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Theranostic Nanoplatforms in Nuclear Medicine: Current Advances, Emerging Trends, and Perspectives for Personalized Oncology

María Jimena Salgueiro * and Marcela Zubillaga

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Theranostic Nanoplatforms in Nuclear Medicine: Current Advances, Emerging Trends, and Perspectives for Personalized Oncology

María Jimena Salgueiro [1,2,*] and Marcela Zubillaga [1,2,3]

[1] Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Cátedra de Física, Buenos Aires, Argentina.

[2] Universidad de Buenos Aires, Instituto de Tecnología Farmacéutica y Biofarmacia (InTecFyB), Buenos Aires, Argentina

[3] Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Buenos Aires, Argentina

* Correspondence: jsalgueiro@ffyb.uba.ar

Abstract

The convergence of nanotechnology with nuclear medicine has led to the development of theranostic nanoplatforms that combine targeted imaging and therapy within a single system. This review provides a critical and updated synthesis of the current state of nanoplatform-based theranostics, with a particular focus on their application in oncology. We explore multifunctional nanocarriers that integrate diagnostic radionuclides for SPECT/PET imaging with therapeutic radioisotopes (α-, β-, or Auger emitters), chemotherapeutics, and biological targeting ligands. We highlight advances in nanomaterial engineering—such as hybrid architectures, surface functionalization, and stimuli-responsive designs—that improve tumor targeting, biodistribution, and therapeutic outcomes. Emphasis is placed on translational challenges including pharmacokinetics, toxicity, regulatory pathways, and GMP-compliant manufacturing. The article closes with a forward-looking perspective on how theranostic nanoplatforms could reshape the future of personalized oncology through precision-targeted diagnostics and radiotherapy.

Keywords: radionuclide imaging; nanotheranostics; nanoplatforms; molecular imaging; nanomedicine

1. Introduction

1.1. Background: From Monotherapy to Integrated Theranostics

The last two decades have witnessed a transformative shift in the conceptualization and clinical management of complex diseases, particularly cancer. Traditional approaches based on monotherapies—whether chemotherapeutic agents or external radiation—have gradually given way to integrated strategies that seek not only to treat but also to understand, monitor, and adapt therapy in real time. At the heart of this transition lies the emergence of theranostics, a hybrid paradigm that integrates diagnostic and therapeutic capabilities within a single platform [1,2].

Theranostics has gained particular relevance in the era of precision medicine, where treatment efficacy depends on individual patient biology and tumor heterogeneity. The underlying principle of theranostics is to deliver molecularly targeted therapy, while simultaneously visualizing its biodistribution, target engagement, and therapeutic outcome. This integrated feedback loop enables patient selection, dose optimization, early assessment of response, and rapid therapeutic adaptation [3].

Among the disciplines that have contributed to the maturation of theranostics, nuclear medicine occupies a uniquely privileged position. This is due to its intrinsic capability to deliver both diagnostic (gamma or positron emitters) and therapeutic (beta or alpha emitters) radioisotopes to

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molecular targets via the same or analogous ligands. In this context, theranostics has evolved not merely as a technological innovation but as a defining framework for the field of nuclear medicine, culminating in what is often referred to as nuclear theranostics [4,5].

In nuclear theranostics, a single molecular targeting vector—such as a peptide, antibody fragment, or small molecule—is labeled with a diagnostic radionuclide for molecular imaging (e.g., 68Ga, 18F, 99mTc) and with a therapeutic radionuclide for targeted radionuclide therapy (e.g., 177Lu, 131I, 225Ac). This dual-use concept enables a "see what you treat, treat what you see" approach, ensuring that only patients whose tumors express the appropriate molecular target receive the corresponding therapy [6,7]. Successful clinical examples include the use of radiolabeled somatostatin analogs in neuroendocrine tumors and Prostate Specific Membrane Antigen (PSMA)-targeting ligands in prostate cancer, both of which have revolutionized disease management and opened new avenues for innovation [8].

1.2. The Convergence of Nanotechnology and Nuclear Medicine

The advent of nanotechnology has added further complexity and versatility to the theranostic field. Nanoplatforms such as liposomes, dendrimers, metal-organic frameworks (MOFs), and inorganic nanoparticles offer multifunctional architectures capable of encapsulating radionuclides, chemotherapeutic agents, imaging probes, and targeting ligands within a single construct [9,10]. These platforms not only improve pharmacokinetics and tumor retention via enhanced permeability and retention (EPR) or active targeting, but also enable multimodal imaging and multivalent interactions, potentially overcoming resistance mechanisms and tumor heterogeneity [11].

The convergence of nuclear medicine and nanotechnology represents a frontier in personalized oncology, aiming to enhance the accuracy, efficacy, and safety of cancer care. However, this convergence also brings forth regulatory, radiochemical, and translational challenges that require coordinated interdisciplinary research to ensure clinical translation [12]. The integration of nanotechnology into nuclear medicine has given rise to a powerful synergy that is redefining the frontiers of diagnosis and therapy. Both fields share a molecular-level approach to disease, and their convergence has enabled the creation of highly sophisticated platforms that simultaneously deliver targeted radionuclide therapy, advanced molecular imaging, and even synergistic chemotherapy or immunomodulation [13,14].

1.3. Advances in Nanoplatform Design and Their Pharmacokinetic and Functional Benefits

Nanoplatforms offer a series of advantages for nuclear medicine applications. Their tunable physicochemical properties—including size, shape, surface charge, and functionalization—allow for precise control over pharmacokinetics, biodistribution, and targeting [15]. These characteristics improve tumor accumulation via EPR effect and facilitate active targeting through the conjugation of ligands that bind to tumor-specific markers, such as integrins, human epidermal growth factor receptor 2 (HER2), or PSMA [16]. Importantly, these platforms provide sufficient surface area to accommodate multiple cargoes, such as radionuclides for imaging and therapy (e.g., 68Ga, 89Zr, 177Lu, 225Ac), fluorescent dyes, chemotherapeutic agents, and immune modulators, within a single multifunctional construct [17].

In recent years, there has been a growing interest in the development of radio-nanomedicines, where nanoparticles are radiolabeled to combine the advantages of nuclear imaging (sensitivity, quantification, real-time biodistribution) with the versatility of nanoscale delivery systems [18]. These radio-nanoplatforms enable multimodal imaging (PET, SPECT, MRI, optical) and theranostic capabilities, such as image-guided drug delivery or radionuclide-chemotherapy combination therapy. For instance, liposomes and dendrimers labeled with therapeutic radionuclides such as 177Lu or 90Y have been explored for their ability to deliver both radiation and chemotherapeutics deep into solid tumors [19]. Furthermore, emerging inorganic nanomaterials such as gold nanoparticles, silica nanoparticles, and hafnium oxide particles have demonstrated potential in radioenhancement, whereby the local radiation dose is increased due to the interaction of the

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nanoparticle with ionizing radiation [20]. When combined with radioisotopes, these platforms can act as amplifiers of radiobiological effects, expanding the potential of internal radiotherapy.

