not cause any harmful effects on organisms. This gentle yet efficient drive opens new avenues for precise drug delivery and disease treatment. The use of magnetic materials allows for a high degree of flexibility and customizability in the design of micro/nanorobots. By adjusting the magnetic configuration or programming control, the robot behavior mode can be easily diversified to meet different application scenarios and treatment needs. This feature is of great significance for precision medicine and personalized treatment in the biomedical field.

3.3. Challenges and Opportunities

Although nanodrug delivery systems have shown great potential and wide application prospects in scientific research and have attracted the attention of a large number of scientists and research institutions, they face many challenges in the process of clinical translation. Despite the sheer volume of scientific reports and research projects, only a handful of nanomedicines have actually made it to clinical trials and successfully approved by regulatory agencies. This is mainly due to the high complexity and uncertainty that nanodrugs need to overcome in the research and development process, including the long-term safety, stability, vivo observation, and imaging modalities of the carrier.

3.3.1. Vivo observation and imaging modalities

At present, achieving real-time and high-resolution observation in vivo is still a very challenging problem. Traditional imaging techniques have their own limitations that are difficult to overcome: although ultrasound imaging is widely used, its resolution is limited; Magnetic resonance imaging (MRI), although the images are clear, cannot achieve true real-time tracking; Although CT scans can provide detailed structural information, they carry a high risk of radiation; Methods involving invasive tests, such as barium swallow imaging, often cause intense discomfort to patients.

In this context, magnetic particle imaging (MPI) [15], as an emerging technology, has shown potential candidates to solve the problem of real-time observation in vivo. With its unique advantages, such as high temporal resolution and radiation-free properties, MPI opens up new possibilities for in vivo imaging. In the future, the integration of MPI with advanced magnetron systems to achieve accurate and real-time monitoring of targets in vivo will be an important research direction in this field. Although the research is still in its infancy, its broad application prospects are worthy of in-depth exploration by researchers.

In addition, from the perspective of interdisciplinary integration, the multi-field coupling effect of physics provides rich possibilities for the manipulation of micro-nano robots. Through the synergy of sound, light, electromagnetism and other physical fields [15], more accurate and flexible in vivo navigation and control can be realized, thereby improving the efficiency and safety of human-computer interaction. Research in this field not only helps to promote the development of micro and nanorobotics but also injects new vitality into biomedical engineering.

Finally, bio-based materials, as a bridge between technology and life, play a crucial role in solving the problem of nanorobots entering the human body and playing a role. The development of bio-based materials with good biocompatibility, degradability, and functionality will be the key to realizing the wide application of nanorobots in the biomedical field. In the future, research in this field will require joint efforts and continuous innovation of interdisciplinary teams.

3.3.2. Long-term safety

When exploring the enormous potential of nanorobots in biomedical applications, especially in the field of cancer treatment, ensuring their safety and preventing potential adverse effects on patients has become a key issue to be addressed. There is widespread concern that any technical omission or misapplication could pose an immediate threat to patients, potentially causing harm and inducing a complex and unpredictable set of side effects that can make the treatment process more difficult.

This challenge is particularly acute for patients with malignancies with complex pathological features, such as angiodysplasia [16]. In this context, traditional treatments, such as interventions using tubular DNA nanobots containing thrombin, may encounter efficacy bottlenecks due to the specificity of the tumor microenvironment, making it difficult to achieve the established treatment goals, and may even fail altogether in some cases.

To ensure the safe and effective application of nanorobots in cancer treatment, there is an urgent need to adopt a comprehensive and rigorous evaluation system, which should include in-depth preclinical research and rigorous clinical trials. This process requires not only a comprehensive evaluation of the biocompatibility of nanorobots in multiple biological environments, but also a deep understanding of their pharmacokinetic and pharmacodynamic properties to ensure their stability [16], distribution, and therapeutic efficacy in vivo.

In short, although the application of nanorobots in cancer treatment is promising, their safety and efficacy still need to be achieved through systematic research, rigorous evaluation, and a high-quality production process. Only in this way can people better harness the potential of nanotechnology and bring more precise and effective treatment options to patients.

4. Conclusion

With the rapid development of science and technology and the increasing intensification of interdisciplinary collaboration, the application of nanorobots in targeted cancer therapy has shown great potential and far-reaching transformative impact. This paper deeply discusses the challenges and opportunities of nanorobots in drug delivery, precise control, and other aspects, and further verifies their wide application prospects and social value in the medical field.

As an extension of robot technology to the microscopic world, nanorobots integrate the essence of physics, chemistry, materials science, bioengineering, and other disciplines, and are the frontier representatives of modern science and technology. Its unique size effect and versatility have shown significant advantages in targeted drug delivery, not only improving the solubility of the drug, and optimizing the distribution path in vivo, but also achieving precise regulation of the drug release rate. By combining active targeting strategies, nanobots can accurately identify and direct tumor cells, significantly improving the accuracy and effectiveness of treatment, and opening up a new path for cancer treatment.

In terms of drive and control mode, the research and development of optical drive, chemical drive, and magnetic drive technology provide diversified options for the motion control of nanorobots. Magnetic drive technology has become a hot topic of current research because of its non-invasive, safe, and efficient characteristics. By programming the magnetic field, scientists were able to precisely manipulate the nanorobot's behavior, ensuring that it moves according to a preset trajectory and accurately reaches the lesion area to perform the treatment task.

However, nanorobots still face many challenges in the clinical process, including safety, stability, biocompatibility, production cost control, and limitations of in vivo observation and imaging technologies. The solution to these problems requires multidisciplinary collaborative efforts to continuously promote technological innovation and R&D progress. In particular, the real-time and high-resolution observation technology in vivo is not perfect, and new imaging methods need to be developed to accurately monitor the behavior of nanorobots. At the same time, long-term safety issues cannot be ignored, and comprehensive and rigorous preclinical studies and clinical trials must be conducted to ensure the safe and effective application of nanorobots in the human body.

Looking to the future, the application of nanorobots in cancer treatment and other medical fields is promising. With the continuous progress of materials science, bioengineering, information technology, and other related fields and the in-depth development of interdisciplinary integration, nanorobots will continue to break through technical bottlenecks and provide more accurate, efficient, and safe solutions for disease treatment. At the same time, nanomedicine, as a fusion of science and technology, will further promote the development of personalized medicine and preventive health management, and open a new era of human health management.

As a representative of cutting-edge technology, nanorobots and related technologies not only demonstrate great potential in the medical field but also provide strong support for promoting social development and improving human health. With the continuous deepening of research and continuous progress in technology, nanorobots will play a more important role in the future and make greater contributions to human health and well-being.

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