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Advanced Nanotechnology in Nuclear Medicine: *A Review*

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تكنولوجيا النانو المتقدمة في الطب النووي

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ABSTRACT

Radiolabeled nanoparticles significantly enhance the clinical applications of nuclear medicine particularly in nuclear diagnosis and therapy. Combining nuclear medicine and nanotechnology allows for targeted delivery of radionuclides to desired tissue, reduces damage to healthy tissues. This review article presents an overview for some commonly used radiolabeled nanoparticles, describes its clinical applications in nuclear medicine, and illustrates related advantages, challenges, and future directions. Nanotechnology facilitates the development of nanoparticles for attaching medical radionuclides, enabling molecular imaging. Moreover, the incorporation of nanotechnology in nuclear medicine offers promising prospects for targeted nuclear therapy. Recent advances in nanotechnology offer the promise clinical applications of nanotechnology in nuclear medicine, especially in the diagnosis and treatment of various diseases. The nanoparticles displaying encouraging outcomes for precise radionuclide delivery at designated tissues within the body. The clinical implementation of radiolabeled nanoparticles encounter some challenges such as enhancing targeting efficiency, attaching targeting ligands, and ensuring safety. The future work of advanced nanotechnology in nuclear medicine should involve the design of nanoparticles tailored to enhance the efficiency of disease detection and treatment.

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Keywords: Nuclear medicine, Nanotechnology, Nanoparticle, Nuclear Imaging, Nuclear therapy

الملخص

تعمل تكنولوجيا النانو المتقدمة على تعزيز جودة التطبيقات السريرية للطب النووي بشكل كبير وخاصة في التشخيص والعلاج النووي. إن الجمع بين الطب النووي وتكنولوجيا النانو يسمح بتوصيل النظائر المشعة إلى الأنسجة المستهدفة، ويقلل من الأضرار التي تلحق بالأنسجة السليمة المحيطة، وتهدف هذه المراجعة البحثية إلى عرض أهم الجسيمات النانوية المستخدمة في تركيب المستحضرات الصيدلانية المشعة في التطبيقات السريرية في مجال الطب النووي واستعراض أهم المميزات والتحديات واتجاهات الأبحاث المستقبلية في هذا المجال. حيث تسهل تكنولوجيا النانو تطوير الجسيمات النانوية لربط النظائر المشعة الطبية وتوصيلها إلى أعضاء الجسم المستهدفة، مما يتيح التصوير الجزيئي بالإضافة إلى أن دمج تكنولوجيا النانو في الطب النووي يوفر آفاقا واعدة للطب النووي التشخيصي والعلاجي.

وقد أظهرت العديد من الدراسات لدور جسيمات النانو في تقنيات الطب النووي نتائج واعدة في توصيل المواد المشعة إلى الأنسجة المستهدفة في التصوير والعلاج النووي حيث ساعد استخدام تكنولوجيا النانو المتقدمة في تحسين جودة التطبيقات السريرية في الطب النووي، وخاصة في تشخيص وعلاج الأمراض المختلفة. كما تواجه التطبيقات السريرية للجسيمات النانوية الممكن تحميلها بالنظائر المشعة بعض التحديات مثل تعزيز كفاءة الاستهداف للأنسجة المحددة، وتحسين روابط الاستهداف، وضمان السلامة للمستحضرات المشعة الناتجة. ولذلك يتضمن العمل المستقبلي لتقنية النانو المتقدمة في الطب النووي تصميم جسيمات نانوية مصممة خصيصًا لتعزيز كفاءة اكتشاف الأمراض وعلاجها.

الكلمات المفتاحية: الطب النووي، تكنولوجيا النانو، الجسيمات النانوية، التصوير النووي، العلاج النووي

1. Introduction

The field of nanotechnology, which deals with the manipulation of matter at the nanoscale, has shown promise in the medical profession [1]. These advancements demonstrate the versatility and potential of nanotechnology in revolutionizing medical applications, since nanotechnology offers new approaches to accurate drug delivery for disease detection and treatment, and plays a vital role in the advancement medicine [2, 3].

Nuclear medicine occupies a crucial position in modern healthcare by employing radiolabeled compounds for the diagnosis and treatment of diverse diseases [4, 5]. The discipline of nuclear medicine facilitates the non-invasive visualization and tracking of radiotracers within the body, providing three-dimensional and quantitative imaging to aid in disease identification and treatment response evaluation. This field includes the use of radiopharmaceuticals in cancer diagnostic modalities such as single-photon emission computed tomography (SPECT), and positron emission tomography (PET), as well as, cancer treatment such as brachytherapy [6]. Moreover, nuclear medicine techniques offer functional information that could hold predictive and prognostic implications for patients undergoing immunotherapy or adoptive T-cell therapy. By advancing imaging technology and radiopharmacy, nuclear medicine is increasingly contributing to personalized and image-guided interventions for a wide array of illnesses, underscoring its importance as a fundamental component of contemporary healthcare [7].

