

Unlocking Precision: Inorganic Nanoparticles Sparking the Next Revolution in Cancer Theranostics

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ABSTRACT

Nanotechnology has profoundly transformed Drug Delivery Systems (DDS), with Inorganic Nanoparticles (INPs) emerging as promising and versatile carriers owing to their exceptional stability, tunable size, and unique physicochemical properties. This review highlights the pivotal role of INPs—such as Gold Nanoparticles (AuNPs), Mesoporous Silica Nanoparticles (MSNs), and Superparamagnetic Iron Oxide Nanoparticles (SPIONs)—in *theranostics*, a cutting-edge approach that integrates diagnosis and therapy within a single nanosystem. INPs have demonstrated remarkable potential across diverse biomedical applications: AuNPs and SPIONs are extensively employed in Photothermal Therapy (PTT) and magnetic resonance Imaging (MRI) contrast enhancement for cancer, Silver Nanoparticles (AgNPs) exhibit potent antimicrobial activity, and Cerium Oxide Nanoparticles (CeO₂ NPs) offer neuroprotective benefits. In oncology, these nanocarriers overcome multidrug resistance, facilitate RNA interference (RNAi)-based treatments, and exploit the Enhanced Permeability and Retention (EPR) effect for passive tumor targeting. Notable advancements include the use of AuNPs for precise PTT and Hafnium Oxide Nanoparticles (HfO₂ NPs) as effective radiosensitizers. Despite significant progress, challenges such as long-term biocompatibility, rapid clearance by the Reticuloendothelial System (RES), and scalability limitations hinder clinical translation. Future directions emphasize the design of stimuli-responsive and multifunctional nanoplateforms that actively modulate the tumor microenvironment, integrate immunotherapeutic strategies, and enable personalized, precision-driven cancer treatment.

Keywords: Cancer Theranostics, Drug Delivery Systems, EPR Effect, Immunotherapy, Inorganic Nanoparticles, MRI Contrast Agents, Photothermal Therapy, Stimuli-Responsive Nanomedicine, Tumor Microenvironment.

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INTRODUCTION

One of the biggest global health burdens is still cancer. Approximately 10.3 million fatalities and 19.3 million new cases of cancer were reported worldwide, according to GLOBOCAN 2020 (Sung *et al.*, 2021). Modern medicine has seen a revolution thanks to nanotechnology, particularly in the creation of advanced medication delivery methods. Because of their distinct physicochemical characteristics, Inorganic Nanoparticles (INPs) like calcium phosphate, iron oxide, cerium oxide, silica, gold, and silver have garnered a lot of interest among the many different types of nanocarriers that have been researched. These nanostructures' large surface area, adjustable size, controllable porosity, and simplicity of surface modification allow them to

encapsulate or conjugate a variety of medicinal compounds, including tiny medicines, proteins, and nucleic acids (Naz *et al.*, 2019). Compared to organic carriers like liposomes and polymeric nanoparticles, inorganic nanoparticles have more imaging potential, greater structural stability, and the possibility to combine therapeutic and diagnostic properties—a process known as Theranostics (Vallet-Regí *et al.*, 2022). For instance, gold nanoparticles have been utilized for photothermal therapy and targeted chemotherapy in solid tumors, while iron oxide nanoparticles have been utilized as dual MRI contrast agents and drug delivery vehicles (Tella *et al.*, 2022). Similar to this, mesoporous silica nanoparticles offer better solubility and controlled drug release for medications that are not very soluble in water, which makes them attractive options for treating infectious diseases and cancer (Mercan *et al.*, 2022). Inorganic nanoparticles are being investigated more and more for neurological, cardiovascular, antimicrobial, and metabolic conditions outside of oncology. Their adaptability is demonstrated by their capacity to administer molecules in a site-specific manner and to penetrate biological barriers including the blood brain barrier (Hudson *et al.*, 2023). However, before these nanocarriers can be regularly



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employed in clinical practice, issues like possible long-term toxicity, biodegradability, and clinical translation still need to be resolved (Singh *et al.*, 2024).