Another rapidly expanding area is that of pretargeting strategies, where radiolabeled small molecules are administered after a nanocarrier loaded with a tumor-targeting moiety, improving specificity and reducing off-target exposure [21]. These approaches further demonstrate the flexibility of nanosystems to accommodate complex architectures compatible with radiolabeling techniques, including click chemistry, chelator-based coordination, or intrinsic doping for metallic nanoparticles [22].

Nevertheless, the successful clinical translation of nanotheranostic systems remains challenged by several critical factors, including radiolabeling stability, reproducibility in large-scale synthesis, immunogenicity, and regulatory compliance [11]. Furthermore, the complexity of these hybrid systems requires interdisciplinary collaboration among radiochemists, nanotechnologists, clinicians, and pharmacologists to ensure safety, efficacy, and standardization [23]. Despite these hurdles, the convergence of nanotechnology and nuclear medicine is paving the way for next-generation precision theranostics, offering a route to tailor treatments not only to the molecular profile of the tumor but also to its dynamic evolution during therapy. In this context, *nanotheranostics* represents not just a research niche but a strategic paradigm for the future of oncologic imaging and therapy.

1.4. Scope of This Review

The rapid expansion of nanotechnology-based platforms and their integration with radionuclide imaging and therapy has transformed the landscape of cancer management, particularly within the emerging paradigm of personalized nanotheranostics. However, the heterogeneity of nanoplatform architectures, radionuclide choices, functionalization strategies, and combinatorial therapeutic approaches calls for a systematic synthesis of current knowledge, translational progress, and persistent challenges.

This review aims to provide a comprehensive, critical overview of the current state, technological advances, and future directions of nanoplatform-based theranostics in nuclear medicine, with a strong emphasis on oncological applications. Our objective is not only to catalog recent developments, but also to highlight the mechanistic rationales that support the design and functional integration of nanocarriers with diagnostic and therapeutic radionuclides. Moreover, we seek to elucidate how these hybrid systems are evolving toward clinically relevant platforms capable of multimodal imaging, image-guided therapy, and combinatorial treatment delivery (e.g., radiotherapy plus chemotherapy or immunotherapy).

2. Theranostic Principles and the Role of Nanoplatforms

2.1. Definition and Conceptual Evolution of Theranostics

The term *theranostics*—a portmanteau of "therapy" and "diagnostics"—was formally introduced in the early 2000s to describe integrated strategies that combine therapeutic and diagnostic functions within a single system, enabling real-time treatment monitoring and individualized medical interventions [24]. However, the conceptual foundation of theranostics predates its nomenclature and is deeply rooted in the legacy of nuclear medicine. As early as the 1940s and 1950s, radiopharmaceuticals such as 131I were used for both diagnostic imaging and treatment of thyroid diseases, effectively embodying the "see what you treat, and treat what you see" paradigm decades before the field adopted the term "theranostics" [25,26].

Over time, technological and scientific advancements have refined and expanded the scope of theranostic applications. The development of hybrid imaging systems such as Positron Emission Tomography (PET)/ Computed Tomography (CT) and PET/ Magnetic Resonance Imaging (MRI) has enabled the concurrent acquisition of anatomical and functional data with high resolution and precision [27]. Simultaneously, the rise of nanotechnology has led to the engineering of multifunctional platforms capable of loading multiple payloads—such as radionuclides,

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chemotherapeutic agents, photosensitizers, and gene-editing components—and delivering them selectively to disease sites [28]. These advances have contributed to a reconceptualization of theranostics as a cornerstone of precision medicine, with applications now extending beyond oncology into cardiology, neurology, and infectious diseases [2,14].

Importantly, the chemical and structural diversity of nanoplatforms—including organic, inorganic, and hybrid systems—has enhanced their adaptability to different biomedical contexts, offering tailored solutions for various disease pathophysiologies. For instance, liposomes and polymeric micelles are often employed for drug delivery and diagnostic imaging in solid tumors, while inorganic structures such as gold or iron oxide nanoparticles have shown promise in treating and monitoring metastatic or hematologic malignancies [29]. Thus, nanoplatforms serve not only as physical carriers but as customizable theranostic architectures capable of integrating molecular targeting, real-time imaging, and controlled therapy.

The evolution of theranostics has also been shaped by a broader shift in healthcare paradigms—from reactive to predictive and personalized medicine. This transition emphasizes biomarker-guided approaches that allow for patient stratification, early intervention, and continuous monitoring of disease progression and response to therapy [30]. In this context, theranostics directly addresses the clinical challenge of biological heterogeneity, enabling clinicians to identify, characterize, treat, and track disease using a unified technological platform. By minimizing the diagnostic–therapeutic gap, such systems not only enhance treatment efficacy but also reduce systemic toxicity and unnecessary exposure to ineffective interventions [31].

While the full potential of nanotheranostics is still being explored, its trajectory builds on decades of innovation and clinical experience. As will be discussed in the following section, the integration of diagnostic and therapeutic functionalities into a single platform reflects a rational, technologically enabled evolution that responds to both the limitations of conventional therapies and the opportunities of precision medicine.

2.2. Main categories of Nanoplatoforms used in nuclear theranostics

Nanoplatforms employed in theranostics are diverse in origin, composition, and functionality. Literature taxonomies often reveal (i) the chemical nature (organic, inorganic, hybrid), (ii) structural characteristics (size, morphology, porosity), and (iii) functionalization potential (targeting ligands, imaging agents, therapeutic payloads, or surface chemistry for radiolabeling). For the purpose of systematization in this article, we propose an analysis from a chemical point of view.

2.2.1. Organic nanoplatforms

This group includes polymeric nanoparticles, liposomes, dendrimers, micelles, and lipid nanocarriers. These classical nanoplatforms have long been at the forefront of nanomedicine and have played a foundational role in shaping the current field of nuclear theranostics. Their intrinsic biocompatibility, biodegradability, capacity to encapsulate both hydrophilic and hydrophobic agents and tunable surface properties [32] make them ideal for radiolabeling, multifunctionalization and clinical translation [33,34]. Polymeric nanoparticles, especially those made from Food and Drug Administration (FDA)-approved materials like poly(lactic-co-glycolic acid) (PLGA) or PEGylated polymers, offer controlled and sustained drug release, long circulation times, and low immunogenicity.