Nuclear medicine imaging vary from conventional imaging modalities (such as: X-rays, MRI, or CT scans) by utilizing radiopharmaceutical to observe physiological processes at a molecular level. By tracking the movement and behavior of radioactive materials all through the body, radiopharmaceutical provides high-sensitivity and specificity functional information which will be utilized to evaluate illness processes, organ function, and treatment results [5],[8]. Its value is particularly evident in the diagnosis of infections, inflammations, cancers, and other conditions where functional insights play a crucial role. Furthermore, nuclear medicine techniques can help with treatment planning by evaluating the effects of radiation therapy on healthy tissues and creating plans to reduce toxicity while optimizing therapeutic efficacy [9]. On the other hand, nuclear medicine practitioners encounter challenges and constraints when it comes to the implementation of personalized radionuclide therapies due to the absence of regular patient-specific treatment strategies and dosimetry calculations, leading to inadequate delivery of radioactivity to tumors [6].

2. Nanotechnology in Nuclear Medicine

Nanoscale materials are instrumental in the enhancement of radiological imaging techniques, as they offer benefits such as heightened resolution, enhanced sensitivity, and the capacity to produce contrast, thereby improving the visualization of physiological structures [10, 11]. The field of nanotechnology has a notable influence on the detection, management, and surveillance of illnesses by facilitating the creation of targeted therapeutic delivery systems, bioanalytical devices, and miniature probes for the early identification of ailments such as cancer [11], [12]. Nanomaterials, by virtue of their distinctive characteristics and controllability, enable precise medication conveyance to malignant cells, resulting in more efficacious interventions [13]. Furthermore, nanoparticles find application in a range of imaging techniques like MRI, nuclear imaging, and optical imaging, thereby augmenting the effectiveness of disease identification and monitoring. The incorporation of nanomaterials in medical contexts represents a propitious progression in enhancing healthcare outcomes through pioneering diagnostic and healing methodologies.

Nanotechnology plays an essential part within the progression of nuclear medicine by displaying novel arrangements to progress the usefulness, safety, and effectiveness of nuclear systems [14]. The utilization of designed nanomaterials in nuclear medicine shows potential in different perspectives such as improving thermal conductivity, efficacy of stage alter materials, and enhancing nuclear fuel manufacturing, increasing safety and fuel burn up through advanced cladding, and reducing radiation effects inside nuclear reactors [15]. Nanoparticles, an essential component of nanotechnology, serve as proficient carriers for delivering therapeutic agents like mRNA, siRNA, and DNA, which are ordinarily non-bioavailable, hence broadening the extend and viability of radiopharmaceutical applications [16]. The integration of nanotechnology in nuclear medicine not only tackles current obstacles but also paves the way for significant advancements in the field.

The incorporation of nanoparticles within the field of nuclear medicine, as evidenced in a variety of previous studies, facilitates heightened therapeutic effectiveness by enabling exact nuclear drug delivery, enhanced biodistribution, and the creation of radiopharmaceuticals that target tumors. Nanoparticles can be customized in terms of dimensions, morphology, electrical charge, and surface characteristics to enhance drug encapsulation, targeting approaches, and accumulation within tumors, consequently optimizing treatment results while minimizing harm to healthy tissues [17, 18]. The application of nanotechnology in nuclear medicine opens doors for novel combination therapies, theranostic uses, and safe and efficient radionuclide nanocarrier design, indicating significant advancements in cancer diagnostics and therapy [19].

Nanotechnology has made significant progress within the nuclear medicine domain, resulting in the emergence of nanomedicine, which concentrates on precise nanoparticles designed for targeted drug delivery and imaging [2]. The application of nanoparticles has been employed for the transportation of radionuclides for both imaging and therapy purposes [20]. The integration of nanotechnology with nuclear medicine has broadened the landscape of cancer diagnosis and treatment, presenting tumor-specific radiopharmaceuticals that reduce harm to healthy tissues [21]. Nanoparticles have surfaced as viable nuclear imaging agents, facilitating non-invasive imaging via the labeling of isotopes and modifications to surfaces for biodistribution and best targeting as it shown in animal experiments [3]. These progresses in nanotechnology exhibit the potential to transform nuclear medicine by heightening imaging sensitivity, resolution, and specificity, while also facilitating precise and efficient cancer treatments.

Nanotechnology is transforming the field of nuclear medicine through the enhancement of both diagnostic and therapeutic capabilities. The incorporation of nanotechnology into radiopharmaceutical envelops the creation of advanced nanoparticles (NPs) custom-made for exact drug delivery and accurate medical imaging [2]. The exploitation of nanoparticles' distinct attributes, such as heightened surface area-to-volume ratio, passive/active targeting functionalities, and substantial loading capacity, is utilized to craft radiopharmaceuticals aimed at tumors for the diagnosis and treatment of cancer [3]. Nanoparticles can be specifically engineered with defined features like dimensions, structure, and electric charge to govern their distribution within the body, elimination, and targeting efficiency in vivo, thereby facilitating the encapsulation or surface attachment of diverse molecules, including radionuclides, for diagnostic and therapeutic purposes [22]. Additionally, the creation of radioisotope-tagged nanoparticles like 177Lu-SN201 exhibits encouraging anti-cancer efficacy and the ability to target solid tumors locally, underscoring the notable influence of nanotechnology on the progression of nuclear medicine [21].