Types Of Inorganic Nanoparticles

A versatile family of nanocarriers, INPs been extensively studied for drug administration due to their stability, unique physicochemical characteristics, and capacity to combine therapeutic and diagnostic purposes. Gold nanoparticles are beneficial in photothermal and cancer therapeutic applications because of their surface plasmon resonance, biocompatibility, and ease of conjugation with medicines or biomolecules (Tarudji and Kievit, 2020; Puente and Azab, 2017; Durfee *et al.*, 2016). Silver nanoparticles have been utilized to improve the administration of antibiotics against diseases that are resistant to them because of their potent antimicrobial action. In oncology, AgNPs demonstrate significant cytotoxicity through ROS generation, mitochondrial dysfunction, and DNA damage, selectively targeting malignant cells. Moreover, AgNP coatings on implants and catheters can prevent tumor-associated infections and biofilm formation, reducing postoperative complications (Srikar *et al.*, 2016; Gurunathan *et al.*, 2020). Because of their large surface area and pore size flexibility, which enable superior drug loading capacity and regulated release, MSNs have shown promise in the treatment of cancer and tuberculosis (Durfee *et al.*, 2016).

SPIONs superparamagnetic properties make them suitable for use as MRI contrast agents and in magnetically guided drug delivery, which may have applications in cancer and neurological disorders. Because of their function in glucose regulation, zinc oxide nanoparticles are being researched for diabetes treatment. They have also shown antibacterial and anticancer effects as represented in Table 1. Because of their exceptional capacity for redox cycling, cerium oxide nanoparticles offer neuroprotective and antioxidant properties, making them promising therapeutic candidates for neurodegenerative illnesses (Amreddy *et al.*, 2015; Palui, Aldeek, Wang, and Mattoussi, 2015). Recent studies highlight that CeO₂ nanoparticles can mimic superoxide dismutase and catalase activity, thereby reducing oxidative stress-induced neuronal and cancer cell damage. Their dual ability to scavenge ROS and modulate inflammatory cytokines enhances not only neuroprotection but also anticancer efficacy when combined with immunotherapeutic agents (e.g., PD-L1 inhibitors) (Harris and DeNicola, 2020; Pirmohamed *et al.*, 2010; Asati *et al.*, 2010). CeO₂-based systems are also being explored to polarize macrophages toward an Anti-Tumor (M1) phenotype, suggesting a key role in immune modulation within the tumor microenvironment. Calcium phosphate nanoparticles can be used as carriers for the oral administration of proteins and peptides and are biocompatible and biodegradable, making them appropriate for bone regeneration (Li *et al.*, 2015). Furthermore, quantum dots have remarkable fluorescent qualities for imaging and drug delivery integration, despite being constrained by

toxicity considerations. When combined, these nanoparticles provide a number of benefits, including high drug loading, targeted delivery, real-time imaging, and stimuli-responsive release; however, issues with toxicity, clearance, and large-scale manufacturing still exist.

Applications In Oncology

Inorganic nanoparticles for drug delivery in cancer treatment offer a number of potential advantages because they can target ligands to enhance therapeutic efficacy and decrease off-target unfavorable effects through drug adsorption and penetration. Synergistic platforms for RNA interference and synergistic drug delivery agents for the inhibition of cancer cell signaling pathways are the most promising advanced cancer therapy approaches (Bhattacharyya *et al.*, 2010). Numerous factors, such as uneven structure and vasculature, different hypoxic or anoxic conditions, low glucose and high lactate levels, enhanced permeability, and irregular pH gradients, cause the tumor environment to differ from that of healthy tissue presented in Figure 1 (Babu *et al.*, 2023).