Liposomes, spherical vesicles composed of phospholipid bilayers, were among the first nanocarriers used for drug delivery and have since been adapted for theranostic applications by incorporating imaging agents and therapeutic payloads, including radionuclides [35] and they can be functionalized with antibodies or peptides for active targeting. Their aqueous core allows encapsulation of hydrophilic drugs or radionuclides, while lipophilic agents can be integrated into the bilayer. In nuclear imaging, liposomes radiolabeled with technetium-99m (99mTc) or indium-111 (111In) have been used for Single Photon Emission Tomography (SPECT)/CT applications [36]. A representative example includes 111In-PEGylated immunoliposomes functionalized with

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monoclonal antibodies and single-chain variable fragments (scFv), enabling specific targeting and high-contrast tumor imaging [37]. Therapeutically, liposomes have been employed to encapsulate β-emitting radionuclides such as 177Lu and α-emitters like 225Ac. For example, thermosensitive liposomes co-loaded with 64Cu and doxorubicin (DOX) have demonstrated PET-guided release and enhanced chemoradiotherapeutic synergy in preclinical tumor models [38]. This design allows for externally triggered drug release in response to mild hyperthermia while simultaneously enabling real-time PET imaging.

Dendrimers are synthetic, branched macromolecules characterized by highly controlled architecture and multivalency. Their size and surface characteristics can be fine-tuned to optimize biodistribution and clearance profiles. Their internal cavities and numerous surface functional groups enable simultaneous loading of radionuclides, targeting moieties, and therapeutic agents. Poly(amidoamine) (PAMAM) dendrimers have been functionalized with chelators like 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid (DOTA) or 1,4,7-Triazacyclononane-1,4,7-triacetic acid (NOTA) to stably bind 68Ga, 177Lu, or 64Cu, enabling their use in both diagnostic and therapeutic applications [39]. 68Ga and 99mTc-labeled PAMAM dendrimers have demonstrated prolonged circulation, high tumor uptake, and favorable pharmacokinetics for PET/SPECT imaging [40]. In addition, 177Lu-conjugated dendrimers targeting HER2 or PSMA have shown promising antitumor effects in xenograft models [7]. Their multivalency also supports the development of multimodal platforms for PET/MRI imaging or radio-chemo-immunotherapy.

Polymeric nanoparticles (PNPs) are solid colloidal systems synthesized from biodegradable and biocompatible polymers such as PLGA, polycaprolactone (PCL), chitosan, or PEGylated copolymers. These systems offer high versatility in terms of size, drug-loading capacity, degradation rate, and compatibility with a wide range of therapeutic and imaging agents. Structurally, they can be formulated as nanospheres, in which the therapeutic or diagnostic agents are uniformly distributed throughout the polymer matrix, or as nanocapsules, where the active compounds are confined within a polymeric shell surrounding a core. In the context of nuclear medicine, PNPs have been extensively explored as vehicles for both diagnostic and therapeutic radionuclides. For example, 177Lu-labeled PLGA nanoparticles have been developed for targeted radionuclide therapy, showing favorable stability and prolonged blood circulation times in preclinical tumor models [41]. When combined with anticancer agents such as paclitaxel or cisplatin, these platforms enable co-delivery strategies that enhance therapeutic efficacy via synergistic mechanisms [42]. Importantly, polymeric particles can be engineered to offer controlled and sustained release profiles, which is critical in maintaining therapeutic levels of radionuclides or drugs within tumors while minimizing systemic exposure. Several studies have also demonstrated the ability of radiolabeled PNPs to improve imaging contrast. For instance, 99mTc-labeled chitosan nanoparticles have been evaluated for sentinel lymph node imaging and inflammation tracking [43]. Similarly, 64Cu- or 89Zr-labeled PLGA nanoparticles have enabled PET imaging of biodistribution and tumor accumulation with high tumor-to-background ratios [44]. Due to their modular design, PNPs can be adapted to carry multiple imaging probes and radionuclides, enabling dual- or multimodal imaging with PET, SPECT, and optical readouts. Polymeric micelles, a subcategory of PNPs, are formed by the self-assembly of amphiphilic block copolymers in aqueous environments. These nanostructures feature a hydrophobic core suitable for encapsulating poorly soluble drugs or lipophilic radionuclide complexes, surrounded by a hydrophilic corona (often PEG), which enhances their solubility and stability in biological fluids. Micelles typically range from 10 to 100 nm in size, favoring passive accumulation in tumors via the EPR effect. Radiolabeled polymeric micelles have shown promising results in theranostic applications. For example, 64Cu-labeled micelles have been employed for PET imaging of tumors, exhibiting high in vivo stability and favorable pharmacokinetics [45]. In therapeutic settings, micelles co-loaded with radionuclides and cytotoxic drugs have demonstrated potent antitumor activity in various xenograft models [14]. Owing to their dynamic assembly and tunable release behavior, micelles offer particular advantages in designing stimuli-responsive systems, which are discussed in later sections. Taken together, polymeric nanoparticles—both solid particles and micellar systems—

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constitute a robust and adaptable platform for radiotheranostics. Their physicochemical tunability, capacity for multimodal cargo loading, and compatibility with a variety of radionuclides make them ideal candidates for the development of personalized nanomedicines. While many polymer-based systems are currently in preclinical stages, their clinical translation is actively being pursued.

2.2.2. Inorganic nanoplatforms

Inorganic nanomaterials have emerged as critical tools in nuclear theranostics due to their structural robustness, tunable physicochemical properties, and capacity for intrinsic imaging. Their high surface-area-to-volume ratio, stability under irradiation, and ability to incorporate or chelate a wide range of radionuclides make them ideal for dual diagnostic and therapeutic use. Among the most studied platforms are gold nanoparticles (AuNPs), quantum dots (QDs), iron oxide nanoparticles (SPIONs), and mesoporous silica nanoparticles (MSNs).

AuNPs exhibit excellent biocompatibility, high atomic number for X-ray attenuation, and facile surface chemistry. They have been radiolabeled with both diagnostic (64Cu, 68Ga) and therapeutic radionuclides (198Au, 177Lu) using chelator-free or chelator-based methods. For example, 64Cu-doped AuNPs have been used for PET imaging with favorable tumor accumulation and pharmacokinetics, while 198Au-labeled AuNPs functionalized with targeting ligands such as Arginylglycylaspartic acid (RGD) peptides demonstrated combined radionuclide therapy and photothermal ablation capabilities in preclinical models [46].

QDs—semiconductor nanocrystals with size-tunable fluorescence—have been functionalized with chelators such as NOTA and labeled with 64Cu or 68Ga for PET-optical imaging applications. A representative example is the use of CdSe/ZnS QDs PEGylated and radiolabeled with 68Ga for imaging U87MG glioma xenografts [47]. Despite concerns over heavy-metal toxicity, strategies such as encapsulation within polymer shells or protein-based carriers (e.g., ferritin) have improved their biocompatibility for in vivo use.

