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Theragnostic Nanoplatforms in Pathology: Simultaneous Imaging, Drug Delivery, and Treatment Monitoring

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Abstract

The growing complexity of modern pathology demands integrated approaches that unify diagnosis, targeted treatment, and real-time monitoring, driving the urgent need for a comprehensive understanding of theragnostic nanoplatforms. This review consolidates current advancements to clarify their pivotal role in advancing precision medicine and overcoming limitations of conventional, disjointed therapeutic strategies. We systematically examine the design and synthesis strategies of multifunctional nanoplatforms, detailing core targeting mechanisms and the enabling of key imaging modalities such as magnetic resonance imaging (MRI), positron emission tomography (PET), fluorescence, and photoacoustics. The review further explores the diverse therapeutic payloads—including small molecules, nucleic acids, radionuclides, and photosensitizers—that these platforms deliver, alongside the innovative stimuli-responsive systems for controlled release. Critical analysis is provided on their integration with digital pathology for quantitative monitoring and an overview of promising clinical studies. The significant challenges hindering clinical translation, encompassing regulatory, technical, and economic barriers, are also discussed. Future progress hinges on translating multifunctional laboratory designs into robust, scalable, and clinically viable constructs, while simultaneously establishing standardized frameworks for safety, efficacy, and seamless integration into diagnostic and therapeutic workflows.

Keywords: Active targeting, Drug delivery, Imaging, Nanomedicine, Pathology, Theragnostics, Treatment monitoring, Tumor microenvironment

Introduction

Theragnostics holds a pivotal role in modern medicine by bridging the gap between diagnosis and therapy, thereby enabling more precise, effective, and individualized patient management [1-10]. Its importance is underscored by the ability to select appropriate therapeutic agents based on specific molecular and biological markers, monitor treatment response in real-time, and adjust interventions accordingly. This approach enhances treatment efficacy while minimizing adverse effects, which is particularly critical in oncology, neuroendocrine tumors, and other complex diseases. The evolution of theragnostics has also facilitated the development of novel radiopharmaceuticals and imaging modalities, expanding the scope of personalized medicine. As a result, theragnostics is increasingly recognized as an essential component of modern clinical practice, offering the potential to improve patient outcomes, reduce healthcare costs, and advance the understanding of disease mechanisms [10].

Theragnostics fundamentally bridges the gap between diagnosis and therapy by utilizing personalized biologic characteristics to inform targeted treatment strategies. Historically rooted in the use of radioiodine for thyroid pathologies in the 1940s, theragnostics has evolved into a sophisticated approach that combines diagnostic imaging with therapeutic interventions using radiopharmaceuticals [10]. Modern techniques employ radiolabeled compounds such as somatostatin receptor analogs (e.g., In-octreotide, DOTATATE) and prostate-specific membrane antigen (PSMA) ligands, which serve dual roles in staging, monitoring, and treating neuroendocrine tumors and prostate cancer respectively [10]. The integration extends further with advanced molecular imaging modalities like PET/computed tomography (CT), which not only detect primary and metastatic lesions with high sensitivity but also predict tumor biology and response to therapy, exemplified by fluorodeoxyglucose-PET's role in renal cell carcinoma evaluation [11]. Additionally, nanotechnology-based diagnostic and therapeutic systems, such as folate receptor-targeted nanocarriers, exemplify the convergence of molecular targeting with personalized treatment, enhancing drug delivery while enabling precise diagnostics [12]. The synergy of these technologies underscores the importance of combining diagnostic accuracy with therapeutic precision, ultimately fostering a more individualized approach to patient care.

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Numerous case studies highlight the practical application of theragnostics across various pathological conditions. For instance, in neuroendocrine neoplasia, radiolabeled somatostatin analogs facilitate disease staging, therapy planning, and monitoring, demonstrating the seamless integration of diagnosis and treatment [10]. Similarly, in prostate carcinoma, radiolabeled PSMA compounds enable personalized diagnosis and systemic therapy, exemplifying theragnostic principles [10]. In lung cancer, the detection of pre-invasive adenocarcinoma spectrum lesions through advanced imaging techniques allows for early intervention before invasive disease develops, emphasizing the role of molecular and radiological diagnostics in guiding treatment decisions [13]. The use of PET/CT in renal cell carcinoma further exemplifies how hybrid imaging enhances staging accuracy and response assessment, even when not yet standard in guidelines [11]. These case studies exemplify the versatility of theragnostics in identifying disease at early stages, tailoring interventions, and improving overall management outcomes.

The integration of theragnostics into clinical practice has demonstrated significant benefits in patient outcomes. By enabling early detection of lesions, predicting tumor behavior, and monitoring therapeutic response, theragnostics facilitates more precise and timely interventions. For example, in neuroendocrine tumors, peptide receptor radionuclide therapy has transformed management paradigms, leading to improved disease control and survival rates [10]. In prostate cancer, PSMA-targeted diagnostics and therapeutics have enhanced treatment personalization, reducing unnecessary interventions and side effects [10]. Moreover, the ability to visualize and quantify disease activity through advanced imaging techniques like PET/CT and MRI allows clinicians to adapt treatment plans dynamically, potentially leading to better prognoses. The development of molecular markers and artificial intelligence-assisted diagnostics further refines this impact by increasing diagnostic accuracy and reducing interpretative discordance [14]. Overall, the adoption of theragnostics fosters a more individualized, effective, and patient-centered approach, ultimately improving survival, quality of life, and treatment satisfaction.

Design and Synthesis Strategies for Multifunctional Nanoplatforms

The development of multifunctional nanoplatforms has garnered significant attention in various fields, particularly in biomedicine, due to their potential for targeted therapy and diagnostics [15-25]. These platforms integrate multiple functionalities into a single nanostructure, enabling synergistic effects and improved performance compared to single-function materials. Design and synthesis strategies of multifunctional nanoplatforms are crucial in determining their efficacy and applicability.

Design strategies

Targeting and delivery

Efficient delivery of therapeutic agents to target cells is a primary goal in nanomedicine. Various strategies have been employed to achieve targeted delivery, including the use of aptamers [26, 27], peptides [26], and antibodies. For example, Tang et al. [26] designed a nanoplatform using trans-activator of transcription (TAT) peptide and aptamer for targeted gene editing and tumor therapy. The integration of an active cell targeting group (aptamer) and nuclear targeting peptide (TAT), the multifunctional nanoplatform can elicit the targeted cellular internalization and efficient nuclear targeting transportation to realize endogenous RNase H activated gene editing of the tumor-associated gene polo-like kinase 1 [26]. Similarly, Hao et al. [28] utilized AS1411 aptamers to functionalize ruthenium-doped carbon quantum dot nanozymes (Ru-CQDs), enhancing active tumor-targeting capability. Furthermore, Kang et al. [29] camouflaged nanoparticles with macrophage cell membrane for tumor-targeting.

Multimodal functionality

Multifunctional nanoplatforms often combine multiple therapeutic modalities to achieve synergistic effects. Common combinations include chemotherapy, photothermal therapy (PTT), photodynamic therapy (PDT), chemodynamic therapy (CDT), and immunotherapy [27, 30]. For instance, Qiu et al. [30] developed polyamino acid calcified nanoparticles for chemotherapy, CDT, and PDT. Wu et al. [31] constructed a nanoplatform to alleviate tumor hypoxia and increase the efficacy of PDT using rationally designed peptide fibrils to encapsulate chlorin e6 inside and to mineralize manganese(II) oxide (MnO) nanoparticles on the surface. Chen et al. [32] designed a single near-infrared (NIR) light-regulated nanoplatform for combined PTT/PDT and chemotherapy.

Stimuli-responsiveness

Nanoplatforms can be designed to respond to specific stimuli, such as pH, light, or enzymes, to trigger drug release or activate therapeutic functions [27, 30]. Qiu et al. [30] utilized pH-responsive nanocarriers to release chemotherapeutic drugs in the acidic tumor microenvironment. Yan et al. [27] designed a nanoplatform that releases resveratrol upon NIR illumination for chemo-photothermal treatment. Tian et al. [33] fabricated a novel acid-responsive oxidized dextran-based nanoplatform for photodynamic antibacterial therapy. Zhang et al. [34] prepared nanomotors responsive to NIR light and acidic tumor conditions for multimodal therapy. Liu et al. [35] reported a folic acid (FA)-targeted photothermal multifunctional nanoplatform by encapsulating CQDs and the anticancer drug doxorubicin (DOX) in the liposomes for synergistic chemo-photothermal tumor therapy. Kang et al. [29] reported a self-accelerated nanoplatform combining an aggregation-induced emission luminogen (AIEgen) and a hypoxia-responsive paclitaxel prodrug for multifunctional image-guided combination immunotherapy.

Imaging capabilities

Integrating imaging modalities into nanoplatforms allows for real-time monitoring of drug delivery, therapeutic response, and disease progression [36, 37]. Zhang et al. [36] synthesized europium-doped iron oxide nanoparticle clusters (EuIO NCs) for multimodal *in vivo* imaging. Zhao et al. [37] developed a lanthanide europium metal-organic frameworks (MOF) nanocomposite for fluorescence imaging and microwave thermo-chemotherapy. Yan et al. [27] demonstrated the ability of CeONP-Res-PCM@zeolite imidazole framework (ZIF)-8/PDA/Apt as the fluorescent sensing platform for AβO detection and intracellular imaging. Hao et al. [28] engineered Ru-CQDs for photoacoustic imaging-

guided cancer therapy. Kang et al. [29] integration of fluorescence and PA imaging helps to delineate tumor site sensitively, providing accurate guidance for tumor treatment. Hu et al. [38] constructed an indocyanine green (ICG) modified platinum nanoclusters (Pt NCs) decorated gold nanobipyramids (Au NBPs) to form the multifunctional nanocomposites (Au NBPs@Pt NCs-ICG) for multimodal imaging mediated phototherapy and chemodynamic cancer therapy.

Synthesis strategies

One-pot synthesis

One-pot synthesis methods offer simplicity and efficiency in producing multifunctional nanoplatforms. Zhang et al. [36] directly synthesized water-soluble biocompatible and superparamagnetic EuIO NCs by a simple one-pot method.

Self-assembly

Self-assembly processes allow for the spontaneous formation of complex nanostructures with precise control over their architecture [31, 32, 39]. Wu et al. [31] constructed a multifunctional composite nanoplatform using rationally designed peptide fibrils. Wu et al. [39] constructed a multifunctional DNA nanoplatform as a versatile carrier for bacteria-specific delivery of clinical antibiotic ciprofloxacin and classic nanoantibiotic silver nanoparticles. Chen et al. [32] designed a signal NIR light-regulated nanoplatform via the self-assembly process of reactive oxygen species (ROS)-sensitive prodrug, human serum albumin, and IR780 for combined PTT/PDT and chemotherapy.

In situ encapsulation

In situ encapsulation involves the incorporation of therapeutic agents or imaging probes within a pre-formed nanostructure [27, 37]. Yan et al. [27] synthesized a core-shell nanocomposite by encapsulating resveratrol, ceria nanoparticles, and PCM into a ZIF-8/PDA matrix. Zhao et al. [37] assembled the ZIF structure on the surface of EuMOF to realize the protection and drug loading.

Layer-by-layer assembly

Layer-by-layer assembly involves the sequential deposition of different materials onto a core nanoparticle to create a complex, multifunctional structure [40]. Wang et al. [40] reported a multifunctional MnO-NCs-decorated Cu-doped mussel-inspired mesoporous polydopamine (CM) nanoplatform, which is further engineered by co-loading sorafenib and ICG with the help of a cargo-loading and targeting-capable hyaluronic acid (HA) shell.

Specific materials used

Gold nanoparticles

Gold nanoparticles are widely used in nanoplatforms due to their unique optical properties, biocompatibility, and ease of surface modification [26, 38]. Tang et al. [26] utilized gold nanorods for targeted gene editing and combined tumor therapy. Hu et al. [38] constructed an ICG modified Pt NCs decorated Au NBPs to form the multifunctional nanocomposites (Au NBPs@Pt NCs-ICG) for multimodal imaging mediated phototherapy and chemodynamic cancer therapy.