While conventional antioxidant therapies have limited success, excess reactive ROS contribute to the development and metastasis of cancer (Arvizo *et al.*, 2013). Nanoparticles and nano-mediated ROS techniques use the tumor's leaky vasculature (EPR effect) to deliver drugs precisely while improving drug stability and retention (Babaei and Ganjalikhani, 2014). However, recent research indicates that the EPR effect is highly heterogeneous across tumor types and patients, often being less pronounced in human tumors than in preclinical models. Strategies such as active targeting ligands, vascular normalization, and immune-modulatory nanoparticles are being investigated to enhance and standardize EPR-mediated delivery (Danhier, 2016; Wilhelm *et al.*, 2016). One promising approach to precise and effective oncology treatment is nanomedicine, since nanoparticles can also function as radiosensitizers, control hypoxia, and shield healthy tissue (Harris and DeNicola, 2020). Initially discovered as a strong thrombin inhibitor obtained from medicinal leeches, hirudin is becoming more well-known for its many therapeutic uses, particularly its anti-tumor effects and functions in wound healing and anti-fibrosis. Inhibiting tumor cell motility, invasion, metastasis, and proliferation while inducing apoptosis is its anti-cancer strategy. These effects are mediated by the downregulation of critical pathways, including HGF/C-met, VEGF/VEGF-R (which controls angiogenesis), and ERK (Chen *et al.*, 2021). The various types of cancer therapies and their respective proportions are presented in Figure 2.

Diagnosis Of Cancer With Nanoparticles

Numerous nanoparticles, are used in the diagnosis of breast, colon, and cervical cancer, prior to arriving at their intended cells, they engage with biological systems and cross a range of biological barriers, including cell membranes, nanoparticles

have been found to spend a significant period of time in the circulation (Alrushaid *et al.*, 2023). MRI is one important use for magnetic nanoparticles. Typically, highly sensitive electronics use magnetic nanoparticles (Chan Zuckerberg Initiative, 2021). There are various forms of metallic nanoparticles (size 1-100 nm), including conventional (spherical) nanoparticles, nanowires, nanoplatelets, and nanostructures. Stabilization in liquid media is crucial because of their propensity to agglomerate due to their high surface energy. There are two main stabilization strategies: steric stabilization, in which the nanoparticles are coated with polymers, surfactants, or ligands that prevent close approach, and electrostatic (static) stabilization, which uses the creation of an electrical double layer via adsorbed charged ions to repel neighboring particles.

Platinum Nanoparticles (PtNPs), one of the metallic nanoparticles, have garnered interest in biomedicine due to their special anticancer properties (such as antioxidant effects) and their ability to improve tumor targeting, drug loading, and controlled release when functionalized with targeting ligands. However, size-dependent toxicity and organ accumulation are still issues (Wang *et al.*, 2018). Because of their customizable sizes and shapes, which enable adjustment of circulation time and tumor targeting, Gold Nanoparticles (AuNPs) are particularly helpful in biomedical imaging and therapy. They have been utilized for drug administration, nucleic acid delivery, photothermal ablation, and radiotherapy (Aygün *et al.*, 2019; Chen *et al.*, 2022). Biocompatibility, magnetic responsiveness, and favorable binding characteristics are all combined in magnetic nanoparticles (10-50 nm) (Yang *et al.*, 2018). Because of their quick assay durations and reduced detection limits, they are often used as labels in MRI, magnetically guided drug administration, and biomarker detection. Because they are degradable and can produce reactive oxygen or nitrogen species when exposed to external fields, iron oxide nanoparticles are particularly appealing *in vivo*. When loaded with anticancer medications, they allow for localized therapy with less off-target toxicity. Metallic and magnetic nanoparticles can be synthesized chemically (sol-gel, co-precipitation) or physically (laser ablation, spray pyrolysis), with control over size, shape, and surface chemistry and used in advanced cancer diagnosis as presented in Figure 3 (Sankaranarayanan *et al.*, 2022). Beyond diagnostic and therapeutic functions, inorganic nanoparticles—particularly AgNPs, ZnO NPs, and CuO NPs—play a crucial role in tumor-associated infection control. Surgical site infections and opportunistic bacterial colonization in cancer patients undergoing chemotherapy or radiotherapy increase morbidity. Nanoparticles with intrinsic antimicrobial properties provide dual benefits by reducing microbial load while simultaneously supporting anticancer therapy, marking an important advancement in infection-controlled oncology (Gurunathan *et al.*, 2020).