SPIONs are established MRI contrast agents but have also been explored for multimodal nuclear imaging. PEGylated SPIONs radiolabeled with 68Ga or 64Cu have shown dual PET/MRI functionality, enabling combined anatomical and functional imaging [48]. In therapeutic contexts, SPIONs have been loaded with Auger or α-emitting radionuclides, enhancing tumoricidal effects. Furthermore, 177Lu-labeled Fe–gallic acid coordination complexes have demonstrated tumor retention and improved survival in murine models [49].

MSNs offer large pore volumes and tunable surface chemistry, making them versatile for co-loading of chemotherapeutics and radionuclides. Radiolabeled with 64Cu, 89Zr, or 177Lu, MSNs have demonstrated utility in PET imaging and radionuclide therapy. Their mesoporous structure facilitates controlled release and multimodal combinations. For example, 177Lu-labeled MSNs co-loaded with DOX have achieved synergistic antitumor effects and reduced systemic toxicity [50].

Despite their promise, inorganic nanoplatforms face translational hurdles including long-term toxicity, reticuloendothelial system (RES) sequestration, and challenges in radiometal retention. However, their intrinsic imaging properties and stability under radiolabeling continue to position them at the forefront of next-generation radiotheranostic development.

2.2.3. Hybrid and Multifunctional Nanostructures

Hybrid nanoplatforms combine organic and inorganic components to create multifunctional theranostic agents capable of simultaneous imaging, therapy, targeting, and controlled release. By integrating structural elements such as lipids, polymers, silica, metals, and biomolecules, these platforms offer modularity to fine-tune pharmacokinetics, biodistribution, and payload co-delivery.

These systems often incorporate diagnostic radionuclides (64Cu, 68Ga, 89Zr) and therapeutic isotopes (177Lu, 225Ac), alongside chemotherapeutics or photosensitizers. For instance, 64Cu-doped PdCu@Au nanoparticles functionalized with D-Ala-peptide T-amide (DAPTA) peptides have enabled PET-guided photothermal therapy in CCR5-expressing breast tumors, showcasing synergy between imaging and treatment modalities [51].

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Another example is the development of dendrimer–gold nanoparticle hybrids functionalized with folate and bombesin, radiolabeled with 177Lu. These constructs achieved dual-targeting of Gastrin-Releasing Peptide Receptor (GRPr) and Folate Receptor (FR) receptors, enabling combined radionuclide therapy and photothermal ablation with improved tumor specificity [52].

Yolk–shell silica-metal hybrids, such as CuS@MSN, combine the porous framework of MSNs with photothermal metal cores. These systems can be co-loaded with 64Cu and chemotherapeutics for PET-guided chemoradiotherapy. Their responsiveness to acidic tumor environments allows site-specific drug release and enhanced antitumor effects.

Ferritin nanocages (Fn) have also been used to encapsulate CuS nanoparticles, producing CuS-Fn constructs radiolabeled with 64Cu. These particles demonstrated high photothermal efficiency and PET signal in glioblastoma models, highlighting the utility of biomimetic carriers for deep-tissue imaging and treatment [53–55].

MOFs are another emerging class of hybrid nanoplatforms. These crystalline porous materials support high loading of drugs and radionuclides, and their structure can be tuned for stability and targeting. Radiolabeled MOFs with 64Cu or 177Lu have been evaluated for PET imaging and combined immunomodulatory therapy [56,57].

Overall, hybrid nanostructures address key limitations of single-component systems by combining high imaging contrast, therapeutic payloads, and targeting specificity. Although their clinical translation is limited by complexity of synthesis, reproducibility, and regulatory demands, early clinical studies (e.g., Cornell dots labeled with 124I) demonstrate feasibility. Continued development hinges on scalable manufacturing and long-term biocompatibility evaluation.

2.3. Rationale for Combining Diagnostic and Therapeutic Modalities

While the conceptual and historical foundations of theranostics were outlined above, this section explores the clinical and technological motivations behind the integration of diagnostic and therapeutic functionalities into a single nanoplatform. This convergence is not merely a theoretical ideal, but a practical strategy that addresses several critical limitations of conventional oncology, particularly the need for individualized treatment, real-time therapy monitoring, and reduced systemic toxicity.

The incorporation of radiodiagnostic agents and therapeutic payloads within a single nanosystem enables image-guided therapy, whereby the biodistribution, tumor uptake, and clearance of the agent can be tracked in vivo. This capability allows for real-time dosimetry and adaptive treatment planning based on patient-specific tumor biology, rather than relying on empirically fixed dosing regimens [58]. For example, PET- or SPECT-labeled nanocarriers enable visualization of drug delivery pathways, quantification of tumor accumulation, and longitudinal tracking of therapeutic efficacy in both preclinical and clinical settings [59]. Moreover, nanoplatforms enhance selective tumor targeting via a combination of passive and active mechanisms. The EPR effect facilitates preferential accumulation of nanoparticles in tumor tissue due to leaky vasculature and impaired lymphatic drainage. This passive accumulation can be further refined through active targeting strategies, where ligands such as monoclonal antibodies, peptides (e.g., RGD, bombesin), or aptamers are conjugated to the nanoparticle surface to recognize and bind specific tumor-associated receptors [2,32].

Another important rationale for nanotheranostics is the reduction of systemic toxicity. By confining the delivery of cytotoxic drugs or radioisotopes to tumor sites, these systems limit exposure to healthy tissues, thereby minimizing adverse effects often associated with conventional chemotherapy or external beam radiotherapy [60]. This is particularly advantageous in pediatric or frail patient populations, where minimizing collateral damage is essential. In addition, nanoplatforms offer a versatile scaffold for multimodal therapeutic integration. Hybrid nanostructures can co-deliver chemotherapeutics and radionuclides or combine radiotherapy with photothermal or photodynamic therapy to enhance cytotoxicity, overcome resistance mechanisms, and improve treatment efficacy [49]. For instance, 177Lu-labeled gold nanoparticles co-loaded with

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paclitaxel have demonstrated synergistic effects in HER2+ breast cancer models by simultaneously inducing DNA damage and microtubule disruption [43].

Finally, the theranostic paradigm supports biomarker-guided stratification and treatment personalization. By conjugating nanocarriers with ligands targeting molecular markers such as PSMA, Epidermal Growth Factor Receptor (EGFR), or HER2, nanotheranostics can be tailored to individual patient profiles. This not only enhances treatment specificity but also enables predictive imaging that informs therapeutic decisions [61].

As this field progresses, integration with digital health technologies, artificial intelligence, and systems biology is expected to refine patient selection, optimize therapeutic regimens, and predict clinical outcomes more accurately. These developments mark a shift from standardized, protocol-driven oncology toward adaptive, feedback-informed treatment frameworks that capitalize on the full potential of theranostic nanomedicine [62].