MOFs

MOFs are crystalline materials with high surface areas and tunable pore sizes, making them suitable for drug delivery and imaging [27, 37, 41]. Yan et al. [27] used ZIF-8 as a matrix for encapsulating therapeutic agents. Zhao et al. [37] designed a lanthanide europium MOF nanocomposite for theragnostics. Lv et al. [41] designed a multifunctional nanoplatform (called BSArGO@ZIF-8 NSs) by growth of MOF nanoparticles (ZIF-8 NPs) onto the graphene oxide surface, subsequently reduced by ascorbic acid and modified by bovine serum albumin.

Carbon-based nanomaterials

Carbon-based nanomaterials, such as CQDs and graphene oxide, offer excellent biocompatibility, photostability, and tunable properties [27, 28, 35]. Liu et al. [35] used CQDs, was initially synthesized and then rationally constructed a FA-targeted photothermal multifunctional nanoplatform. Hao et al. [28] engineered Ru-CQDs for photoacoustic imaging-guided cancer therapy. Lv et al. [41] designed a multifunctional nanoplatform (called BSArGO@ZIF-8 NSs) by growth of MOF nanoparticles (ZIF-8 NPs) onto the graphene oxide surface.

Polymers

Polymers, including polysaccharides and polyamino acids, are frequently employed for their biocompatibility, biodegradability, and ease of modification [30, 33]. Qiu et al. [30] exploited tumor-specific activated polyamino acid calcified nanoparticles as new-type oxidative stress amplification of anticancer drugs building a safe and biodegradable multifunctional nanoplatform. Tian et al. [33] fabricated a novel acid-responsive oxidized dextran-based nanoplatform for photodynamic antibacterial therapy.

In summary, multifunctional nanoplatforms represent a promising avenue for advancing targeted therapy and diagnostics. The rational design and synthesis of these platforms, incorporating targeting ligands, multiple therapeutic modalities, stimuli-responsive elements, and imaging capabilities, are crucial for maximizing their efficacy. As research progresses, these nanoplatforms hold the potential to revolutionize disease treatment and improve patient outcomes.

Mechanisms of Targeted Delivery: Passive vs Active Targeting in Diseased Tissues

Targeted delivery mechanisms in nanomedicine are broadly categorized into passive and active strategies, each leveraging different biological and physicochemical principles to enhance therapeutic specificity within diseased tissues (Table 1) [42-53]. Passive targeting primarily exploits the unique physiological features of pathological tissues, such as the enhanced permeability and retention (EPR) effect observed in tumors, which allows nanocarriers to accumulate preferentially at the disease site without specific ligand-receptor interactions [53]. This process relies on the natural leakiness of abnormal vasculature and impaired lymphatic drainage, facilitating the extravasation and retention of nanoparticles within the diseased tissue. Conversely, active targeting involves the functionalization of nanocarriers with specific ligands—such as peptides, antibodies, or aptamers—that recognize and bind to molecular markers or receptors overexpressed on diseased cells or tissues, thereby promoting receptor-mediated endocytosis or adhesion [54]. This ligand-receptor interaction enhances the precision of delivery, reducing off-target effects and increasing therapeutic efficacy.

Passive targeting leverages the inherent physiological and pathological features of diseased tissues to facilitate drug accumulation without the need for specific ligands or external guidance. One of its primary advantages is simplicity in design and implementation, as it relies on natural phenomena such as the EPR effect observed in tumor tissues [55]. This effect allows nanoparticles of appropriate size and surface properties to extravasate through leaky vasculature and accumulate preferentially in the diseased tissue interstitium, thereby increasing local drug concentration. Additionally, passive targeting does not require complex surface modifications or ligand conjugation, which simplifies manufacturing and reduces production costs [56]. Its broad applicability across various disease models, including tumors and inflamed tissues, makes passive targeting a versatile approach. For instance, nanoparticles designed with optimal size, charge, and shape can exploit tissue-specific vascular abnormalities, as demonstrated in kidney-targeted nanocarriers where physicochemical properties influence renal accumulation [57]. Moreover, passive targeting strategies have been successfully integrated into theragnostic platforms, enabling simultaneous diagnosis and therapy with minimal off-target effects [58].

Active targeting enhances delivery specificity by functionalizing nanocarriers with ligands such as antibodies, peptides, or aptamers that recognize and bind to specific receptors overexpressed on diseased cells or tissues [55]. This approach offers several advantages over passive targeting, including increased binding affinity and cellular uptake, leading to higher therapeutic payload delivery at the target site [54]. Active targeting can overcome biological barriers and heterogeneity within diseased tissues, ensuring more uniform and efficient drug distribution [59]. For example, ligand-modified nanoparticles can selectively bind to integrins expressed on tumor cells or to receptors on inflamed endothelium, thereby improving therapeutic efficacy while reducing systemic toxicity [55]. Additionally, active targeting strategies facilitate stimuli-responsive drug release, as seen in DNA tetrahedron nanostructures designed for on-site cargo release upon environmental triggers [54]. This precision reduces off-target effects and enhances the therapeutic index, making active targeting particularly valuable in complex pathologies such as cancer and inflammatory diseases [60].

Despite their advantages, both passive and active targeting approaches face inherent limitations. Passive targeting's reliance on the EPR effect can be inconsistent due to tumor heterogeneity, abnormal vasculature, and variations in microenvironmental factors, which may lead to suboptimal accumulation and distribution of nanocarriers [54]. Moreover, passive targeting lacks specificity at the molecular level, increasing the risk of off-target effects in non-diseased tissues with similar vascular features. Additionally, the size and surface properties optimized for passive targeting may inadvertently promote clearance by the mononuclear phagocyte system, reducing bioavailability [56].

Active targeting, while offering higher specificity, introduces complexity in nanocarrier design and manufacturing. The conjugation of targeting ligands can increase production costs, affect nanoparticle stability, and potentially induce immunogenic responses [54]. Furthermore, receptor expression levels can vary among patients and disease stages, leading to inconsistent targeting efficiency. The presence of the protein

Table 1: Comparison of passive and active targeting mechanisms in nanomedicine.

Feature	Passive targeting	Active targeting
Core principle	Exploits the unique physiological and pathological features of diseased tissues, primarily the EPR effect.	Utilizes ligand-receptor interactions by functionalizing nanocarriers with targeting moieties (e.g., antibodies, and peptides, aptamers).
Key mechanism	Relies on leaky vasculature and impaired lymphatic drainage in pathological tissues (e.g., tumors and inflammation) to allow nanocarrier extravasation and accumulation.	Ligands on the nanocarrier surface specifically bind to molecular markers (e.g., integrins and receptors) overexpressed on target cells, promoting receptor-mediated endocytosis.
Primary advantages	• Simpler design without complex ligand conjugation. • Broad applicability across various disease models with vascular abnormalities. • Lower production costs.	• Higher specificity and binding affinity for target cells. • Enhanced cellular uptake and therapeutic payload delivery. • Can overcome biological barriers and tissue heterogeneity.
Common targeting ligands/ strategies	Relies on physicochemical properties like size, charge, and shape.	Antibodies, peptides (e.g., TAT and RGD), aptamers (e.g., AS1411), small molecules (e.g., FA).
Inherent limitations	• Inconsistent due to tumor heterogeneity and variable EPR effect. • Lacks molecular specificity, leading to potential off-target accumulation. • Optimized physicochemical properties may promote clearance by the mononuclear phagocyte system.	• Increased complexity, cost, and potential immunogenicity from ligand conjugation. • Variable receptor expression among patients and disease stages. • Protein corona formation can mask ligands, reducing targeting efficiency.
Representative examples	• Exploitation of leaky tumor vasculature via the EPR effect. • Kidney-targeted nanocarriers using optimized size and charge.	• TAT peptide and aptamer for nuclear-targeted gene editing. • AS1411 aptamer for tumor targeting of Ru-CQDs. • Macrophage cell membrane camouflage for tumor homing.
Therapeutic outcome	Increased local drug concentration in diseased tissue interstitium, but with limited cellular precision.	Precise delivery to specific cell types, enhancing therapeutic index and reducing systemic toxicity.

corona formed in biological fluids can also mask targeting ligands, diminishing their binding capacity and overall effectiveness [56]. Additionally, active targeting strategies often require stimuli-responsive release mechanisms to ensure payload delivery, which can complicate nanocarrier design and pose challenges in clinical translation [54].

In summary, while passive targeting provides a straightforward and broadly applicable method exploiting tissue microenvironment features, its efficacy can be limited by biological variability and off-target accumulation. Conversely, active targeting offers enhanced specificity and cellular uptake but faces challenges related to complexity, stability, and biological barriers. Combining both strategies or developing innovative approaches may help overcome these limitations and optimize targeted delivery in diseased tissues [1].

Imaging Modalities Enabled by Nanoplatforms: MRI, PET, Fluorescence, and Photoacoustics

Nanoplatforms have emerged as pivotal tools in advancing medical imaging by overcoming limitations of conventional contrast agents and enabling multimodal, targeted, and theragnostic applications [61-72]. Their nanoscale size allows for enhanced tissue penetration, prolonged circulation, and functionalization with targeting ligands, which improves specificity and reduces off-target effects [73]. Nanomaterials such as MOF, protein-based constructs, and inorganic nanoparticles can be engineered to carry multiple imaging agents, enabling simultaneous use of MRI, PET, fluorescence, and photoacoustic modalities within a single platform [61, 73, 74]. This multimodal capability not only provides comprehensive diagnostic information but also facilitates image-guided therapy, known as theragnostics, where diagnosis and treatment are integrated [75, 76]. Furthermore, nanoplatforms can be designed to respond to specific biological stimuli, releasing therapeutic agents or enhancing imaging signals in diseased tissues, thus enabling precision medicine approaches [77-79]. The versatility, tunability, and multifunctionality of nanoplatforms are driving innovations that promise to improve diagnostic accuracy, enable real-time monitoring of therapeutic responses, and ultimately transform pathology management (Table 2).

MRI

Nanoplatforms have significantly advanced MRI by serving as contrast agents that improve signal specificity and sensitivity. Superparamagnetic iron oxide nanoparticles (SPIONs) and other magnetic nanomaterials are commonly employed to induce local magnetic field inhomogeneities, resulting in T2-weighted signal darkening that enhances lesion detectability [80]. The high surface area of nanomaterials allows for functionalization with targeting ligands, enabling selective accumulation in diseased tissues. Additionally, the integration of multimodal functionalities into nanoplatforms, such as combining MRI with optical or photoacoustic imaging, further enhances diagnostic accuracy [73].

Table 2: Comparative analysis of imaging modalities enabled by theragnostic nanoplatforms.