3. Types of nanoparticles commonly used in nuclear medicine applications

Nanoparticles utilized in the nuclear medicine applications can be categorized according to their composition, dimensions, and characteristics; there exist various classifications such as inorganic nanoparticles including gold, iron oxide, carbon nanotubes, and quantum dots, as well as organic nanoparticles such as liposomes, micelles, dendrimers, and polymers/biomolecules [23, 24], as it depicted in Figure 1. A variety of radiolabeling techniques are at disposal, tailored to the specific characteristics of the nanoparticle and the isotopes employed. The utilization of radiolabeled nanoparticles has exhibited promise in both therapeutic interventions and diagnostic procedures. These nanoparticles exhibit diversity in their chemical and physical attributes, dimensions, morphology, chemical makeup, and electrical charge, all of which influence their distribution within biological systems, elimination from the body, and ability to target specific sites in vivo. They possess the capability to encapsulate or attach to various molecules, such as radionuclides, for purposes of diagnosis or treatment, thereby forming theragnostic tools. The adaptability in terms of core materials, surface modifications, and radiolabeling methodologies presents a broad spectrum of opportunities for the preparation of nanoparticles tailored for applications in the field of nano-nuclear medicine [25].

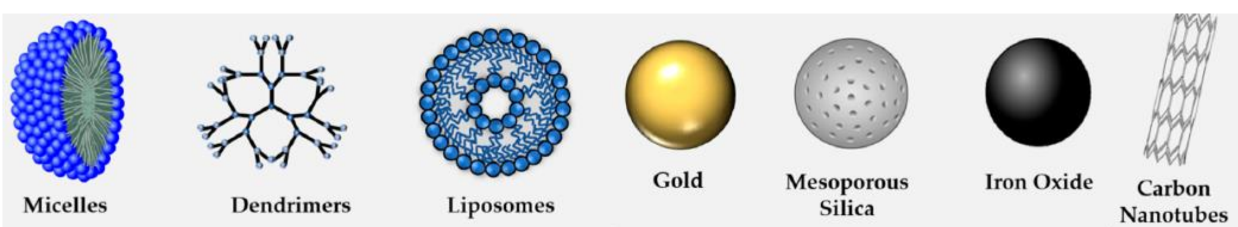

Figure (1): Common radiolabeled nanoparticles, adapted from [26]

Table 1 illustrates the main properties of common radiolabeled nanoparticles, and its clinical applications.

Table (1): The clinical applications of some radiolabeled nanoparticles

Nanoparticle Type	Description	Clinical Applications
Liposomes	Microscopic vesicles from phospholipids	Targeted drug delivery, diagnostic imaging, theranostics, gene therapy, vaccine delivery
Inorganic Nanoparticles (gold, iron oxide)	Made of metals, oxides, semiconductor	Imaging (CT, MRI), radionuclide therapy, photothermal therapy
Dendrimers	Branched polymers like tree-structure	Drug delivery, imaging, theranostics
Polymeric Nanoparticles	Made of biodegradable or non-biodegradable polymers	Sustained drug release, improved drug stability, imaging
Carbon Nanotubes	Have a cylindrical framework made of carbon atoms	Drug delivery, excellent imaging properties, therapeutic potential
Quantum Dots	Nano-crystals composed of semiconductor substance.	High-resolution imaging, biosensing

There are various approaches for radiolabeled on nanoparticles with surface modification as it illustrated in Figure 2.

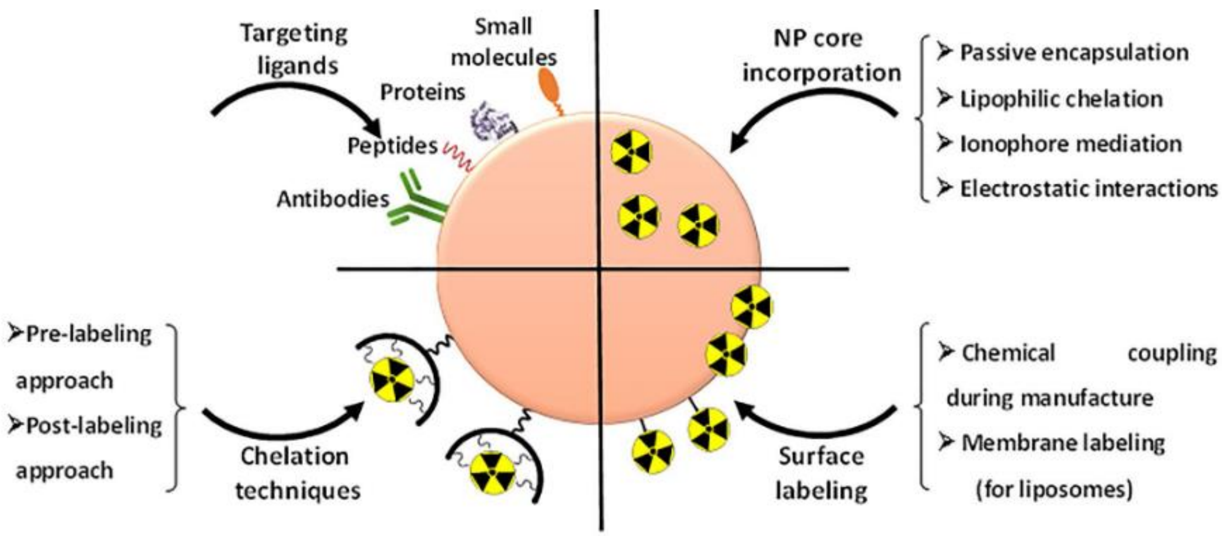

Figure (2): Nanoparticles surface modification by targeted ligands and radiolabeling approaches, adapted from [27].