3. Radioisotope Selection, Radiolabelling Strategies and Stability Concerns

3.1. Radioisotopes for Diagnostic

In nuclear medicine, the choice of radioisotopes for diagnostic purposes is primarily based on their decay characteristics, which determine the nature and energy of the emitted radiation. Diagnostic radiopharmaceuticals typically incorporate radioisotopes that undergo electromagnetic decay, emitting gamma (γ) photons or positrons (β+). Gamma-emitting isotopes are used in planar scintigraphy and SPECT imaging, as the emitted photons exit the body and are detected by gamma cameras. Table 1 summarizes commonly used γ-emitting radionuclides for scintigraphic imaging. In contrast, positron-emitting isotopes, employed in PET imaging, decay via β+ emission. These positrons travel a short distance in tissue before annihilating with electrons, resulting in the emission of two 511 keV annihilation photons in opposite directions, which are detected in coincidence by PET scanners. The selection of appropriate diagnostic radioisotopes must therefore consider not only the decay mode and photon energy, but also their compatibility with radiolabelling strategies and the physicochemical stability of the resulting radioconjugates. [63].

Table 1. Physical characteristics of candidate radioisotopes currently used in diagnostics.

Radioisotope	Decay mode	$T_{1/2}$	Energy of the main photon in keV (abundance %)	Diagnostic method
^{99m}Tc	γ	6 h	140 (89)	SPECT
^{131}I	β^-	8 d	364 (81)	SPECT
^{123}I	EC	13.2 h	159 (83)	SPECT
^{67}Ga	EC	78.3 h	93 (37); 185 (20); 300 (17); 395 (5)	SPECT
^{111}In	EC	2.8 d	171 (90); 245 (94)	SPECT
^{11}C	B^+	20 min	511	PET
^{18}F	β^+	110 min	511	PET
^{68}Ga	β^+	68 min	511	PET

EC: Electron Capture.

3.2. Radioisotopes for therapy

For therapeutic applications, the radioisotopes of choice are those that emit charged particles—either heavy particles such as alpha (α) particles or lighter ones such as beta minus (β−) particles—which deposit their energy directly into the surrounding tissue through ionization events. The specific ionization capacity of these particles, which depends on their mass and charge, results in limited penetration depths: typically in the micrometer range for α-particles and a few millimeters for β−-particles. Unlike photons, these emissions constitute directly ionizing radiation and are

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capable of inducing localized cytotoxic effects. Within a restricted radius from the decay site, determined by the particle's energy, they can cause significant DNA damage in tumor cells, leading to impaired replication and ultimately cell death. Table 2 summarizes several of the most commonly used therapeutic radioisotopes in nuclear medicine [63].

Table 2. Physical characteristics of particle-emitting radionuclides currently used for therapy in Nuclear Medicine.

Radioisotope	$T_{1/2}$	Emitted particle (Energy MeV)	Max range in soft tissue
^{131}I	8 d	β^- (0.606)	2.3 mm
^{223}Ra	11.43 d	4α 2β^- (5.64, 5.715)	<100 μm
^{90}Y	64.1 h	β^- (2.27)	11.3 mm
^{177}Lu	6.65 d	β^- γ (0.497)	1.8 mm
^{188}Re	0.7 d	β^- (2.12)	10 mm
^{225}Ac	10 d	4α 2β^- (6.83)	47-85 μm

3.3. Radioisotopes pairing strategies

The clinical success of theranostic radiopharmaceuticals relies not only on the biological specificity of the targeting vector but also on the chemical properties of the radioisotopes and their coordination with appropriate chelators. In nanotheragnosis, where radiometals are incorporated into nanoparticle systems, the stability and versatility of these chemical complexes are critical to ensure effective in vivo performance, minimize off-target radiation, and enable matched diagnostic and therapeutic functionalities.

Among the most widely used theranostic pairs is the combination of 68Ga and 177Lu coordinated via DOTA. DOTA forms highly stable octadentate complexes with trivalent radiometals, making it ideal for both diagnostic (68Ga, positron emitter) and therapeutic (177Lu, β− emitter) applications. This chemical similarity allows the development of chemically identical radioconjugates, such as [68Ga/177Lu]Ga/Lu-DOTA-TATE, used in the management of somatostatin receptor-expressing neuroendocrine tumors. The DOTA chelator can also be conjugated to nanocarriers (e.g., liposomes, micelles, polymeric nanoparticles), preserving radiolabeling efficiency and in vivo stability under physiological conditions [64,65].

Similarly, the PSMA-targeting theranostic pair 68Ga-PSMA-11 / 177Lu-PSMA-617 employs DOTA-based or similar macrocyclic chelators (e.g., N, N′-bis(2-hydroxybenzyl)ethylenediamine-N,N′-diacetic acid (HBED) or 2-[1,4,7,10-Tetraazacyclododecane-4,7,10-tris(t-butyl acetate)]-pentanedioic acid-1t-butyl ester (DOTAGA)), selected based on the coordination preferences of each metal ion. These structures not only ensure high thermodynamic and kinetic stability but also allow site-specific conjugation to PSMA ligands or nanostructures, facilitating targeted delivery and controlled biodistribution. The availability of long-lived therapeutic isotopes such as 177Lu and emerging alpha-emitters like 225Ac further extends the potential of these systems for nanotheragnostic applications [66].

The metal–chelator pairing is central to theranostic design: radiometals such as 64Cu, 89Zr, 90Y, and 67Ga offer diverse decay properties and coordination chemistries that can be matched with appropriate chelators (e.g., NOTA, Deferoxamine (DFO), diethylenetriaminepentaacetic acid (DTPA)), enabling tailored pharmacokinetics and optimized imaging or therapeutic windows. Importantly, many of these chelators can be functionalized for covalent attachment to nanoparticles, providing multivalency, enhanced circulation time, and improved tumor accumulation via the EPR effect [67,68].

These chemical considerations—metal ion coordination geometry, charge, oxidation state, and chelator denticity—are especially relevant in the context of nanotheragnosis, where radiolabeling conditions must preserve the structural and functional integrity of the nanoplatform. The use of matched diagnostic/therapeutic radiometals that bind to a common chelator scaffold not only

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streamlines the synthesis of theranostic agents but also facilitates regulatory translation and clinical implementation.

Table 3 summarizes selected clinically established and emerging theranostic pairs used in nuclear medicine, highlighting their radiophysical properties, commonly used chelators, and suitability for integration into nanotheragnostic platforms. The choice of chelator is critical to ensure radiolabeling efficiency and in vivo stability. DOTA and its derivatives are particularly favored for their capacity to form kinetically inert complexes with a variety of diagnostic and therapeutic radiometals. Nanotheragnostic compatibility is assessed based on the ability to conjugate or encapsulate the radiolabeled compound within nanocarriers without compromising its stability or bioactivity

Table 3. Theranostic pairs in nuclear medicine: chemical and clinical characteristics relevant to nanotheragnosis.