Feature	MRI	PET	Fluorescence imaging	PAI
Core principle	Detects relaxation of hydrogen nuclei in a strong magnetic field to produce anatomical images.	Detects gamma rays from positron-emitting radiotracers to map metabolic and molecular activity.	Detects emitted light from fluorescent probes (e.g., quantum dots, dyes) excited by external light.	Detects ultrasound waves generated by tissue expansion after absorption of pulsed laser light (photoacoustic effect).
Key role of nanoplatforms	Serve as high-performance contrast agents (e.g., SPIONs for T2-weighting). Enable multimodal integration and targeted delivery via surface functionalization.	Act as versatile carriers for radionuclides (e.g., in NMOFs, liposomes). Enhance stability, enable multi-agent loading, and facilitate targeted theragnostics.	Function as carriers to improve probe stability, brightness, and targeting. Enable multimodal imaging (e.g., quantum dots with tunable emission).	Engineered as contrast agents with strong NIR absorption (e.g., specialized NMOFs, gold nanostructures) to amplify signals and enable targeted accumulation.
Primary advantages	• Excellent soft tissue contrast and high spatial resolution. • Deep tissue penetration. • No ionizing radiation.	• Very high sensitivity for molecular processes. • Quantitative capabilities. • Excellent for detecting metastases and metabolic activity.	• High sensitivity and specificity. • Real-time imaging capability. • High temporal resolution.	• Combines optical contrast with ultrasound resolution. • Good depth penetration with high spatial resolution. • Provides functional and molecular information.
Primary limitations	• Relatively low sensitivity compared to nuclear/optical methods. • Long acquisition times. • High cost and complex equipment.	• Exposure to ionizing radiation. • Lower spatial resolution than MRI or CT. • Requires cyclotron/proximity for short-lived isotopes.	• Limited tissue penetration depth (especially in visible spectrum). • Tissue autofluorescence can create background noise. • Primarily for superficial or intraoperative use.	• Limited by optical penetration depth (though better than fluorescence). • Requires specialized laser/ultrasound equipment. • Can be affected by tissue optical properties.
Common nanomaterial examples	Superparamagnetic iron oxide nanoparticles (SPIONs), Gadolinium-based complexes, Manganese oxides.	NMOFs, Radiolabeled liposomes, Polymeric nanoparticles.	Quantum Dots, Carbon Dots, Dye-loaded liposomes/polymers, NIR-II fluorescent probes.	Gold nanostructures (nanorods, bipyramids), ICG nanocomposites, Carbon-based nanomaterials, Absorbing NMOFs.
Key applications in pathology	• Detailed tumor characterization and margin delineation. • Neuroinflammatory and neurodegenerative disease monitoring. • Imaging-guided therapy.	• Cancer diagnosis, staging, and treatment response monitoring. • Neurodegenerative disease biomarker visualization (e.g., amyloid). • Cardiovascular plaque assessment.	• Intraoperative guidance and tumor margin delineation. • Real-time cellular/molecular event visualization. • Lymph node mapping and immune cell tracking.	• Brain tumor detection and surgical guidance. • Visualization of atherosclerotic plaques and vasculature. • Monitoring of therapeutic responses in deep tissues.
Synergy in multimodal platforms	Often combined with PET (PET/MRI) for complementary anatomical and metabolic data, or with fluorescence/PAI for surgical guidance.	Integrated with MRI or CT (PET/MRI and PET/CT) to merge high sensitivity with high-resolution anatomy.	Integrated with MRI or PAI to add real-time, high-sensitivity molecular data to structural imaging.	Combined with MRI for deep structural context or with fluorescence for comprehensive multi-scale imaging.

These engineered nanostructures can be tailored for optimal biocompatibility, stability, and targeted delivery, thereby overcoming limitations of traditional contrast agents and enabling more precise imaging in pathological contexts [80].

In pathology, nanoplatform-enhanced MRI has been instrumental in detecting and characterizing various disease states. For instance, in neuroinflammatory diseases and neurodegenerative disorders, MRI with nanoparticle contrast agents facilitates the visualization of immune responses and tissue degeneration [77]. In oncology, nanomaterials enable detailed tumor imaging, delineation of tumor margins, and monitoring of therapeutic responses. The development of omniparticle contrast agents capable of multimodal imaging—combining MRI with PET, fluorescence, photoacoustic, and CT—has opened new avenues for comprehensive disease assessment [80]. Such platforms allow for real-time tracking of disease progression, evaluation of therapeutic efficacy, and precise localization of pathological features, thereby significantly advancing diagnostic capabilities in clinical and research pathology [73, 80].

PET

Recent advances in nanotechnology have significantly expanded the capabilities of PET imaging through the development of nanoplatforms for radiotracer design. Nanomaterials such as nanoscale MOF (NMOFs,) liposomes, polymeric nanoparticles, and other hybrid systems serve as versatile carriers for positron-emitting isotopes [73]. These nanoplatforms offer several advantages, including high surface area for functionalization, improved stability of radiotracers, and the ability to incorporate multiple imaging agents or therapeutic payloads within a single construct [73]. For instance, NMOFs can be engineered to load and deliver radiometal ions, enabling multimodal imaging and theranostic applications [73]. Surface modification of nanoplatforms allows for targeted delivery to specific tissues or cellular markers, enhancing imaging specificity and reducing off-target effects [73]. Moreover, the porosity and tunable chemistry of nanomaterials facilitate the co-loading of diagnostic and therapeutic agents, paving the way for integrated theranostic systems [73].

Nanoplatform-enabled PET radiotracers have demonstrated significant potential in clinical settings, particularly in cancer diagnosis, staging, and treatment monitoring. For example, multifunctional nanoconstructs have been used to target tumor-specific biomarkers, improving the sensitivity and specificity of PET imaging in detecting primary and metastatic lesions [73]. In neurodegenerative diseases, nanoplatforms facilitate the delivery of radiotracers across the blood-brain barrier, enabling better visualization of pathological hallmarks such as amyloid plaques or neuroinflammation [73]. Additionally, in cardiovascular diseases, nanomaterials loaded with PET isotopes assist in the assessment of atherosclerotic plaques and vascular inflammation, aiding in risk stratification and therapeutic planning [73]. The integration of nanotechnology with PET imaging not only enhances diagnostic accuracy but also supports personalized medicine approaches by enabling real-time monitoring of therapeutic efficacy and disease progression [73]. As nanoplatforms continue to evolve, their translation into clinical practice promises to improve disease detection, facilitate targeted therapy, and ultimately enhance patient outcomes across a broad spectrum of pathologies.

Fluorescence imaging

Nanoplatforms have revolutionized fluorescence imaging by serving as carriers for fluorescent agents, enhancing their stability, brightness, and targeting capabilities. These nanocarriers include liposomes, polymeric nanoparticles, quantum dots, and biomimetic systems, which can be engineered to carry multiple imaging labels and therapeutic agents simultaneously [73]. For instance, quantum dots exhibit exceptional photostability and tunable emission spectra, making them ideal for long-term imaging applications [73]. Surface functionalization of nanoplatforms with targeting ligands such as peptides, antibodies, or aptamers allows for specific accumulation in diseased tissues, improving contrast and reducing off-target effects [61]. Moreover, the integration of fluorescent probes into multifunctional nanoplatforms enables multimodal imaging, combining fluorescence with modalities like MRI or photoacoustic imaging, thus providing comprehensive diagnostic information [75]. The porosity and surface chemistry of nanomaterials also facilitate loading of therapeutic agents, paving the way for theranostic applications that combine diagnosis and treatment [73].

Fluorescence imaging, enabled by nanoplatforms, has found extensive applications in pathology, including cancer detection, neurodegenerative disease monitoring, and immune response assessment. Its high sensitivity allows for early detection of pathological changes at the molecular level, often before morphological alterations become apparent [77]. In cancer, fluorescence-guided surgery improves tumor margin delineation, leading to more complete resections and better patient outcomes [81]. The ability to visualize specific biomarkers with targeted fluorescent probes enhances diagnostic accuracy and enables real-time intraoperative decision-making [82]. Additionally, fluorescence imaging's non-ionizing nature and high spatial resolution make it suitable for longitudinal studies and dynamic monitoring of disease progression or therapeutic response [83]. The development of NIR-II fluorescent probes has further extended the depth and clarity of *in vivo* imaging, facilitating the detection of deep-seated lesions with minimal tissue damage [84]. Overall, the advantages of fluorescence imaging include its high sensitivity, specificity, real-time capability, and compatibility with multimodal approaches, making it an indispensable tool in modern pathology and personalized medicine.

Photoacoustic imaging

The effectiveness of photoacoustic imaging heavily depends on the development of suitable contrast agents that can efficiently absorb light and generate acoustic signals. Recent advances have focused on engineering nanoplatforms to amplify photoacoustic signals and improve imaging specificity. As highlighted by Duman and Forgan [73], NMOFs and other nanomaterials can be tailored to possess strong NIR absorption, biocompatibility, and targeted delivery capabilities. These nanoplatforms can be loaded with functional molecules or designed with intrinsic optical properties to enhance contrast. Zhang et al. [81] further demonstrate the use of multifunctional nanotheragnostics that combine photoacoustic agents with therapeutic functionalities, enabling simultaneous imaging and treatment of diseases such as brain tumors. The integration of nanomaterials not only boosts signal strength but also allows for targeted accumulation in pathological tissues, thereby increasing the sensitivity and specificity of photoacoustic detection.

Photoacoustic imaging, augmented by nanoplatforms, has shown significant potential in diagnosing and monitoring a variety of diseases. Its high spatial resolution and deep tissue penetration make it particularly suitable for oncological applications, such as brain tumor detection and cancer margin delineation. Zhang et al. [81] highlight the use of NIR contrast agents for brain tumors, where PAI provides real-time guidance during surgical procedures and therapy monitoring. Similarly, in cardiovascular diseases, ICG-based nanotheragnostics enable visualization of atherosclerotic plaques and vascular inflammation with high contrast and specificity [85]. The ability to combine PAI with other modalities, such as MRI and fluorescence imaging, facilitates comprehensive disease assessment, tracking molecular changes, and evaluating therapeutic responses over time. As research progresses, the development of targeted nanoplatforms promises to further enhance the diagnostic accuracy and therapeutic efficacy of photoacoustic imaging in clinical pathology.

Comparative analysis of imaging modalities

Each imaging modality enabled by nanoplatforms offers distinct advantages that make them suitable for specific pathological applications, yet they also possess inherent limitations. MRI provides excellent soft tissue contrast, high spatial resolution, and deep tissue penetration without ionizing radiation, making it highly valuable for detailed anatomical imaging and functional studies, such as tumor characterization and immune response monitoring [73, 77]. However, MRI often suffers from relatively lower sensitivity compared to optical methods and can require long acquisition times and high-cost equipment. PET offers high sensitivity and quantitative capabilities, enabling detection of molecular and metabolic processes at very low concentrations, which is particularly useful in cancer and neurodegenerative disease diagnostics [73, 86]. Its main limitations include exposure to ionizing radiation and relatively lower spatial resolution. Fluorescence imaging, especially in the NIR-II window, provides high sensitivity, real-time imaging, and the ability to visualize cellular and molecular events with excellent temporal resolution [82, 84]. Nonetheless, its limited tissue penetration depth and potential for tissue autofluorescence restrict its use to superficial tissues or intraoperative settings. Photoacoustic imaging combines optical contrast with ultrasound resolution, allowing for high-contrast, deep tissue imaging with functional and molecular information [81, 84, 87]. Despite its advantages, photoacoustic imaging can be limited by optical penetration depth and the need for specialized equipment. Multimodal approaches, integrating these techniques, aim to leverage their respective strengths while compensating for individual limitations, thus providing comprehensive insights into pathological processes [80-82].

The integration of multiple imaging modalities using nanoplatforms has emerged as a powerful strategy to achieve comprehensive and precise pathological assessment. Multifunctional nanoplatforms can be engineered to carry contrast agents suitable for MRI, PET, fluorescence, and photoacoustic imaging, enabling simultaneous or sequential multimodal imaging [61, 80, 81]. Such integration allows clinicians and researchers to combine the high spatial resolution of MRI, the molecular sensitivity of PET, the real-time visualization of fluorescence, and the deep tissue contrast of photoacoustics, thereby overcoming the limitations inherent to individual modalities [61, 80, 82]. For example, the development of omniparticle contrast agents demonstrates the feasibility of a single nanoparticle platform capable of producing signals across multiple imaging techniques, facilitating comprehensive disease diagnosis, monitoring, and therapy guidance [80]. Moreover, multimodal imaging enhances the accuracy of disease detection, enables better delineation of pathological features, and supports real-time assessment of therapeutic responses, especially in complex conditions such as brain tumors, neurodegenerative diseases, and cardiovascular disorders [76, 81, 88]. The synergistic use of these modalities not only improves diagnostic confidence but also paves the way for integrated theranostic applications, where diagnosis and treatment are combined within a single nanoplatform, advancing personalized medicine [61, 75, 76]. As research progresses, the focus remains on optimizing biocompatibility, targeting specificity, and clinical translatability of these multimodal nanoplatforms to fully realize their potential in pathology.