4. Clinical applications of nanotechnology in nuclear medicine

Nanotechnology assumes a pivotal role in diverse applications within the nuclear medicine field. One example is radiolabeled nanoparticles for diagnostic imaging; also, the nanoparticle-based radiopharmaceuticals employed in nuclear therapy systems. These instances highlight the adaptability and promise of nanotechnology in transforming imaging, targeted drug delivery, and theranostics in the field of nuclear medicine [2, 22, 24].

4.1 Nuclear medicine imaging

Nanoparticle-based imaging within the field of nuclear medicine has exhibited promising potential in various clinical trials. Diverse types of nanoparticles, such as quantum dots, liposomes, and inorganic nanoparticles, have been applied in nuclear imaging procedures [2]. These nanoparticles have the capacity to undergo radiolabeling with isotopes to serve diagnostic objectives, thereby facilitating targeted delivery and improved imaging capabilities [22]. By incorporating complementary imaging probes within nanoparticles, the opportunity arises for multimodal molecular imaging with heightened sensitivity and specificity [28]. Furthermore, the modification of nanoparticle surfaces plays a crucial role in enabling specific targeting and enhancing biocompatibility, thereby further amplifying their effectiveness in diagnostic applications [20]. The distinctive characteristics of nanoparticles, encompassing their capability to encapsulate drugs and enhance drug accumulation at designated sites, have resulted in successful clinical trials and usage within the field of nuclear medicine [29]. This highlights the potential of nanoparticles as potent instruments for the diagnosis.

Nanoparticles have become increasingly important as contrast agents in nuclear imaging, improving both sensitivity and specificity across different modalities [30]. Gold nanoparticles show promise for use in optical coherence tomography and photoacoustic imaging in ophthalmology [31] . On the other hand, nanoscale contrast agents (NCAs) designed for magnetic resonance imaging demonstrate high relaxivity and specific targeting of tumors. Moreover, cloneable Selenium Nanoparticles (cSeNPs) offer contrast enhancement in electron microscopy, fluorescence microscopy, and X-ray computed tomography, facilitating the correlation of proteins-of-interest at various length scales [32]. Furthermore, the possibility of nanomaterials like liposomes and quantum dots as nuclear imaging probes, which would enable multimodal molecular imaging with increased sensitivity and resolution [33]. The utilization of nanoparticles as contrast agents in nuclear imaging methodologies shows significant promise in advancing medical diagnostics.

Variety of nanoparticles can be radiolabeled in nuclear imaging such as SPECT and PET techniques including both inorganic nanoparticles and organic nanoparticles [34, 35]. For instance, the radiolabeled iron oxide nanoparticles combine exceptional sensitivity and precise spatial resolution to enable the accurate diagnosis of early-stage diseases [22]. They can be employed as dual-modality contrast agents for SPECT/MRI or PET/MRI imaging applications [29].

4.2 Targeted Drug Delivery

Nanoparticles play a vital role in the targeted transportation of drugs to specific tissues, while simultaneously reducing side effects. Several mechanisms facilitate the ability of nanoparticles to accomplish this task, which includes both passive and active targeting techniques [35, 36]. Nanoparticles can be labeled with alpha emitters for nuclear therapy, resulting in localized cell destruction owing to the high linear energy transfer and limited reach of alpha emitters, passive targeting capitalizes on the enhanced permeability and retention effect, which enables nanoparticles to amass in affected tissues due to leaky vasculature. On the other hand, active targeting entails precise interactions between targeting agents present on nanoparticles and disease-specific biomarkers, ensuring accurate delivery to the designated site [37, 38]. Essential attributes such as stability, biocompatibility, and optimal size are imperative for nanoparticle carriers to avert leakage and guarantee secure delivery to target tissues. Furthermore, novel strategies like magnet-enhanced targeting and nanoparticles inhibiting macropinocytosis contribute to heightening the specificity and effectiveness of targeted drug delivery systems. These innovations aid in diminishing off-target effects and enhancing therapeutic results [39, 40].

Nanoparticles have been recognized as highly adaptable vehicles for both radioactive isotopes and pharmaceutical agents in the field of medical practice. To deliver radionuclides to targets, a variety of nanoparticle forms, including liposomes, gold nanoparticles, iron oxide nanoparticles, silica nanoparticles, micelles, and dendrimers, have been studied [41]. Moreover, specially designed nanoparticles such as polymeric nanoparticles, carbon nanotubes, and metallic nanoparticles have been employed for drug distribution systems, enriching drug bioavailability, absorption duration, and solubility while simultaneously decreasing release duration and aggregation [21]. These nanocarriers have undergone thorough examination both in controlled laboratory settings and within living organisms, displaying encouraging outcomes for precise delivery at designated locations within the body [41]. The integration of nanoparticles in nuclear medicine for both diagnostic and therapeutic intentions is experiencing rapid growth, holding the potential to transform treatment methodologies through the amalgamation of imaging and therapy in a theranostic approach [43].