Diagnostic / Therapeutic Pair	Chelator	Nanotheragnostic Suitability	Clinical Application
[68Ga]/[177Lu]-DOTA-TATE	DOTA	High – stable coordination, mild labeling conditions	NETs (neuroendocrine tumors)
[68Ga]/[177Lu]-PSMA-617	DOTA / DOTAGA	High – widely adapted to nanocarriers	Prostate cancer
[64Cu]/[67Cu]-Chelate	NOTA / SarAr	Moderate–High – versatile chelation, redox sensitivity requires stabilization	Experimental – solid tumors
[89Zr]/[90Y]-Chelate	DFO (for 89Zr), DOTA (for 90Y)	Moderate – DFO less stable long-term, 90Y well adapted	Antibody labeling / solid tumors
[123I]/[131I]-MIBG	Direct iodination	Low for nanoplatforms – instability in vivo without encapsulation	Neuroblastoma, pheochromocytoma
[68Ga]/[225Ac]-PSMA	DOTA / Macropa	High – α-emitter integration into nanoparticles for targeted delivery	mCRPC, α-therapy under investigation

3.4. Radiolabeling Strategies

Radiolabeling of nanoplatforms is a critical step in designing nuclear theranostic agents, directly influencing their in vivo behavior, imaging signal, therapeutic efficacy, and biocompatibility. The choice of radiolabeling strategy must account for the physicochemical characteristics of both the radionuclide and the nanoparticle, the intended biological application, and the stability requirements of the final construct [43,69].

Radiolabeling methods may be categorized into three main strategies: chelator-based, chelator-free, and encapsulation or surface sorption [70]. Each approach offers distinct advantages and is suited for different classes of radionuclides and nanomaterials. Importantly, although 99mTc remains a cornerstone of nuclear medicine and has been successfully radiolabeled via all three of these approaches [71–76], the present section emphasizes strategies applicable to emerging radionuclides—such as 64Cu, 89Zr, 68Ga, and 177Lu—that are increasingly used in next-generation nuclear theranostics [77].

Chelator-based strategies remain the gold standard for radiolabeling metallic radionuclides, offering excellent radiochemical yields and in vivo stability. These approaches involve the conjugation of bifunctional chelating agents (BFCAs)—such as DOTA, NOTA, 2-[4,7-bis(carboxymethyl)-1,4,7-triazonan-1-yl]-5-(2,5-dioxopyrrolidin-1-yl)oxy-5-oxopentanoic acid (NODAGA), or DTPA—to the nanoparticle surface via reactive functional groups (e.g., –NH_2, –SH, –

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COOH). The chelators tightly bind radiometals such as 64Cu, 68Ga, 89Zr, and 177Lu, forming thermodynamically and kinetically stable complexes [41,78]. For instance, DOTA-conjugated polymeric micelles and lipid-based nanoparticles have been radiolabeled with 177Lu under mild aqueous conditions (pH 5–6, 30–90 °C), achieving >95% radiochemical yield [41]. Likewise, NOTA and NODAGA provide high labeling efficiency with 64Cu, enabling PET imaging of tumor biodistribution and clearance [70]. Chelators can also be pre-attached to targeting moieties or embedded within PEGylated nanocarriers, which prolong circulation and enhance tumor uptake, as demonstrated in studies using 68Ga- or 99mTc-labeled liposomes and micelles [78]. Chelator-based methods allow modular nanoparticle design and are compatible with a wide range of imaging and therapeutic applications. Nonetheless, the choice of chelator must be carefully matched to the coordination chemistry of the radionuclide, as instability may result in transchelation or loss of signal [79–82].

Chelator-free strategies offer an attractive alternative for radiolabeling nanoparticles without the use of exogenous chelating agents. These methods rely on the direct chemical interaction between the radionuclide and specific functional groups or structural features of the nanomaterial. They simplify synthesis, reduce potential immunogenicity, and often preserve the native physicochemical characteristics of the platform [69]. A widely employed mechanism in this category is doping, where radionuclides are embedded within the crystal lattice of inorganic nanomaterials during or after synthesis. For instance, 64Cu can be doped into copper sulfide (CuS) or palladium-copper-gold (PdCu@Au) nanoparticles under mildly basic aqueous conditions (pH ~9, 65–90 °C), achieving high radiochemical yields (>98%) and excellent in vivo stability [43,51,83]. This approach not only ensures robust labeling but also endows the particles with photothermal properties for synergistic therapy. Another chelator-free approach involves surface bonding or sorption. Nanoparticles containing thiol (-SH), catechol, or carboxylate functional groups—such as melanin, iron oxide, or carbon-based nanostructures—can coordinate with metallic radionuclides like 64Cu, 89Zr, or 177Lu directly on their surface. For example, melanin nanoparticles labeled with 64Cu via spontaneous metal–phenol interactions have shown strong in vivo retention and effective tumor imaging [84,85]. Neutron activation is a less common but powerful chelator-free technique, where stable isotopes within the nanoparticle are activated via neutron irradiation. This method generates radiolabeled constructs without altering their morphology or surface chemistry. For example, 198Au-labeled gold nanoparticles, prepared via this route, may be use for both SPECT imaging and β-therapy in preclinical tumor models [86]. The adsorption-based method relies on physical sorption of radionuclides onto high-affinity surfaces such as hydroxyapatite, TiO_2, or carbon nanotubes [87–89]. For example, 223Ra has been successfully sorbed onto calcium-based nanocarriers through ionic interactions, achieving high labeling efficiency and mitigating recoil-induced daughter loss [90–93]. While chelator-free techniques offer simplicity and versatility, their success depends heavily on the nanoparticle's surface chemistry and compatibility with the chosen radionuclide. The absence of a defined chelating scaffold means that achieving long-term stability requires careful engineering of surface charge, hydrophilicity, and protective coatings.

3.4.1. Regulatory Perspectives and GMP Considerations

The regulatory landscape for nuclear theranostic agents—defined as radiolabeled nanostructures for combined diagnostic and therapeutic purposes—presents unique challenges at the intersection of nanomedicine, radiopharmacy, and pharmaceutical regulation. While traditionally categorized under the umbrella of radiopharmaceuticals, nuclear theranostics involve complex multicomponent constructs that may include radionuclides, nanocarriers, targeting ligands, and therapeutic drugs, each subject to distinct regulatory scrutiny. Consequently, the clinical translation of these agents requires a harmonized and risk-based regulatory framework that adequately considers their dual functionality, nanometric nature, and radiation-emitting properties [94].