Therapeutic Payloads: Small Molecules, Nucleic Acids, Radionuclides, and Photosensitizers

Therapeutic payloads incorporated into theragnostic nanoplatforms encompass a diverse array of agents, each with unique mechanisms and applications. Small molecules are widely used for their ability to modulate specific molecular targets, such as ion channels or enzymes, and are central to many cancer therapies [89, 90]. Nucleic acids, including siRNAs, antisense oligonucleotides, and microRNAs, offer gene-specific regulation and gene therapy potential, although their delivery remains challenging [91-93]. Radionuclides serve dual roles in imaging and radiotherapy, enabling precise tumor localization and destruction through radiation emission [94, 95]. Photosensitizers are employed in PDT to generate reactive oxygen species upon light activation, inducing tumor cell death and immune responses [92, 94, 96]. The integration of these payloads into nanoplatforms aims to harness their individual strengths while overcoming delivery barriers, ultimately advancing theranostic strategies in pathology [97, 98].

Small molecules have been extensively explored in cancer therapy due to their capacity to target key molecular pathways involved in tumor growth and immune evasion. For example, the development of Mn-based hollow nanoplatforms encapsulating small-molecule chemotherapeutics enables MRI-guided combination therapies, including chemotherapy, PDT, and CDT [95]. These nanoplatforms facilitate targeted delivery and controlled release of small-molecule drugs within tumor microenvironments, enhancing therapeutic efficacy while minimizing systemic toxicity. Moreover, small molecules such as photosensitizers (e.g., pheophorbide A) can be combined with nucleic acids like siRNA within nanogels to achieve synergistic tumor cell killing and immune activation [92]. Small-molecule inhibitors targeting immune checkpoints or signaling pathways are also under investigation, with some progressing into clinical trials for various cancers [99]. The ability to conjugate small molecules with targeting ligands or incorporate them into nanocarriers further broadens their application scope, enabling precise and effective cancer treatments.

Effective delivery of nucleic acids remains a critical challenge due to their large size, negative charge, and susceptibility to degradation. To overcome these barriers, various nanocarrier systems have been developed, including lipid nanoparticles, polymeric nanoparticles, exosomes, and DNA nanostructures [91, 97, 100]. Lipid nanoparticles and ligand conjugation approaches have shown promise in improving cellular uptake and stability of nucleic acid therapeutics [91]. For example, lipid-based nanoparticles can encapsulate nucleic acids, protecting them from enzymatic

degradation and facilitating endosomal escape [97]. Exosomes, naturally occurring vesicles, are being explored as delivery vehicles owing to their biocompatibility and ability to cross biological barriers, including the blood-brain barrier [91]. Additionally, DNA origami nanostructures can be engineered for targeted delivery, enabling rapid cytosolic uptake and deep tissue penetration [100]. Cell-based delivery systems, such as erythrocytes and stem cells, also offer innovative platforms for transporting nucleic acids with prolonged circulation times and tissue-homing capabilities [101].

Radionuclides play a pivotal role in enabling precise imaging and effective treatment within theragnostic nanoplatforms. Diagnostic imaging benefits from radionuclides like technetium-99m and fluorine-18, which facilitate non-invasive visualization of tumor localization, metastasis, and treatment response with high sensitivity and spatial resolution [94]. These imaging capabilities allow clinicians to accurately delineate disease extent and monitor therapeutic outcomes in real-time. On the therapeutic front, radionuclides such as lutetium-177 and actinium-225 deliver cytotoxic radiation directly to cancer cells, minimizing damage to surrounding healthy tissue [94]. The integration of radionuclides into nanocarriers enhances targeted delivery, improves retention within tumor sites, and enables combination therapies that synergize radiotherapy with other modalities like chemotherapy or immunotherapy [94]. Moreover, the development of hollow manganese-based nanoplatforms exemplifies how radionuclides can be incorporated into multifunctional systems for MR imaging-guided cancer therapies, where the radionuclide serves both as a contrast agent and a therapeutic payload [95].

Photosensitizers have been extensively explored in clinical settings for the treatment of various cancers, including skin, lung, and esophageal cancers, owing to their ability to induce localized cell death upon light activation [94]. Their application extends beyond oncology to antimicrobial therapies, where PDT can effectively eradicate resistant bacterial infections [92]. Recent advances involve the development of multifunctional nanoplatforms that co-deliver photosensitizers with immunomodulatory agents, such as PD-L1 siRNA, to enhance therapeutic efficacy and immune activation [9]. Moreover, photosensitizers are integrated into theranostic nanoplatforms for real-time imaging-guided therapy, leveraging their inherent fluorescence or photoacoustic properties [95]. The ability to visualize tumor margins and monitor treatment response *in vivo* has significantly improved the precision and outcomes of PDT [102]. These clinical applications demonstrate the versatility of photosensitizers in targeted, minimally invasive therapies with potential for synergistic effects when combined with other therapeutic payloads.

Combining multiple therapeutic agents within a single nanoplatform can produce synergistic effects that surpass the efficacy of individual treatments. For example, the co-delivery of photosensitizers and immune checkpoint siRNA, such as PD-L1 siRNA, within a nanogel framework enables simultaneous PDT and immune modulation, resulting in enhanced antitumor immune responses [92]. Similarly, hollow manganese-based nanostructures can encapsulate chemotherapeutic drugs, photosensitizers, and photothermal agents, facilitating multimodal therapy that integrates chemotherapy, PDT, and CD) [95]. The synergistic interaction between these modalities can induce immunogenic cell death, amplify immune activation, and improve overall therapeutic outcomes [102]. Moreover, the co-delivery of nucleic acids and small molecules, such as antisense oligonucleotides with small-molecule inhibitors, can target multiple pathways simultaneously, reducing the likelihood of resistance and increasing treatment potency [103]. The design of nanoplatforms that enable controlled, sequential, or stimuli-triggered release of combined payloads is critical to harnessing these synergistic effects effectively [104].

Recent advances exemplify the potential of integrating diverse therapeutic payloads into nanoplatforms for enhanced pathology treatment. Mollé et al. demonstrated nanoparticles capable of delivering nucleic acids and photosensitizers for vaccine and gene therapy applications, overcoming delivery barriers and achieving targeted gene silencing and tumor ablation [97]. Guo et al. developed a nucleic acid nanogel co-packaging photosensitizers and PD-L1 siRNA, which synergistically induced tumor cell death and immune activation, showcasing the potential for combined photodynamic and immunotherapeutic strategies [92]. Manganese-based hollow nanoplatforms exemplify multifunctional systems capable of encapsulating small molecules for chemotherapy, PDT, and PTT, while simultaneously serving as imaging contrast agents and mediators of CDT [95]. Additionally, innovative approaches such as the CytoDirect DNA nanodevice enable rapid cytosolic delivery of nucleic acids and small molecules, bypassing endosomal entrapment and enhancing intracellular therapeutic effects [100]. These case studies highlight ongoing research efforts aimed at optimizing nanoplatform design for multimodal, synergistic therapy, emphasizing the importance of tailored physicochemical properties, stimuli-responsiveness, and multifunctionality to address complex pathological conditions effectively.

Theragnostic Nanoplatforms: Clinical Studies

The fabricated GPRD NPs [105] demonstrated excellent MR and fluorescence dual-modality imaging capabilities for vulnerable atherosclerotic plaques *in vivo* (Figure 1). GPRD NPs effectively utilized the nano-enzyme activity of Gd-doped Prussian blue to scavenge ROS. This ROS scavenging led to a reduction in inflammation, apoptosis, and foam cell formation, thereby inhibiting the progression of atherosclerosis. The study concluded that these multimodal imaging nanoparticles, with their ROS-scavenging ability, offer a new approach for both the diagnosis and treatment of vulnerable AS plaques. In summary, the research successfully developed GPRD nanoparticles that serve a dual purpose: enabling precise imaging of vulnerable plaques and actively treating atherosclerosis by mitigating oxidative stress and its downstream effects.

A study by Pan et al. [106] successfully developed and evaluated a macrophage-targeted, *in situ* stimuli-triggered T1–T2 switchable MRI nanoprobe for the non-invasive diagnosis of vulnerable atherosclerotic plaques (Figure 2). The nanoprobe, consisting of single-dispersed IONPs modified with HA and denoted as IONP-HP, demonstrated macrophage targetability and exhibited T1 MRI enhancement. In this state, its r2/r1 ratio was measured at 3.415. When exposed to the low pH environment characteristic of macrophage lysosomes, the single-dispersed IONP-HP transformed into a cluster analogue. This transformation led to a switch in its MRI enhancement mode. The clustered form of the nanoprobe displayed T2 MRI enhancement, with a significantly higher r2/r1 ratio of 13.326. After intravenous administration of the nanoprobe, vulnerable plaques showed strong T1 enhancement initially. This enhancement subsequently switched to T2 enhancement after 9 hours. This dynamic switch is crucial for distinguishing plaque types. In contrast, stable plaques exhibited only slight T1 enhancement and did not show any T2 enhancement. This lack of T2 enhancement in stable plaques provides a clear differentiation from vulnerable ones. The intelligent and

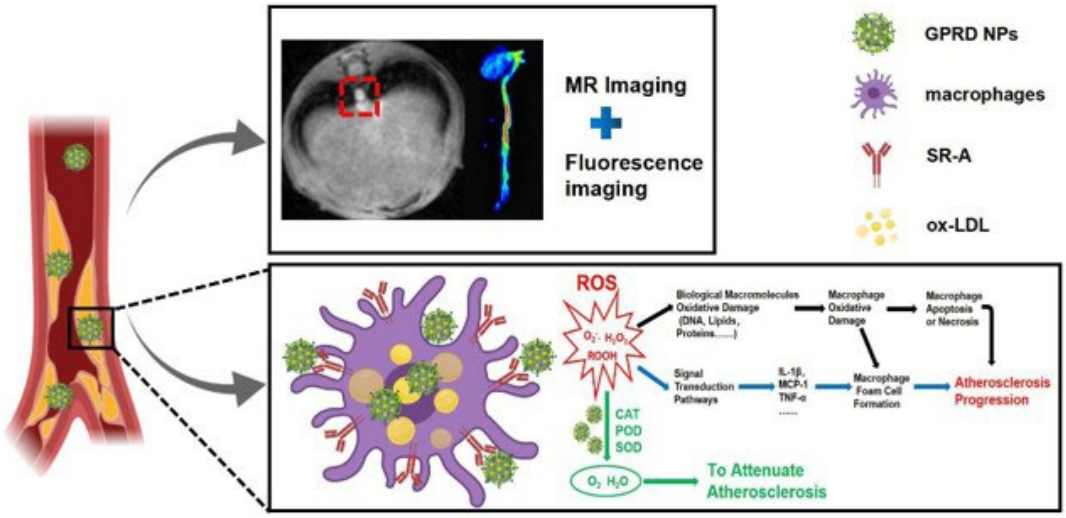


Figure 1: Targeted therapy of atherosclerosis vulnerable plaque by ROS-scavenging nanoparticles and MR/fluorescence dual-modality imaging tracing [105].

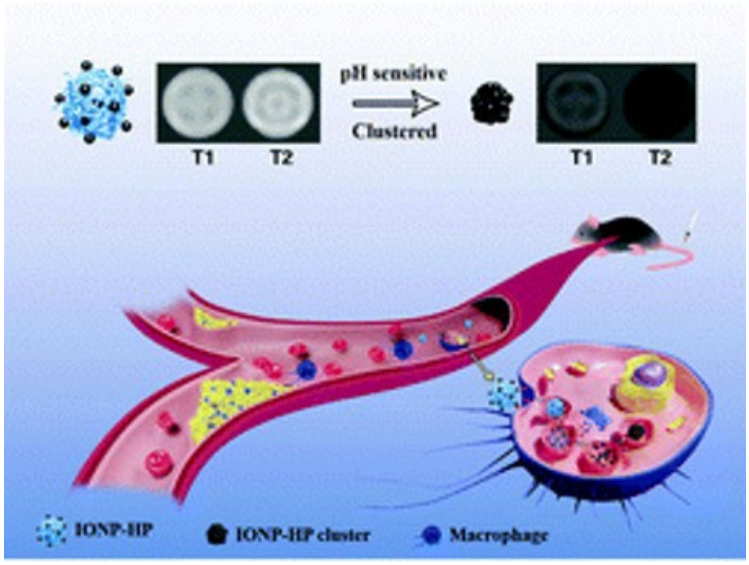


Figure 2: An intelligent T1-T2 switchable MRI contrast agent for the non-invasive identification of vulnerable atherosclerotic plaques [106].

novel nanoplatform presented in this study achieved a substantial non-invasive diagnosis of vulnerable plaques. This was accomplished through a facile but effective T1–T2 switchable process, which is expected to significantly contribute to applying materials science to clinical problems.