Treatment Of Cancer With Nanoparticles

Systems based on nanoparticles that can target tumor cells specifically while preserving healthy tissues are essential for effective cancer treatment. In order to accomplish this, nanocarriers need to get past a number of biological obstacles, stay steady in the bloodstream, avoid immune clearance, build up in the tumor microenvironment, enter tumor tissues, and precisely deliver therapeutic agents to cancer cells for increased effectiveness and decreased toxicity (Gavas, Quazi, and Karpiński, 2021; Zheng *et al.*, 2022). Cancer treatments based on nanoparticles improve drug delivery through passive and active targeting. As demonstrated by formulations such as Doxil and Abraxane used to treat breast and ovarian cancers, the foundation of passive targeting is the increased EPR effect, in which leaky tumor vasculature permits nanoparticles (10-200 nm) to concentrate in tumor tissues. Alternatively, active targeting entails surface modification of nanoparticles with antibodies and peptides (e.g., RGD, GE11) that bind specific receptors overexpressed in tumors such as breast, lung, ovarian, and prostate cancers. This improves selective uptake by cancer cells and enhances therapeutic efficacy while reducing systemic toxicity, but factors like tumor heterogeneity, immune clearance, and receptor variability can limit efficiency (Jain, 2012). Drug resistance is the main concern in cancer treatment because it works against all types of cancer and treatments. Drug resistance is a phenomenon that occurs when illnesses develop tolerance to

Table 1: Characteristics and primary therapeutic applications of several major inorganic Nanoparticles (AmalDoss *et al.*, 2022).

Nanoparticle Type	Key Properties	Significance in Drug Delivery
Gold (AuNPs)	Biocompatible, surface plasmon resonance	Cancer targeting, photothermal therapy
Silver (AgNPs)	Antimicrobial, ROS generation	Enhance antibiotic delivery, infection therapy
Silica (MSNs)	High surface area, tunable pore size	Controlled release, cancer and TB therapy
Iron Oxide (SPIONs)	Magnetic, MRI contrast	Magnetic targeting, brain and cancer therapy
Zinc Oxide (ZnO NPs)	Antimicrobial, anticancer activity	Diabetes therapy, antimicrobial systems
Cerium Oxide (CeO ₂ NPs)	Redox activity, antioxidant	Neuroprotection, Alzheimer's, Parkinson's
Calcium Phosphate (CaP NPs)	Biodegradable, bone compatibility	Bone regeneration, oral peptide delivery
Quantum Dots (QDs)	Fluorescence, strong imaging capability	Theranostics, imaging (toxicity concern)