From a regulatory standpoint, nuclear theranostics are generally classified as investigational medicinal products (IMPs) or radiopharmaceuticals under both U.S. FDA and European Medicines

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Agency (EMA) guidelines. In Europe, Directive 2001/83/EC and its subsequent adaptations (including Directive 2013/59/Euratom for radiation protection) provide the overarching legal framework [95,96]. These agents must meet the regulatory requirements related to pharmaceutical quality, radioprotection, and preclinical safety, regardless of their intended use in diagnosis or therapy. The heterogeneous definitions and classifications of radiopharmaceuticals across jurisdictions complicate international clinical trials and market authorization. Therefore, initiatives from the International Atomic Energy Agency (IAEA), World Health Organization (WHO) and the EMA have sought to harmonize guidance documents and promote regulatory convergence for these compounds [94]. Non-clinical development of nuclear theranostics involves comprehensive characterization of the nanoplatform's pharmacokinetics, dosimetry, biodistribution, and toxicological profile. Regulatory guidance such as ICH M3(R2) and ICH S9 provides general frameworks, yet often lacks specificity for radiolabeled nanoparticles [97-98). In response, the EMA drafted a dedicated guideline addressing non-clinical requirements for radiopharmaceuticals (EMA/CHMP/QWP/306970/2018), which remains applicable to theranostic nanomaterials [94,99]. A notable challenge is that conventional toxicity testing under Good Laboratory Practice (GLP) is difficult for radioactive compounds. Instead, the non-radioactive components (e.g., the nanocarrier or ligand) are evaluated under GLP, while pharmacokinetics and dosimetry are conducted under radiation safety conditions in specialized facilities [94]. Depending on the novelty and pharmacological activity of the non-radioactive component, different regulatory scenarios may apply [94]. For example, if a theranostic nanoplatform uses an established vector and only the radionuclide is changed (e.g., 64Cu instead of 68Ga), limited additional testing may be sufficient. Conversely, entirely new constructs require full toxicological and pharmacokinetic assessment in one or more animal models [94].

Diagnostic nuclear theranostics often fall within the scope of "microdose" regulation, particularly when used at sub-pharmacological mass levels. The FDA and EMA allow streamlined non-clinical testing for such agents, provided that dosimetry and radiation safety are adequately justified [94]. This includes demonstrating that the administered activity and molar quantity remain below thresholds defined by ICH M3(R2) guidelines [94,97]. Therapeutic nuclear theranostics, however, generally require full toxicology packages, including genotoxicity, hematology, histopathology, and repeat-dose studies. In certain cases—such as advanced oncology—ICH S9 guidelines allow for the omission of reproductive or carcinogenicity studies if the clinical context justifies it [94,98].

Compliance with Good Manufacturing Practices (GMP) principles is essential for the clinical production of nuclear theranostics. However, current GMP guidelines, such as those in Annex 3 of the WHO Technical Report Series No. 1025, were primarily developed for small-molecule radiopharmaceuticals and may not sufficiently address nanomaterials [100].

Key GMP considerations include:

- **Radiochemical and pharmaceutical purity**: Must be above 95%, verified by radio-Thin Layer Chromatography, High-Performance Liquid Chromatography, or gamma spectrometry.
- **Sterility and apyrogenicity**: Especially critical for parenteral formulations.
- **Batch reproducibility**: Challenging in nanoscale systems, requiring robust standard operating procedures (SOPs).
- **Molar activity control**: Particularly relevant for receptor-saturating theranostic agents.
- **Documentation and traceability**: Extensively detailed records for precursor synthesis, labeling conditions, and control quality testing are mandatory.

A comparative overview of regulatory scenarios is presented in Table 4, highlighting how the level of technological innovation and the nature of the radionuclide influence the expected non-clinical studies, regulatory classification, and GMP considerations for nuclear theranostic platforms.

Table 4. Regulatory Scenarios for Nuclear Theranostics.

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Technological Innovation Level	Radionuclide Type	Regulatory Classification	Non-Clinical Requirements	GMP Considerations
Incremental (e.g., liposomes + 99mTc)	Conventional (99mTc, 111In, 131I)	IMP / Radiopharmaceutical	Reduced studies if vector known	Standard GMP processes apply
Intermediate (e.g., new polymers + 177Lu)	Emerging therapeutic (177Lu, 90Y)	Radiotherapeutic	Toxicology (S9), biodistribution, dosimetry	Process validation, radiochemical stability
Disruptive (e.g., hybrid NP + 225Ac)	High-risk a-emitter (225Ac, 213Bi, 223Ra)	Advanced Radiotherapeutic / ATMP	Full toxicology, genotoxicity, organ dosimetry	Custom GMP: shielding, purity, retention
? Increasing Regulatory Complexity	Greater innovation and risk demand more stringent regulatory oversight and tailored GMP solutions.			

*ATMP = Advanced Therapy Medicinal Product (producto medicinal de terapia avanzada, según EMA).

As nuclear theranostics become more sophisticated and widespread, regulatory authorities must evolve to accommodate their unique features. This includes the development of nanotechnology-specific pharmacopoeial monographs, dedicated EMA or FDA guidance for radiolabeled nanomaterials, and training programs for reviewers and inspectors. Moreover, collaborative platforms such as the IAEA's Radiopharmaceuticals Program and the EANM Dosimetry and Regulatory Committees can foster dialogue and consensus building across regions. A harmonized, science-driven, and risk-based regulatory model is essential to unlock the full potential of nuclear theranostics in personalized medicine.

3.4.2. Final Remarks and Conclusion

This comprehensive review highlights the diverse classes of radiolabeled nanoplatforms being developed for nuclear theranostic applications, emphasizing their chemical versatility, structural tunability, and capacity for dual diagnostic and therapeutic functionality. Organic systems such as liposomes, dendrimers, and polymeric micelles continue to evolve with increasingly sophisticated designs for radiolabeling and drug co-loading. Inorganic and hybrid nanostructures offer inherent imaging contrast, improved stability, and multifunctional capabilities—though their long-term biocompatibility remains under scrutiny. Radiolabeling strategies have expanded beyond traditional chelator-based approaches to include chelator-free, doping, surface sorption, and encapsulation techniques. These methods improve radiochemical yields, pharmacokinetics, and site-specific delivery, while supporting the integration of both established and emerging radionuclides, including α-emitters. Moreover, the co-delivery of chemotherapeutic agents with radionuclides has demonstrated promising synergistic effects in preclinical models, potentially addressing tumor heterogeneity and therapeutic resistance. Despite these advances, the translational gap remains considerable. Most of the current evidence originates from animal models, and only a limited number of formulations have entered clinical trials. Critical challenges persist in standardizing production, achieving regulatory approval, and demonstrating long-term safety. The lack of robust clinical outcome data, particularly in the last five years, limits our ability to conclude that radiolabeled nanomaterials represent the immediate future of radiopharmacy.