A study by Fujiwara et al. [107] successfully developed a smart and versatile theranostic nanoplatform, named DOX/ Gd3+-based carbon quantum dots (GCDs)- hollow mesoporous Prussian blue nanoparticles, by encapsulating GCDs and DOX within hollow mesoporous Prussian blue nanoparticles (Figure 3). At physiological pH, both GCDs and DOX molecules are contained within the nanoparticles' mesoporous hollow network. The metal–ligand coordination bonding between Gd species and DOX molecules restricts water access to the Gd3+ center, thereby minimizing proton relaxivity. In the acidic tumor microenvironment, GCDs and DOX drug molecules are simultaneously released from the nanoparticles. This release leads to an enhancement in both MR contrast and fluorescence, which in turn increases chemotherapeutic activities. The innovative platform facilitates targeted drug release and simultaneous MR/fluorescence imaging specifically at the tumor site. The system demonstrated strong pH-switching theranostic performance for 4T1 cells, exhibiting high-efficiency chemotherapy and considerable photothermal conversion. This indicates its practical application for synergistic chemo-photothermal treatment of tumors. This study introduces a promising strategy for developing a theranostic platform for cancer treatment and diagnosis, integrating multiple modalities into a single entity for effective cancer treatment

A study by Huang et al. [108] on FeOOH-loaded mesoporous silica nanoparticles (Fe@MSNs) revealed several significant findings regarding their potential as a theranostic platform. The synthesized Fe@MSNs demonstrated activatable T1 MRI performance. This means their MRI signal can be 'turned on' in response to specific environmental cues. This activation is specifically triggered by the acidic microenvironment

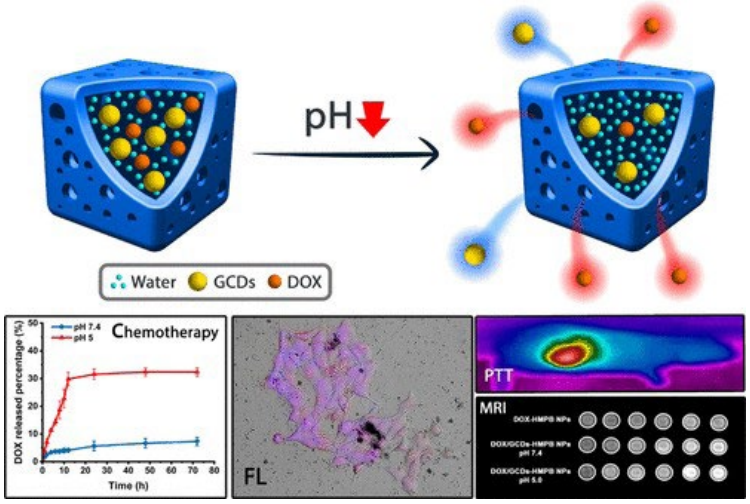


Figure 3: Hollow Mesoporous Prussian blue nanoparticles for *in vivo* synergistic chemo-photothermal cancer therapy and dual-mode magnetic resonance/fluorescence imaging [107].

characteristic of solid tumors. In such conditions, the Fe@MSNs release paramagnetic Fe^{3+} ions, which are responsible for enhancing the T1 MRI signals. The Fe@MSNs were found to be biocompatible, indicating they are well-tolerated by biological systems. Crucially, they exhibited no appreciable cytotoxicity, meaning they do not cause significant harm or death to cells. The unique mesoporous structure of the Fe@MSNs provides a significant advantage for effective drug delivery. This structure allows them to carry and effectively deliver chemotherapeutic drugs, which can inhibit the growth of solid tumors.

A phase I trial by Chargari et al. [109] investigating AGuIX nanoparticles in combination with chemoradiation and brachytherapy for locally advanced cervical cancer yielded several significant results. The AGuIX nanoparticles, when combined with chemoradiation, appeared well tolerated among the 12 treated patients. No dose-limiting toxicity was observed during the trial. AGuIX nanoparticles, administered intravenously, accumulated appropriately within tumors in a dose-dependent manner. This accumulation was assessed using T1-weighted MRI. Uncaught nanoparticles demonstrated a rapid urinary clearance. The observed tumor accumulation of the compounds supports the precise delineation of functional target volumes at the time of brachytherapy. This delineation is based on gadolinium enhancement, leveraging the paramagnetic properties of gadolinium. The nanoparticles also enhance the radiotherapeutic activity of conventional X-rays, a 'theragnostic' action explained by the generation of high densities of secondary radiation following interaction with high-Z atoms, leading to enhanced radiation dose deposits within tumors. The treatment resulted in excellent local control, with all patients achieving complete remission of the primary tumor. One patient experienced a distant tumor recurrence. These results collectively demonstrate the clinical feasibility of using theranostic nanoparticles like AGuIX to enhance the accuracy of MRI-based treatments and focally augment radiation activity in tumors, particularly for cervical cancer patients.

Integration with Digital Pathology and Computational Analysis for Quantitative Monitoring

The integration of digital pathology with computational analysis offers numerous synergistic benefits that significantly advance diagnostic precision, research capabilities, and personalized treatment strategies. Digital pathology, characterized by high-resolution whole-slide imaging (WSI), provides a comprehensive and standardized platform for capturing tissue morphology, which, when combined with sophisticated computational algorithms, enables objective, reproducible, and high-throughput analysis [110-112]. This synergy facilitates the automation of routine and complex tasks such as tissue segmentation, biomarker quantification, and spatial analysis, thereby reducing inter- and intra-observer variability and increasing diagnostic accuracy [113-115]. Moreover, machine learning and AI-driven tools can extract hidden image patterns and quantify features that are often imperceptible to the human eye, leading to improved disease grading, prognosis, and biomarker discovery [116]. The seamless flow of digital data into computational pipelines supports large-scale biobanking, enabling translational research and the development of digital biobanks that underpin precision medicine initiatives [110]. Additionally, the integration enhances workflow efficiency, allowing rapid analysis of vast datasets, which is crucial for timely clinical decision-making and monitoring therapeutic responses [111, 117]. Overall, this combined approach fosters a more objective, scalable, and insightful understanding of tissue pathology, ultimately improving patient outcomes and advancing theragnostic nanoplatforms' monitoring capabilities.

Several case studies exemplify the impactful applications of integrating digital pathology with computational analysis. Griem et al. developed a clinical-grade AI tool for multiclass tissue segmentation in colorectal specimens, demonstrating high accuracy in tumor detection and tissue classification, with the ability to analyze most biopsy cases in under a minute—highlighting its potential for routine clinical use [114]. Similarly, Cazzaniga et al. [118] utilized fluorescence-enhanced Congo Red imaging combined with AI algorithms to improve the diagnosis of cardiac amyloidosis, achieving high diagnostic agreement and demonstrating the feasibility of applying AI to specialized staining techniques in digital slides [118]. In the realm of neurodegenerative diseases, Ramaswamy et al. created an automated pipeline employing Mask R-CNN for amyloid detection in Alzheimer's disease, enabling rapid, unbiased, and scalable neuropathological assessments that correlated well with clinical severity measures. Quantitative analysis tools have also been successfully applied in systemic sclerosis, where digital image analysis of skin

biopsies provided objective metrics of fibrosis correlating with histopathological scores, thus supporting personalized fibrosis evaluation [119]. Furthermore, in low- and middle-income countries, digital pathology combined with AI has been leveraged to extend molecular diagnostics remotely, overcoming infrastructural barriers and enabling scalable, objective assessments [120]. These case studies underscore the versatility and transformative potential of integrated digital and computational approaches across various disease contexts, facilitating more accurate, efficient, and scalable pathology workflows.

The methods of quantitative analysis in digital pathology encompass a range of computational techniques designed to extract meaningful data from histopathological images. Image analysis algorithms, including machine learning and deep learning models, are employed to perform tissue segmentation, cell counting, and feature extraction with high precision [121]. For instance, convolutional neural networks (CNNs) and mask R-CNN architectures have been successfully trained to detect, classify, and quantify specific tissue components, such as amyloid deposits in Alzheimer's disease or collagen density in systemic sclerosis [119]. Stain normalization techniques improve consistency across large datasets, facilitating more accurate quantitative comparisons [122]. Additionally, specialized software like QuPath and CurveAlign enable objective measurement of histological features, such as collagen alignment and cellularity, which correlate with disease severity [119]. Advanced methods also include spatial omics data integration, allowing for the analysis of molecular and cellular spatial patterns within tissue architecture [123]. These approaches collectively enable high-throughput, reproducible, and detailed quantitative assessments that are essential for theragnostic nanoplatforms and biomarker discovery [113].

The integration of quantitative monitoring through digital and computational pathology significantly impacts patient outcomes by enabling more accurate diagnoses, risk stratification, and personalized therapies. Quantitative biomarkers derived from tissue analysis can predict disease progression, treatment response, and prognosis with greater confidence than traditional qualitative assessments. For example, AI-driven tools for tumor detection and tissue segmentation have demonstrated high sensitivity and specificity, facilitating early diagnosis and tailored treatment plans [114]. Quantitative immune profiling, such as the immunoscore, has shown to outperform conventional staging systems in predicting patient prognosis, thereby guiding more effective therapeutic interventions [112]. Furthermore, automated and unbiased analysis pipelines reduce diagnostic variability and turnaround times, leading to faster clinical decision-making. In resource-limited settings, digital pathology combined with AI can extend expert diagnostic capabilities, improving access to high-quality care and reducing disparities [120]. Overall, these advancements foster a more precise, efficient, and personalized approach to patient management, ultimately improving survival rates and quality of life [124].

Despite the promising benefits, the integration of digital pathology and computational analysis faces several challenges and limitations. One major obstacle is the variability in data quality and standardization across different laboratories and imaging systems, which can affect the robustness and generalizability of AI models [116]. The need for large, well-annotated datasets for training and validation remains a significant bottleneck, often requiring extensive expert input and consensus annotation, as exemplified by neuropathology and cancer studies [119]. Additionally, the interpretability and transparency of complex AI models, such as deep neural networks, pose concerns for clinical adoption, as clinicians require explainable results to trust and act upon computational outputs [116, 124]. Regulatory and ethical considerations, including data privacy, validation standards, and integration into existing clinical workflows, further complicate implementation [111, 117]. Technical challenges also include domain shifts across institutions, differences in staining protocols, and scanner variability, which can impair model performance outside training environments [121]. Moreover, the human-in-the-loop paradigm emphasizes the continued importance of pathologist oversight to ensure accuracy, contextual understanding, and responsible use of AI-generated insights [117, 125]. Addressing these limitations requires ongoing research into model robustness, standardization protocols, explainability techniques, and collaborative efforts to develop universally applicable frameworks for digital pathology and computational analysis integration.

Challenges in Clinical Translation

Regulatory and ethical considerations

The development and implementation of theragnostic techniques face significant regulatory and ethical challenges that can hinder their widespread adoption. As Frangos et al. [10] highlight, the integration of personalized biologic characteristics into diagnostic and therapeutic protocols necessitates rigorous regulatory oversight to ensure safety, efficacy, and standardization. The novelty of many radiopharmaceuticals and nanotechnologies used in theragnostics raises concerns regarding their approval processes, long-term safety profiles, and potential environmental impacts. Ethical considerations also emerge around patient consent, especially given the complex nature of personalized treatments that may involve genetic profiling and novel agents with limited long-term data. Ensuring informed consent and addressing privacy issues related to genetic and molecular data are paramount to maintaining patient trust and adherence to ethical standards. Moreover, the disparity in regulatory frameworks across different regions can lead to inconsistencies in the approval and clinical application of theragnostic agents, potentially delaying access to innovative therapies [10].