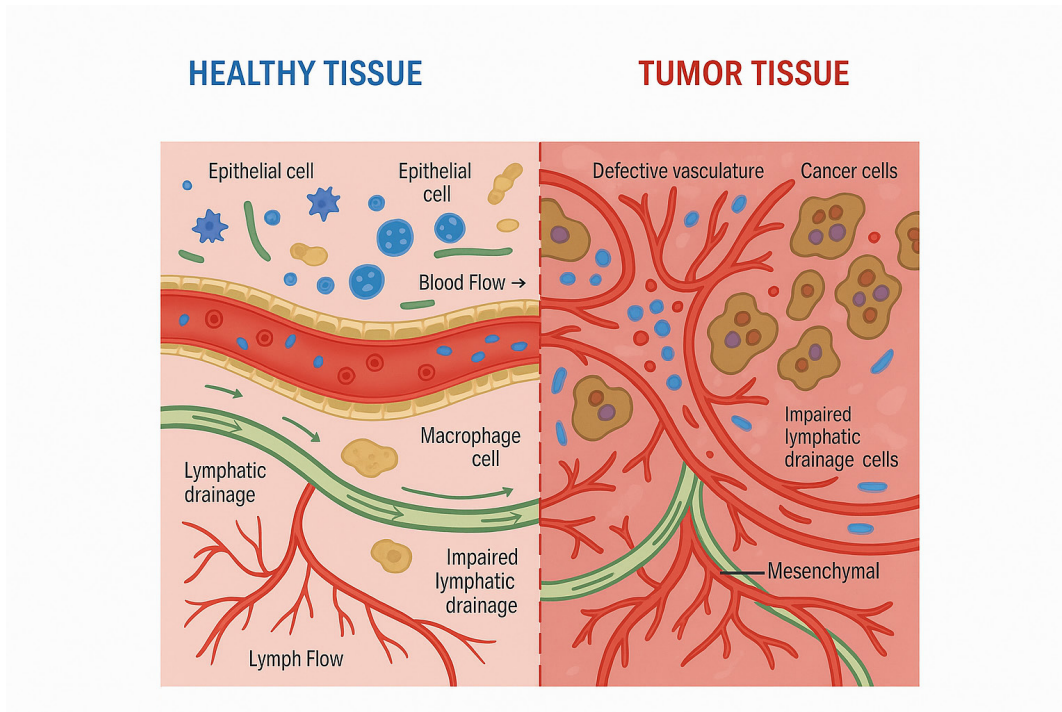


Figure 1: The difference between healthy tissue and tumour tissue.

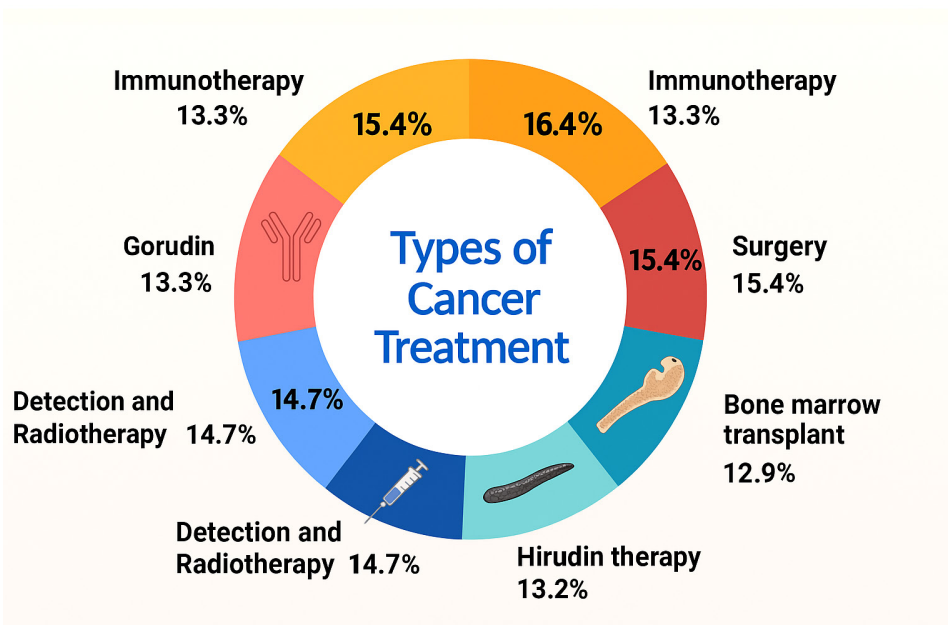


Figure 2: The various types of cancer therapies and their respective proportions.