Clinical trials and successful applications of targeted drug delivery utilizing nanoparticles have exhibited encouraging outcomes in diverse medical domains. By precisely targeting specific areas, nanomaterial-based radiopharmaceutical delivery systems have been used to improve the safety and efficacy of nuclear therapy, overcoming obstacles like insufficient stability and solubility [44]. Liposomes and dendrimers are two illustrations of nanoparticles that have been effectively utilized in targeted nuclear therapy delivery since of their biocompatibility and capacity to gather at particular target tissue without influencing non-targeted tissues [45]. Mesoporous nanocarriers have garnered attention for their prospective application in targeted drug delivery systems, facilitating the regulated discharge of biomolecules and displaying potential in areas such as bone regeneration and microfluidic-templated encapsulation [46]. The amalgamation of clinical and engineering principles in nuclear drug delivery systems has empowered the controlled discharge of therapeutic agents at designated sites, diminishing systemic side effects and heightening efficacy in diverse clinical scenarios, encompassing cancer treatment and inflammatory diseases [47].

Nanoparticle-based nuclear therapy provide notable benefits in the domains of drug delivery, and therapeutics owing to their distinct physicochemical characteristics and interactions at the biological level [44]. These systems enhance the stability, solubility, and duration of circulation of drugs, while simultaneously mitigating toxic effects, rendering them well-suited for the precise targeting of intravascular and extravascular ailments [43]. Nanoparticles based radionuclides have demonstrated a high level of efficacy in delivering medications across the blood-brain barrier to treat neurodegenerative disorders, improving pharmacological efficacy and streamlining the use of combination therapeutic techniques [48]. Furthermore, nanoparticles have brought about a transformation in the treatment of cancer by enhancing drug stability, specificity, and sensitivity, which in turn results in improved drug release and therapeutic results in the context of bone cancer and other intricate health disorders [49]. Besides, nanoparticles such as silica nanoparticles expect a basic part in nano-nuclear therapy, advertising easy synthesis, controllability, and compatibility with biological frameworks for the proficient diagnosis and treatment of inflammatory [50].

4.3 *Theranostics*

The advancement of theranostic nano-radiopharmaceuticals, which amalgamate diagnostic and therapeutic functionalities, signifies a notable progression in the field of cancer therapy. These innovative drugs combine radiopharmaceuticals and nanotechnology to offer better imaging and therapy choices for a range of illnesses [3, 51, 52]. Nanoparticles, distinguished by their unique characteristics, act as efficient vehicles for both diagnostic substances and therapeutic medications, facilitating precise delivery to tumor locations while reducing general toxicity levels. Some studies have concentrated on the utilization of nanomaterials for cancer diagnosis, treatment, and observation, displaying the promise of versatile nanoparticles in improving treatment results and patient well-being . The merger of nanotechnology with nuclear medicine has laid the groundwork for the creation of tumor-targeted nanoparticles for cancer radiotherapy, offering the potential for synergistic combination treatments and heightened treatment effectiveness [53, 54].

Theranostics nano-radiopharmaceuticals present notable benefits for personalized medicine and the real-time assessment of treatment efficacy. These sophisticated compounds integrate therapeutic and diagnostic imaging functions, thereby enabling precise treatment selection and monitoring of responses [55]. These nano-radiopharmaceuticals enhance the effects of radiation therapy by incorporating chemical radiosensitizers like diselenide and nitroimidazole. The effects of radiation therapy can be applied through a variety of mechanism including the monitoring of reactive oxygen species (ROS) levels during treatment [56]. Moreover, the employment of blood-oxygen-level-dependent/diffusion-weighted imaging permits the noninvasive monitoring of tumor responses to hypoxic radiosensitization induced by radiation-activated nanoagents, thus facilitating the assessment of treatment efficacy and enhancements in tumor oxygenation levels. In essence, theranostics nano-radiopharmaceuticals assume a pivotal role in personalized cancer therapy by providing targeted treatment modalities, real-time monitoring capabilities, and enhanced treatment outcomes [57].

Theranostic nano-radiopharmaceuticals represent a promising field of study within the field of nuclear medicine, with the objective of integrating both diagnostic and therapeutic functionalities to facilitate targeted therapy. Illustrative instances of such nano-pharmaceuticals encompass iodine nanoparticles (INPs), which serve dual roles in the imaging and treatment of malignancies, as emphasized in a critique delineating their viability in medical imaging and cancer management [3]. Furthermore, the emergence of an innovative 27 nm nanoparticle labeled with radioisotopes, denoted as 177Lu-SN201, exhibits potential in specifically homing in on solid tumors for radionuclide therapy, showcasing efficacy in combatting tumors in mice models [58]. Moreover, some studies were conducted on the nuclear therapy application of nanoparticle-based targeted alpha-particle to localized cell destruction in cancer treatment, utilizing a variety of nanoparticles, including liposomes, polymersomes, and inorganic nanoparticles. These instances serve to exemplify the varied strategies and materials that are currently under scrutiny for theranostic nano-pharmaceuticals in the sphere of nuclear medicine applications [59].