Technical and operational challenges

Despite the promising advancements, technical and operational hurdles remain a barrier to the seamless integration of theragnostics into routine clinical practice. The complexity of developing and standardizing sophisticated imaging modalities, such as molecular imaging techniques and AI-assisted diagnostic tools, requires substantial technical expertise and infrastructure. Morrison et al. [126] emphasize that the digitization of pathology workflows and the application of deep learning models demand high-quality digital data, robust computational resources, and specialized training for personnel. Additionally, the variability in image quality, data interpretation, and the need for validation across different platforms pose challenges to achieving consistent and reliable results. Operational issues such as workflow integration, data management, and

interdepartmental coordination further complicate the deployment of theragnostic technologies. The lack of universally accepted protocols and the need for multidisciplinary collaboration can slow down clinical translation and limit the scalability of these approaches [126].

Cost and accessibility issues

Cost considerations and accessibility remain critical limitations in the broader implementation of theragnostics. The high costs associated with advanced imaging systems, radiopharmaceutical production, and nanotechnology-based diagnostics can restrict availability primarily to well-funded centers, creating disparities in patient access. Jena et al. [11] note that although PET/CT and emerging tracers like 68Ga-PSMA are effective, their routine use is limited by economic factors and infrastructure requirements, especially in low-resource settings. Furthermore, the expenses related to personalized molecular profiling, such as liquid biopsies and genetic testing, can be prohibitive for many healthcare systems and patients. This economic barrier hampers the equitable distribution of theragnostic benefits and may lead to inequalities in cancer care and diagnosis. Ensuring affordability and developing cost-effective, scalable solutions are essential to making theragnostics a viable option for a broader patient population [11].

Conclusion

Theragnostic nanoplatforms represent a transformative convergence of diagnostic precision and targeted therapeutic intervention, poised to redefine the landscape of modern pathology. By engineering a single nanostructure to integrate imaging capabilities, targeted drug delivery, and stimuli-responsive release mechanisms, these systems offer a powerful paradigm for personalized medicine—enabling simultaneous disease localization, treatment, and real-time monitoring of therapeutic efficacy. The successful application of such platforms in preclinical and emerging clinical studies, from cancer to cardiovascular disease, underscores their potential to improve diagnostic accuracy, enhance treatment specificity, and minimize systemic toxicity. However, the full realization of these potential hinges on overcoming persistent challenges in clinical translation, including biocompatibility, scalable manufacturing, regulatory harmonization, and cost-effective accessibility. As interdisciplinary research continues to advance the design, functionality, and integration of these multifunctional systems, theragnostic nanoplatforms are set to become indispensable tools in the pathologist's arsenal, driving a future where diagnosis and therapy are seamlessly unified for optimized patient outcomes.

Acknowledgements

None.

Conflict of Interest

None.

References

1. Gheisari F, Vali R (2024) Revolutionizing diagnostic precision: emerging trends and innovations in theranostics for nuclear medicine. Mathews J Case Rep 9: 1-9. https://doi.org/10.30654/MJCR.10155
2. Sergeeva OV, Luo L, Guiseppi-Elie A (2025) Cancer theragnostics: closing the loop for advanced personalized cancer treatment through the platform integration of therapeutics and diagnostics. Front Bioeng Biotechnol 12: 1-24. https://doi.org/10.3389/fbioe.2024.1499474
3. Omidian H, Gill EJ (2025) Multifunctional nanoplatforms bridging diagnostics and therapeutics in cancer. Micromachines 16: 1323. https://doi.org/10.3390/mi16121323
4. Rituraj, Pal RS, Wahlang J, Pal Y, Chaitanya MVNL, et al. (2025) Precision oncology: transforming cancer care through personalized medicine. Med Oncol 42: 246. https://doi.org/10.1007/s12032-025-02817-y
5. Dessale M, Mengistu G, Mengist HM (2022) Nanotechnology: a promising approach for cancer diagnosis, therapeutics and theragnosis. Int J Nanomedicine 17: 3735—3749. https://doi.org/10.2147/ijn.s378074
6. Rajapaksha W, Khetan R, Johnson IR, Blencowe A, Garg S, et al. (2024) Future theranostic strategies: emerging ovarian cancer biomarkers to bridge the gap between diagnosis and treatment. Front Drug Deliv 4: 1-19. https://doi.org/10.3389/fddev.2024.1339936
7. Bogdanovic B, Hugonnet F, Montemagno C (2025) Theranostics in hematological malignancies: cutting-edge advances in diagnosis and targeted therapy. Cancers 17: 1247. https://doi.org/10.3390/cancers17071247
8. Zhuang L, Lian Y, Zhu T (2025) Multifunctional gold nanoparticles: bridging detection, diagnosis, and targeted therapy in cancer. Mol Cancer 24: 1-37. https://doi.org/10.1186/s12943-025-02431-6
9. Marques L, Costa B, Pereira M, Silva A, Santos J, et al. (2024) Advancing precision medicine: a review of innovative in silico approaches for drug development, clinical pharmacology and personalized healthcare. Pharmaceutics 16: 332. https://doi.org/10.3390/pharmaceutics16030332
10. Morgan KA, Rudd SE, Noor A, Donnelly PS (2023) Theranostic nuclear medicine with gallium-68, lutetium-177, copper-64/67, actinium-225, and lead-212/203 radionuclides: focus review. Chem Rev 123: 12004-12035. https://doi.org/10.1021/acs.chemrev.3c00456
11. Jena R, Narain TA, Singh UP, Srivastava A (2021) Role of positron emission tomography/computed tomography in the evaluation of renal cell carcinoma. Indian J Urol 37: 125-132. https://doi.org/10.4103/iju.iju_268_20
12. Ahmadi M, Ritter CA, von Woedtke T, Bekeschus S, Wende K (2024) Package delivered: folate receptor-mediated transporters in cancer therapy and diagnosis. Chem Sci 15: 1966-2006. https://doi.org/10.1039/d3sc05539f
13. Succony L, Rassl DM, Barker AP, McCaughan FM, Rintoul RC (2021) Adenocarcinoma spectrum lesions of the lung: detection, pathology and treatment strategies. Cancer Treat Rev 99: 102237.
14. Choi S, Kim S (2023) Artificial intelligence in the pathology of gastric cancer. J Gastric Cancer 23: 410-427. https://doi.org/10.5230/jgc.2023.23.e25

15. Tang L, Li J, Pan T, Yin Y, Mei Y, et al. (2022) Versatile carbon nanoplatforms for cancer treatment and diagnosis: strategies, applications and future perspectives. Theranostics 12: 2290. https://doi.org/10.7150/thno.69628

16. Kazi RNA, Hasani IW, Khafaga DS, Kabba S, Farhan M, et al. (2025) Nanomedicine: the effective role of nanomaterials in healthcare from diagnosis to therapy. Pharmaceutics 17: 987. https://doi.org/10.3390/pharmaceutics17080987

17. Li M, Luo Z, Zhao Y (2018) Self-assembled hybrid nanostructures: versatile multifunctional nanoplatforms for cancer diagnosis and therapy. Chem Mater 30: 25-53. https://doi.org/10.1021/acs.chemmater.7b03924

18. Yin W, Pan F, Zhu J, Xu J, Gonzalez-Rivas D, et al. (2021) Nanotechnology and nanomedicine: a promising avenue for lung cancer diagnosis and therapy. Engineering 7: 1577-1585. https://doi.org/10.1016/j.eng.2020.04.017

19. Zhu W, Wei Z, Han C, Weng X (2021) Nanomaterials as promising theranostic tools in nanomedicine and their applications in clinical disease diagnosis and treatment. Nanomaterials 11: 3346. https://doi.org/10.3390/nano11123346

20. Zhu YF, He MQ, Lin CS, Ma WH, Ai Y, et al. (2025) Multifunctional nanocarrier drug delivery systems: from diverse design to precise biomedical applications. Adv Healthc Mater e02178. https://doi.org/10.1002/adhm.202502178

21. Lan HR, Zhang YN, Han YJ, Yao SY, Yang MX, et al. (2023) Multifunctional nanocarriers for targeted drug delivery and diagnostic applications of lymph nodes metastasis: a review of recent trends and future perspectives. J Nanobiotechnology 21: 1-16. https://doi.org/10.1186/s12951-023-01990-4

22. Yasir M, Mishra R, Tripathi AS, Maurya RK, Shahi A, et al. (2024) Theranostics: a multifaceted approach utilizing nano-biomaterials. Discov Nano 19: 1-29. https://doi.org/10.1186/s11671-024-03979-w

23. Yao J, Yang M, Duan Y (2014) Chemistry, biology, and medicine of fluorescent nanomaterials and related systems: new insights into biosensing, bioimaging, genomics, diagnostics, and therapy. Chem Rev 114: 6130-6178. https://doi.org/10.1021/cr200359p

24. Umadevi K, Sundeep D, Vighnesh AR, Misra A, Krishna AG (2025) Current trends and advances in nanoplatforms-based imaging for cancer diagnosis. Indian J Microbiol 65: 137-176. https://doi.org/10.1007/s12088-024-01373-9

25. Xu M, Han X, Xiong H, Gao Y, Xu B, et al. (2023) Cancer nanomedicine: emerging strategies and therapeutic potentials. Molecules 28: 5145. https://doi.org/10.3390/molecules28135145

26. Tang W, Han L, Lu X, Wang Z, Liu F, et al. (2021) A nucleic acid/gold nanorod-based nanoplatform for targeted gene editing and combined tumor therapy. ACS Appl Mater Interfaces 13: 20974-20981. https://doi.org/10.1021/acsami.1c02122

27. Yan X, Pan Y, Ji L, Gu J, Hu Y, et al. (2021) Multifunctional metal–organic framework as a versatile nanoplatform for Aβ oligomer imaging and chemo-photothermal treatment in living cells. Anal Chem 93: 13823-13834. https://doi.org/10.1021/acs.analchem.1c02459

28. Hao Y, Wang Z, Chen Y, Li C, Wang H, et al. (2025) Aptamer-engineered NIR-II Ru-doped carbon quantum dot nanozyme for photoacoustic imaging-guided synergistic photothermal and catalytic cancer therapy. J Nanobiotechnology 24: 1-16. https://doi.org/10.1186/s12951-025-03919-5

29. Kang X, Zhang Y, Song J, Wang L, Li W, et al. (2023) A photo-triggered self-accelerated nanoplatform for multifunctional image-guided combination cancer immunotherapy. Nat Commun 14: 1-17. https://doi.org/10.1038/s41467-023-40996-2

30. Qiu W, Liang M, Gao Y, Yang X, Zhang X, et al. (2021) Polyamino acid calcified nanohybrids induce immunogenic cell death for augmented chemotherapy and chemo-photodynamic synergistic therapy. Theranostics 11: 9652. https://doi.org/10.7150/thno.64354

31. Wu J, Liu Y, Cao M, Zheng N, Ma H, et al. (2023) Cancer-responsive multifunctional nanoplatform based on peptide self-assembly for highly efficient combined cancer therapy by alleviating hypoxia and improving the immunosuppressive microenvironment. ACS Appl Mater Interfaces 15: 5667-5678. https://doi.org/10.1021/acsami.2c20388

32. Chen Y, Lu Z, Wang D (2024) Multifunctional nanoplatform for single NIR laser-regulated efficient PDT/PTT/chemotherapy. Biomacromolecules 25: 1038-1046. https://doi.org/10.1021/acs.biomac.3c01100

33. Tian Y, Zhang R, Guan B, Zhu Y, Chen L (2023) Oxydextran-based photodynamic antibacterial nanoplatform with broad-spectrum antibacterial activity. Int J Biol Macromol 236: 123917. https://doi.org/10.1016/j.ijbiomac.2023.123917

34. Zhang S, Liu X, Hao Y, Yang H, Zhao W, et al. (2023) Synergistic therapeutic effect of nanomotors triggered by near-infrared light and acidic conditions of tumor. J Colloid Interface Sci 650: 67-80. https://doi.org/10.1016/j.jcis.2023.06.120

35. Liu C, Chang Q, Fan X, Meng N, Lu J, et al. (2025) Rational construction of CQDs-based targeted multifunctional nanoplatform for synergistic chemo-photothermal tumor therapy. J Colloid Interface Sci 677: 79-90. https://doi.org/10.1016/j.jcis.2024.08.037