medicinal treatments. It can be either innate or acquired (Wang *et al.*, 2023). By increasing the effectiveness and lowering the toxicity of traditional treatments, nanoparticles have emerged as crucial instruments for transforming the therapy of different malignancies, including breast, ovarian, lung, and prostate cancer (Blanco *et al.*, 2015; Bobo *et al.*, 2012; Jahromi *et al.*, 2021). Drugs like doxorubicin can be encapsulated using the versatility of nanocarriers like liposomes and polymeric nanoparticles, which greatly reduces systemic side effects like cardiotoxicity while

promoting passive accumulation in tumors through the EPR effect (Dadwal *et al.*, 2020; Zang *et al.*, 2021). AuNPs are used for highly localized PTT in head/neck cancers, by effectively converting Near-Infrared light into heat to selectively destroy malignant cells. In addition, inorganic nanoparticles introduce new, highly targeted treatment modalities (Tardi *et al.*, 1996; How Doxorubicin-Based Liposomal Agents Would Effect on Breast Cancer Tumors, 2023; Rivetti *et al.*, 2024). At the same time, carbon based materials like graphene oxide and carbon

nanotubes improve medication and gene delivery for a variety of malignancies, while magnetic nanoparticles are essential for magnetic hyperthermia and active, targeted drug delivery in diseases like liver and prostate cancer (Cao, 2022; Abadeer and Murphy, 2016). For example, dendrimers and functionalized polymeric nanoparticles are designed to overcome drug resistance and navigate the dense stroma in tumors like lung and pancreatic cancer (Raza *et al.*, 2017; Chen *et al.*, 2021). The use of nanomedicine is highly tailored to individual tumor difficulties. Additional specialized uses include the integration of hafnium oxide nanoparticles to improve radiation in locally advanced tumors such as pancreatic and esophageal cancer, for photodynamic treatment (Balzani *et al.*, 2008). This wide range

of applications and ongoing improvement highlight a significant trend toward developing complex multimodal Theranostics platforms that combine highly localized therapy and diagnosis for individualized cancer treatment (Dadwal *et al.*, 2023; Patil *et al.*, 2010). Additionally, the incorporation of materials such as these into nano-platforms enables the in-situ production of oxygen within hypoxic tumors, increasing imaging contrast and sensitizing the cancer cells to both chemotherapy and radiation (Feng *et al.*, 2019; Fan *et al.*, 2021; Zhang *et al.*, 2021). For the effective treatment of tumors that are difficult to treat, such as gliomas and recurrent ovarian cancer, where drug penetration and resistance are significant challenges, this advanced control over drug release kinetics and localized regulation of the is

Table 2: Nano-particles used in different cancer therapies, indication and current clinical status (Gholizadeh *et al.*, 2022; Huang *et al.*, 2020; Sun *et al.*, 2021; U.S. Food and Drug Administration, 2025; U.S. Food and Drug Administration, 2015; U.S. Food and Drug Administration, 2017; European Medicines Agency, 2025; Samyang Biopharmaceuticals, 2025).

Brand (Trade name)	Type / Platform	Indication / Notes	Present clinical status (as of Oct 6, 2025)
Doxil (Caelyx)	PEGylated liposomal doxorubicin	Liposomal doxorubicin for multiple myeloma (varies by region)	FDA/EMA approved (widely marketed)
Abraxane	Albumin-bound (nab) paclitaxel	Albumin-bound paclitaxel for breast, lung, pancreatic cancers	FDA approved (widely marketed)
Onivyde	Liposomal irinotecan	Irinotecan liposome for metastatic pancreatic adenocarcinoma (in combination)	FDA approved; additional regimens approved
Marqibo	Liposomal vinorelbine sulfate	Multiple myeloma resistant to Kaposi's sarcoma associated with AIDS.	FDA approved
Vyxeos (CPX-351)	Fixed-combination liposomal (daunorubicin+cytarabine)	For therapy in MDS	FDA approved
Myocet	Non-PEGylated liposomal doxorubicin	Management of Non-Hodgkin's B-cell lymphoma.	EMA approved / marketed in some regions
Genexol-PM	Polymeric micelle paclitaxel	Cremophor-free paclitaxel (approved in South Korea for several indications)	Approved in South Korea; in clinical use
NanoTherm (NanoActivator)	Iron-oxide magnetic nanoparticles (device-based hyperthermia)	Intratumoral iron-oxide nanoparticles activated by alternating magnetic field for GBM	CE-marked in Europe for recurrent glioblastoma; clinical trials ongoing
CRLX101	Cyclodextrin-based polymeric nanoparticle (camptothecin payload)	Investigational camptothecin nanoparticle in various solid tumors	Clinical trials (Phase I/II ongoing historically; investigational)
BIND-014	PSMA-targeted polymeric nanoparticle (docetaxel)	PSMA-targeted docetaxel nanoparticle (investigational)	Development discontinued / company bankrupt; clinical trials halted