4.4 Other Applications

Nanotechnology's application in nuclear medicine presents a wide range of emerging possibilities extending beyond radioimmunotherapy, gene therapy, and tissue engineering. Nanoparticles (NPs) are of significant importance in targeted alpha-particle therapy (TAT) for localized cell destruction during cancer treatment, owing to their high linear energy transfer and short ranges of alpha emitters [60]. Furthermore, the distinct characteristics of NPs facilitate the development of efficient drug delivery systems, allowing for the encapsulation of medications to boost accumulation at specific sites and enhance effectiveness [20]. Within the field of tissue engineering, nanoparticles are employed to improve cell adhesion, regulated growth factor release, and non-invasive monitoring of tissue regeneration processes [61]. Moreover, nanotechnology provides opportunities for precise management of protein adsorption and cellular interactions, confirming its adaptability in diverse medical contexts [62].

Advanced nanotechnology is transforming the field of radioimmunotherapy within nuclear medicine through the augmentation of targeted cancer treatment [60]. Nuclear nanomedicines are specifically engineered to integrate tumor antigens, immuno- or radio-regulators, and imaging agents, thereby eliciting biological responses such as immunogenic cell death and overcoming resistance to radiation. Moreover, nanoparticles serve as a foundation for the precise transportation of radionuclide payloads to tumors, thus reducing the harmful effects on healthy tissues [3]. The incorporation of high-atomic number nanoparticles or radiosensitizing elements with immunotherapy agents in nanoplatforms elevates the efficacy of immunotherapy responses, potentially enhancing the clinical results in cancer treatment [63]. Additionally, the advancement of multifunctional nanoplatforms, for instance, gold nanoparticles co-functionalized with radioactive iodine and peptides, facilitates the synergistic fusion of internal radiation therapy with immunotherapy, thus expanding the scope of clinical applications in radioimmunotherapy [64].

5. Advantages and limitations of nanoparticles in nuclear medicine applications

Targeted cancer therapy has significantly improved thanks to nanotechnology, which has solved problems with conventional treatments' toxicity, lack of specificity, and multidrug resistance. [65]. Researchers have engineered sophisticated nanosystems with distinctive characteristics such as magnetic targeting, thermal therapy, and increased drug loading capacity to enhance bioavailability and reduce toxicity in cancer treatment [66]. Strategies such as incorporating tumor-targeting peptides and proteins into iron oxide nanoparticles have driven to the creation of exceptionally successful tumor-targeted nanocarriers that can enter deeply into tumors, progressing the viability of drug delivery and therapeutic viability [67]. Also, the utilize of transporter-targeted nanocarriers, which take advantage of certain transporters expressed in cancer cells, has appeared promise in terms of upgrading drug delivery to tumors and getting overcome biological boundaries, which is able eventually improve the effectiveness of cancer treatments [68]. Nanocarriers have transformed the delivery of anticancer radiopharmaceuticals by enhancing drug accumulation at precise locations, ensuring sustained release, and promoting increased apoptosis of cancer cells while minimizing impacts on healthy cells, underscoring the substantial contribution of nanotechnology in advancing targeted cancer therapy [69].

Various categories of nanoparticles present distinct benefits and limitations for particular applications within the nuclear medicine [2]. Liposomes, for example, have exhibited potential in clinical scenarios but are yet to be commercialized due to inherent limitations [20]. Nanoparticles can be customized to encapsulate or attach to molecules like radionuclides, thereby enabling theragnostic applications in the field of nuclear medicine [70]. Furthermore, advancements in nanotechnology have streamlined the creation of nanoparticle drug delivery systems equipped with precise targeting capabilities for tailored cancer treatment [3]. The fusion of nanotechnology with nuclear medicine holds the potential to improve cancer diagnosis and therapy through the exploitation of nanoparticles' distinctive characteristics, including their high loading capacity, surface attributes, and targeting prowess [22]. Table 2 presents the advantages and limitation/ challenges of some common radiolabeled nanoparticles used in nuclear imaging and therapy. Nonetheless, obstacles persist in the optimization of these systems for effective and safe clinical deployment, highlighting the necessity for further exploration and enhancement in this domain .

Polymeric nanoparticles, which encompass micelles and dendrimers, offer a flexible foundation for regulating therapy or imaging agents like radionuclides, thereby enabling theranostic applications [1]. Inorganic nanoparticles, characterized by their adjustable physical attributes, serve as effective carriers for drug delivery owing to their small dimensions and capacity to reach intricate sites, thereby heightening drug concentration and efficacy [3]. Moreover, inorganic nanoparticles have the capacity to be labeled with isotopes, facilitating theranostic functionalities through the amalgamation of diagnostic and therapeutic roles in a unified system. Nonetheless, impediments such as managing recoil energy in alpha-particle therapy and the necessity for precise nuclear targeting strategies in nanoparticle-based drug delivery systems persist as areas requiring attention [58].