36. Zhang T, Wang Z, Xiang H, Xu X, Zou J, et al. (2021) Biocompatible superparamagnetic europium-doped iron oxide nanoparticle clusters as multifunctional nanoprobes for multimodal *in vivo* imaging. ACS Appl Mater Interfaces 13: 33850-33861. https://doi.org/10.1021/acsami.1c07739

37. Zhao L, Zhang W, Wu Q, Fu C, Ren X, et al. (2022) Lanthanide europium MOF nanocomposite as the theranostic nanoplatform for microwave thermo-chemotherapy and fluorescence imaging. J Nanobiotechnology 20: 1-16. https://doi.org/10.1186/s12951-022-01335-7

38. Hu P, Xu J, Li Q, Sha J, Zhou H, et al. (2024) Tumor microenvironment-activated theranostic nanozymes for trimodal imaging-guided combined therapy. J Colloid Interface Sci 660: 585-596. https://doi.org/10.1016/j.jcis.2024.01.114

39. Wu T, Fu Y, Guo S, Shi Y, Zhang Y, et al. (2024) Self-assembly multifunctional DNA tetrahedron for efficient elimination of antibiotic-resistant bacteria. Aggregate 5: 1-30. https://doi.org/10.22541/au.168566222.23448157/v1

40. Wang Y, Zheng G, Li X, Shi Y, Tian F, et al. (2025) A dual-function hyaluronic acid-encapsulated nanoplatform enables triple GSH depletion for apoptosis-ferroptosis synergistic oncotherapy. Int J Biol Macromol 308: 142650. https://doi.org/10.1016/j.ijbiomac.2025.142650

41. Lv C, Kang W, Liu S, Yang P, Nishina Y, et al. (2022) Growth of ZIF-8 nanoparticles *in situ* on graphene oxide nanosheets: a multifunctional nanoplatform for combined ion-interference and photothermal therapy. ACS Nano 16: 11428-11443. https://doi.org/10.1021/acsnano.2c05532

42. Manzari MT, Shamay Y, Kiguchi H, Rosen N, Scaltriti M, et al. (2021) Targeted drug delivery strategies for precision medicines. Nat Rev Mater 6: 351-370. https://doi.org/10.1038/s41578-020-00269-6

43. Attia MF, Anton N, Wallyn J, Omran Z, Vandamme TF (2019) An overview of active and passive targeting strategies to improve the nanocarriers efficiency to tumour sites. J Pharm Pharmacol 71: 1185-1198. https://doi.org/10.1111/jphp.13098

44. Dey S, Hassan S, Pandey RK (2024) Nanomedicine in targeted drug delivery: precision therapeutics for personalized medicine. In Nanomedicine: innovations, applications, and breakthroughs in the quest for health and medicine's future. Cham: Springer Nature Switzerland, pp 179-231.

45. Xu M, Han X, Xiong H, Gao Y, Xu B, et al. (2023) Cancer nanomedicine: emerging strategies and therapeutic potentials. Molecules 28: 5145. https://doi.org/10.3390/molecules28135145

46. Narum SM, Le T, Le DP, Lee JC, Donahue ND, et al. (2020) Passive targeting in nanomedicine: fundamental concepts, body interactions, and clinical potential. In Nanoparticles for biomedical applications. Elsevier, pp 37-53.

47. Sun W, Hu Q, Ji W, Wright G, Gu Z (2017) Leveraging physiology for precision drug delivery. Physiol Rev 97: 189-225. https://doi.org/10.1152/physrev.00015.2016

48. Sabit H, Pawlik TM, Radwan F, Abdel-Hakeem M, Abdel-Ghany S, et al. (2025) Precision nanomedicine: navigating the tumor microenvironment for enhanced cancer immunotherapy and targeted drug delivery. Mol Cancer 24: 1-37. https://doi.org/10.1186/s12943-025-02357-z

49. Chattopadhyay S, Goswami A, Sil M (2025) Nanobiotechnology: traditional re-interpreting personalized medicine through targeted therapies and regenerative solutions. Naunyn Schmiedebergs Arch Pharmacol 398: 10025–10048. https://doi.org/10.1007/s00210-025-04038-6

50. Youden B, Jiang R, Carrier AJ, Servos MR, Zhang X (2022) A nanomedicine structure-activity framework for research, development, and regulation of future cancer therapies. ACS Nano 16: 17497-17551. https://doi.org/10.1021/acsnano.2c06337

51. Milcovich G, Jesus CF, Esteves MI, Calzaferri F, Antunes FE, et al. (2026) Advances in nanomedicine: from design and formulation to regenerative application and theranostics. Nanoscale 18: 1765–1802. https://doi.org/10.1039/d5nr02064f

52. Zhu YF, He MQ, Lin CS, Ma WH, Ai Y, et al. (2025) Multifunctional nanocarrier drug delivery systems: from diverse design to precise biomedical applications. Adv Healthc Mater 15: e02178. https://doi.org/10.1002/adhm.202502178

53. Kiran AVR, Kumari GK, Krishnamurthy PT, Khaydarov RR (2021) Tumor microenvironment and nanotherapeutics: intruding the tumor fort. Biomater Sci 9: 7667-7704. https://doi.org/10.1039/d1bm01127h

54. Tian T, Zhang T, Shi S, Gao Y, Cai X, Lin Y (2023) A dynamic DNA tetrahedron framework for active targeting. Nat Protoc 18: 1028-1055. https://doi.org/10.1038/s41596-022-00791-7

55. Gong Z, Liu X, Zhou B, Wang G, Guan X, et al. (2021) Tumor acidic microenvironment-induced drug release of RGD peptide nanoparticles for cellular uptake and cancer therapy. Colloids Surf B Biointerfaces 202: 111673. https://doi.org/10.1016/j.colsurfb.2021.111673

56. Fu L, Zhang Y, Farokhzad RA, Mendes BB, Conde J, et al. (2023) 'Passive' nanoparticles for organ-selective systemic delivery: design, mechanism and perspective. Chem Soc Rev 52: 7579-7601. https://doi.org/10.1039/d2cs00998f

57. Cheng HT, Ngoc Ta YN, Hsia T, Chen Y (2024) A quantitative review of nanotechnology-based therapeutics for kidney diseases. Wiley Interdiscip Rev Nanomed Nanobiotechnol 16: e1953. https://doi.org/10.1002/wnan.1953

58. Yuan L, Chen Q, Riviere JE, Lin Z (2023) Pharmacokinetics and tumor delivery of nanoparticles. J Drug Deliv Sci Technol 83: 104404. https://doi.org/10.1016/j.jddst.2023.104404

59. Fernández-Rhodes M, Lorca C, Lisa J, Batalla I, Ramos-Miguel A, et al. (2024) New origins of yeast, plant and bacterial-derived extracellular vesicles to expand and advance compound delivery. Int J Mol Sci 25: 7151. https://doi.org/10.3390/ijms25137151

60. Bourgonje AR, Andreu-Sánchez S, Vogl T, Hu S, Vich Vila A, et al. (2022) DOP53 In-depth characterisation of the serum antibody epitope repertoire in inflammatory bowel disease by high-throughput phage-displayed immunoprecipitation sequencing. J Crohns Colitis 16: i100-i102. https://doi.org/10.1093/ecco-jcc/jjab232.092

61. Tiwari H, Singh S, Kumar R, Mandal A, Pathak A, et al. (2025) Novel advancements in nanomaterials-based contrast agents across multimodal imaging and theranostic applications. Nanoscale Adv 7: 6753-6773. https://doi.org/10.1039/d5na00596e

62. Cinar O, Kimiz-Gebologlu I, Oncel SS (2025) Nanoparticle-based therapeutic strategies in respiratory diseases: current approaches and future perspectives. Thorac Res Pract 26: 31-33. https://doi.org/10.4274/thoracrespract.2025.s012

63. Mishra V, Kumari N, Vyas M, Aljabali AA, Chattaraj A, et al. (2025) Advances in multimodal imaging techniques in nanomedicine: enhancing drug delivery precision. RSC Adv 15: 27187-27209. https://doi.org/10.1039/d5ra03255e

64. Bonlawar J, Setia A, Challa RR, Vallamkonda B, Mehata AK, et al. (2024) Targeted nanotheranostics: integration of preclinical MRI and CT in the molecular imaging and therapy of advanced diseases. Nanotheranostics 8: 401-426. https://doi.org/10.7150/ntno.95791

65. Huang H, Lovell JF (2017) Advanced functional nanomaterials for theranostics. Adv Funct Mater 27: 1603524. https://doi.org/10.1002/adfm.201603524

66. Zhuang D, Zhang H, Hu G, Guo B (2022) Recent development of contrast agents for magnetic resonance and multimodal imaging of glioblastoma. J Nanobiotechnology 20: 1-21. https://doi.org/10.1186/s12951-022-01479-6

67. Habeeb M, Vengateswaran HT, Tripathi AK, Kumbhar ST, You HW, et al. (2024) Enhancing biomedical imaging: the role of nanoparticle-based contrast agents. Biomed Microdevices 26: 42. https://doi.org/10.1007/s10544-024-00725-y

68. Hsu JC, Tang Z, Eremina OE, Sofias AM, Lammers T, et al. (2023) Nanomaterial-based contrast agents. Nat Rev Methods Primers 3: 30. https://doi.org/10.1038/s43586-023-00211-4

69. Butt A, Bach H (2025) Advancements in nanotechnology for diagnostics: a literature review, part II: advanced techniques in nuclear and optical imaging. Nanomedicine 20: 183-206. https://doi.org/10.1080/17435889.2024.2439778

70. Bartusik-Aebisher D, Wilk I, Aebisher D (2025) Nanomedicine in ovarian cancer: advances in imaging, targeted delivery, and theranostic therapeutic platforms. Cancers 18: 86. https://doi.org/10.3390/cancers18010086

71. Thangam R, Paulmurugan R, Kang H (2021) Functionalized nanomaterials as tailored theranostic agents in brain imaging. Nanomaterials 12: 18. https://doi.org/10.3390/nano12010018

72. Yasir M, Mishra R, Tripathi AS, Maurya RK, Shahi A, et al. (2024) Theranostics: a multifaceted approach utilizing nano-biomaterials. Discov Nano 19: 1-29. https://doi.org/10.1186/s11671-024-03979-w

73. Duman FD, Forgan RS (2021) Applications of nanoscale metal-organic frameworks as imaging agents in biology and medicine. J Mater Chem B 9: 3423-3449. https://doi.org/10.1039/d1tb00358e

74. Chu S, Wang AL, Bhattacharya A, Montclare JK (2021) Protein based biomaterials for therapeutic and diagnostic applications. Prog Biomed Eng 4: 012003. https://doi.org/10.1088/2516-1091/ac2841

75. Omidian H, Gill EJ, Cubeddu LX (2025) Conjugate nanoparticles in cancer theranostics. J Nanotheranostics 6: 24. https://doi.org/10.3390/jnt6030024

76. Wang Y, Hu C, Li Y, Chen ZS, Zhang L (2025) Advancing cancer treatment: innovative materials in PDT and diagnostic integration. Int J Nanomedicine 31: 7037-7060. https://doi.org/10.2147/ijn.s514937

77. Amor S, Nutma E, Owen D (2021) Imaging immune responses in neuroinflammatory diseases. Clin Exp Immunol 206: 248-250. https://doi.org/10.1111/cei.13670

78. Younis MH, Tang Z, Cai W (2022) Multimodality imaging of nanoparticle-based vaccines: shedding light on immunology. Wiley Interdiscip Rev Nanomed Nanobiotechnol 14: e1807. https://doi.org/10.1002/wnan.1807

79. Singh D, Bedi N (2025) Nano-immunoconjugates in immune checkpoint blockade: a dual approach to precision immunotherapy and real-time imaging. Asia Pac J Clin Oncol 22:369-380. https://doi.org/10.1111/ajco.70036

80. Robertson N, Sempere L, Kenyon E, Mallet C, Smith K, et al. (2023) Omniparticle contrast agent for multimodal imaging: synthesis and characterization in an animal model. Mol Imaging Biol 25: 401-412. https://doi.org/10.1007/s11307-022-01770-w

81. Zhang L, Liu Y, Huang H, Xie H, Zhang B, et al. (2022) Multifunctional nanotheranostics for near infrared optical imaging-guided treatment of brain tumors. Adv Drug Deliv Rev 190: 114536. https://doi.org/10.1016/j.addr.2022.114536

82. Nguyen VP, Zhe J, Hu J, Ahmed U, Paulus YM (2023) Molecular and cellular imaging of the eye. Biomed Opt Express 15: 360-386. https://doi.org/10.1364/BOE.502350

83. Saygin D, Albayda J (2024) Current approach to muscle imaging in myositis. Curr Opin Rheumatol 36: 445-452. https://doi.org/10.1097/bor.0000000000001043

84. Mu J, Xiao M, Shi Y, Geng X, Li H, et al. (2022) The chemistry of organic contrast agents in the NIR-II window. Angew Chem Int Ed Engl 61: e202114722. https://doi.org/10.1002/anie.202114722

85. Verma N, Setia A, Mehata AK, Randhave N, Badgujar P, et al. (2024) Recent advancement of indocyanine green based nanotheranostics for imaging and therapy of coronary atherosclerosis. Mol Pharm 21: 4804-4826. https://doi.org/10.1021/acs.molpharmaceut.4c00495

86. Chen P, Scarpelli ML, Healey DR, Mehta S, Quarles CC (2023) MRI and amino acid PET detection of whole-brain tumor burden. Front Oncol 13: 1-9. https://doi.org/10.3389/fonc.2023.1248249

87. Yang JM, Ghim CM (2021) Photoacoustic tomography opening new paradigms in biomedical imaging. In Advanced imaging and bio techniques for convergence science. Singapore: Springer Singapore, pp 239-341.