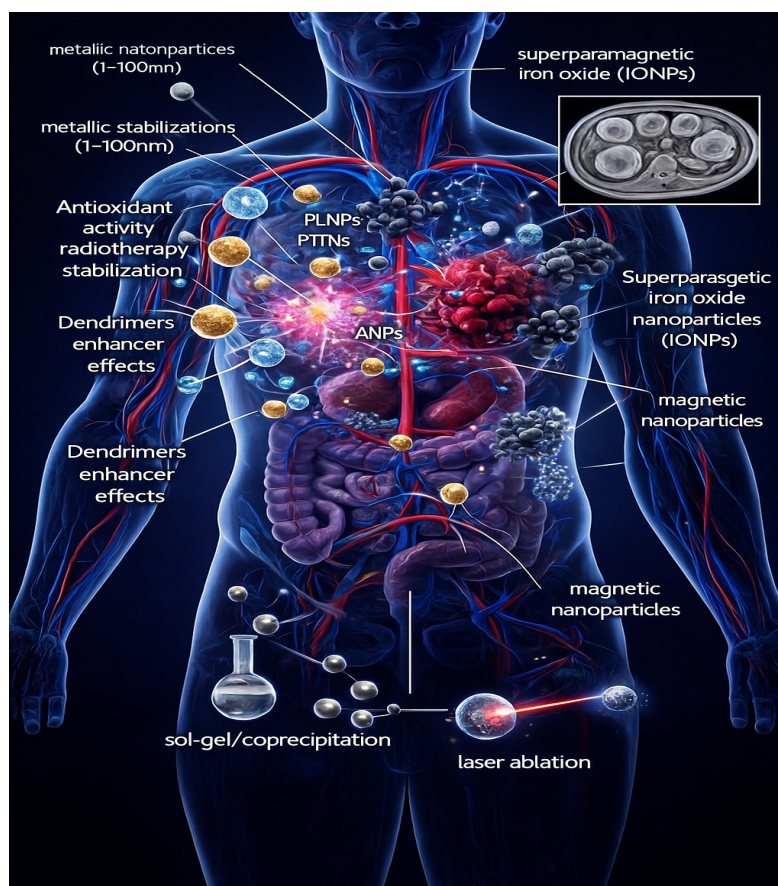


Figure 3: Various metallic and magnetic nanoparticle's role in advanced cancer diagnosis.

essential (Chen *et al.*, 2022; Cheng, Wang, and Yang, 2024; Zang *et al.*, 2021). The next phase of precision oncology is represented by the move toward these stimuli-responsive nanomedicines, which go beyond passive targeting to actively engage the tumor's pathophysiology for better therapeutic outcomes as mentioned in Table 2 (Hardman, 2006; Chiboub *et al.*, 2019).