Table (2): Some radiolabeled nanoparticles advantages and limitations/ challenges

Nanoparticle Type	Advantages	Limitations / challenges
Liposomes	Due to its biochemical interactions with cellular components membrane it can travel through membrane cell into cytoplasm	Stability issues, potential for off-target accumulation
Inorganic Nanoparticles (gold, iron oxide)	High stability, good imaging contrast, therapeutic potential	Potential for toxicity, limited drug loading capacity
Dendrimers	Controlled release, improved biodistribution, attractive modality for drug delivery and imaging	Potential for immunogenicity, limited in vivo stability
Polymeric Nanoparticles	Versatile, tunable properties, good biocompatibility	Potential for immunogenicity, limited drug loading capacity
Carbon Nanotubes	Their needle-like shape enables them to penetrate cellular membranes and enter into intracellular content without significant damage to cell	Potential for toxicity, limited biocompatibility
Quantum Dots	High sensitivity, Easily modifiable	Potential for toxicity, limited in vivo stability

Nanotechnology represents a promising avenue for addressing current constraints in nuclear medicine through the provision of enhanced imaging resolution, improved treatment effectiveness, and reduced adverse effects [2]. Tailoring nanoparticles for precise drug delivery to solid tumors can enhance therapeutic outcomes while minimizing harm to healthy tissues. Moreover, nanomaterials can function as nuclear imaging agents, enabling multimodal molecular imaging with heightened sensitivity and specificity, thereby propelling the advancement of theranostic medical imaging tools [18]. In addition, nanotechnology streamlines the advancement of targeted alpha-particle therapy (TAT) utilizing nanoparticles, which promise precise cell destruction with minimal side effects, underscoring the promise of nanotechnology in nuclear medicine [28].

The translation of nanotechnology into clinical applications within the field of nuclear medicine is confronted by some obstacles, these challenges encompass the necessity for expertise in regulatory affairs, establishment of standard methods for characterization, and the requirement for cost-effectiveness in comparison to conventional methodologies [71]. Furthermore, the creation of drug delivery systems based on nanoparticle targeting the cell nucleus presents difficulties in terms of strategies for nucleus-specific targeting, as well as mechanisms for efficient drug loading and release [72]. Moreover, the fusion of nanomedicine and nuclear medicine for the treatment of cancer necessitates the overcoming of barriers associated with the production of radionuclides, scalability issues, and the assurance of consistent manufacturing processes [2]. To tackle these hurdles, a collaborative approach involving regulatory bodies from the initial phases of development is imperative to ensure harmonization and expedite the clinical application of nanotechnology in nuclear medicine [3].

Regulatory and safety considerations concerning nanomaterials in nuclear medicine are of paramount importance due to the distinctive challenges they present. The field of nanotechnologies in medicine, which encompasses nanomedicines, demands rigorous safety evaluation techniques, particularly in relation to the potential adverse impacts on the immune system [73]. The concept of Nanomedicine highlights the advancement of intricate nanoparticles tailored for precise drug delivery, highlighting the necessity of focusing on nuclear delivery to enhance therapeutic effectiveness [74]. The combination of nuclear medicine with nanomedicine represents a critical leap forward within the domain of cancer diagnosis and treatment, utilizing nanoparticles for targeted nuclear radiation therapy characterized by a high level of specificity Nevertheless, the regulatory pathway for products based on nanomaterials such as nano-imaging agents remains intricate, involving complexities in classification and safety assessment that call for regulatory flexibility and personalized safety evaluation approaches [75]. These perceptions emphasize the critical significance of progressing collaboration between administrative bodies and developers to guarantee the secure and effective utilization of nanomaterials within the field of nuclear medicine.

6. Advances and Innovations

Advanced Nanotechnology within the nuclear medicine field has exhibited notable progress and discoveries, many of recent studies have devised intricate nanoparticles for precise drug transportation, imaging, and detection, with a particular emphasis on nuclear distribution to amplify therapeutic effectiveness [2]. The Integration of nanotechnology with nuclear medicine has broadened the horizons by employing nanoparticles for the diagnosis and treatment of cancer, providing both passive and active targeting, substantial loading capacity, and versatility within a single framework [21]. Innovatively engineered radioisotope-tagged nanoparticles have been created to target specific solid tumors offering effectiveness against tumors in experimental models [28]. Nanomaterials have surfaced as encouraging nuclear imaging agents for theranostic applications, enabling multifaceted molecular imaging with heightened sensitivity and specificity. Furthermore, the utilization of nanotechnology in targeted alpha-particle therapy (TAT) introduces prospects for localized cell eradication in cancer therapy, underscoring the necessity for fresh radiolabeling methodologies to handle recoil energy and enhance therapy delivery [58].

Nanoparticles play a significant part within the progression of personalized medicine through molecular imaging (MI) techniques, encouraging accurate diagnosis and treatment choice for individual patients. These nanoparticles are essential components of theranostics, which combines therapy and diagnostics in one step. Nanoparticles are used in a number of molecular imaging techniques including nuclear imaging, and optical imaging, to enhance disease monitoring and treatment administration [76]. Furthermore, the creation of platforms for multimodal imaging contributes significantly to the field by offering comprehensive insights into disease pathology and treatment outcomes. Thus, nanomaterials and nanodevices are essentially impacting the healthcare scene by giving customized arrangements for patients based on their particular molecular profiles.