Nuclear theranostics represents a paradigm shift toward personalized medicine, offering tailored treatment regimens guided by real-time molecular imaging. The convergence of nanotechnology and nuclear medicine enables precise tumor targeting, adaptive dosing, and the integration of multimodal therapies within a single platform. Advances in ligand design, radiochemistry, and image-guided drug release are expected to further enhance therapeutic efficacy

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while minimizing off-target toxicity. In particular, the potential of nanoradiotheranostics lies in their ability to selectively accumulate in diseased tissues, reduce multi-step procedures, and act as individualized precision tools for complex diseases such as prostate cancer, glioblastoma, and neuroendocrine tumors. Integration with artificial intelligence, systems biology, and digital health platforms is poised to further refine patient selection, improve outcome prediction, and support biomarker-driven stratification in clinical practice. However, a comprehensive understanding of radionanotechnology is essential to improve success rates in human applications. Optimizing nanoparticle design for specific tumor microenvironments, controlling in vivo degradation and clearance, and achieving scalable GMP-compliant manufacturing remain high priorities for the field.

While radiolabeled nanomaterials hold undeniable promise for transforming the landscape of nuclear medicine, the path to clinical adoption is still complex and requires collaborative efforts across disciplines. From engineering and radiochemistry to regulatory science and clinical oncology, the successful translation of nanoradiotheranostics will depend on harmonized regulatory frameworks, robust toxicological assessment, and the generation of clinical evidence that demonstrates safety, efficacy, and cost-effectiveness. Although challenges remain, the future of nuclear theranostics is undeniably bright. As novel formulations continue to mature, and regulatory and technical hurdles are progressively addressed, radiolabeled nanoplatforms are expected to play a central role in the evolution of personalized oncology—ultimately contributing to improved patient outcomes and enhanced quality of life. As illustrated in Figure 1, the successful clinical implementation of nuclear theranostics requires a stepwise progression from robust nanomaterial design to compliance with complex regulatory standards, ultimately enabling their adoption in precision oncology workflows.

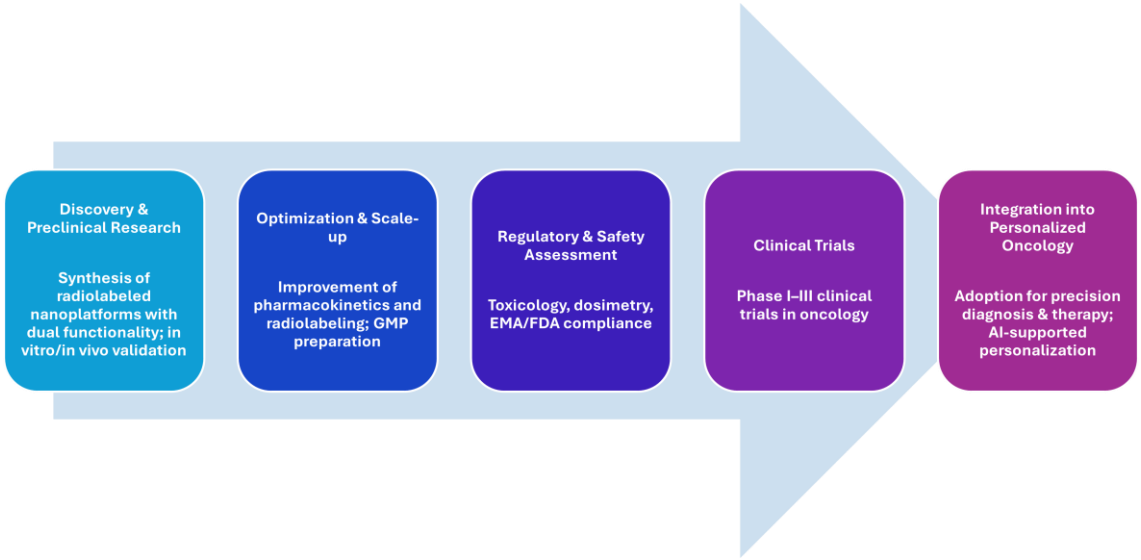

Figure 1. Roadmap to Clinical Implementation of Nuclear Theranostics. Schematic representation of the translational steps required for the clinical adoption of nuclear theranostic nanoplatforms. The pathway includes (1) discovery and preclinical validation, (2) optimization and scale-up under GMP-compatible conditions, (3) regulatory and safety assessment under EMA/FDA/IAEA guidelines, (4) clinical trial execution, and (5) final integration into personalized oncology practice. Color intensity increases with regulatory complexity and translational maturity.

Conflicts of Interest: "The authors declare no conflicts of interest."

Abbreviations

The following abbreviations are used in this manuscript:

ATMP: Advanced Therapy Medicinal Product

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AuNPs: Gold nanoparticles
BFCAs: Bifunctional Chelating Agents
CT: Computed Tomography
DAPTA: D-Ala-peptide T-amide
DFO: Deferoxamine
DOTA: 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid
DOTAGA: 2-[1,4,7,10-Tetraazacyclododecane-4,7,10-tris(t-butyl acetate)]-pentanedioic acid-1t-butyl ester
DOX: Doxorubicin
DTPA: diethylenetriaminepentaacetic acid
EC: Electron Capture
EGFR: Epidermal Growth Factor Receptor
EMA: European Medicines Agency
EPR: Enhanced Permeability and Retention
FDA: Food and Drug Administration
Fn Ferritin nanocages
FR: Folate Receptor
GLP: Good Laboratory Practice
GMP: Good Manufacturing Practices
GRPR: Gastrin-Releasing Peptide Receptor
HBED: N, N′-bis(2-hydroxybenzyl)ethylenediamine-N,N′-diacetic acid
HER2: Human Epidermal Growth Factor Receptor 2
IAEA: International Atomic Energy Agency
IMPs: investigational Medicinal Products
MOFs: Metal Organic Frameworks
MRI: Magnetic Resonance Imaging
MSNs: Mesoporous silica nanoparticles
NODAGA: 2-[4,7-bis(carboxymethyl)-1,4,7-triazonan-1-yl]-5-(2,5-dioxopyrrolidin-1-yl)oxy-5-oxopentanoic acid
NOTA: 1,4,7-Triazacyclononane-1,4,7-triacetic acid
NP: Nanoparticles
PAMAM: Poly(amidoamine)
PCL: Polycaprolactone
PEG: Polyethylene glycol
PET: Positron Emission Tomography
PLGA: poly(lactic-co-glycolic acid)
PNPs: Polymeric nanoparticles
PSMA: Prostate Specific Membrane Antigen
QDs: Quantum Dots
RES: Reticuloendothelial System
RGD: Arginylglycylaspartic acid
SPECT: Single Photon Emission Tomography
SPIONs: iron oxide nanoparticles
WHO: World Health Organization

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