Challenges and Future Perspectives

A number of significant obstacles pertaining to safety, effectiveness, and scalability limit the clinical development of inorganic nanoparticles in the field of therapeutics (MagForce AG, 2025). Since many inorganic NPs, like metal oxides, have the potential to develop long-term problems due to slow degradation and the release of toxic ions, safety and toxicity concerns are still present. To improve biocompatibility and avoid the immune system's quick clearance by the reticuloendothelial system, advanced surface modifications are necessary (ClinicalTrials.gov, 2025). The Enhanced Permeability and Retention effect's fluctuating nature limits its effectiveness, calling for more dependable active targeting methods to particular tumor receptors. Furthermore, maintaining strict quality control and attaining batch-to-batch uniformity in size and surface qualities throughout large-scale production continue to be important obstacles to clinical approval and commercial viability, making the economic and industrial constraints substantial (Choi and Choy, 2021).

Using internal TME cues or external triggers for on-demand drug release and activation, the area is heading toward the development of stimuli-responsive nanomedicines that integrate numerous functions (Luan *et al.*, 2021). The development of multimodal Theranostics platforms that seamlessly integrate improved therapeutic delivery with real-time imaging (such as MRI contrast) and contemporary immunotherapy techniques to modify the tumor microenvironment for better and more individualized cancer outcomes is essential for future success.

CONCLUSION

A flexible and potent platform for improving cancer treatment, inorganic nanoparticles provide tailored therapeutic action, multimodal imaging, and accurate drug administration while reducing systemic toxicity. Their adaptable physicochemical characteristics allow for active and passive targeting, synergistic combination therapies, and incorporation into Theranostics techniques, thereby tackling important issues like tumor heterogeneity and drug resistance. Notwithstanding challenges with biodegradability, safety, and large-scale clinical translation, sustained advancements in stimuli-responsive, multifunctional nanocarriers hold the potential to revolutionize personalized oncology by offering highly efficient, site-specific therapies and better patient outcomes.

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ABBREVIATIONS

INPs: Inorganic Nanoparticles; **DDS:** Drug Delivery Systems; **AuNPs:** Gold Nanoparticles; **AgNPs:** Silver Nanoparticles; **MSNs:** Mesoporous Silica Nanoparticles; **SPIONs:** Superparamagnetic Iron Oxide Nanoparticles; **CeO₂ NPs:** Cerium Oxide Nanoparticles; **HfO₂ NPs:** Hafnium Oxide Nanoparticles; **ZnO NPs:** Zinc Oxide Nanoparticles; **CaP NPs:** Calcium Phosphate Nanoparticles; **QDs:** Quantum Dots; **PTT:** Photothermal Therapy; **MRI:** Magnetic Resonance Imaging; **EPR Effect:** Enhanced Permeability and Retention Effect; **RNAi:** RNA Interference; **TME:** Tumor Microenvironment; **RES:** Reticuloendothelial System; **ROS:** Reactive Oxygen Species; **VEGF:** Vascular Endothelial Growth Factor; **ERK:** Extracellular Signal-Regulated Kinase; **GBM:** Glioblastoma Multiforme; **FDA:** Food and Drug Administration; **EMA:** European Medicines Agency; **PSMA:** Prostate-Specific Membrane Antigen; **MDS:** Myelodysplastic Syndrome; **PEG:** Polyethylene Glycol; **NIR:** Near-Infrared; **RNA:** Ribonucleic Acid; **DNA:** Deoxyribonucleic Acid.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

SUMMARY

Inorganic Nanoparticles (INPs) such as gold, silica, and iron oxide have emerged as promising tools in cancer theranostics by integrating diagnosis and therapy within a single nanoplatform. Their unique physicochemical properties enable targeted drug delivery, real-time imaging, and multimodal treatment approaches like photothermal and magnetic hyperthermia therapies. INPs enhance therapeutic precision through the Enhanced Permeability and Retention (EPR) effect and active targeting mechanisms while reducing systemic toxicity. Despite challenges related to biocompatibility, biodegradation, and large-scale production, advances in stimuli-responsive and multifunctional nanocarriers are paving the way for personalized and precision-based cancer treatments. Continued innovation and translational research will be key to realizing their full clinical potential.

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