88. Jost WH, Rau A, Brumberg J, Urbach H, Meyer PT, et al. (2025) Neuroimaging in multiple system atrophy: clinical implications and novel developments. J Neural Transm133: 891–902. https://doi.org/10.1007/s00702-025-02921-3

89. Morris G, O'Brien D, Henshall DC (2021) Opportunities and challenges for microRNA-targeting therapeutics for epilepsy. Trends Pharmacol Sci 42: 605-616. https://doi.org/10.1016/j.tips.2021.04.007

90. Komatsu H (2021) Innovative therapeutic approaches for Huntington's disease: from nucleic acids to GPCR-targeting small molecules. Front Cell Neurosci 15: 1-10. https://doi.org/10.3389/fncel.2021.785703

91. Yamada Y (2021) Nucleic acid drugs—current status, issues, and expectations for exosomes. Cancers 13: 5002. https://doi.org/10.3390/cancers13195002

92. Guo Y, Zhang Q, Zhu Q, Gao J, Zhu X, et al. (2022) Copackaging photosensitizer and PD-L1 siRNA in a nucleic acid nanogel for synergistic cancer photoimmunotherapy. Sci Adv 8: 1-13. https://doi.org/10.1126/sciadv.abn2941

93. Mikutis S, Rebelo M, Yankova E, Gu M, Tang C, et al. (2023) Proximity-induced nucleic acid degrader (PINAD) approach to targeted RNA degradation using small molecules. ACS Cent Sci 9: 892-904. https://doi.org/10.1021/acscentsci.3c00015

94. Basu S, Middya S, Banerjee M, Ghosh R, Pryde DC, et al. (2022) The discovery of potent small molecule cyclic urea activators of STING. Eur J Med Chem 229: 114087. https://doi.org/10.1016/j.ejmech.2021.114087

95. Liang S, Liao G, Zhu W, Zhang L (2022) Manganese-based hollow nanoplatforms for MR imaging-guided cancer therapies. Biomater Res 26: 32. https://doi.org/10.1186/s40824-022-00275-5

96. Zeng YL, Liu LY, Ma TZ, Liu Y, Liu B, et al. (2024) Iridium (III) photosensitizers induce simultaneous pyroptosis and ferroptosis for multi-network synergistic tumor immunotherapy. Angew Chem 136: e202410803. https://doi.org/10.1002/anie.202410803

97. Mollé LM, Smyth CH, Yuen D, Johnston AP (2022) Nanoparticles for vaccine and gene therapy: overcoming the barriers to nucleic acid delivery. Wiley Interdiscip Rev Nanomed Nanobiotechnol 14: e1809. https://doi.org/10.1002/wnan.1809

98. Chingarande RG, Tian K, Kuang Y, Sarangee A, Hou C, et al. (2023) Real-time label-free detection of dynamic aptamer–small molecule interactions using a nanopore nucleic acid conformational sensor. Proc Natl Acad Sci U S A 120: 1-11. https://doi.org/10.1073/pnas.2108118120

99. Pascual-Gilabert M, Artero R, López-Castel A (2023) The myotonic dystrophy type 1 drug development pipeline: 2022 edition. Drug Discov Today 28: 103489. https://doi.org/10.1016/j.drudis.2023.103489

100. Yu L, Xu Y, Al-Amin M, Jiang S, Sample M, et al. (2023) CytoDirect: a nucleic acid nanodevice for specific and efficient delivery of functional payloads to the cytoplasm. J Am Chem Soc 145: 27336-27347. https://doi.org/10.1021/jacs.3c07491

101. Yang L, Yang Y, Chen Y, Xu Y, Peng J (2022) Cell-based drug delivery systems and their *in vivo* fate. Adv Drug Deliv Rev 187: 114394. https://doi.org/10.1016/j.addr.2022.114394

102. Sun X, Setrerrahmane S, Li C, Hu J, Xu H (2024) Nucleic acid drugs: recent progress and future perspectives. Signal Transduct Target Ther 9: 1-31. https://doi.org/10.1038/s41392-024-02035-4

103. Cuoghi S, Caraffi R, Anderlini A, Baraldi C, Enzo E, et al. (2024) Challenges of enzyme therapy: why two players are better than one. Wiley Interdiscip Rev Nanomed Nanobiotechnol 16: e1979. https://doi.org/10.1002/wnan.1979

104. Li C, Shi K, Zhao S, Liu J, Zhai Q, et al. (2024) Natural-source payloads used in the conjugated drugs architecture for cancer therapy: recent advances and future directions. Pharmacol Res 207: 107341. https://doi.org/10.1016/j.phrs.2024.107341

105. Dai Y, Sha X, Song X, Zhang X, Xing M, et al. (2022) Targeted therapy of atherosclerosis vulnerable plaque by ROS-scavenging nanoparticles and MR/fluorescence dual-modality imaging tracing. Int J Nanomedicine 17: 5413-5429. https://doi.org/10.2147/ijn.s371873

106. Pan C, Lin J, Zheng J, Liu C, Yuan B, et al. (2021) An intelligent T1–T2 switchable MRI contrast agent for the non-invasive identification of vulnerable atherosclerotic plaques. Nanoscale 13: 6461-6474. https://doi.org/10.1039/d0nr08039j

107. Fujiwara Y, Maruyama H, Toyomaru K, Nishizaka Y, Fukamatsu M (2018) Quantitative T 1 and T 2* carotid atherosclerotic plaque imaging using a three-dimensional multi-echo phase-sensitive inversion recovery sequence: a feasibility study. Radiol Phys Technol 11: 156-164. https://doi.org/10.1007/s12194-018-0449-2

108. Huang G, Liu R, Hu Y, et al. (2018) FeOOH-loaded mesoporous silica nanoparticles as a theranostic platform with pH-responsive MRI contrast enhancement and drug release. Sci China Chem 61: 806-811. https://doi.org/10.1007/s11426-017-9217-4

109. Chargari C, Maury P, Texier M, Genestie C, Morice P, et al. (2024) Theragnostic gadolinium-based nanoparticles safely augment X-ray radiation effects in patients with cervical cancer. ACS Nano 18: 16516-16529. https://doi.org/10.1021/acsnano.3c12537

110. Bonizzi G, Zattoni L, Fusco N (2022) Biobanking in the digital pathology era. Oncol Res 29: 229-233. https://doi.org/10.32604/or.2022.024892

111. Hanna MG, Ardon O (2023) Digital pathology systems enabling quality patient care. Genes Chromosomes Cancer 62: 685-697. https://doi.org/10.1002/gcc.23192

112. Hijazi A, Bifulco C, Baldin P, Galon J (2024) Digital pathology for better clinical practice. Cancers 16: 1686. https://doi.org/10.3390/cancers16091686

113. Wu B, Moeckel G (2023) Application of digital pathology and machine learning in the liver, kidney and lung diseases. J Pathol Inform 14: 100184. https://doi.org/10.1016/j.jpi.2022.100184

114. Griem J, Eich ML, Schallenberg S, Pryalukhin A, Bychkov A, et al. (2023) Artificial intelligence-based tool for tumor detection and quantitative tissue analysis in colorectal specimens. Mod Pathol 36: 100327. https://doi.org/10.1016/j.modpat.2023.100327

115. Mezei T, Kolcsár M, Joó A, Gurzu S (2024) Image analysis in histopathology and cytopathology: from early days to current perspectives. J Imaging 10: 252. https://doi.org/10.3390/jimaging10100252

116. Hosseini MS, Bejnordi BE, Trinh VQ, Chan L, Hasan D, et al. (2024) Computational pathology: a survey review and the way forward. J Pathol Inform 15: 100357. https://doi.org/10.1016/j.jpi.2023.100357

117. Rau TT, Cross W, Lastra RR, Lo RCL, Matoso A, Herrington CS (2024) Closing the loop – the role of pathologists in digital and computational pathology research. J Pathol Clin Res 10: e12366. https://doi.org/10.1002/2056-4538.12366

118. Cazzaniga G, De Gaspari M, L'Imperio V, Beretta C, Greco A, et al. (2025) Congo red fluorescence enhances digital pathology workflow in cardiac amyloidosis. Sci Rep 15: 1-12.

119. Oganesyan R, Pouli D, Shi B, Carns M, Dennis-Aren K, et al. (2025) Quantitative digital image analysis for assessing cutaneous fibrosis correlates with histopathological scoring in patients with systemic sclerosis. Lab Invest 105: 104177. https://doi.org/10.1016/j.labinv.2025.104177

120. Rahman A, Cheng CL, Salim R, Goh Di Shen H, Gallagher WM, et al. (2025) Digital pathology and AI: enhancing molecular diagnostics in low- and middle-income countries. Expert Rev Mol Diagn 25: 859-867. https://doi.org/10.1080/14737159.2025.2581687

121. Komura D, Ochi M, Ishikawa S (2024) Machine learning methods for histopathological image analysis: updates in 2024. Comput Struct Biotechnol J 27: 383-400. https://doi.org/10.1016/j.csbj.2024.12.033

122. Agraz JL, Agraz C, Chen AA, Rice C, Pozos RS, et al. (2024) Optimized whole-slide-image H&E stain normalization: a step towards big data integration in digital pathology. IEEE Open J Eng Med Biol 6: 35-40. https://doi.org/10.1109/ojemb.2024.3455011

123. Kim H, Kim J, Yeon SY, You S (2024) Machine learning approaches for spatial omics data analysis in digital pathology: tools and applications in genitourinary oncology. Front Oncol 14: 1-9. https://doi.org/10.3389/fonc.2024.1465098

124. Saba L, Pinna A, Faa G, Balestrieri A, Politi C, et al. (2025) The evolution from qualitative to quantitative analysis in medical sciences: a historical perspective and the impact of AI. Imaging 17: 15-25. https://doi.org/10.1556/1647.2025.00281

125. Bhajaj P, Nalubolu S, Gurram B, Srinivas M, Choudhary R, et al. (2025) ClinSegAI: a post-processing framework for superior histopathology segmentation accuracy, radiomics feature preservation, and quantitative analysis. Comput Biol Med 199: 111298. https://doi.org/10.1016/j.compbiomed.2025.111298

126. Morrison D, Harris-Birtill D, Caie PD (2021) Generative deep learning in digital pathology workflows. Am J Pathol 191: 1717-1723. https://doi.org/10.1016/j.ajpath.2021.02.024