The nuclear therapy and the treatment of cancer have significantly changed as a result of recent advancements in nanotechnology in nuclear medicine field. The utilization of nanomaterials is pivotal in augmenting the therapeutic effectiveness of alpha-emitting radionuclides like actinium-225 (225Ac) by impeding the migration of daughter nuclides to unintended organs, thereby diminishing toxicity [77]. Moreover, the introduction of innovative nanoparticles, for instance, 177Lu-SN201, has exhibited encouraging outcomes in the precise targeting of solid tumors and the delivery of effective intratumoral irradiation [78]. The combination of nanomedicine and nuclear medicine has broadened the horizons of cancer diagnosis and treatment by leveraging nanoparticles for their passive/active targeting capabilities, substantial loading capacity, and multifaceted attributes [21]. Furthermore, the progression towards nuclear nanomedicine highlights the significance of nuclear-targeted nanoparticle-based drug delivery systems to enhance therapeutic efficacy through the delivery of nuclear drugs. These advancements highlight the vast potential of nanotechnology in advancing nuclear medicine towards more accurate and efficient cancer therapies.

7. Future Directions

The future directions in nuclear nanomedicine research entail the exploration of novel approaches to augment cancer diagnosis and treatment. The possibility for producing tumor-targeted nanoparticles through the combination of nuclear medicine and advanced nanotechnology will make way for more effective radiation therapy with less harm to healthy tissues [79]. Current research is concentrated on manufacturing radionuclides and utilizing laser ablation techniques to create nano-radiopharmaceuticals with heightened imaging precision and therapeutic selectivity [21]. Moreover, progress in the field of nanosized radiopharmaceuticals, like 177Lu-SN201 and 99mTc-G-PNP, demonstrates encouraging prospects for targeting solid tumors and enhancing imaging capabilities [53]. Global collaborative endeavors among proficient researchers have established protocols and standards for the delivery mechanisms of nanoradiopharmaceuticals, facilitating the path towards clinical application and personalized treatment of cancer. Further exploration into the synergy of radiotherapy with diverse nanomaterials, such as metal nanoparticles, can potentially enhance radiosensitization and elevate treatment effectiveness across various types of cancer [80].

The Future works in nanoradiopharmaceuticals may focus on improving tumor-targeted imaging and therapy through the fusion of radionuclide and nanoparticle [79]. With this combination, multifunctional nanoplatforms for improved cancer diagnostics and treatment might be created by utilizing the passive/active targeting capabilities, high loading capacity, and surface properties of nanoparticles. Furthermore, progress in radionuclide synthesis and laser ablation technologies could result in the development of nanoradiopharmaceuticals characterized by exceptional purity, rapid biodegradability, and improved imaging or therapeutic properties [53]. Initiatives like the coordinated research project led by the International Atomic Energy Agency have already set the stage for the establishment of well-defined and efficient nanoscale delivery systems for radiopharmaceuticals, emphasizing site-specific targeting and optimal radiolabeling techniques [80]. Subsequent investigations may delve into the integration of nanoradiopharmaceuticals with other therapeutic modalities to facilitate synergistically enhanced combination therapies, ultimately revolutionizing the field of nuclear medicine [58].

The investigations in the field of nanoradiopharmaceuticals should be directed towards addressing various crucial knowledge gaps that have been identified in the provided contexts.

These gaps include the require for more comprehensive biodistribution studies to extend our understanding of how nanoparticles behave in living cells [79], The examination of novel radioisotope-labeled nanoparticles to move forward tumor targeting and treatment adequacy [21], the combination of nuclear medicine and advanced nanotechnology to make more proficient tumor-targeted to improve cancer diagnosis and therapy [3], the development of accurate and profoundly effective delivery systems for radiopharmaceuticals utilizing procedures from nanotechnology field [53], and the investigation of how tumor microenvironment and immunogenicity are altered by radioenhancing nanoparticles to maximize clinical outcomes. The future work may encompass the evolution of nanomaterials specifically designed for more efficient disease detection and treatment [81].

8. Conclusions

The advanced nanotechnology offers best quality clinical applications in nuclear medicine field by introducing novel approaches to nuclear diagnosis and therapy. The unique characteristics of nanoparticles, such as their dimensions, morphology, and surface alterations, allow for their labeling with radioisotopes, leading to the creation of theranostic tools that merge diagnostic and therapeutic functions into a unified system, as well as, the nanoparticles enhance the targeted delivery and retention of radionuclides in tumors, maximizing therapeutic outcomes while ensuring safe elimination from the body.

Some of radiolabeled nanoparticles have undergone thorough different examination in controlled laboratory settings, within living organisms, and preclinical studies for all the findings displaying encouraging outcomes for precise delivery at designated locations within the body. The utilization of advanced nanotechnology in nuclear medicine presents numerous opportunities, including the development of tumor-targeted by radiolabeled nanoparticles for cancer diagnosis and treatment by leveraging the special qualities of nanoparticles such as increased surface area-to-volume proportion, active targeting capabilities. Nanoparticles have demonstrated significant potential as nuclear imaging agents, enabling multimodal molecular imaging with superior sensitivity and specificity, thereby creating new possibilities for theranostic applications.

On the other hand, the combination of nanotechnology with nuclear medicine encounters various challenges such as the inadequate delivery of radionuclides to tumor sites, attaching targeting ligands, safety standards, and addressing regulatory issues. The future works in advanced nanotechnology within nuclear medicine entail the design of nanomaterials tailored to enhance the efficiency of disease detection and treatment.

List of Abbreviations:

NPs ➔ Nanoparticles
SPECT ➔ single-photon emission computed tomography
PET ➔ positron emission tomography
CT ➔ computed tomography
MRI ➔ Magnetic resonance imaging
TAT ➔ Targeted alpha-particle therapy

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